“HISTOMORPHOLOGICAL STUDY OF LUNG CHANGES SEEN AT AUTOPSY”

By

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IN

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Under the guidance of

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DEDICATED
TO
My Father, Late MR.ALEXY THOMAS,
who is always watching over me

ABSTRACT

TITLE OF THE TOPIC: Histomorphological Study of Lung Changes seen at Autopsy

BACKGROUND: Organ specific pathological changes that are seen during autopsy give a clearer picture of the cause of death and help to correlate with the clinical scenario on what went wrong. Pulmonary histomorphological alterations seen at autopsy remain a relatively unstudied domain of forensic pathology.

OBJECTIVES:

1. To study the histomorphological lung changes seen at autopsy.
2. To correlate the clinical cause of death with pathological findings seen at autopsy wherever data is available.

METHODS: Lung specimens were collected from 120 autopsies conducted at R.L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar in coordination with the Department of Forensic Medicine. These autopsies were performed beginning from October 2009 till August 2011. Grossly, both lungs were carefully examined for any morphological changes like collapse, non-collapse or inflation. Histological studies were done from the bits taken by routine tissue processing and H & E staining. The sections were examined for congestion, edema, haemorrhage, hyaline membranes, inflammation, alveolar collapse and thickening, alveolar wall disturbances and capillary dilatation. All the data obtained were analysed using SPSS package version 14.

RESULTS: Majority of patients belonged to the 3rd decade of life. Most common cause of death was Road Traffic Accidents. Most common morphological features were Pulmonary congestion, Pulmonary edema and Alveolar Haemorrhage. Diffuse Alveolar Damage (DAD) was only seen in 13.5 % cases.

CONCLUSION: The main pathologic cause of death (86.5%) could be due to circulatory failure from inciting causes like RTA, Trauma, Burns, Snake bites and Chemicals. This could have had multi-organ effects in addition to lung microvascular injury. Remaining 13.5 % cases had DAD changes or acute respiratory failure as cause of death.

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INTRODUCTION:

The lung is unique among all internal organs in that it exposes itself directly and constantly to the surrounding atmosphere.[1]

The lungs are the essential organs of respiration and are responsible for the uptake of oxygen into the blood and the removal of carbon dioxide. The process of breathing exposes the lung to noxious agents, including gases, dust particles, bacteria and viruses. The mucous barrier, mucociliary escalator, branching pattern of the airways and the cough reflex are all anatomical defences against these insults.[1]

"At first glance the lungs may seem uncomplicated, but many wise men have gone astray in their labyrinths", stated Dr. A.A. Liebow, in a foreword to the first edition of Pathology of the Lung by H. Spencer.[2] This same thought can also be applied to the field of medicolegal autopsies.

Any observed histopathology is highly dependent on when the lung biopsy is performed relative to the onset of a given injury.[3]

In biological systems, the extent and type of pathologic and toxicologic findings can often be correlated with the specific circumstances of the fatal event. While such correlations are never perfect, their use in forensic scientific investigations forms an important component of the experienced investigator's repertoire. In addition, enlightened interpretation of postmortem findings may assist in elucidating the circumstances of death when they either are unresolved or later are found to have been confabulated.[4]

Post-mortem examinations, although suffering a decline in usage during the past few decades, remain a valuable contributor to our medical education and toward the understanding of medicine's limitations.[5]

Necropsy or Autopsy is the gold standard for clinicopathological discrepancy studies and epidemiological surveys. Inadequate sampling or lack of tissue may hamper the final interpretation and quality of the necropsy.[6]

The World Health Organization has predicted that traffic fatalities will be the sixth leading cause of death worldwide and the second leading cause of disability-adjusted life-years lost in developing countries by the year 2020.[7,8]

Organ specific pathological changes that are seen during autopsy give a clearer picture of the cause of death and help to correlate with the clinical scenario on what went wrong. Pulmonary histomorphological alterations seen at autopsy remain a relatively unstudied domain of forensic pathology and hence the need for such a study.

OBJECTIVES

OBJECTIVES OF THE STUDY:

1. To study the histomorphological lung changes seen at autopsy.
2. To correlate the clinical/forensic cause of death with pathological findings seen at autopsy wherever data is available.

REVIEW OF LITERATURE

REVIEW OF LITERATURE:

ANATOMY:[1]

PLEURA-

Each lung is covered by inner visceral pleura and the outer parietal pleura. The potential space between them is the pleural cavity, which is maintained at a negative pressure by the inward elastic recoil of the lung and the outward pull of the chest wall.

LUNGS-

They are situated on either side of the heart and other mediastinal contents. When removed from the thorax, a fresh lung is spongy, can float in water, and crepitates when handled, because of the air within its alveoli. Its surface is smooth, shiny and is separated by fine, dark lines into numerous small polyhedral domains.

At birth, the lungs are pink, but in adults they are dark grey and patchily mottled. As age advances, this maculation becomes black, as granules of inhaled carbonaceous material are deposited in the loose connective tissue near the lung surface. Darkening is often more marked in men than women, especially in those who have dwelt in industrial areas and are smokers.

The adult right lung weighs 625 gm and the left 565 gm.

Each lung has an apex, base, three borders and two surfaces.

The basal surface is semilunar, concave, and rests upon the superior surface of the diaphragm, which separates the right lung from the right lobe of the liver and the left lung from the left lobe

of the liver, the gastric fundus and spleen. Since the diaphragm extends higher on the right than on the left, the concavity is deeper on the base of the right lung.

Right Lung –

The right lung is divided into superior, middle and inferior lobes by an oblique and a horizontal fissure.

The upper, oblique fissure separates the inferior from the middle and upper lobes. The short horizontal fissure separates the superior and middle lobes. It passes from the oblique fissure, near the mid axillary line, horizontally forwards to the anterior border of the lung.

Left Lung –

The left lung is divided into a superior and an inferior lobe by an oblique fissure, which extends from the costal to the medial surfaces of the lung both above and below the hilum. Superficially this fissure begins on the medial surface at the posterosuperior part of the hilum. It ascends obliquely backwards to cross the posterior border of the lung 6 cm below the apex, and then descends forwards across the costal surface, to reach the lower border almost at its anterior end.

The left oblique fissure is usually more vertical than the right. At the lower end of the cardiac notch, a small process, the lingula, is usually present.

Bronchopulmonary segments:

Each of the principal bronchi divides into lobar bronchi. Primary branches of the right and left lobar bronchi are termed segmental bronchi because each ramifies in a structurally separate, functionally independent, unit of lung tissue called a bronchopulmonary segment.

Pulmonary Hila-

The pulmonary root is formed by a group of structures which enter or leave the hilum. These are the principal bronchus, pulmonary artery, two pulmonary veins, bronchial vessels, a pulmonary autonomic plexus, lymph vessels, Bronchopulmonary lymph nodes and loose connective tissue, all of which are enveloped by a sleeve of pleura.

Right hilum- Usual sequence of hilar structures from above downwards is: superior lobar bronchus, pulmonary artery, principal bronchus, and lower pulmonary vein.

Left hilum – The usual vertical sequence is pulmonary artery, principal bronchus, and lower pulmonary vein.

Each segmental bronchus supplies a Bronchopulmonary segment. Progressive subdivisions of the bronchus occur within each segment and the bronchi become increasingly narrow. All intrapulmonary bronchi are kept patent by cartilaginous plates, which decline in size and number and finally disappear when the tubes are less than 1 mm in diameter (bronchioles).

The terminal bronchiole is the most peripheral bronchiole not to have alveoli in its wall. Distal to each terminal bronchiole is an acinus, which consists of three to four orders of respiratory

bronchioles, leading to three to eight orders of alveolar ducts. The walls of these ducts consist of alveolar sacs or the mouths of alveoli.

The major vascular supply is the pulmonary vascular system. The main pulmonary arterial trunk divides into right and left pulmonary arteries. The main right and left pulmonary arteries enter the lungs at the lung hila alongside the main bronchus.

HISTOLOGY:[9,10]

Main Bronchus –

The basic structure is similar to that of the trachea but differs in several details:

- The respiratory epithelium is less tall and contains fewer goblet cells.
- The lamina propria contains more elastin in its upper layers.
- The lamina propria is separated from the submucosa by a layer of smooth muscle which becomes more prominent in more distal bronchi.
- The cartilage support is in flattened interconnected plates rather than distinct rings.

Tertiary (Segmental) Bronchus –

The respiratory epithelium is tall and columnar with little pseudostratification and goblet cell numbers are greatly diminished.

Seromucinous glands are sparse in the submucosa.

The cartilage framework is reduced to a few irregular plates.

Small aggregations of lymphocytes are seen in the adventitia.

Bronchiole –

It is an airway of less than 1mm diameter which has neither cartilage nor submucosal glands in its wall. The epithelium is composed of ciliated columnar cells and few goblet cells.

In the terminal and respiratory bronchioles, goblet cells are replaced by Clara cells – tall columnar cells with apical secretory granules. The wall is composed of smooth muscle.

Terminal Portion of the respiratory tree –

These are the smallest diameter passages of the purely conducting portion of the respiratory tree.

Each terminal bronchiole divides to form short, thinner-walled branches called respiratory bronchioles which contain a small number of single alveoli in their walls. The epithelium consists of ciliated cuboidal cells and smaller numbers of Clara cells.

Each respiratory bronchiole divides further into several alveolar ducts which have numerous alveoli.

Each alveolus is lined by flattened epithelial cells (pneumocytes). The alveolar septal wall is composed of a central area of alveolar capillaries surrounded by a fine sparse network of elastin and collagen fibres, with the flat epithelial layer of the two adjacent alveoli on each side of the capillary network.

Most of the alveolar lining epithelium surface area is covered by large, squamous cells – Type 1 Pneumocytes. Type 2 Pneumocytes cover 5 % of the alveolar surface area.

Type 1 Pneumocytes constitute part of the extremely thin gaseous diffusion barrier, whereas Type 2 Pneumocytes secrete surfactant which reduces surface tension within the alveoli.

The lung contains alveolar macrophages, both free within the alveolar spaces and in the alveolar septa. Their function is the phagocytosis and removal of unwanted material which gain access to the air spaces such as inhaled particulate matter and bacteria. The most common particles are carbon, in city dwellers from car exhaust fumes and industrial smoke, and in cigarette smokers.

Commensal Microbes of Respiratory Tract:[11]

Mouth/Throat: Actinomyces spp, Fusobacterium spp., Lactobacillus spp., Leptotrichia spp., Mycoplasma spp., Neisseria spp., Staphylococcus spp., Streptococcus spp.

Nasal cavity/pharynx: Corynebacterium spp., Haemophilus influenza, Neisseria meningitides, Staph spp., Strep spp.

Upper Respiratory Tract: Moraxella catarrhalis, Neisseria meningitides, Strep spp (alpha – haemolytic)

TECHNIQUES OF LUNG FIXATION:[12]

1. Wet Inflation Fixation of lungs – It helps in reconstitution of size, better fixation and better specimen for museum.

   Principle – Inflate the lungs using a syringe or by a gravitational technique with 10 % formalin till the lungs are fully inflated and then the bronchus is clamped. Both lungs can be fixed simultaneously by infusing through trachea. Infused lungs must be kept in a tub of formalin covered with cotton gauze. Proper fixation takes 2-3 days.
2. Pressure Fixation (Vacuum fixation) – Isolated lung is kept in airtight container containing 10% formalin. A tube is tied to the bronchus and is connected to another

formalin container. Air in the first container is removed to create vacuum which causes lungs to expand and formalin from 2nd container flows into the bronchial tree.

3. Gaseous Fixation – Formaldehyde gas or formalin vapour is used. This method is not used routinely as it leads to desiccation of lungs.

TECHNIQUES OF LUNG GROSSING:[12]

It includes dissection of fresh and fixed lungs.

Caution: If the lungs contain active tuberculous lesions or those of other hazardous infections, wear a surgical mask and spectacles when you section the tissue.[13]

Dissection of Fresh Lungs –

1. **Dissection from Hilus** – The pulmonary arteries and bronchi are opened from the hilus toward the periphery of the mediastinal surface of the lung. Subsequently, the lungs are cut into several sagittal slices parallel to the mediastinal surface. This method permits study of many cross-sections of bronchovascular units and gives a good overall view of the parenchyma. The continuity of the organ is lost in this method.[12]
2. **Dissection from Incisions along Lateral Surface of Lung** – An incision is made from the apex to the base of the pulmonary lobes along their longest lateral axis. For the right middle lobe, this axis lies almost in the horizontal plane. The incisions into the upper and lower lobes reach toward but not into the hilus and are connected by a third incision that lies at a right angle to the first and second. This third incision divides part of the wall of a

main pulmonary artery. One blade of a pair of scissors is introduced into this opening and the pulmonary arteries are opened radially in all directions. Subsequently, the bronchial tree is dissected in the same fashion. This method requires more practice, but leaves the dissected lung in continuity.[12]

Dissection of Fixed Lungs –

Slicing of lungs is advisable using a long bladed knife (78cm long) to cut with uninterrupted pulling motion and to have smooth cut surface.

Using a knife and a slicing board, slice the whole lung in one uninterrupted pulling motion. This ensures a smooth and even cut surface without knife marks. The lung usually is cut in the frontal or sagittal plane in slices about 1.5 cm thick. For frontal sectioning, the lung is placed so that the hilus is uppermost. The first cut is made immediately adjacent to the hilus. This method cuts from hilus towards the mediastinal surface.[12]

Another method from anterior surface of lung towards hilus – With the large knife, an incision is made along the anterior surface starting from the apex of the upper lobe and extending to the base of the upper lobe. This cut can also extend to the middle lobe in case of right lung. Before the second incision is made, the lung is rotated 90 degrees about an imaginary longitudinal axis, so that its lateral margin faces the dissector. The second incision goes along the lateral margin, starting at the upper portion of the upper lobe and extending through the lower lobe to its base. Both incisions cut towards the hilus. Similar parallel slices can be made in a similar fashion at 1-

2 cm apart. During this procedure, cross sections of the bronchi, their ramifications and blood vessels can also be seen.[14]

Special Techniques: [12]

1. Mounted Gross Sections – Technique of Gough: Paper mounted sections are prepared especially for quantitative estimation of pulmonary changes with the use of suitable grids, such as in cases of Emphysema and Bronchitis. The technique is elaborate and consists of perfusing the lungs with formalin under pressure. Slices of fixed lungs (approximately 2 cm thick) are vacuum embedded in gelatin. The whole block is kept at 25^{o}C overnight and cut on a large section microtome. The thickness of the section is approximately 400µ. These slices are then taken on a plexiglass and covered by a sheet of Whatmann No.1 filter paper. The preparation is dried and the paper with the tissue slice is lifted off the plexiglass.
2. Post mortem – Pulmonary Angiography and Bronchography: The lungs have to be well inflated. Barium gelatin mixture is injected through a cannula inserted through the pulmonary artery/ bronchus or pulmonary vein as the case may be.
3. Vascular or bronchial casts: A solution of polyvinyl chloride in acetone with green or red or blue pigment is injected and the tissue is subsequently treated with concentrated Hydrochloric acid for 24-48 hrs.
4. Particle Identification: It can be done with the help of electron microscope, chemical analysis or complicated physical and chemical techniques such as X-ray diffraction.

Autopsy:

An autopsy, literally meaning self study of a dead body, is carried out for clinical as well as medico-legal purposes. Clinical autopsy is carried out to diagnose the disease which has caused the mortality when ante-mortem efforts have failed. Medico-legal autopsy is performed with the aim of providing answers to questions about the identity, cause of death, time of death, circumstances of death, etc. thus helping the law enforcing agencies to solve the crime.[15]

Though necropsy is the most accurate term for the investigative dissection of a dead body, the term autopsy is used more commonly.[16]

Autopsy has double roles: it is both a method by which to detect diagnostic errors and a source of knowledge to be applied to future cases, influencing learning and adding data on local epidemiology of diseases and quality control for technical investigations.[17]

Atelectasis and Collapse - Atelectasis signifies the absence of air in the lungs. Airless areas may be small, dark blue and fleshy in consistency.[14]

Collapse is often the result of compression of the lung by fluids in the pleural cavity, by air and by tumours pressing upon the lung etc. It may also be caused by obstruction of a bronchus.[14]

Chronic Passive Hyperaemia – The lungs are firm, air containing and of typical rust brown colour.[14]

Pulmonary Edema –

Pulmonary edema can result from hemodynamic disturbances (hemodynamic or cardiogenic pulmonary edema) or from direct increases in capillary permeability, as a result of alveolar septal

microvascular injury.[18] The organs are enlarged, firm and heavier than normal. The cut surface contains a large amount of a distinctly foamy liquid which can be easily expressed from the lungs. Histologically, the alveolar capillaries are engorged, and an intra-alveolar granular pink precipitate is seen.[18]

In hemodynamic pulmonary edema, Alveolar micro-haemorrhages and Hemosiderin-laden macrophages ("heart failure" cells) may be present.[18]

Table 1: Classification and causes of Pulmonary Edema[18]

HEMODYNAMIC EDEMA
Increased hydrostatic pressure (increased pulmonary venous pressure) • Left-sided heart failure • Volume overload • Pulmonary vein obstruction Decreased oncotic pressure • Hypoalbuminemia • Nephrotic syndrome • Liver disease • Protein-losing enteropathies
EDEMA DUE TO MICROVASCULAR INJURY (ALVEOLAR INJURY)
• Infections: pneumonia, septicaemia • Inhaled gases: oxygen, smoke • Liquid aspiration: gastric contents, near-drowning • Drugs and chemicals: chemotherapeutic agents (bleomycin), other medications (Amphotericin B), heroin, kerosene, paraquat • Shock, trauma • Radiation • Transfusion related
EDEMA OF UNDETERMINED ORIGIN
• High altitude • Neurogenic (central nervous system trauma)

Hemorrhagic infarcts – The infarcted areas are firm, project above the pleura and are often triangular. The apex of the triangle contains the blocked artery and points towards the hilum of

the lung. Most commonly, they are seen in the lower lobes. There is no air in the infarcted areas. On section, the infarct is dry, distinctly granular of a dark colour.[14]

Pulmonary Embolus – The embolus may be large, coiled, snake-like and smooth. It is found in the main pulmonary artery and may extend into one or both of its branches. They are best seen on the cut surfaces of the lungs.[14]

Bronchopneumonia – The lung is heavier than normal and firm. On cut section, the surface presents well-circumscribed areas that are finely granular and drier than the surrounding lung tissues. The colour varies from reddish to dark gray and light gray.[14] Foci of bronchopneumonia are consolidated areas of acute suppurative inflammation. The consolidation may be patchy through one lobe but is more often multilobar and frequently bilateral and basal. Histologically, the reaction usually elicits a suppurative, neutrophil-rich exudate that fills the bronchi, bronchioles, and adjacent alveolar spaces.[18]

Lobar Pneumonia – Usually one whole lobe is involved, sometimes also adjacent parts of another lobe. The lungs are much heavier and firmer than normal. Depending upon the stage of pneumonia, the surface is diffusely red, gray or yellowish.[18] Four stages of the inflammatory response have classically been described: congestion, red hepatization, gray hepatization, and resolution. In the first stage of **congestion** the lung is heavy, boggy, and red. It is characterized by vascular engorgement, intra-alveolar fluid with few neutrophils, and often the presence of numerous bacteria. The stage of **red hepatization** that follows is characterized by massive confluent exudation with neutrophils, red cells, and fibrin filling the alveolar spaces. On gross

examination, the lobe now appears distinctly red, firm, and airless, with a liver-like consistency. The stage of **gray hepatization** follows with progressive disintegration of red cells and the persistence of a fibrinosuppurative exudate, giving the gross appearance of a grayish brown, dry surface. In the final stage of **resolution** the consolidated exudate within the alveolar spaces undergoes progressive enzymatic digestion to produce granular, semifluid debris that is resorbed, ingested by macrophages, expectorated, or organized by fibroblasts growing into it.[18]

Abscesses of the lungs – Yellowish, sometimes dark reddish yellow areas filled with pus are often found in the midst of a pneumonic area.

Pneumoconiosis – Anthracosis, silicosis, siderosis and asbestosis are classified under this category. The lungs are large, firm and black.

Pulmonary Fissure Abnormalities:

Lobar anatomy and Bronchopulmonary segments can be appreciated better with knowledge of variations that abound in fissures of the lungs. Knowledge of anatomical variations is essential for interpreting radiological images, performing lobectomies and also for general knowledge to medical personnel.[19,20,21]

Fissures separate individual Bronchopulmonary segments as the lungs grow. These fissures become obliterated except along two planes which is seen in fully developed lungs as oblique or horizontal fissures. If pulmonary development is defective, it will give rise to variations in lobes and fissures of lung.[19,20,21]

A fissural classification based on both the degree of completeness of the fissures and the location of the pulmonary artery at the base of the oblique fissure. Four stages have been described:
Grade I- complete fissure with entirely separate lobes.
Grade-II- complete visceral cleft but parenchymal fusion at the base of the fissure.
Grade III- visceral cleft evident for a part of the fissure.
Grade IV- complete fusion of lobes with no evident fissural line.[21,22]

Aspergillus:

Aspergillus species are the cause of a variety of pulmonary abnormalities that range in severity from commensal overgrowth of airways to invasion of the lung and its blood vessels, leading to sepsis and death.[23]

Aspergillus species are readily isolated from both soil and decaying vegetation, but they have been isolated from a wide range of organic substances, including foodstuffs, paint, medications, refrigerator walls, dialysis bags, etc. The fungal spores of Aspergillus spp are released into the ambient air, and viable organisms can survive extreme climatic conditions.[23]

Aspergillus species hyphae tend to branch dichotomously, progressively, and primarily at acute angles of approximately 45^{o}, mimicking an arborizing tree branch. The hyphae range in diameter from 2.5 to 4.5 µm and exhibit frequent septation.[23]

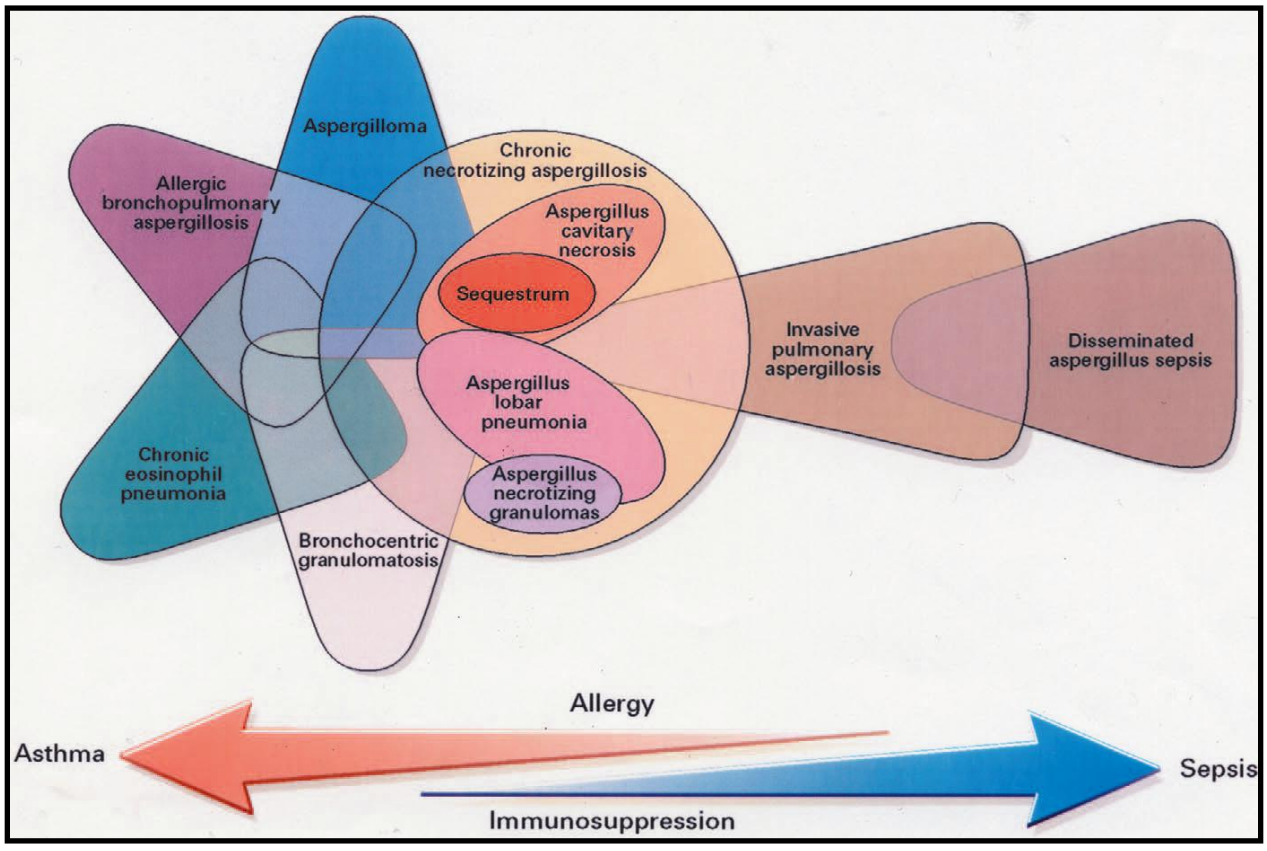
The gold standard for the diagnosis of Aspergillus infection is isolation and culture of the organisms in the microbiology laboratory.[23] Since confirmatory microbial cultures may not be available for all cases, establishing expertise in discerning the morphologic features of

Aspergillus species and the spectrum of histopathologies caused by them is critical in directing appropriate therapy.[23]

It evokes histologic responses by the host that reflect the level of immunocompetence and thus determines the spectrum of lung disorders it cause.[24]

Invasive Aspergillus infections are characterized by tissue necrosis accompanied by neutrophilic exudates. Eosinophils are variably present. Macrophages are invariably present, and granulomatous inflammation with giant cell formation is common.

Figure 1 - showing the spectrum of diseases caused by Aspergillosis[23]



ANGIOINVASIVE ASPERGILLOSIS - Grossly targetoid lesions with central thrombosed vessels secondary to angioinvasion surrounded by a rim of consolidated lung, confluent bronchopneumonia, or dense lobar consolidation may be seen. Identification of fungal angioinvasion is enhanced with the aid of silver and elastic stains.

Type 2 Pneumocyte Hyperplasia:

Type 2 pneumocyte hyperplasia is a universal reaction in injured lung. It is most striking in diffuse alveolar damage (DAD), but is also seen in organizing pneumonia, non-specific interstitial pneumonia, and in a variety of other settings, including acute bronchopneumonia, in the lung surrounding granulomas, lesions of pulmonary Langerhans' cell histiocytosis, tumours and abscesses.[25,26,27]

Pneumocyte hyperplasia is commonly observed in the lung adjacent to pleuritis.[25,26,27]

Pathology of Small Airways Disease:

Features of the various small airways diseases overlap, and a firm diagnosis may not be possible on limited endobronchial or transbronchial biopsy tissue, and diagnoses are often descriptive rather than specifically diagnostic of a specific entity. Clinical and radiologic correlation is necessary to provide the most accurate diagnosis.

Small airways may be involved with disease primarily or may be involved secondarily by diseases primarily affecting bronchi or lung parenchyma. Although etiologies are numerous, small airways disease may be generally divided into small airways disease related to tobacco; to various other exposures, including mineral dusts; to diseases involving other areas of the lung, with secondary bronchiolar involvement; and to idiopathic causes.

The term small airways include membranous bronchioles, respiratory bronchioles, and alveolar ducts.[28]

Table 2: Classification of Small Airways Disease, 2008[29]

Cellular bronchiolitis
Acute bronchiolitis
Acute and chronic bronchiolitis
Chronic bronchiolitis, with or without fibrosis
Subtypes of cellular bronchiolitis
Follicular bronchiolitis
Diffuse panbronchiolitis
Bronchiolitis obliterans with intraluminal polyps
Constrictive bronchiolitis
Respiratory bronchiolitis
Mineral dust-associated airway disease
Peribronchiolar metaplasia
Bronchiolocentric nodules
Asthmatic-type changes
Chronic bronchitis/emphysema-associated small airways changes

Acute and Chronic Bronchiolitis

Generally found in adults. Although many cases are caused by infections, including respiratory syncytial virus, other noninfectious etiologies exist like Aspiration Pneumonia, Collagen vascular diseases, Inhalation of fumes and toxins, Asthma etc.

Bronchiolar lumen contains purulent exudative material and sloughed bronchiolar mucosal cellular debris and variable amounts of mucus. Bronchiolar mucosa and walls contain a mixed neutrophilic infiltrate and chronic inflammatory cell infiltrate made up predominantly of lymphocytes and plasma cells. The mixed acute and chronic inflammatory cell infiltrate extends into peribronchiolar tissue, and edema may be present.

Chronic Bronchiolitis:

It may be a feature of many diseases like infections, collagen vascular diseases, post transplantation GVHDs, chronic obstructive pulmonary diseases etc.

Bronchioles and peribronchiolar tissues are infiltrated with chronic inflammatory cells.

Interstitial Lung Diseases:

The most common histologic subtype of chronic interstitial lung disease is usual interstitial pneumonia (UIP), which makes up 47% to 71% of cases.[30,31]

Usual interstitial pneumonia can occur in a familial pattern or in the setting of connective tissue disease, hypersensitivity pneumonitis, or drug toxicity.[32] It has alternating zones of interstitial collagen type fibrosis, active fibrosis (fibroblast foci), scant inflammation, normal lung, and honeycomb change, all of which result in architectural distortion.[31]

Non-Specific Interstitial Pneumonia (NSIP) is usually a uniform process characterized by a mixture of inflammation and fibrosis with minimal architectural destruction.[31]

Lymphoid Interstitial Pneumonia (LIP) is an interstitial lung disease characterized by diffuse and dense infiltration of alveolar septae by chronic inflammatory cells, including T lymphocytes, plasma cells, and histiocytes, with prominent germinal centers and hyperplasia of the bronchial-associated lymphoid tissue.[32] LIP is considered an AIDS-defining illness.[33]

Organizing Pneumonia (OP) or Bronchiolitis obliterans organizing pneumonia (BOOP) is another interstitial lung disease which can be idiopathic (Cryptogenic Organizing Pneumonia) or seen in association with infections, collagen vascular diseases and drug reactions.[32,34] The OP pattern is characterized by patchy accumulation of intra-alveolar organizing fibroblastic tissue,

which is primarily centered around bronchioles. Intra-bronchiolar fibroblastic tissue (bronchiolitis obliterans) may or may not be present. The alveolar septa in involved areas generally exhibit mild chronic inflammation. Significant fibrosis should not be present, and the intervening lung tissue should be relatively normal.[34]

Fibrosis associated with architectural derangement (UIP) does not respond to anti-inflammatory therapy and has a poor prognosis, whereas architecture-sparing fibrosis (NSIP) may respond to anti-inflammatory therapy and has a better prognosis.[31]

Acute Lung Injury:

Acute pulmonary injury may occur secondary to an extensive number of direct or indirect pulmonary insults and often results in acute hypoxemic respiratory failure. Most patients with this condition will have acute respiratory distress syndrome (ARDS) or Acute Lung Injury (ALI) clinically.[34]

ARDS is defined as the presence of acute hypoxemia with

(1) A ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO_2:FIO_2) of 200 mm Hg or less,

(2) Bilateral infiltrates that are consistent with pulmonary edema radiographically, and

(3) No clinical evidence of cardiac failure.

A less severe category, termed Acute lung injury (ALI), was defined by the same criteria but with a PaO2 to FIO2 of 300 mm Hg.[35]

The incidence of ALI was 78.9 per 100 000 person-years and the incidence of ARDS was 58.7 per 100 000 person-years with an average mortality rate of 41.1% for ARDS and 38.5% for ALI.[36]

Histologically, cases from patients with clinical acute lung injury typically exhibit diffuse alveolar damage, but other histologic patterns may occasionally be encountered such as acute fibrinous and organizing pneumonia, acute eosinophilic pneumonia, and diffuse alveolar hemorrhage with capillaritis.[34]

Diffuse Alveolar Damage (DAD):

Acute Respiratory Distress Syndrome/Acute Lung Injury is a well-recognized complication of numerous and diverse conditions, including both direct injuries to the lungs and systemic disorders. In many cases, a combination of predisposing conditions are present.[18,37]

ARDS and ALI both have inflammation-associated increase in pulmonary vascular permeability, and epithelial and endothelial cell death. The histologic manifestation of these diseases is diffuse alveolar damage (DAD). Most cases of ALI are associated with an underlying etiology such as sepsis. In the absence of any etiologic association, such cases are called Acute Interstitial Pneumonia (AIP) (Hamman-Rich Syndrome).[34]

Table 3: Conditions Associated with Development of Acute Respiratory Distress Syndrome[18]

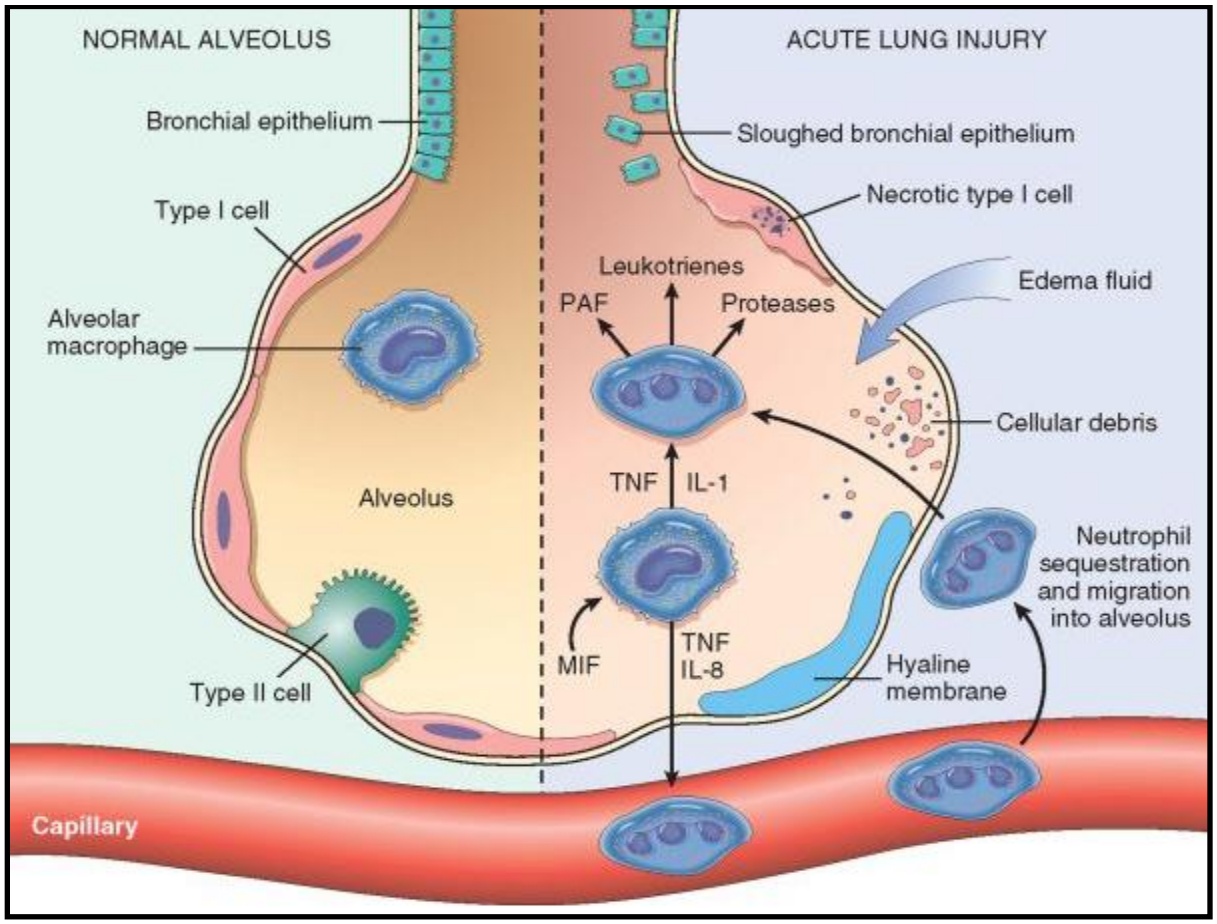
INFECTION
• Sepsis* • Diffuse pulmonary infections* - Viral, *Mycoplasma*, and *Pneumocystis* pneumonia; miliary tuberculosis • Gastric aspiration*
PHYSICAL/INJURY
• Mechanical trauma, including head injuries* • Pulmonary contusions • Near-drowning • Fractures with fat embolism • Burns • Ionizing radiation
INHALED IRRITANTS
• Oxygen toxicity • Smoke

• Irritant gases and chemicals
CHEMICAL INJURY
• Heroin or methadone overdose • Acetylsalicylic acid • Barbiturate overdose • Paraquat
HEMATOLOGIC CONDITIONS
• Multiple transfusions • Disseminated intravascular coagulation
PANCREATITIS
UREMIA
CARDIOPULMONARY BYPASS
HYPERSENSITIVITY REACTIONS
• Organic solvents • Drugs
* More than 50% of cases of acute respiratory distress syndrome are associated with the first four conditions.

Pathogenesis

The alveolar capillary membrane is formed by two separate barriers: the microvascular endothelium and the alveolar epithelium. In ARDS the integrity of this barrier is compromised by either endothelial or epithelial injury or, more commonly, both. The acute consequences of damage to the alveolar capillary membrane include increased vascular permeability and alveolar flooding, loss of diffusion capacity, and widespread surfactant abnormalities caused by damage to type II pneumocytes. Endothelial injury also triggers the formation of micro thrombi that add to the insult of ischemic injury (Fig 2). Hyaline membranes result from inspissation of protein rich edema fluid that entraps debris of dead alveolar epithelial cells.

Figure 2: Pathogenesis of DAD[18]



Morphology

DAD is a diffuse process as the name implies, but it is not always uniform in severity or appearance from one microscopic field to another. The pathologic features of the lung in ARDS derive from severe injury to the alveolocapillary unit. Extravasation of intravascular fluid dominates the onset of the disease and is equated with permeability pulmonary edema. As the process unfolds, edema is overshadowed by cellular necrosis, epithelial hyperplasia, inflammation and fibrosis. The histologic appearance is temporal which can be divided into three interrelated and overlapping phases that correlated with the clinical evolution of the disease.[38]

(1) Acute/Exudative Phase (Onset of respiratory failure to 1 week)

(2) Proliferative/ Organizing Phase (Day 7 to 21)

(3) Fibrotic Phase (> Day 21)

In the acute stage, the lungs are heavy, firm, red, and boggy. They exhibit congestion, interstitial and intra-alveolar edema, inflammation, fibrin deposition, and diffuse alveolar damage. The alveolar walls become lined with waxy **hyaline membranes.** (Fig 3) Alveolar hyaline membranes consist of fibrin-rich edema fluid mixed with the cytoplasmic and lipid remnants of necrotic epithelial cells. They appear as dense, glassy eosinophilic membranes lining the alveolar ducts and alveolar spaces.[34] In the organizing stage, type II pneumocytes undergo proliferation, and there is a granulation tissue response in the alveolar walls and in the alveolar spaces. Sometimes, however, fibrotic thickening of the alveolar septa ensues, caused by proliferation of interstitial cells and deposition of collagen.

Figure 3: DAD – Acute phase showing Hyaline Membranes[18]

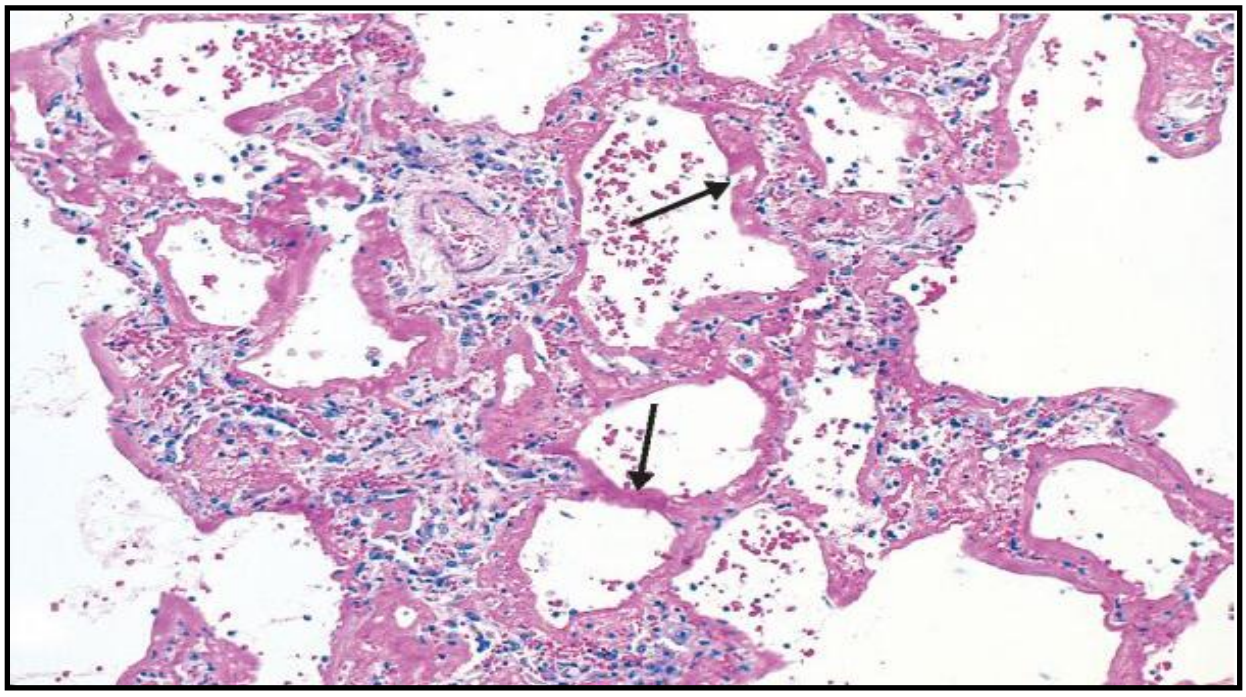


Table 4: Temporal Features of Diffuse Alveolar Damage[38]

EXUDATIVE PHASE	PROLIFERATIVE PHASE	FIBROTIC PHASE
Interstitial and Intra-alveolar edema	Interstitial Myofibroblast reaction	Collagenous fibrosis
Haemorrhage	Luminal Organizing fibrosis	Microcystic Honeycombing
Leukoagglutination	Chronic Inflammation	Traction Bronchiectasis
Necrosis of alveolar cells	Parenchymal Necrosis	Arterial Tortuosity
Hyaline Membrane	Type II cell Hyperplasia	Mural Fibrosis
Platelet-Fibrin Thrombi	Obliterative endarteritis	Medial Hypertrophy
	Macro thrombi	

Regional Alveolar Damage (RAD):

Although ARDS is characterized by extensive bilateral lung involvement, alveolar damage can also affect the lung in a localized fashion. Regional Alveolar Damage is associated with the same clinical risk factors as Diffuse Alveolar Damage, suggesting that there is a spectrum in the extent of lung involvement and disease severity in patients at risk for ARDS.[38]

RAD was defined as one or more macroscopically visible discrete areas of consolidation that had the macroscopic and histologic characteristics of DAD, exudative or proliferative phase; occupied less than 50 % of the bilateral cut surface.[39]

It was speculated that the regional DAD could result from irregular blood flow related to vascular occlusion, irregularly distributed microvascular injury, or from a combination of factors.[39]

Acute Eosinophilic Pneumonia:

It may be associated with underlying etiologies such as toxic inhalation, drug reaction, or infection, particularly with parasites or fungus, or may be idiopathic.[34]

It may be characterized by intra-alveolar fibrin and macrophages in variable proportions, admixed with numerous eosinophils. Eosinophils may also be present in the interstitial tissue and eosinophilic micro abscess formation may be observed along with the additional finding of hyaline membrane.[34]

Acute Fibrinous and Organizing Pneumonia:

Histologic pattern associated with acute lung injury in which the alveolar spaces are filled with organizing fibrin balls.[34,40] The process may be patchy or relatively diffuse. The alveolar septa may show mild interstitial widening or lymphocytic infiltrates, but significant eosinophils or neutrophils should not be seen.[34,40]

Diffuse Alveolar Haemorrhage:

Bleeding from the lung originates from the bronchial vessels, the pulmonary vessels, or the microcirculation of the lung. Diffuse alveolar hemorrhage (DAH) is a clinicopathological syndrome describing the accumulation of intra-alveolar RBCs originating from the alveolar capillaries. All causes of DAH have the common denominator of an injury to the alveolar microcirculation.[41]

Injury to the alveolar microcirculation resulting in DAH may be localized to the lung (inhalation injuries, diffuse alveolar damage) or associated with a systemic disorder (vasculitis or connective tissue disease, immune-mediated disorders).[34,41]

Pulmonary capillaritis is typically seen in patients with Microscopic Polyangiitis, Wegener's Granulomatosis, Systemic Lupus Erythematosis (SLE), and the entire range of collagen vascular

diseases, including polymyositis, mixed connective tissue disease, antiphospholipid syndrome, and rheumatoid arthritis. Medications such as phenytoin, retinoic acid, penicillamine, hydralazine, and propylthiouracil have also been associated with pulmonary capillaritis.[42]

Bland pulmonary hemorrhage is seen secondary to coagulation disorders, inhalational toxins, mitral stenosis and idiopathic pulmonary hemosiderosis.[42]

Diffuse alveolar damage (DAD) associated with hemorrhage can also be seen in the context of SLE, crack cocaine inhalation, bone marrow transplantation, radiation therapy and ARDS.[41,42]

Histopathologic findings may be those of DAH with capillaritis, bland alveolar hemorrhage, and alveolar hemorrhage associated with diffuse alveolar damage.[42] The underlying histopathology of DAH includes the presence of intra-alveolar RBCs and fibrin and the eventual accumulation of Hemosiderin-laden macrophages, which may take up to 48 to 72 hrs to accumulate.[41] The Hemosiderin in these macrophages is characteristically coarsely granular and golden brown. Iron stains may highlight the coarse nature of true Hemosiderin.[34] Pulmonary capillaritis consists of an interstitial neutrophilic predominant infiltration, fibrinoid necrosis of the alveolar and capillary walls, and leukocytoclasis.[41] Other histologic features include alveolar capillary thrombosis, type II alveolar epithelial cell hyperplasia, intra-alveolar organizing pneumonia, and mononuclear cell infiltration of the alveolar interstitium.[43]

Idiopathic Pulmonary Hemosiderosis:

Idiopathic pulmonary hemosiderosis (IPH) is a rare disease characterized by heavy lungs with aggregates of Hemosiderin- laden macrophages due to recurrent diffuse alveolar hemorrhage in the absence of vasculitis or capillaritis and by eventual interstitial fibrosis. Presentation is most often seen in the pediatric age group although adults can also be affected.[32]

Smoker's Macrophages:

Sometimes the pigmented alveolar macrophages of smokers can simulate the siderophages of pulmonary haemorrhage. The fine granularity of the brown pigment in these cells and the consistent presence of dot-like black pigment particles in the cytoplasm helps in their proper identification.[44]

Chronic Respiratory Diseases:

Hundreds of millions of people suffer every day from chronic respiratory diseases. According to the latest WHO estimates (2004), currently 235 million people have asthma; 64 million people have chronic obstructive pulmonary disease (COPD) while millions have allergic rhinitis and other often-under diagnosed chronic respiratory diseases.[45]

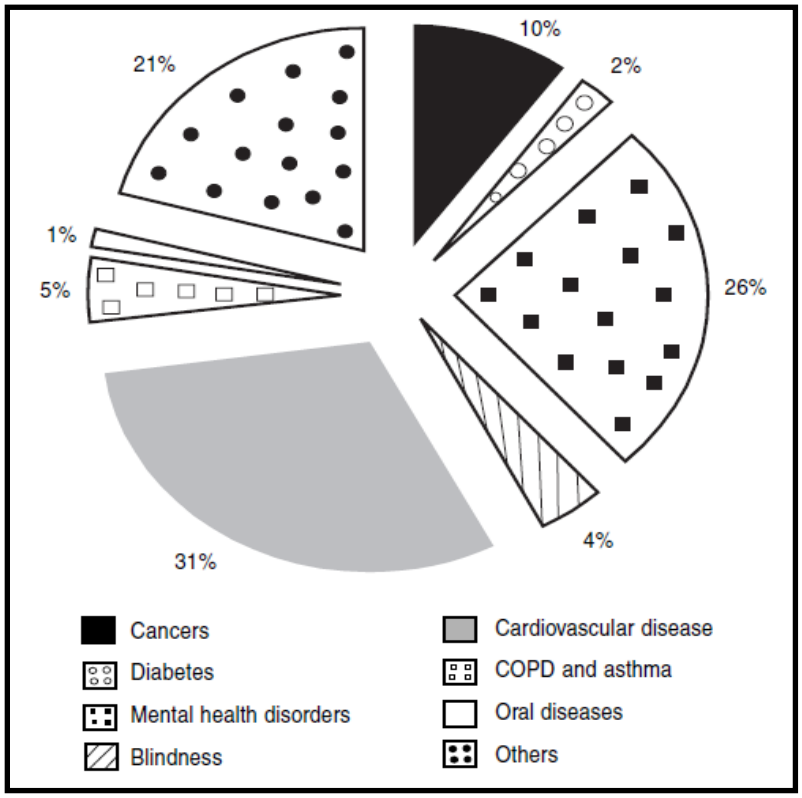
In India, it is estimated that there were roughly 25 million cases of asthma in 2001 which may increase by nearly 50% by 2016.[46]

Table 5: Deaths due to respiratory diseases in India and the world in 1990 and 2020 [47]

	Deaths			
	1990 Estimated numbers (%)		2020 Projected numbers (%)	
	World	India	World	India
Respiratory diseases (total)	2,935,000 (5.8)	267,000 (2.8)	6,366,000 (9.3)	744,000 (6.5)
COPD	2,211,000 (4.4)	140,000 (1.5)	4,726,000 (6.9)	429,000 (3.8)
Asthma	137,000 (0.3)	20,000 (0.2)	326,000 (0.5)	55,000 (0.5)
Other respiratory diseases	587,000 (1.2)	106,000 (1.1)	1,313,000 (1.9)	261,000 (2.3)

COPD: chronic obstructive pulmonary disease
Figures in parentheses indicate respiratory deaths as percentages of total deaths

Figure 4: Priority non-communicable health conditions in India, by share in the burden of disease, 1998 [46]



Chronic Obstructive Pulmonary Diseases:

Chronic obstructive pulmonary disease (COPD) refers to a group of disorders characterized by chronic airflow obstruction/limitation. The airway obstruction is persistent and largely irreversible. It includes two distinct pathophysiological processes—chronic bronchitis and emphysema.[48]

Incidence, Prevalence and Economic Burden

COPD is a leading cause of morbidity and mortality worldwide.[47,49,50] According to the latest WHO estimates (2004), currently 64 million people have COPD and 3 million people died of COPD. COPD is currently the fourth leading cause of death worldwide.[48] WHO predicts that

COPD will become the third leading cause of death worldwide by 2030.[46] It accounted for 5.8% of total deaths in 1990 and is expected to rise to 9.3% of deaths by 2020.[47] It is also a major cause of economic burden in both developed and developing countries.[47,51]

It is estimated that there are around 14.9 million chronic cases of COPD in India in the age group of 30 years and above, and these are projected to increase by nearly 50% by the year 2016, including 'severe' cases, some of whom may require greater levels of care, including hospitalization.[46]

The prevalence of COPD is reported to be around 5% among males and 2.7% among females, with a male to female ratio of 1.85:1. At the all-India level, the male to female smoking ratio was seen to be 11.76:1.[48]

Indian Estimations in 2011 with urban-rural divide:[48]

- Treatment cost of a patient with chronic COPD per year would be Rs 52,645.
- Number of patients with chronic COPD would be 5.15 million in urban areas and 14.19 million in rural areas.
- Number of males with chronic COPD would be 3.43 million in urban areas and 9.35 million in rural areas.
- Number of females with chronic COPD would be 1.72 million in urban areas and 4.83 million in rural areas.
- Total cost of treatment for COPD would be Rs 9.4 billion in urban areas and Rs 25.9 billion in the rural areas.

Risk Factors

The most important risk factors for COPD are:[52]

- Tobacco smoking
- Indoor air pollution (such as biomass fuel used for cooking and heating)
- Outdoor air pollution
- Occupational dusts and chemicals (vapours, irritants, and fumes)

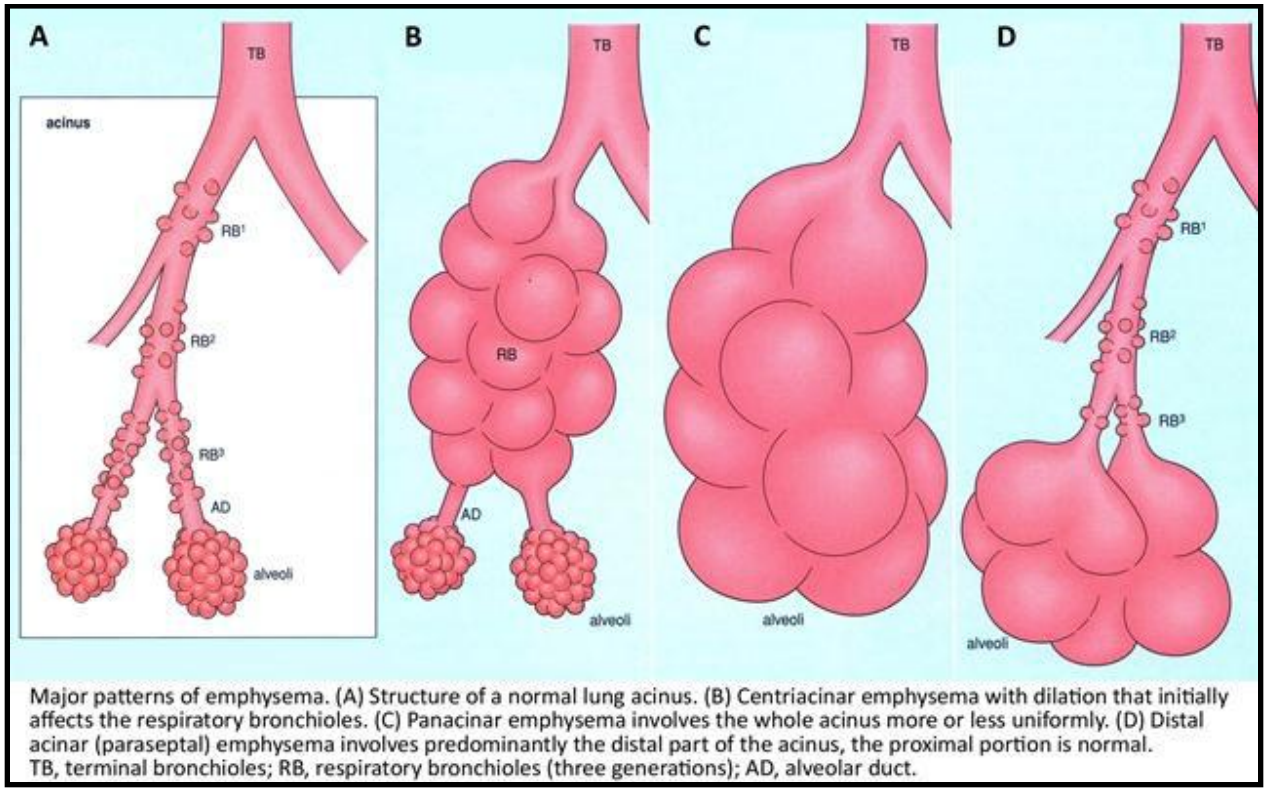
Squamous Metaplasia of Respiratory Epithelium

When the respiratory mucosa is exposed to tobacco smoke, mucosal cells are thought to undergo a variety of pathologic changes prior to the development of carcinoma. With prolonged exposure to tobacco smoke, mucosal lining cells begin to show basal-cell hyperplasia, nuclear atypia, and squamous metaplasia.[53] Squamous metaplasia was characterized by proliferation of polygonal cells with the flattening or stratification of any portion of the mucosa and the total loss of cilia from the biopsy specimen.[53] Squamous metaplasia was also seen in uranium miners, marijuana smokers, and chronic pulmonary diseases like Asthma, Emphysema, Chronic Bronchitis, Bronchiectasis, Tuberculosis and silicosis.[53]

Emphysema

This is a condition of the lung characterized by abnormal, permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls.

Figure 5: Types of Emphysema



Major patterns of emphysema. (A) Structure of a normal lung acinus. (B) Centriacinar emphysema with dilation that initially affects the respiratory bronchioles. (C) Panacinar emphysema involves the whole acinus more or less uniformly. (D) Distal acinar (paraseptal) emphysema involves predominantly the distal part of the acinus, the proximal portion is normal. TB, terminal bronchioles; RB, respiratory bronchioles (three generations); AD, alveolar duct.

Centriacinar/ Centrilobular Emphysema: The central or proximal parts of the acini, formed by respiratory bronchioles, are affected, whereas distal alveoli are spared. Thus, both emphysematous and normal airspaces exist within the same acinus and lobule. It is most severe in the upper zones of the lung, the upper lobe, and the superior segment of the lower lobe.[54]

Panacinar (panlobular) Emphysema: In this type, the acini are uniformly enlarged from the level of the respiratory bronchiole to the terminal blind alveoli. The prefix "pan" refers to the entire acinus. It tends to occur more commonly in the lower zones and in the anterior margins of the lung, and it is usually most severe at the bases. This type is associated with alpha-1-antitrypsin deficiency.[54]

Distal acinar (paraseptal) emphysema: The proximal portion of the acinus is normal, and the distal part is predominantly involved. The emphysema is more striking adjacent to the pleura, along the lobular connective tissue septa, and at the margins of the lobules.[54]

Bullous emphysema: This term is used to describe exceptionally large air spaces, especially within the uppermost portions of lungs that develop secondary to damaged alveoli. It is generally seen in association with centriacinar emphysema and paraseptal emphysema. A bulla is an emphysematous space that is more than 1cm in diameter.[54]

Paracicatricial (irregular) emphysema: Emphysematous destruction occurs adjacent to pulmonary scars. The scars may be consequent to old granulomatous inflammation (example, tuberculosis), healed pulmonary infarcts, organized pneumonia, or pneumoconiosis (such as progressive massive fibrosis in patients with silicosis).[54]

Grossly, the lungs are large. The organs are light in colour and over distended. Sometimes, markedly dilated and fused alveoli are visible grossly, assuming the form of small gas bubbles. Large, well circumscribed air-containing blebs may be found (Bullous emphysema)

Microscopically, there is loss and thinning of alveolar septal walls resulting in fewer alveolar attachments to bronchioles.[18]

Chronic Bronchitis

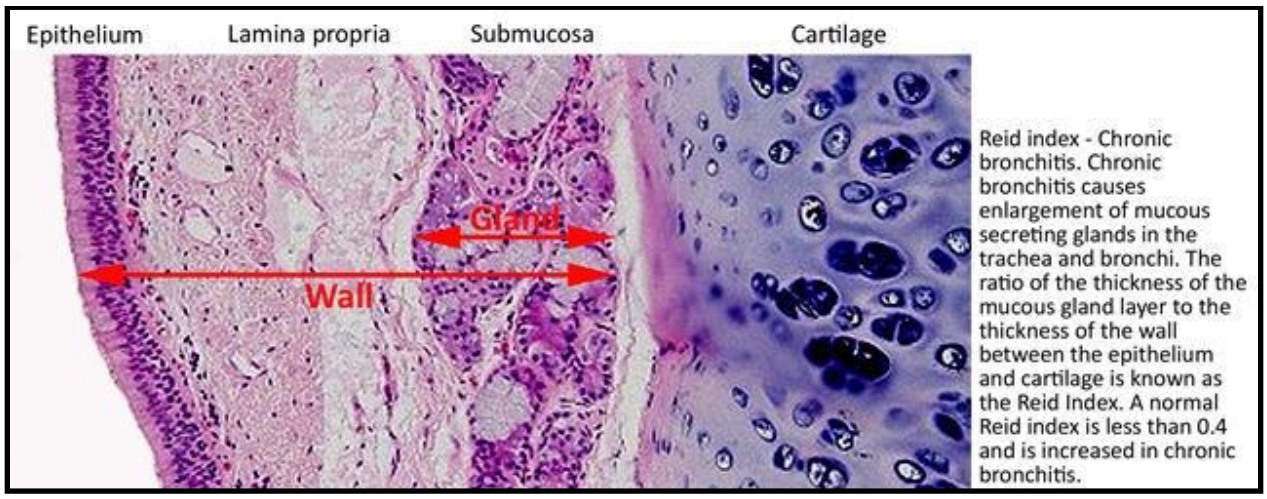
It is a chronic inflammatory condition of the bronchi producing an increase in mucus secretion by the glands of the tracheobronchial tree resulting in the expectoration of mucus at some time of the day for at least three months for two consecutive years.[55]

Pathologically the bronchial wall may be thickened, and the following features may be observed

histologically: enlargement of the mucous glands, dilatation of mucous gland ducts, an increase in the number of mucous cells in the acini of mucous glands, goblet cell hyperplasia and squamous metaplasia of the surface epithelium, a variable degree of chronic inflammatory cell infiltration. Chronic bronchiolitis is often associated with it, and there may be narrowing or obliteration of the lumen.[55]

Reid Index (Gland/wall ratio) is increased in chronic bronchitis and is more than 0.4 due to mucosal gland hypertrophy and hyperplasia.[18,56] This may be done by measuring the ratio of the thickness of the gland layer to the thickness of the wall between the base of the surface epithelium and the internal limit of the cartilage plates.[56]

Figure 6: Shows calculation of Reid's Index



Bronchiectasis:

Bronchiectasis is a disease characterized by permanent dilation of bronchi and bronchioles caused by destruction of the muscle and elastic tissue, resulting from or associated with chronic necrotizing infections.[18]

Causes – Significant portion of cases are idiopathic.[18,55,57]

- Congenital or hereditary conditions, including cystic fibrosis, intralobar sequestration of the lung, immunodeficiency states, and primary ciliary dyskinesia and Kartagener syndromes.
- Post-infectious conditions, including necrotizing pneumonia caused by bacteria (Mycobacterium tuberculosis, Staphylococcus aureus, Haemophilus influenzae, Pseudomonas), viruses (adenovirus, influenza virus, human immunodeficiency virus [HIV]), and fungi (Aspergillus species).
- Bronchial obstruction, due to tumor, foreign bodies, and occasionally mucus impaction, in which the bronchiectasis is localized to the obstructed lung segment.
- Other conditions, including rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, and post-transplantation (chronic lung rejection, and chronic graft-versus-host disease after bone marrow transplantation).

Grossly, Bronchiectasis usually affects the lower lobes bilaterally. The airways are dilated, sometimes up to four times normal size. Characteristically, the bronchi and bronchioles are sufficiently dilated that they can be followed almost to the pleural surfaces. On the cut surface of the lung, the transected dilated bronchi appear as cysts filled with mucopurulent secretions.[18] Two basic patterns of bronchial dilatation can be seen – cylindrical and saccular.[55]

The histologic findings vary with the activity and chronicity of the disease. In the full-blown, active case there is an intense acute and chronic inflammatory exudation within the walls of the bronchi and bronchioles, associated with desquamation of the lining epithelium and extensive areas of necrotizing ulceration. There may be pseudostratification of the columnar cells or squamous metaplasia of the remaining epithelium. Fibrosis of the bronchial and bronchiolar

walls and peribronchiolar fibrosis develop in the more chronic cases, leading to varying degrees of subtotal or total obliteration of bronchiolar lumens.[18]

In chronic bronchitis, there is frequently atrophy of the bronchial wall. This atrophy may be from fibrous development, and in that case the wall can be weakened. With prolonged periods of constant inflammation, there is abundant secretion and therefore frequent coughing, and the forced expirations with closed glottis, acting on the weakened wall, induces dilatation and eventually Bronchiectasis.[18]

Pulmonary Hypertension:

The most recent World Health Organization clinical classification defines 5 groups of pulmonary hypertension: (1) arterial, (2) venous, (3) hypoxemia associated, (4) thrombotic-embolic associated, and (5) miscellaneous.[32]

The morphologic features described, such as changes in small arteries (medial hypertrophy, intimal proliferation, concentric intimal fibrosis, necrotizing arteritis) and changes in arterioles (muscularization, plexiform lesions, angiomatoid lesions) are useful in identifying the range of pathologic conditions encountered.[32] Increases in intimal thickness with longitudinal muscle formation are a common feature in lungs of patients with COPD. Vasculitis, fibrinoid necrosis, and plexiform lesions are never found in COPD.[54]

Fatty streaking or even frank atherosclerotic changes may be seen on the intimal surface and similar intimal changes may be present in the intrapulmonary branches of the pulmonary artery.[54]

FEW SCENARIOS OF CAUSE OF DEATH ON LUNG CHANGES:

RTA:

Road traffic accident trauma is considered as a major cause of morbidity and mortality among young population worldwide.[58]

The actual causes of death according to autopsy reports were classified as central nervous system (CNS) injury, skull vault fractures, skull base fractures, cervical spinal cord injury, airway/ventilation compromise, and hemorrhage from extremities or internal bleeding (hypovolemic shock).[58]

Men were more affected by car crash-related death than women, especially in the second and third decades of life. Not only in car traffic accidents, but also in all types of injuries, men are more susceptible than women as a result of cultural norms and higher level of outdoor activities of men in our society.[58]

The World Health Organization has predicted that traffic fatalities will be the sixth leading cause of death worldwide and the second leading cause of disability-adjusted life-years lost in developing countries by the year 2020.[7]

In India, Road traffic fatalities have been increasing at about 8% annually for the last ten years and show no signs of decreasing.[59]

In India, the number of fatalities per million population remained around 79-83 in the period 1997-2003 and has since increased to 101 in 2007.[59,60] In 2007, only 15% of the victims were females.

In civilian life, chest injuries are responsible for a high mortality and morbidity in victims of road traffic accidents.[61] Penetrating chest trauma is frequently caused by gunshots and non gunshot-related incidents such as stabs, traffic accidents, and impalements.[62] Males are more

often the victims than females.[62] While gunshot wounds are major causes during wars and civil unrest, road traffic accidents account for most of the peace-time chest trauma.[63]

In a review of the management of chest trauma, Adebonojo working in Washington DC noted that 10% of patients with chest injury die at the site of the accident, and 5% die within 1 hour of arrival at the hospital.[63,64]

Lung Lacerations seen in Blunt Trauma:

In lung lacerations, lung lobes have tears with pleural cavity showing blood (Hemothorax).[61] Depending on the severity of chest injury, lung injuries can have congested or hemorrhagic grey-black areas grossly along with the tears. Microscopically, the alveoli are distended with blood and blood elements.[61]

Burns:

Respiratory dysfunction is common after major burns. Respiratory dysfunction after burns is multi-factorial, and ARDS and inhalation injury are most important. The early onset of ARDS, together with the changes in white blood cell count and organ dysfunction, favours a syndrome in which respiratory distress is induced by an inflammatory process mediated by the effect of the burn rather than being secondary to sepsis.[65]

Cases of Poison:

Lung changes seen in poisoning cases are usually histologically characterised by acute lung injury usually in the form of DAD, BOOP, Diffuse Alveolar Haemorrhage (DAH) and acute pulmonary edema. Majority of the poisons taken in medicolegal cases in the rural setup include

organophosphorus compounds, herbicides like paraquat, rat poisons and kerosene. Poisoning medicolegal cases are usually associated with suicides and accidents.

Suicide is a complex phenomenon associated with psychological, biological and social factors involving by and large every corner of the world. It is distinctively a human affair and continues to be a major public health issue. It is an enigma as to why life-caring human beings turn to self-destruction. Suicide by poisoning is attributed to the easy availability of the various poisons like rat poison, organophosphorus poison etc.[66]

Among the poisoning cases, organophosphorus poisoning was the most commonly used method for suicide, which is in contrast to the findings observed in England and Wales, wherein vehicle exhaust gas has been commonly used and carbon monoxide poisoning was common in Japan.[67]

Poison-related Aspiration Pneumonitis:

Aspiration is defined as the inhalation of oropharyngeal or gastric contents into the larynx and lower respiratory tract.

Aspiration pneumonitis (Mendelson's syndrome) is defined as acute lung chemical injury after the inhalation of regurgitated sterile gastric contents.[68] This occurs in patients who have a marked disturbance of consciousness such as that resulting from a drug overdose, seizures, a massive cerebrovascular accident, or the use of anaesthesia.[68] Bacterial infection may occur at a later stage of lung injury. The inflammatory response in the lungs probably results both from bacterial infection and from the inflammatory response to the particulate gastric matter.[68]

Aspiration pneumonia is an infectious process caused by the inhalation of oropharyngeal secretions that are colonized by pathogenic bacteria like Haemophilus influenza and Streptococcus pneumoniae.

In patients who aspirate while in a recumbent position, the most common sites of involvement are the posterior segments of the upper lobes and the apical segments of the lower lobes, whereas in patients who aspirate in an upright or semi recumbent position, the basal segments of the lower lobes are usually affected.[68]

Aspiration of food and other particulate substances causes a characteristic suppurative and granulomatous reaction in the lung. This type of aspiration pneumonia is a common finding at autopsy in debilitated patients.[69] The presence of multinucleated giant cells, foreign-body granulomas, and/or acute bronchopneumonia/ bronchiolitis in the background of a BOOP-like process should suggest the diagnosis, and the finding of foreign material is diagnostic.[69]

Aspirated food is usually identified by the presence of vegetable matter, which is classically characterized by large, usually non-polarizable, multi-septate elongate structures with thick cell walls, and occasional pigmentation. On cross-section, these may appear round with honeycomb like internal septation, dividing the structure into compartments.[69]

Sudden Death:

It must be pointed out that in Greece, every case of sudden death must be subjected to autopsy.[17] The definition of sudden death is rather unclear and varies according to the authority and the convention. The World Health Organization defines it as a death that occurs within 24 hours from the onset of symptoms, although many clinicians and pathologists believe that this is too long.[17]

Fatal Falls from Height:

Deaths due to blunt trauma as a sequel of falls from heights are a common phenomenon especially occurring in urban settings. A fatal fall from height can result from accident, suicide, or homicide.[70]

HIV and Lung changes:

Despite the use of prophylactic antibiotics over the course of infection, the lungs are the organs most frequently affected by HIV/AIDS and, hence, failure of the respiratory system is one of the main causes of death in HIV/AIDS patients.[71]

The present data underline the overwhelming prevalence of tuberculosis in HIV-infected patients in India; it was the most common cause of death in 59% of cadavers. Hence, physicians should remain suspicious of tuberculosis in HIV-infected patients until proven otherwise.[72]

Based upon pulmonary histopathological analysis in HIV autopsy cases, acute interstitial pneumonia (AIP) was the most common pattern observed, followed by diffuse alveolar damage (DAD), pulmonary edema and alveolar haemorrhage.[71]

Pulmonary Complications in Obesity:

In the obese population, left ventricular dysfunction, atherosclerotic heart disease, obstructive sleep apnea (OSA), asthma, and venous thromboembolism are recognized cardiopulmonary causes of morbidity and mortality.[73] Compared with the group without OSA, individuals with morbid obesity and OSA had a higher prevalence of medial hypertrophy of the muscular pulmonary arteries, hemosiderosis, alveolar hemorrhage, and alveolar capillary proliferation.[73]

Histomorphological correlation between clinical diagnosis, macroscopic examination and microscopic findings in autopsy in relation to cause of death:

The carefully examined lungs in medicolegal autopsies show characteristic morphological changes depending on the cause of death. Based on their gross appearance, the lungs were classified into 3 types: collapsed, non-collapsed and inflated type.[74]

The collapsed type of lung was seen in cases of death from exsanguination, and shrunk lungs due to traumatic pneumo- and/or hemo-thorax. The non-collapsed type of lung was seen in cases where lungs were thermo-coagulated, pulmonary embolism and deflating lungs of drowning victims before falling into collapse. The inflated type of lung consisted of lungs that showed ballooning soon after death by drowning, and lungs that had inflated due to emphysema or edema from various causes.[74]

Some of the histopathological lung changes observed in medicolegal cases were pulmonary edema, intra-alveolar hemorrhage, congestion, diffuse alveolar damage, interstitial inflammation, alveolar collapse and alveolar thickening.[75,76,77]

When death had resulted from a hemorrhage or occurred during a state of shock, megakaryocytes in the pulmonary vessels tended to increase.[74]

A meta-analysis based on a College of American Pathologists survey of 248 institutions in the United States noted that nearly 40% of autopsies yield at least 1 unexpected finding that contributed to the patient's death.[78]

Studies regarding correlation of clinical diagnosis and autopsy diagnosis point out the value of the postmortem examination as an educational and audit tool in the Emergency Department

environment. It also showed the discrepancies between the clinical diagnosis and autopsy diagnosis and classified them according to the Goldman Criteria.[5]

Table 6: Errors in Goldman Classification versus Autopsy Findings[5]

Type of Error	Goldman Class	Definition	Example: Death due to:
Major	1	Directly related to death; if recognized, may have altered treatment or survival	Unsuspected myocardial infarction presenting with chest pain
Major	2	Directly related to death; if recognized, would not have altered treatment or survival	Unsuspected myocardial infarction presenting with cardiac arrest
Minor	3	Incidental autopsy finding not directly related to death but related to terminal disease process	Known myocardial infarction with unsuspected left ventricular mural thrombus
Minor	4 (i)	Incidental autopsy finding unrelated to cause of death	Known myocardial infarction with unsuspected lung cancer
Minor	4 (ii)	Incidental autopsy finding contributing to death in an already terminally ill patient	Unsuspected aspiration pneumonia in an already terminally ill patient
No error	5	Clinical and autopsy diagnoses in complete agreement	

The Goldman classification is useful in that it differentiates between major and minor discrepancies and identifies those deaths where the discrepancy had an impact on patient survival.[79]

Discrepancies may be better divided into:

(1) Discrepancies of potentially treatable major conditions (those leading to, or significantly contributing to death)

(2) Discrepancies of untreatable major conditions

(3) Discrepancies of minor/coexistent conditions

This would highlight the most significant discrepancies without requiring a judgement about potential survival.[79]

The clinical diagnoses were further classified as being either concordant or discrepant with respect to the necropsy diagnoses by using another classification system based on that proposed by Underwood as follows:[80]

Category I
– major discrepancy – missed principal diagnosis definitely affecting clinical outcome
Category II
– major discrepancy – missed principal diagnosis possibly affecting clinical outcome
Category III
– minor discrepancy – missed secondary diagnosis, either symptomatic but not treated, or likely to have affected prognosis
Category IV
– minor discrepancy – missed secondary diagnosis that could not have been made clinically
Category V
– concordant diagnosis

The highest frequencies of discrepancies between the gross and microscopic findings were found in the lung. It was found that the lung was the organ where most diagnostic discrepancies or refinements occurred after microscopic examination. There are some entities that maybe similar at gross examination such as bronchopneumonia and diffuse alveolar damage.[6]

The diagnoses with the highest individual discrepancy rates were pneumonia and pulmonary thromboembolism.[5,17,78,79,80]

For certain organs, such as the lung, it has been shown that there are considerable intra-observer and inter-observer discrepancies in the diagnosis of bronchopneumonia using the naked eye and histology.[6]

It was shown that diagnoses made on macroscopic examination were altered by histology and that macroscopically normal organs showed histological abnormalities. Therefore histology is still essential to confirm or refute macroscopic diagnosis.[79]

The study of Tavora et al confirms that autopsy remains an important tool in assessing discrepant diagnoses, especially in the areas of pulmonary embolism, infections, solid tumor diagnosis, and postoperative complications.[78]

Although alternatives to the autopsy are being researched, the autopsy, including histology, remains the most accurate means of determining the cause of death and other significant and incidental diagnoses.[79]

Discrepancy rates will only decrease when more necropsies are requested, allowing clinicians to appreciate the ‘‘different faces’’ of various diseases, and allowing continual audit of diagnostic accuracy.[80]

In Road Traffic Accident autopsies, apart from lung injuries as a cause of death, bronchopneumonia and undiagnosed chest infection also played a role.[7]

Contradiction between autopsy and histopathology examinations:[15]

1. Improper sampling/ preservation of tissues during autopsy.
2. Autolysis of the tissues is quite common.
3. Sections for histopathological examination may be taken from the site where lesion is not present.
4. Necrosed tissues which are visible during gross examination in autopsy may slough out during preservation or during processing of tissues for microscopic examination.
5. Most of the tissues received for histopathological examination show non-specific findings e.g. congestion, cloudy swelling, inflammatory cells etc., which may not be helpful to establish the cause of death.

6. Insufficient priority given to histopathological examination of autopsy specimens by technical staff and pathologist already burdened with increasing workload of surgical resections, biopsies and cytology.
7. Some pathologists do not want to indulge themselves in medico legal complications and to avoid legal queries further they may not write any specific opinion about the pathology found.[15]

RESEARCH METHODOLOGY

RESEARCH METHODOLOGY:

Source of Data:

Lung specimens were collected from autopsies conducted at R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar (Karnataka), India in coordination with the Department of Forensic Medicine.

Clinical data was obtained in each case – name, age, clinical diagnosis and cause of death. Each autopsy subject was identified, examined and post-mortem study was done after obtaining consent from next of kin in case of medical autopsy and requisition from the Police/Department of Forensic Medicine in medicolegal autopsies.

Method of Collection of Data:

a. **Study Setting:**

   This study was carried at Department of Pathology, R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

b. **Study Design:**

   Cross-Sectional Study Design

c. **Study Duration:**

   The study was carried out from 1st October 2009 to 31st August 2011.

d. **Study Population and Sample Size:**

   120 cases that underwent autopsy during the study period mentioned.

e. Study Procedure:

Autopsy was done by conventional technique. Following thoracotomy, both the lungs were taken out at the level of carina. The lungs were fixed with the Wet Inflation Fixation Method

f. Gross Examination & Dissection:

(1) Each lung with the main bronchus was then weighed and dimensions were noted.

(2) On external surface, both lungs were carefully examined for any morphological changes like pleural changes, anthracotic pigments, lung collapse and any other findings. Then it was cut in parallel slices from the costal surface towards the hilus of both lungs.

(3) On cut section, consistency of lung was noted whether it was soft or spongy or firm or hard. Changes of pneumonic consolidations like red or gray hepatizations if seen were recorded. Bronchial changes were noted. Finally, if any other changes like anthracosis, dilated airways, dilated bronchioles etc, were also noted.

g. Tissue Processing:

(a) 2 bits of 1 cm thickness each was taken from each lobe of both lungs amounting to 10 bits and each bit labelled according to the original site. One bit from the bronchus of either side was also taken and labelled. These bits were fixed in 10 % Formalin.

(b) Histological studies were done by routine tissue processing. Paraffin-embedded tissue sections were assessed following haematoxylin and eosin staining.

(c) Special stains like Periodic Acid Schiff (PAS) stain, Gram's stain and Ziehl-Neelsen Stain were done wherever micro-organisms were seen.

h. Microscopic Examination:

The sections were examined for congestion, edema, haemorrhage, inflammation, alveolar collapse and thickening, alveolar wall disturbances, capillary dilatation, hemosiderotic changes, anthracotic changes, bronchiolar and pulmonary vessel pathologies and any other changes if any. Also sections through the main bronchi were also examined and observed for any congestion, inflammatory exudates and any other changes.

Hemosiderosis was graded as

I – Questionable Hemosiderin-laden macrophages

II – Hemosiderin-laden macrophages seen

III - Hemosiderin-laden macrophages seen in large amounts

i. Proforma:

All the details were recorded in a predesigned and pretested Proforma (enclosed in Annexure-A)

j. Analysis of Data:

All the data obtained in the study were entered in the master chart (enclosed in annexure-C). The data was analysed using SPSS package version 14 (Chicago,IL) and presented in the form of tables, figures, graphs and diagrams wherever necessary. Chi Square descriptive analysis was applied.

k. Inclusion Criteria:

(1) Admitted patients who have died and sent for medical autopsy.

(2) Patients on whom medicolegal autopsies have been done to ascertain the cause of death.

h. Exclusion Criteria:

(1) Autopsies on exhumed bodies.

(2) Autopsies on poorly preserved bodies that are more than 3 days old where autolytic changes would have taken place.

(3) Intra uterine and perinatal deaths

(4) Infants and children under 1 year.

- In each case, a clinicopathological correlation was done wherever data was available.
- And wherever necessary, gross and microphotographs were taken.

RESULTS

RESULTS:

The total number of autopsy cases that were studied: 120.

The total number of right lung specimens received and studied: 110.

The total number of left lung specimens received and studied: 107.

The total number of right lung portions received and studied: 6.

The total number of left lung portions received and studied: 4.

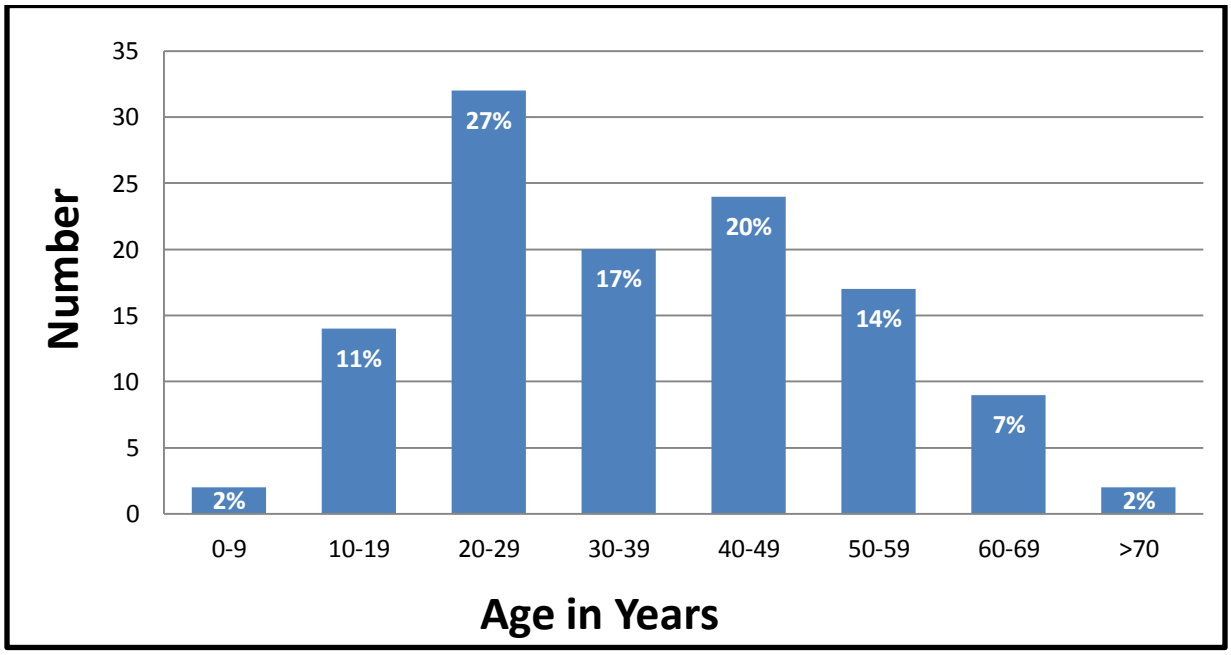
AGE:

In the present study, the ages ranged from 8 to 85 years. Mean age was 36.25±15.71 years. Majority of patients belonged to the 3rd decade of life (27%), followed by 5th decade (20%) and 4th decade (17%).

Table 7: Age Distribution

Age Groups(Years)	Number	Percent(%)
0-9	2	2
10-19	14	11
20-29	32	27
30-39	20	17
40-49	24	20
50-59	17	14
60-69	9	7
>70	2	2
Total	120	100

Chart 1: Age Distribution

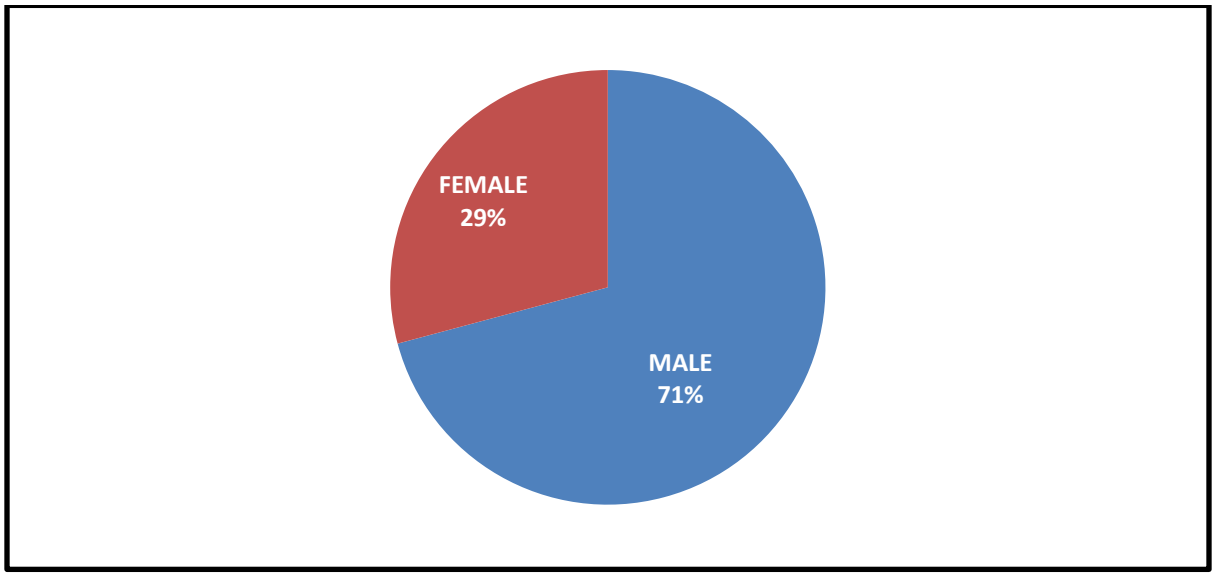


GENDER:

In the present study, number of males were 85 (71%) and number of females were 35 (29%).

Male: female ratio was 2.43:1.

Chart 2: Gender Distribution



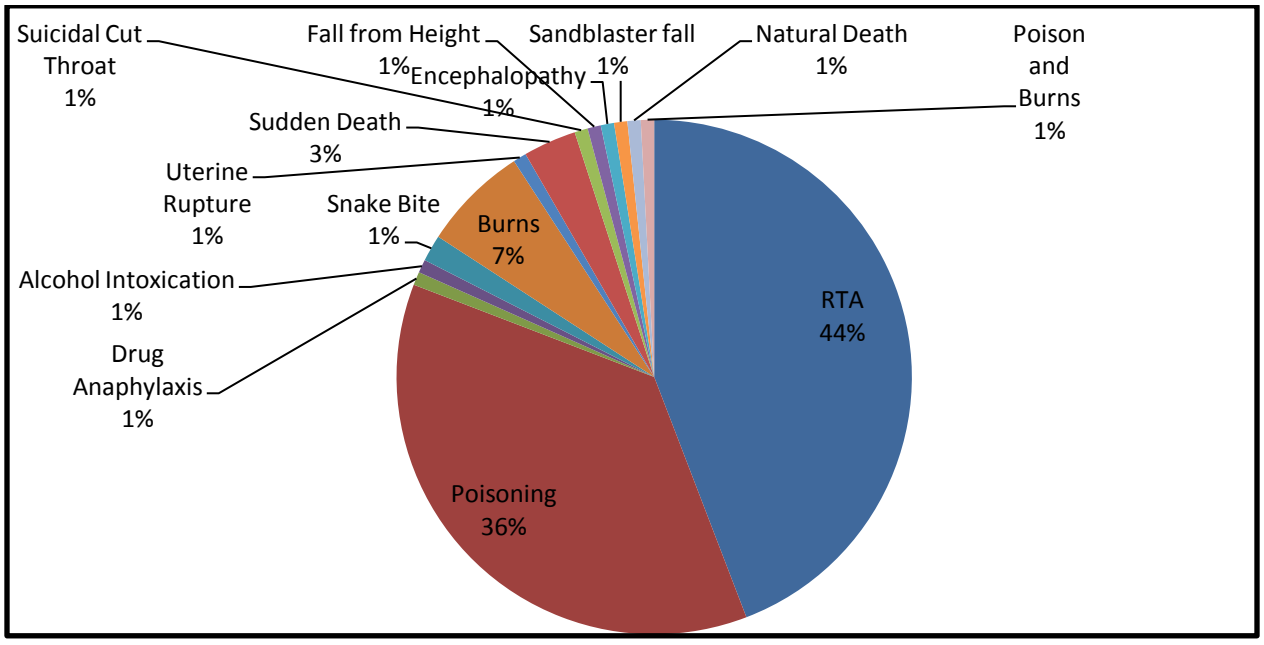
CLINICAL/FORENSIC CAUSE OF DEATH:

In the current study, the most common cause of death was Road Traffic Accidents (RTA)(44%), followed by poisoning (36%) and Burns (7%).

Table 8: Cause of Death Distribution

Clinical Cause of Death	Total	Percent(%)
RTA	53	44%
Poisoning	44	36%
Drug Anaphylaxis	1	1%
Alcohol Intoxication	1	1%
Snake Bite	2	1%
Burns	8	7%
Uterine Rupture	1	1%
Sudden Death	4	3%
Suicidal Cut Throat	1	1%
Fall from Height	1	1%
Encephalopathy	1	1%
Head Trauma from Sandblaster fall	1	1%
Natural Death	1	1%
Poison and Burns	1	1%
Total	120	100%

Chart 3: Cause of Death Distribution



CLINICAL/FORENSIC CAUSE OF DEATH AND AGE DISTRIBUTION:

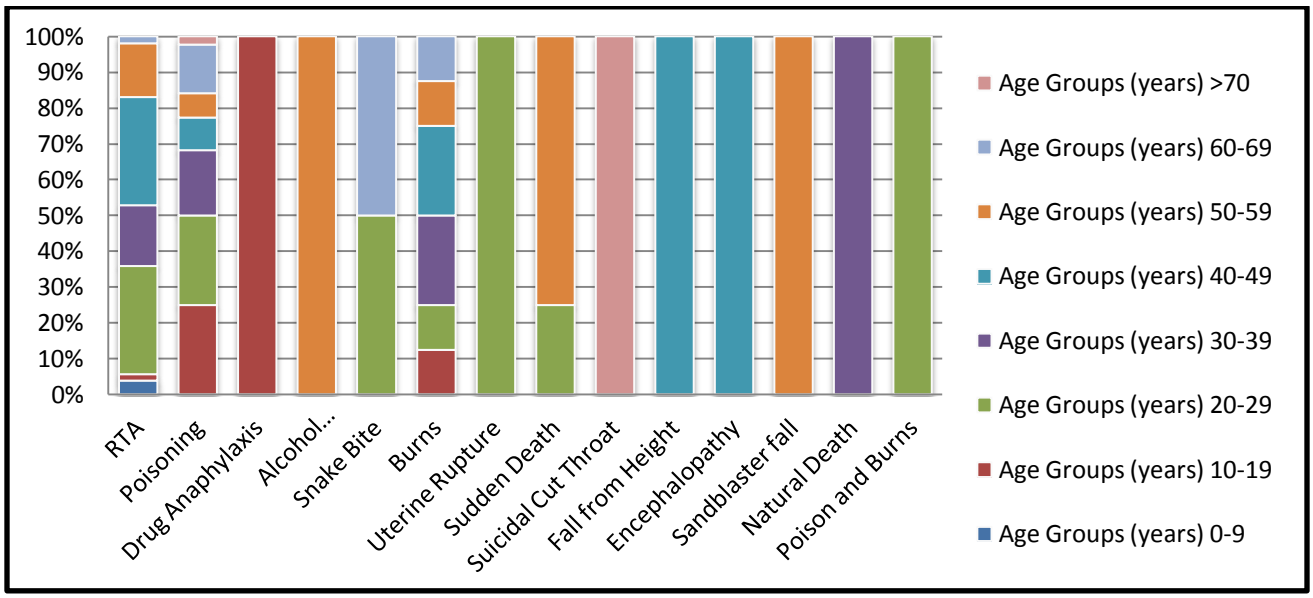
Maximum number of RTAs were seen in the 20-29 age group (13%) and 40-49 age group (13%).

Highest frequency of poisoning was seen in the 10-19 age group(9%) and 20-29 age group (9%).

Table 9: Cause of Death and Age Distribution

Clinical Cause of Death	Age Groups (years)								Total
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	>70	
RTA	2	1	16	9	16	8	1	0	53
Poisoning	0	11	11	8	4	3	6	1	44
Drug Anaphylaxis	0	1	0	0	0	0	0	0	1
Alcohol Intoxication	0	0	0	0	0	1	0	0	1
Snake Bite	0	0	1	0	0	0	1	0	2
Burns	0	1	1	2	2	1	1	0	8
Uterine Rupture	0	0	1	0	0	0	0	0	1
Sudden Death	0	0	1	0	0	3	0	0	4
Suicidal Cut Throat	0	0	0	0	0	0	0	1	1
Fall from Height	0	0	0	0	1	0	0	0	1
Encephalopathy	0	0	0	0	1	0	0	0	1
Sandblaster fall	0	0	0	0	0	1	0	0	1
Natural Death	0	0	0	1	0	0	0	0	1
Poison and Burns	0	0	1	0	0	0	0	0	1
Total	2	14	32	20	24	17	9	2	**120**

Chart 4: Cause of Death and Age Distribution



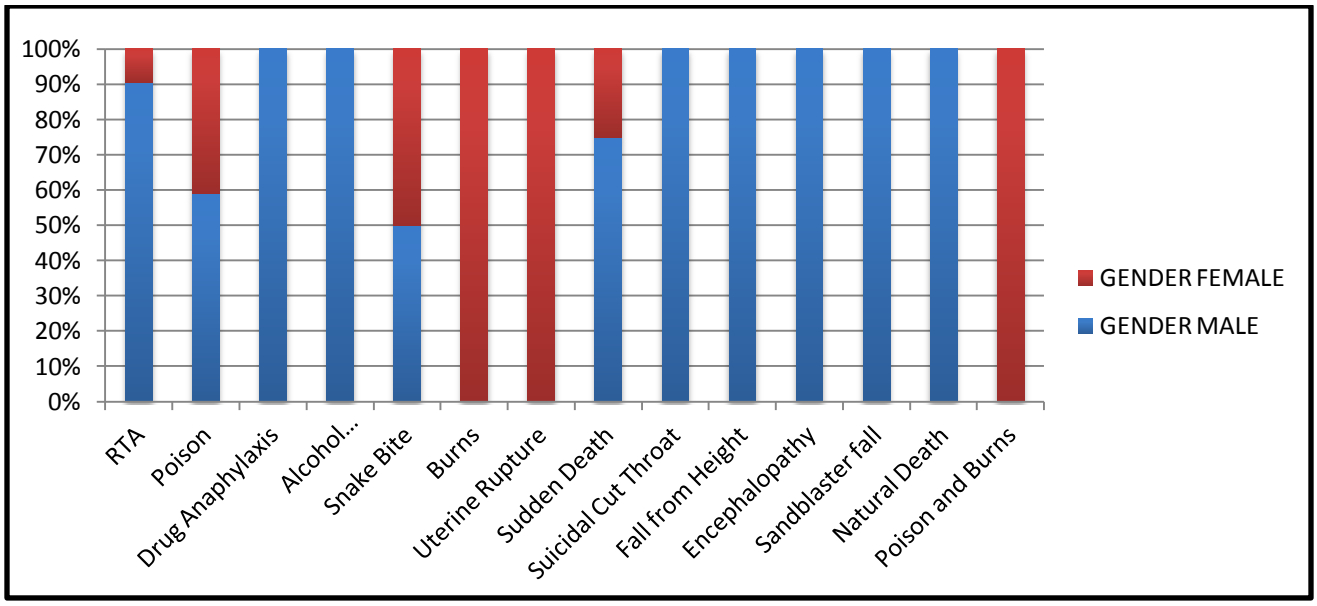
CLINICAL/FORENSIC CAUSE OF DEATH AND GENDER DISTRIBUTION:

In this study, maximum victims of RTAs were males (40 %) and maximum victims of Burns were females (6.67 %).

Table 10: Cause of Death and Gender Distribution

CAUSE OF DEATH	GENDER		TOTAL
	MALE	FEMALE	
RTA	48	5	53
Poison	26	18	44
Drug Anaphylaxis	1	0	1
Alcohol Intoxication	1	0	1
Snake Bite	1	1	2
Burns	0	8	8
Uterine Rupture	0	1	1
Sudden Death	3	1	4
Suicidal Cut Throat	1	0	1
Fall from Height	1	0	1
Encephalopathy	1	0	1
Sandblaster fall	1	0	1
Natural Death	1	0	1
Poison and Burns	0	1	1
TOTAL	85	35	120

Chart 5: Cause of Death and Gender Distribution



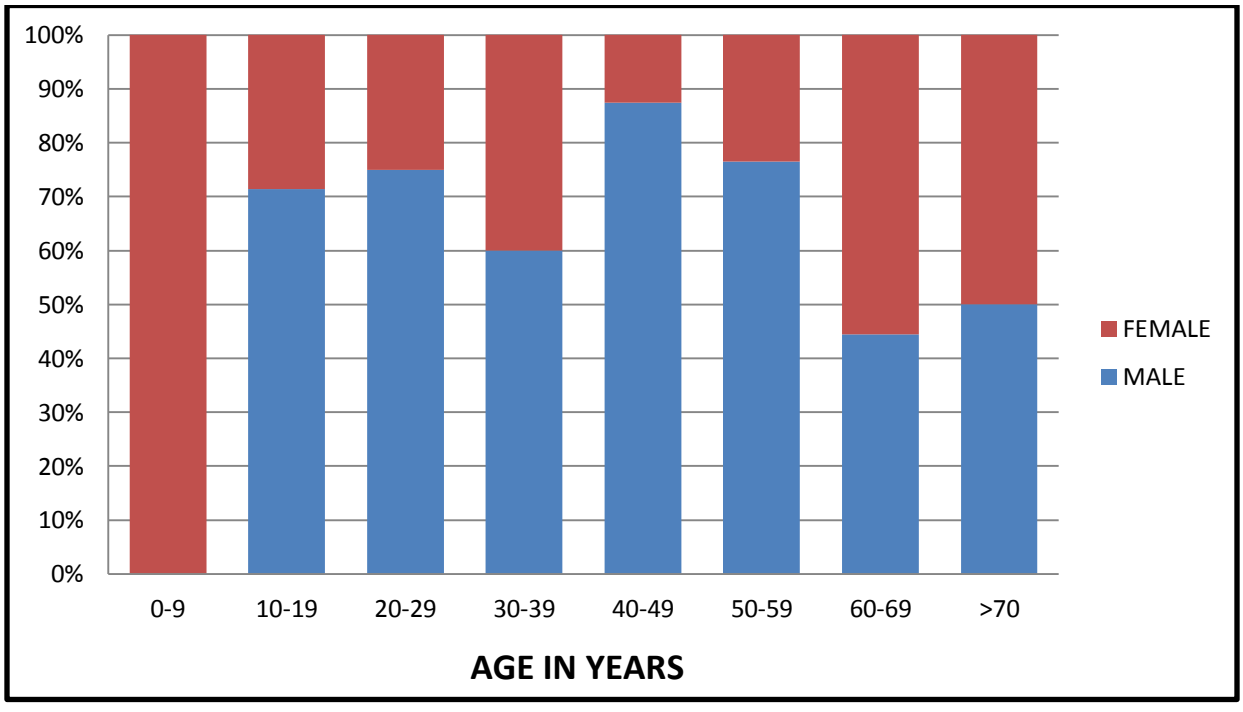
DEMOGRAPHIC ANALYSIS OF AGE AND GENDER DISTRIBUTION:

Maximum number of male victims were seen in the 20-29 age group (20 %) whereas maximum number of female victims were seen in the 20-29 age group (6.67 %) and 30-39 age group (6.67%).

Table 11: Age and Gender Distribution

Age Group (Years)	MALE	FEMALE	TOTAL
0-9	0	2	2
10-19	10	4	14
20-29	24	8	32
30-39	12	8	20
40-49	21	3	24
50-59	13	4	17
60-69	4	5	9
>70	1	1	2
TOTAL	85	35	120

Chart 6: Age and Gender Distribution



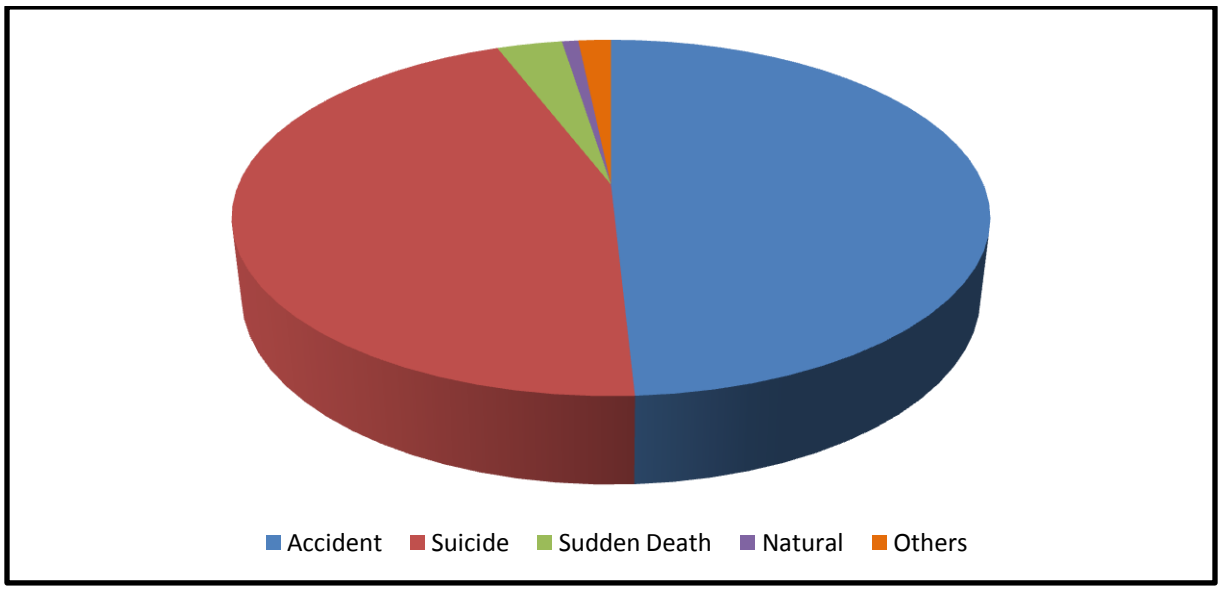
MANNER OF DEATH:

In this study, the most frequent manner of deaths were accidents (49 %), followed by suicides (45 %) and sudden death (3 %).

Table 12: Manner of Death and Number of Cases Distribution

MANNER OF DEATH	Number	Percent(%)
Accident	59	49
Suicide	54	45
Sudden Death	4	3
Natural	1	1
Others	2	2
TOTAL	120	100

Chart 7: Manner of Death and Number of Cases Distribution



GROSS PATHOLOGY:

Weight of Right Lung: In males, it ranged from 120 to 1200 gm and the mean weight was 425.56±135.09 gm. In females, it ranged from 150 gm to 700 gm and the mean weight was 410±99.41 gm.

Weight of Left Lung: In males, it ranged from 100 to 900 gm and the mean weight was 376.6±111.32 gm. In females, it ranged from 140 gm to 600 gm and the mean weight was 387.1±87.06 gm.

Right Pleura: Out of the total 116 (96.7 %) lung specimens and portions studied (110 +6), all 116 cases had pleural membranes. Of the 116 lung specimens/portions, the pleura was normal in 114 cases (95 %) and thickened in 2 cases (1.7 %).

Left Pleura: Out of the total 111 (92.5 %) lung specimens and portions studied (107 + 4), all 111 cases had pleural membranes. Of the 111 lung specimens/portions, the pleura was normal in 109 cases (90.8%) and thickened in 2 cases (1.7 %).

Right Lung: All 116 (96.7 %) lung specimens/portions were non-collapsed.

Left Lung: All 111 (92.5 %) lung specimens/portions were non-collapsed.

External Findings of Right Lung:

Table 13: Distribution of Right Lungs with External findings

S No	EXTERNAL FINDING	NUMBER
1	Unremarkable	60
2	Anthracosis	41
3	Emphysematous Bulla	7
4	Emphysematous changes	1
5	Fixation Artifacts	4
6	Absent Horizontal Fissure	2
7	Gray-Brown Areas	2
8	Gray-Black Areas	1

In the present study, 60 lungs were unremarkable, 41 lungs had anthracotic changes, 7 lungs had emphysematous changes and 2 cases had absence of the right horizontal fissure.

External Findings of Left Lung:

Table 14: Distribution of Left Lungs with External findings

S No	EXTERNAL FINDING	NUMBER
1	Unremarkable	61
2	Anthracosis	40
3	Emphysematous Bulla	6
4	Fixation Artifacts	3
5	Lacerations (LL)	1
6	Gray-White Areas	1

In this study, 61 lungs were unremarkable, 40 lungs had anthracotic changes, 6 lungs had emphysematous changes and 1 lung had lacerations in the lower lobe.

Consistency of Right and Left Lung: All 116 (96.7 %) right and 111 (92.5 %) left lung specimens/portions were spongy in consistency in this study

Cut Section Findings of Right Lung:

Table 15: Distribution of Right Lungs with Cut Section Findings

S No	FINDING	NUMBER
1	Unremarkable	73
2	Gray-White Areas	26
3	Gray-Brown Areas	4
4	Gray-Yellow Areas	2
5	Gray-Black Areas	1
6	Anthracosis	7
7	Clot/Thrombus	2
8	Dilated Airways/Bronchiectatic changes	3
9	Emphysematous changes	1

In this study, 73 lungs were unremarkable, 26 lungs had gray-white areas, 3 lungs had bronchiectatic changes and 2 lungs had clot/thromboembolus in the pulmonary artery and its branches.

Cut Section Findings of Left Lung:

Table 16: Distribution of Left Lungs with Cut Section Findings

S No	FINDING	NUMBER
1	Unremarkable	72
2	Gray-White Areas	20
3	Gray-Brown Areas	7
4	Gray-Yellow Areas	3
5	Gray-Black Areas	1
6	Anthracosis	8
7	Clot/Thrombus	3
8	Dilated Airways/Bronchiectatic changes	2
9	Emphysematous changes	1
10	Fixation Artifacts	1

In this study, 72 lungs were unremarkable, 20 lungs had gray-white areas, 2 lungs had bronchiectatic changes and 3 lungs had clot/thromboembolus in the pulmonary artery and its branches.

MICROSCOPY:

Table 17: Distribution of Lung Lobes with each Microscopic Finding

S No	Feature	Rt UL	Rt ML	Rt LL	Lt UL	Lt LL
1	Pulmonary Congestion	89	85	88	84	84
2	Alveolar Capillary Engorgement	59	63	72	68	67
3	Alveolar Hemorrhage	32	23	36	38	38
4	Pulmonary Edema	61	50	60	54	57
5	Hemosiderosis	39	37	37	41	37
6	Hyaline Membrane	13	12	19	14	9
7	Septal Thickening	20	23	27	25	29
8	Septal Hyperplasia	16	19	14	21	27
9	Pneumonia changes	10	7	9	7	9
10	Microthrombi	3	2	2	4	7
11	Macrothromboembolus	0	0	0	2	0
12	Emphysematous changes	14	9	7	16	16
13	Pulmonary Vessel Thickening	6	9	8	7	11
14	Bronchiolar Fibrosis/Dilatation-changes	5	5	7	3	6
15	Smoker's Macrophages	8	9	9	6	6
16	Carbon Macrophages/Anthracosis	61	59	54	50	50
17	Inflammatory Exudate in alveoli	11	8	6	10	9
18	Fungal Hyphae	4	1	3	2	0
19	Bacteria- Cocci, Bacilli	7	2	6	4	1
20	Vasculitis with Fibrinoid Necrosis	2	2	2	0	2
21	Bronchiolitis with starch/vegetable matter	2	2	2	0	1
22	Bronchiolitis	7	5	9	5	5
23	Interstitial Inflammation	4	3	5	4	4

Table 18: Distribution of Lungs with each Bronchial Finding

S No	Feature	Rt Bronchus	Lt Bronchus
1	Congestion - Bronchus	68	67
2	Squamous Metaplasia	3	0
3	Reid's Index	4	6
4	Bronchitis Changes	3	4
5	Calcification of Bronchial Cartilage	0	1

In this study, maximum number of cases had Pulmonary Congestion, followed by Bronchial Congestion, Anthracosis, Pulmonary Edema, Alveolar Capillary Engorgement and Alveolar Haemorrhage.

Table 19: Distribution of Lungs – Overall Microscopic Impression

S No	Feature	Right Lung	Rt Lung (%)	Left Lung	Lt Lung (%)
1	Pulmonary Congestion	91	77.7	82	73.8
2	Alveolar Capillary Engorgement	49	41.8	50	45
3	Alveolar Hemorrhage	44	37.6	44	39.6
4	Pulmonary Edema	55	47	53	47.7
5	Hemosiderosis(I,II,III)	16,15,7	32.5	17,17,4	34.2
6	Diffuse Alveolar Damage	16	13.6	15	13.5
7	Regional Alveolar Damage	6	5.1	2	1.8
8	Septal Thickening	8	6.8	9	8.1
9	Septal Hyperplasia	8	6.8	15	13.5
10	Pneumonia changes	15	12.8	15	13.5
11	Microthrombi	3	2.5	6	5.4
12	Macrothromboembolus	0	0	2	1.8
13	Emphysematous changes	14	12	16	14
14	Pulmonary Vessel Thickening	16	13.6	12	10.8
15	Bronchiolar Fibrosis/Dilatation-changes	10	8.5	6	5.4
16	Smoker's Macrophages	6	5	5	4.5
17	Carbon Macrophages/Anthracosis	61	52	50	45
18	Fungal Hyphae	6	5	2	1.8
19	Bacteria- Cocci, Bacilli	8	6.8	4	3.6
20	Vasculitis with Fibrinoid Necrosis	2	1.7	2	1.8
21	Bronchiolitis with starch/vegetable matter	4	3.4	1	1
22	Bronchiolitis	11	9	8	7
23	Interstitial Fibrosis	3	2.5	0	0
24	Thrombus-Pulmonary Artery and branches	1	1	1	1
25	Congestion - Bronchus	68	58	67	60
26	Squamous Metaplasia	3	2.5	0	0
27	Reid's Index	4	3.4	6	5.4
28	Bronchitis Changes	3	2.5	4	3.6
29	Calcification of Bronchial Cartilage	0	0	1	1
30	COPD changes	14	12	16	14

Maximum number of cases had Pulmonary Congestion, followed by Anthracosis, Pulmonary Edema, Alveolar Capillary Engorgement and Alveolar Haemorrhage.

Table 20: Distribution of Lung Findings in cases of RTA

S No	Feature	Rt Lung	Lt Lung
1	Pulmonary Congestion	45	40
2	Alveolar Capillary Engorgement	22	26
3	Alveolar Hemorrhage	18	21
4	Pulmonary Edema	25	23
5	Hemosiderosis(I,II,III)	6,6,5	7,6,3
6	Diffuse Alveolar Damage	3	3
7	Regional Alveolar Damage	4	2
8	Septal Thickening	4	6
9	Septal Hyperplasia	5	9
10	Pneumonia changes	4	5
11	Microthrombi	0	2
12	Macrothromboembolus	0	2
13	Emphysematous changes	9	10
14	Pulmonary Vessel Thickening	11	7
15	Bronchiolar Fibrosis/Dilatation-changes	5	2
16	Smoker's Macrophages	4	2
17	Carbon Macrophages/Anthracosis	15	13
18	Inflammatory Exudate in alveoli	0	0
19	Fungal Hyphae	3	0
20	Bacteria- Cocci, Bacilli	4	1
21	Vasculitis with Fibrinoid Necrosis	0	0
22	Bronchiolitis with starch/vegetable matter	0	0
23	Bronchiolitis	2	2
24	Interstitial Inflammation	0	0
25	Interstitial Fibrosis	1	0
26	Thrombus-Pulmonary Artery and branches	0	0
27	Congestion - Bronchus	31	31
28	Squamous Metaplasia	0	0
29	Reid's Index	1	3
30	Bronchitis Changes	0	1
31	Calcification of Bronchial Cartilage	0	0
32	COPD changes	9	10

The main histological findings seen in the RTA cases were Pulmonary Congestion, Pulmonary Edema, Alveolar Haemorrhage, Hemosiderotic changes and coincidental Obstructive Pulmonary Disease changes.

Table 21: Distribution of Lung Findings in Poison cases

S No	Feature	Rt Lung	Lt Lung
1	Pulmonary Congestion	31	29
2	Alveolar Capillary Engorgement	21	17
3	Alveolar Hemorrhage	19	17
4	Pulmonary Edema	21	23
5	Hemosiderosis(I,II,III)	8,9,1	6,11,0
6	Diffuse Alveolar Damage	9	9
7	Regional Alveolar Damage	1	0
8	Septal Thickening	4	2
9	Septal Hyperplasia	3	4
10	Pneumonia changes	9	8
11	Microthrombi	1	2
12	Macrothromboembolus	0	0
13	Emphysematous changes	3	4
14	Pulmonary Vessel Thickening	3	3
15	Bronchiolar Fibrosis/Dilatation-changes	3	2
16	Smoker's Macrophages	1	2
17	Carbon Macrophages/Anthracosis	9	8
18	Inflammatory Exudate in alveoli	0	0
19	Fungal Hyphae	3	2
20	Bacteria- Cocci, Bacilli	3	3
21	Vasculitis with Fibrinoid Necrosis	1	1
22	Bronchiolitis with starch/vegetable matter	4	1
23	Bronchiolitis	8	5
24	Interstitial Inflammation	0	0
25	Interstitial Fibrosis	1	0
26	Thrombus-Pulmonary Artery and branches	1	1
27	Congestion - Bronchus	27	24
28	Squamous Metaplasia	1	0
29	Reid's Index	0	0
30	Bronchitis Changes	1	0
31	Calcification of Bronchial Cartilage	0	1
32	COPD changes	3	4

The main histological findings seen in the cases of Poison were Pulmonary Congestion, Pulmonary Edema, Alveolar Haemorrhage, Hemosiderotic changes, Diffuse Alveolar Damage and Pneumonia.

Table 22: Distribution of Lung Findings in cases of Burns

S No	Feature	Rt Lung	Lt Lung
1	Pulmonary Congestion	7	6
2	Alveolar Capillary Engorgement	6	6
3	Alveolar Hemorrhage	3	4
4	Pulmonary Edema	4	4
5	Hemosiderosis(I,II,III)	0,0,1	0,0,1
6	Diffuse Alveolar Damage	2	2
7	Regional Alveolar Damage	0	1
8	Septal Thickening	0	1
9	Septal Hyperplasia	0	1
10	Pneumonia changes	0	0
11	Microthrombi	1	2
12	Macrothromboembolus	0	0
13	Emphysematous changes	2	2
14	Pulmonary Vessel Thickening	0	0
15	Bronchiolar Fibrosis/Dilatation-changes	0	0
16	Smoker's Macrophages	0	0
17	Carbon Macrophages/Anthracosis	6	5
18	Inflammatory Exudate in alveoli	0	0
19	Fungal Hyphae	0	0
20	Bacteria- Cocci, Bacilli	2	0
21	Vasculitis with Fibrinoid Necrosis	0	0
22	Bronchiolitis with starch/vegetable matter	0	0
23	Bronchiolitis	0	0
24	Interstitial Inflammation	0	0
25	Interstitial Fibrosis	0	0
26	Thrombus-Pulmonary Artery and branches	0	0
27	Congestion - Bronchus	5	7
28	Squamous Metaplasia	0	0
29	Reid's Index	0	0
30	Bronchitis Changes	0	0
31	Calcification of Bronchial Cartilage	0	0
32	COPD changes	2	2

The main histological findings seen in the cases of Burns were Pulmonary Congestion, Anthracosis, Alveolar Capillary Engorgement, Pulmonary Edema, and Alveolar Haemorrhage.

Figure 7: Gross Photograph showing Emphysematous Bulla in the upper lobe

Figure 8: Gross Photograph showing Bronchiectatic Changes in the lung

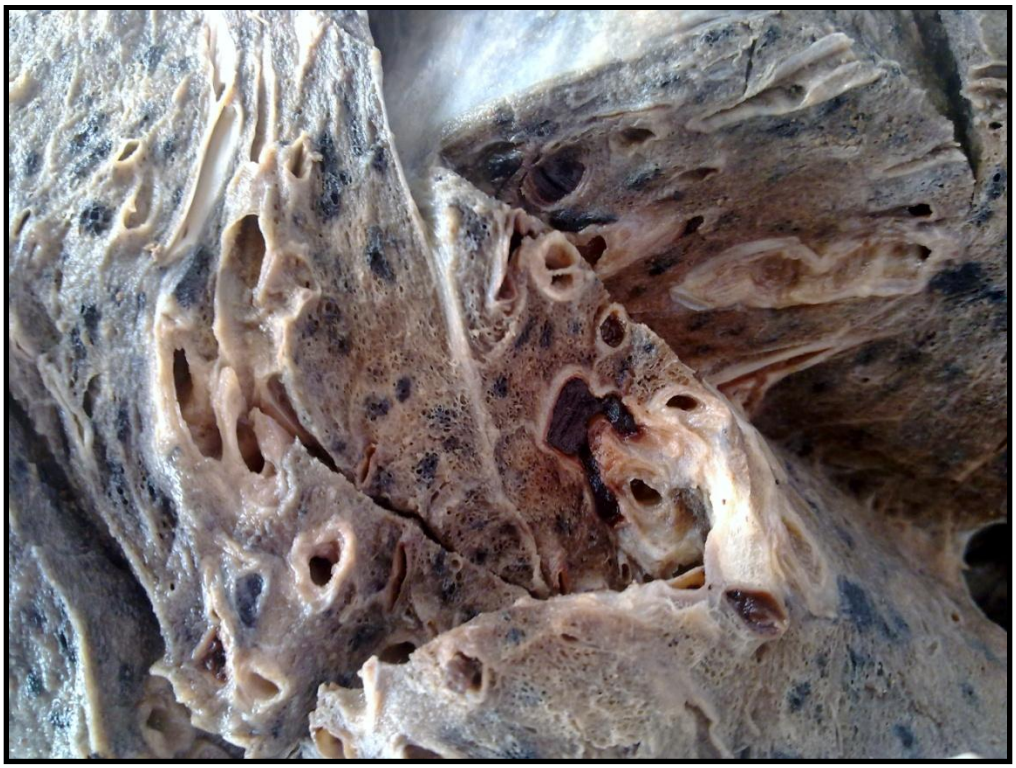


Figure 9: Gross Photograph showing Thickened Pleura

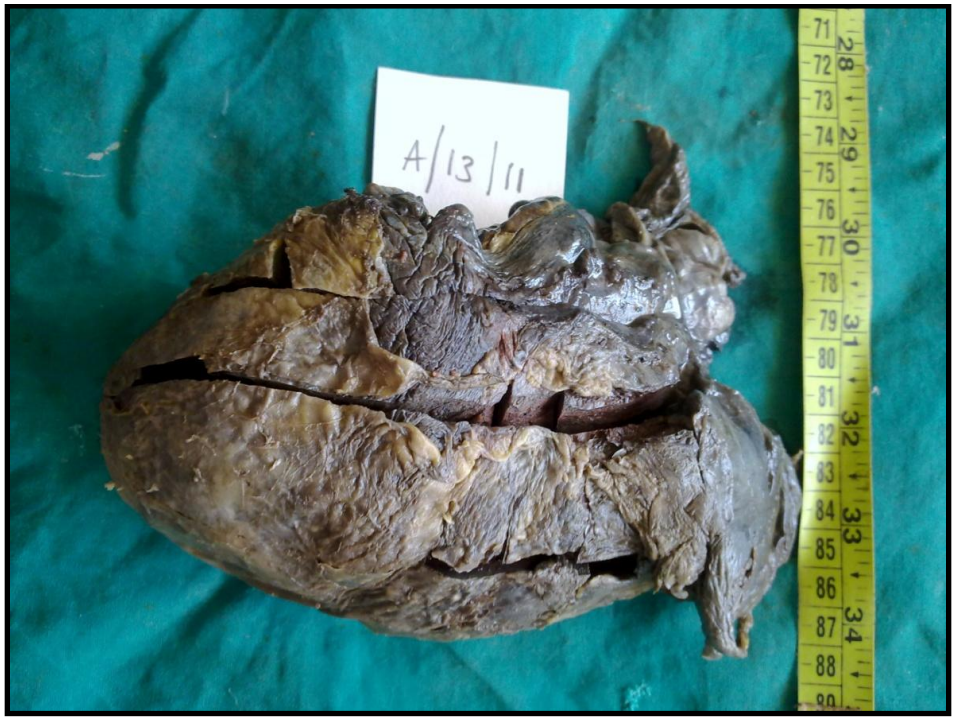


Figure 10: Gross Photograph showing Thromboembolus in the Pulmonary Artery Branch

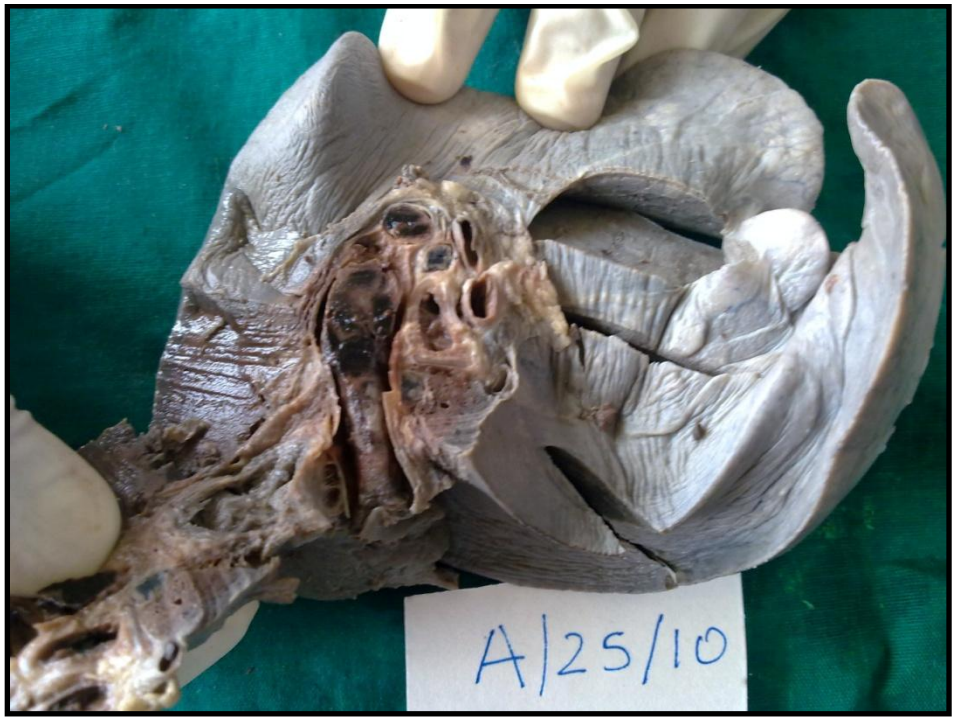


Figure 11: Gross Photograph showing Absent Horizontal Fissure in the right lung

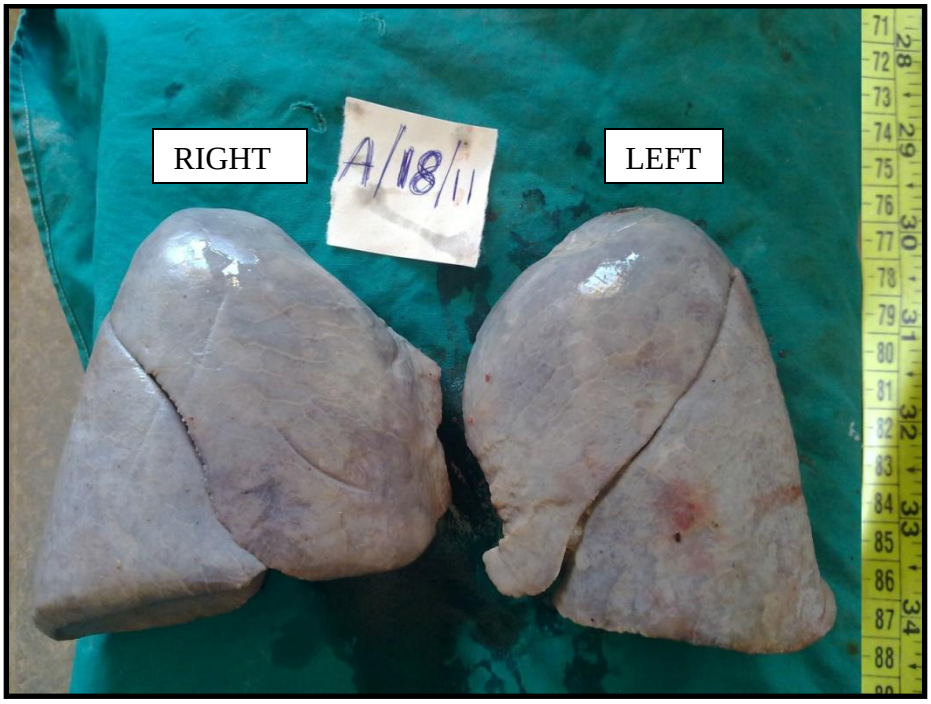


Figure 12: Photomicrograph showing features of Alveolar Capillary Congestion and Pulmonary Edema (H & E Stain, 100X)

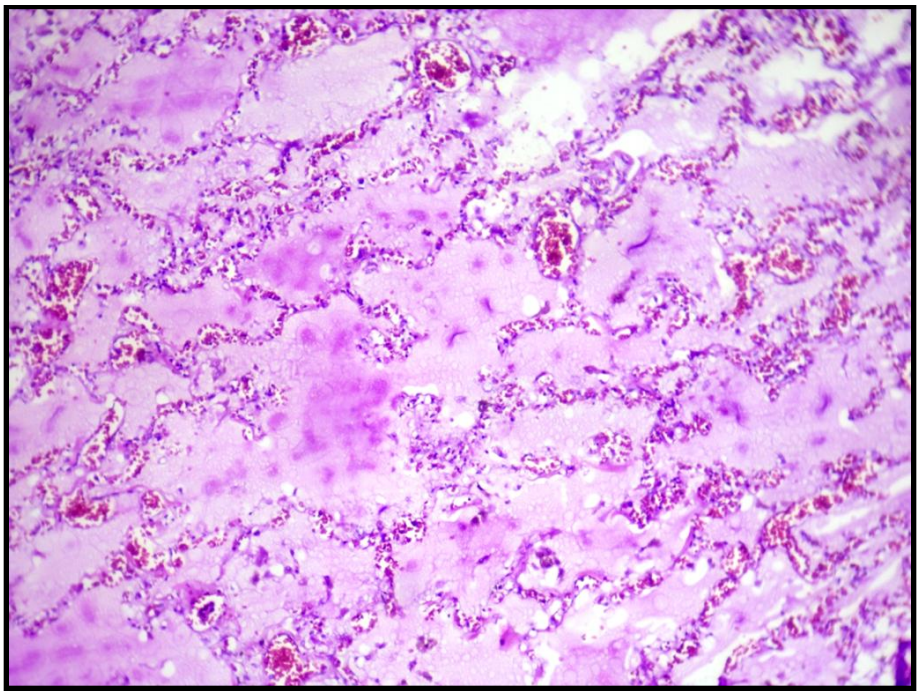


Figure 13: Photomicrograph showing features of Pulmonary Edema - (H & E Stain, 100X)

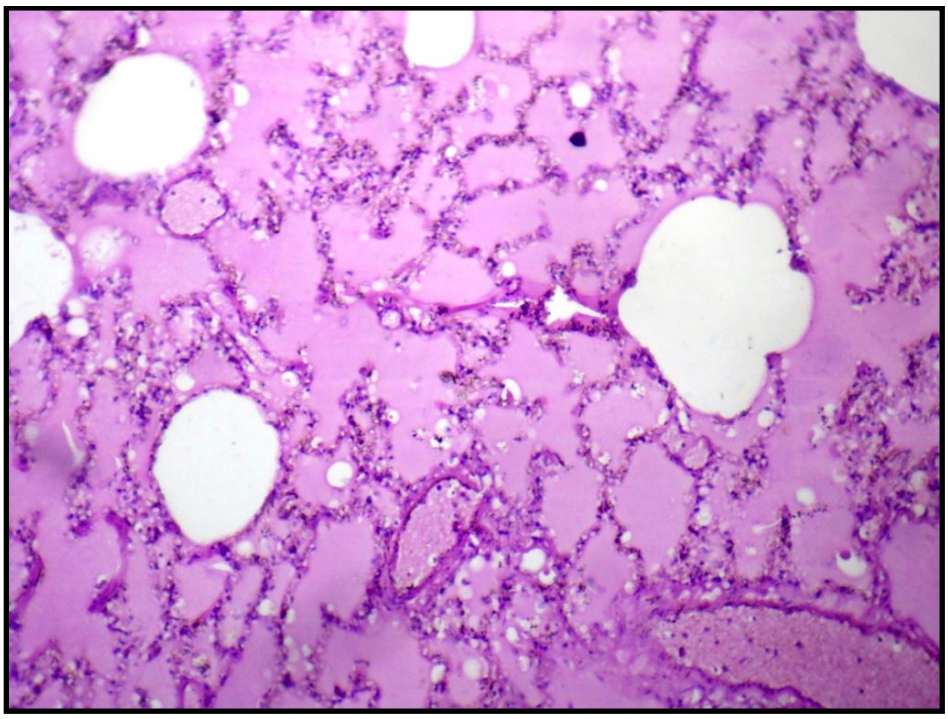


Figure 14: Photomicrograph showing features of Intra-Alveolar Haemorrhage (H & E Stain, 100X)

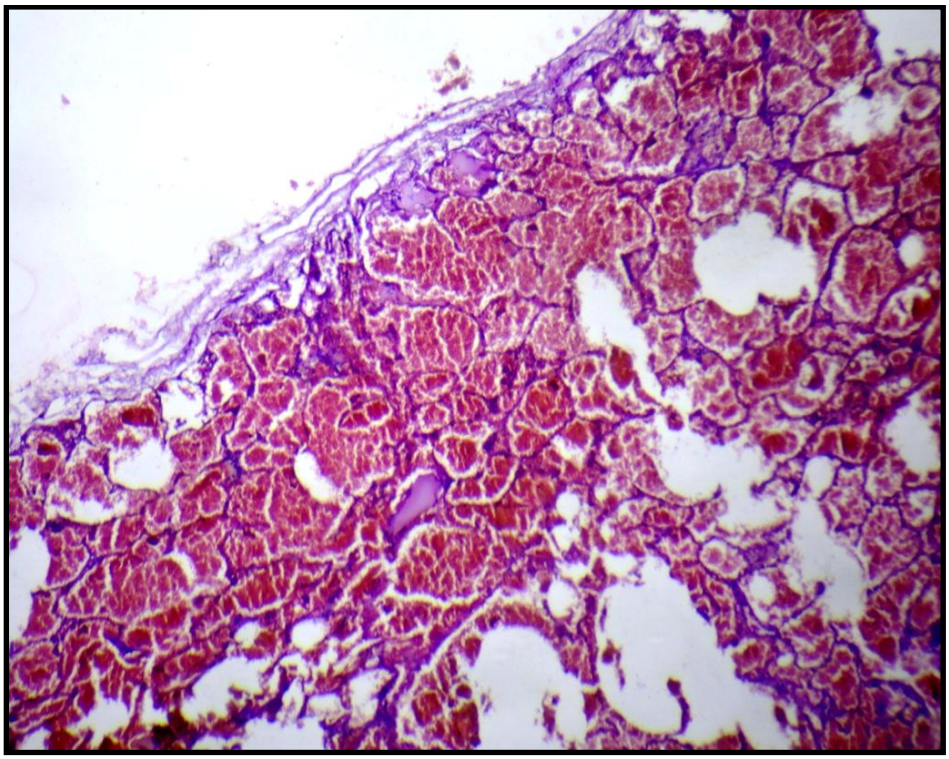


Figure 15: Photomicrograph showing features of thinned out and broken alveolar septae suggestive of emphysema (H & E Stain, 100X)

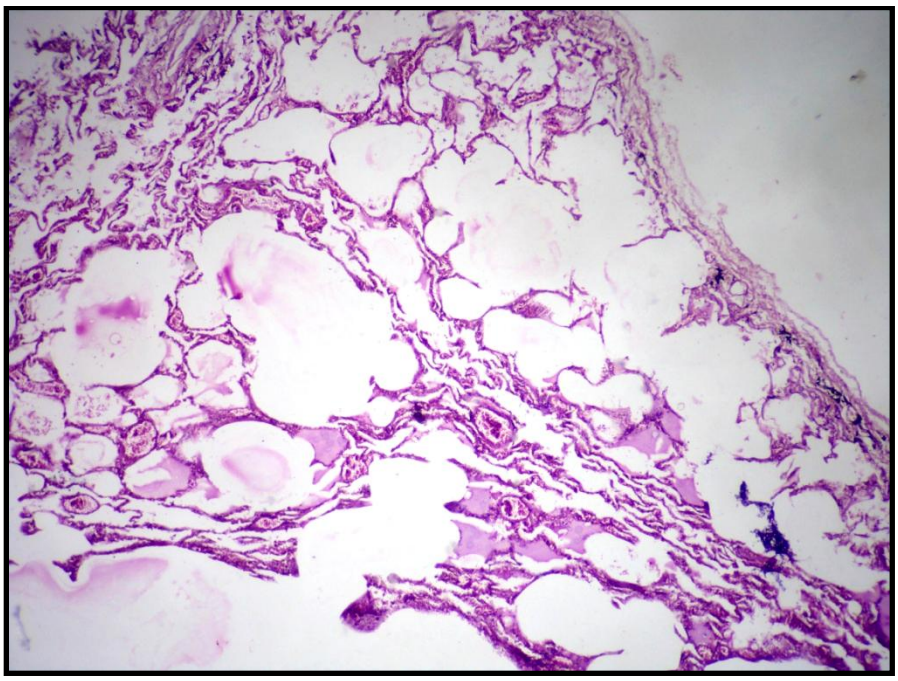


Figure 16: Photomicrograph showing features of peribronchiolar fibrosis and dilatation (H & E Stain, 100X)

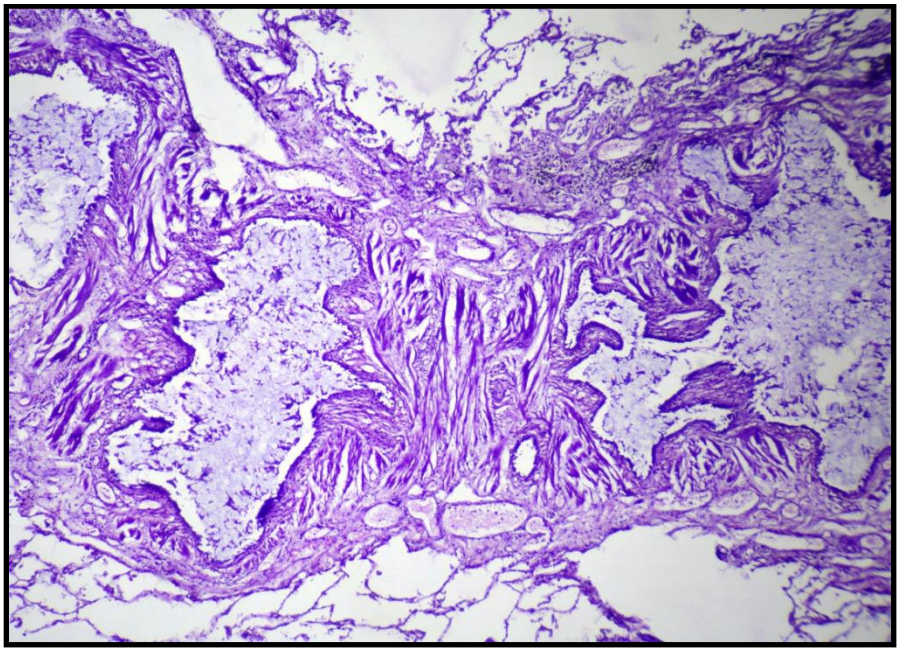


Figure 17: Photomicrograph showing dense eosinophilic hyaline membranes of DAD (H & E Stain, 100X)

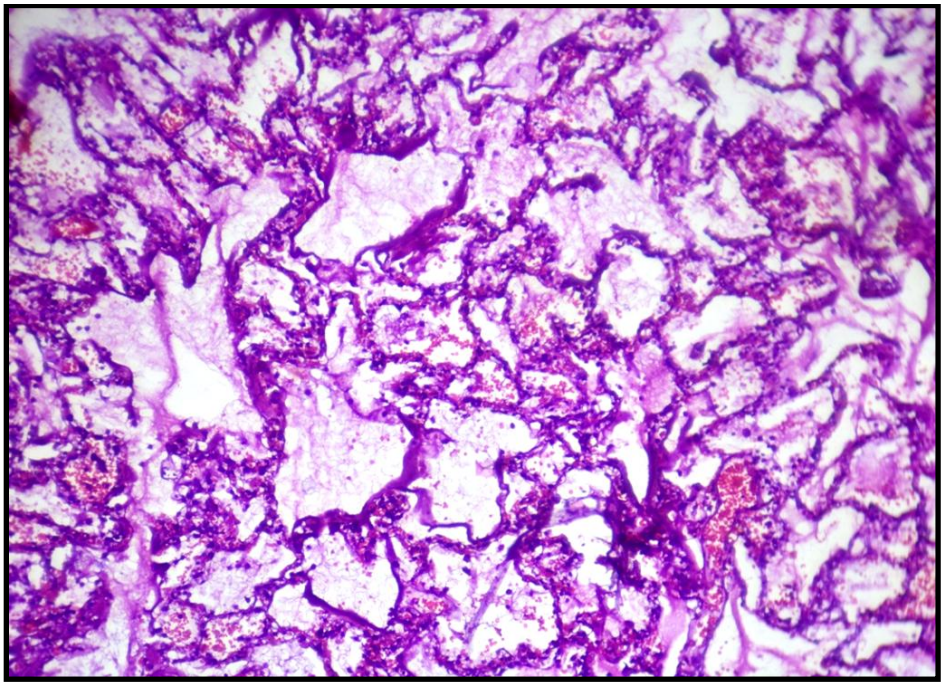


Figure 18: Photomicrograph showing dense eosinophilic hyaline membrane (H & E Stain, 450X)

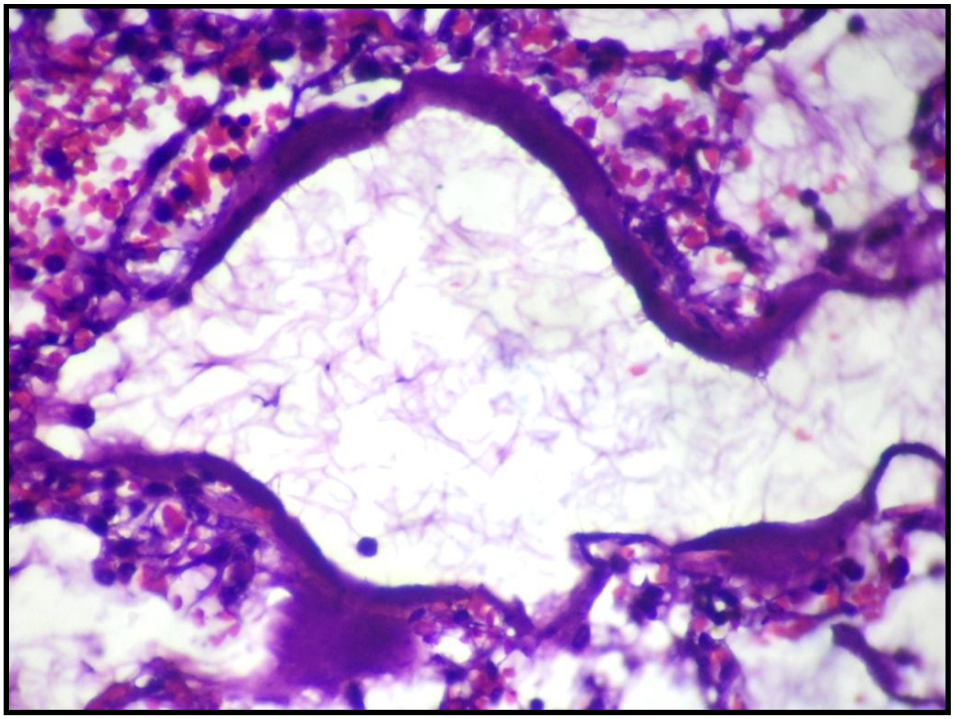


Figure 19: Photomicrograph showing features of many fungal hyphae without inflammatory response (H & E Stain, 100X)

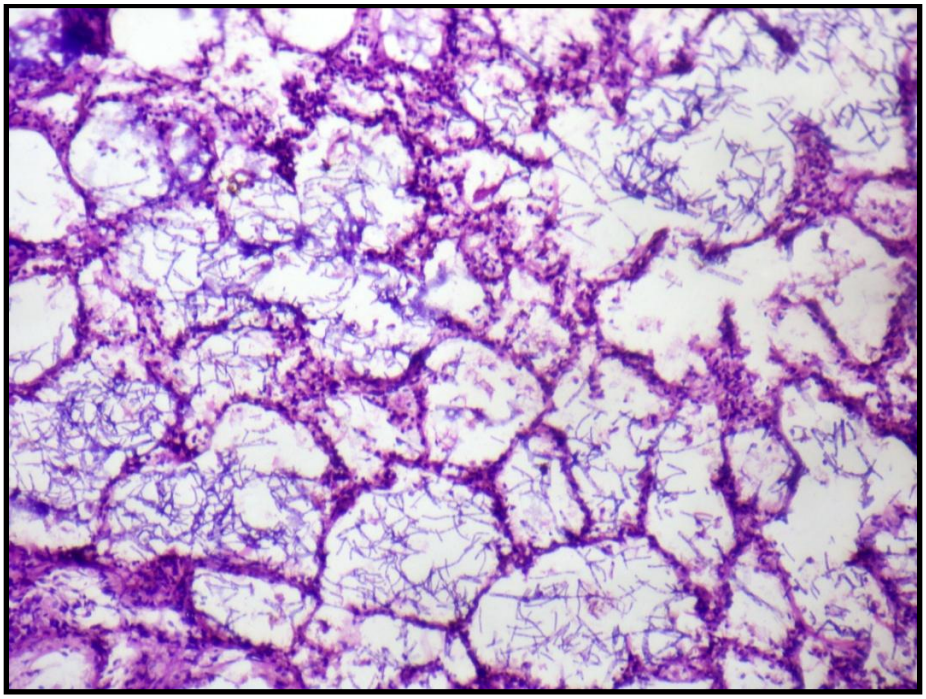


Figure 20: Photomicrograph showing many obtuse angled, broad branched fungal hyphae (H & E Stain, 1000X)

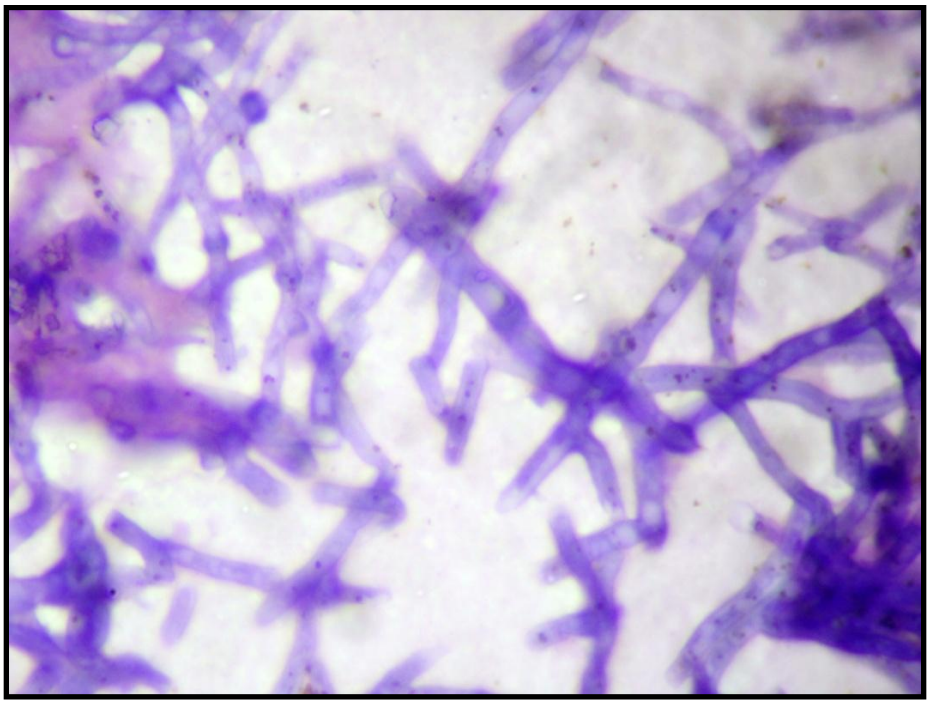


Figure 21: Photomicrograph showing Hemosiderin laden heart failure macrophages (H & E Stain, 450X)

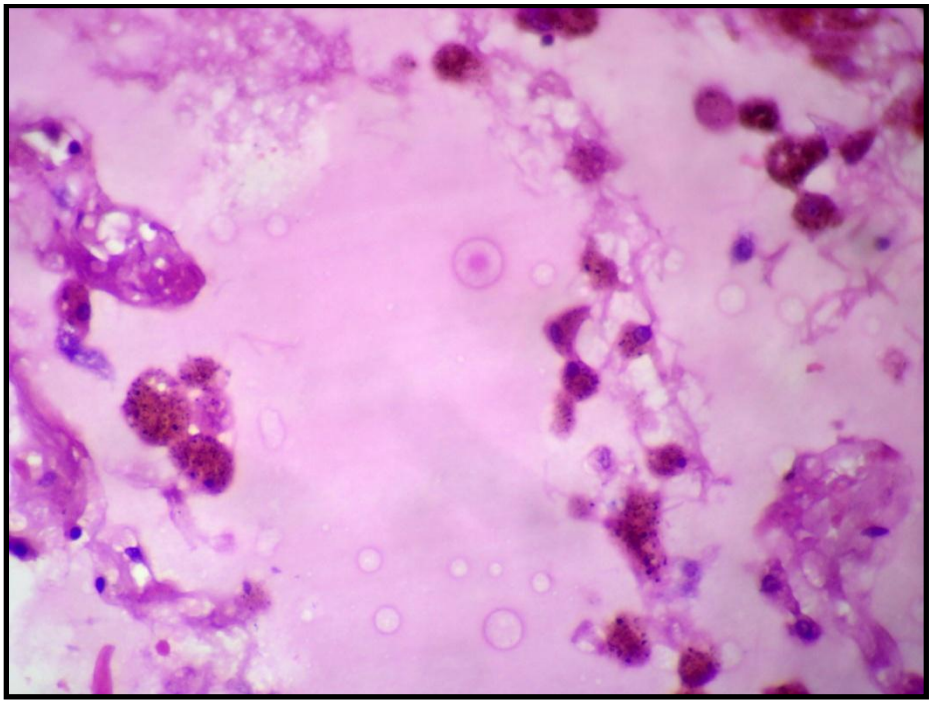


Figure 22: Photomicrograph showing thrombi inside vessels (H & E Stain, 100X)

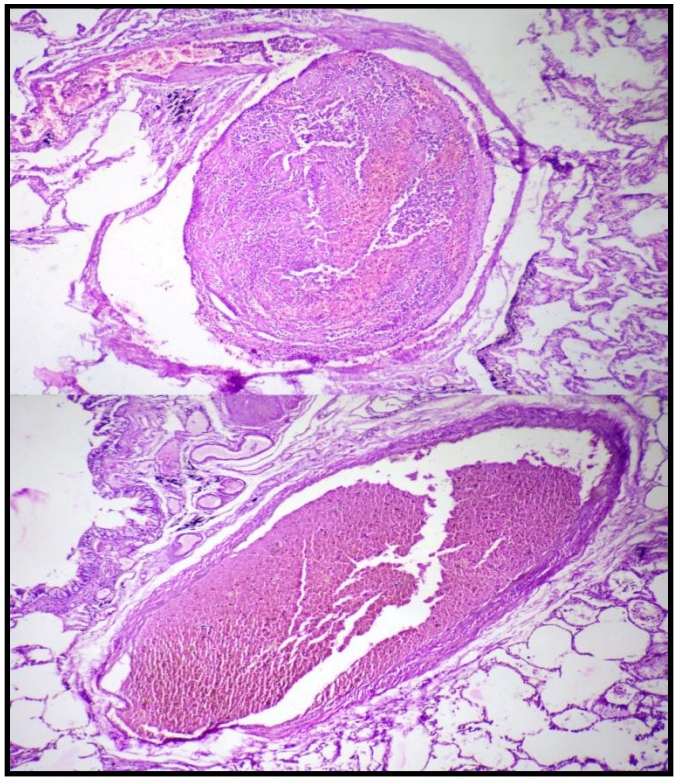


Figure 23: Photomicrograph showing foreign vegetable matter inside a bronchiole in a patient of Poisoning (H & E Stain, 100X)

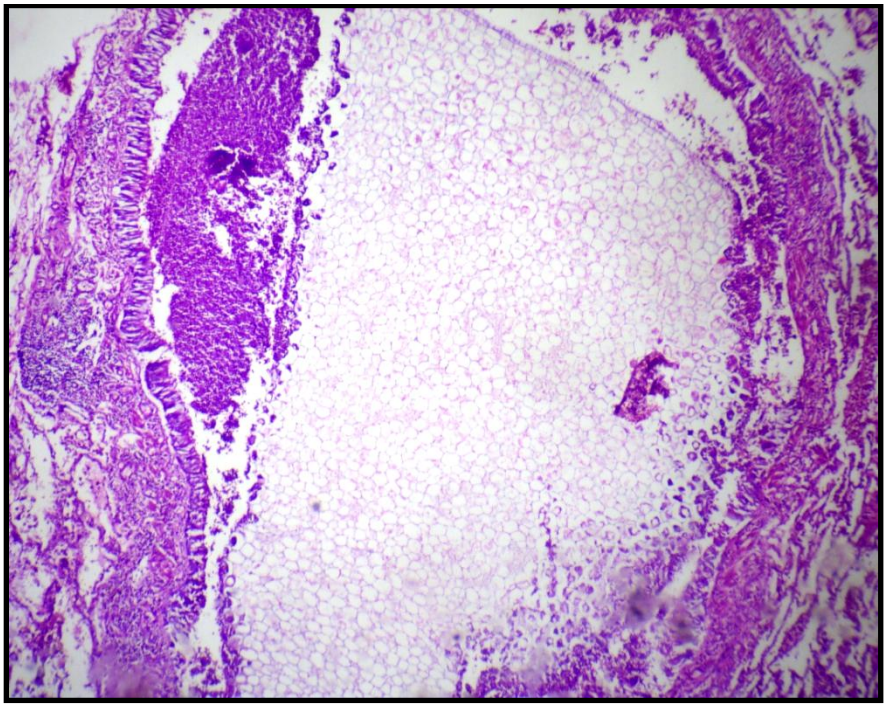


Figure 24: Photomicrograph showing vegetable matter with septation (H & E Stain, 450X)

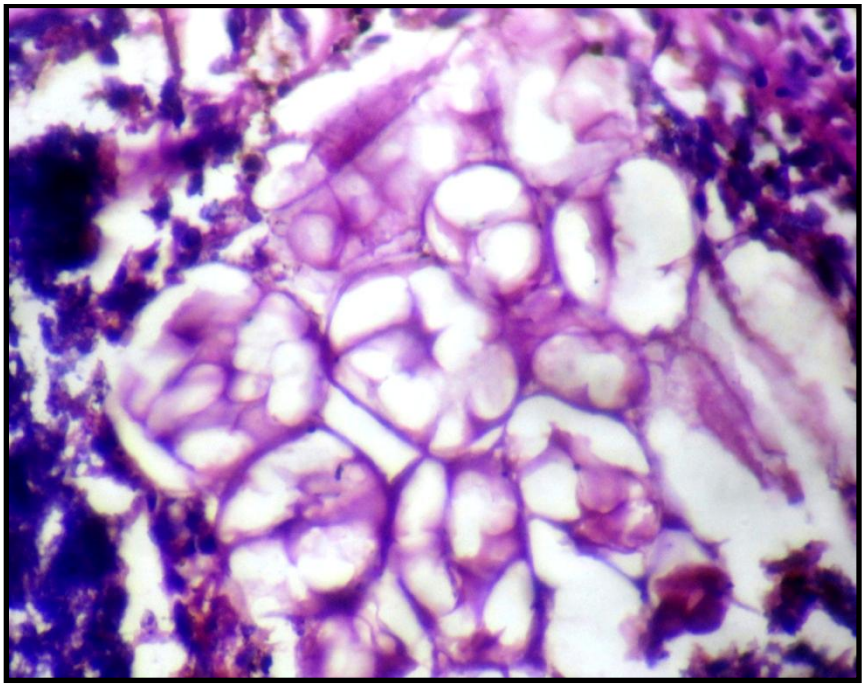


Figure 25: Photomicrograph showing inflammatory and fibrinous exudate inside the alveolar spaces - Pneumonia (H & E Stain, 100X)

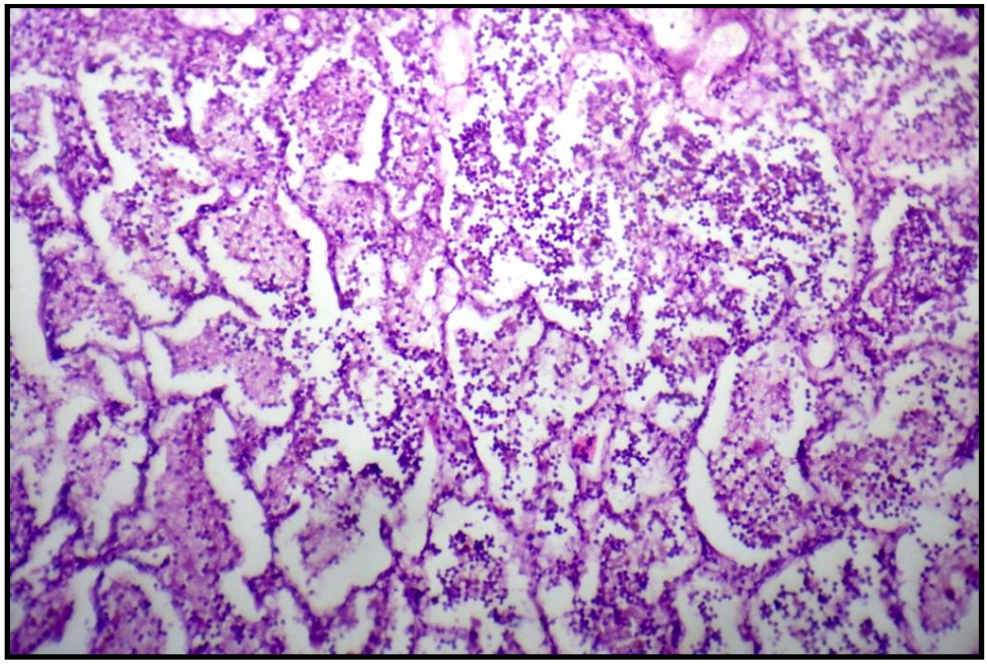
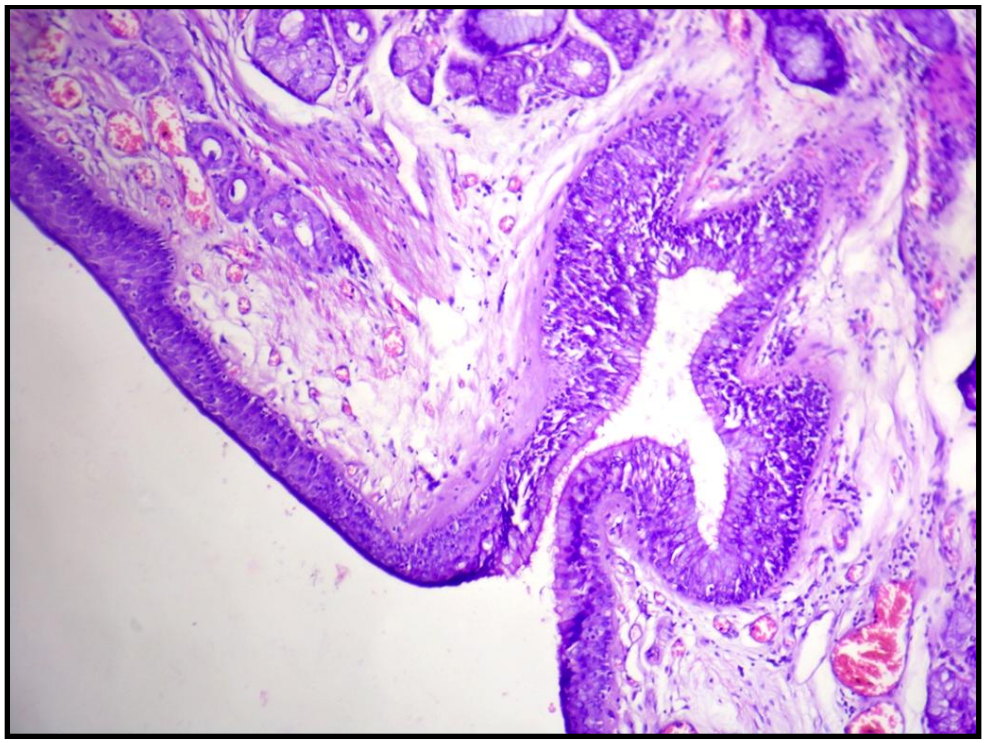


Figure 26: Photomicrograph showing features of squamous metaplasia of the bronchial lining (H & E Stain, 100X)



DISCUSSION

DISCUSSION:

AGE

Incidences of medicolegal and medical autopsies are higher in the 3rd and 4th decades of life.[15,81,82,83]

In the present study, the ages ranged from 8 to 85 years. Mean age was 36.25±15.71 years. Majority of patients belonged to the 3rd decade of life (27%), followed by 5th decade (20%) and 4th decade (17%).

GENDER

Incidence of autopsies were higher in males than in females.[15,81,82,83,84]

In the present study, number of males were 85 (71%) and number of females were 35 (29%).

CAUSE OF DEATH

Unnatural deaths claim a considerable number of lives, with major share being contributed by Road Traffic Accidents (RTA).[82]

Table 23: Comparison of Percentage of RTA in various studies

Most Common Cause of Death	Gouda et al Study[82]	Garg et al Study[83]	Mandong et al Study[84]	Present Study
RTA (%)	56	59.4	39	44

In the current study, the most common cause of death was Road Traffic Accidents (RTA) (44%), followed by poisoning (36%) and Burns (7%). In the semi-urban area of Kolar, poor socioeconomic status of the individual could have contributed to the high frequency of poison deaths in this study.

In the study done by Gouda and Aramani, among the cases of poisoning, majority were due to Organophosphorus pesticide (53.6%). [82] In the present study, of all the 44 cases of poison, 10 were due to Organophosphorus compounds, 1 was due to rat poison, 1 was due to paraquat poison (herbicide) and in the remaining 32 cases, the poison was unknown.

In the current study, sudden death was seen in 3 males in their 5th decade of life and 1 young female. The 3 males had severe atherosclerotic changes in their aorta and coronary arteries and also 2 of them had changes of myocardial infarction. The young female had changes of pulmonary congestion and pneumonia.

There was an autopsy case of death from a fall from tree. This case had microscopic changes of angio-invasive vasculitis, fibrinoid necrosis and Diffuse Alveolar Damage in the lungs. Fungus could not be demonstrated both on H&E and PAS stains.

CLINICAL/FORENSIC CAUSE OF DEATH AND AGE DISTRIBUTION

In this study, maximum number of RTAs were seen in the 20-29 age group (13%) and 40-49 age group (13%) whereas highest frequency of poisoning was seen in the 10-19 age group (9%) and 20-29 age group (9%).

CLINICAL/FORENSIC CAUSE OF DEATH AND GENDER DISTRIBUTION

In this study, maximum victims of RTAs were males (40 %) and maximum victims of Burns were females (6.67 %). A high rate of poisoning in male victims could be again due to poor socioeconomic status of the individual.

DEMOGRAPHIC ANALYSIS OF AGE AND GENDER DISTRIBUTION

Maximum number of male victims were seen in the 20-29 age group (20 %) whereas maximum number of female victims were seen in the 20-29 age group (6.67 %) and 30-39 age group (6.67%).

MANNER OF DEATH:

In this study, the most frequent manner of deaths were accidents (49 %), followed by suicides (45%) and sudden death (3 %). Comparing it to other studies, the following table shows the differences.

Table 24: Comparison of the Studies regarding Manner of Death

MANNER OF DEATH	Molina et al Study[81]		Garg et al Study[83]		Mandong et al Study[84]		Present Study	
	Number	%	Number	%	Number	%	Number	%
Accident	68	36	661	84.3	143	51.3	59	49
Suicide	20	10	65	8.3	0	0	54	45
Sudden Death	5	2	0	0	35	12.5	4	3
Natural	47	25	0	0	0	0	1	1
Others	51	27	58	7.4	101	36.2	2	2
TOTAL	189	100	784	100	279	100	120	100

In the present study, other causes included death due to uterine rupture after 28 weeks of gestation and hypertensive encephalopathy with a history of RTA one year prior to death with fracture of femur. In the other studies, other causes included Homicidal deaths.[81,83,84]

GROSS PATHOLOGY

WEIGHT OF RIGHT LUNG

In males, it ranged from 120 to 1200 gm and the mean weight was 425.56±135.09 gm. In females, it ranged from 150 gm to 700 gm and the mean weight was 410±99.41 gm. Following table shows data comparing it with other studies:

Table 25: Comparison of Right lungs in males and females in other studies

Gender	Singh et al [85]	Kohli et al [86]	Present Study
Male	568.85±174.85 gm	460±50 gm	425.56±135.09 gm
Female	421.2±108.23 gm	410±50 gm	410±99.41 gm

Singh et al study assessed organs from the autopsies of Chandigarh zone (North India), whereas Kohli et al study assessed organs from North Indian cities (Bombay, Uttar Pradesh., Chandigarh, Delhi and Nagpur).

WEIGHT OF LEFT LUNG

In males, it ranged from 100 to 900 gm and the mean weight was 376.6±111.32 gm. In females, it ranged from 140 gm to 600 gm and the mean weight was 387.1±87.06 gm. Following table shows data comparing it with other studies:

Table 26: Comparison of Left lungs in males and females in other studies

Gender	Singh et al [85]	Kohli et al [86]	Present Study
Male	516.62±165.45 gm	420±50 gm	376.6±111.32 gm
Female	392.87±112.54 gm	370±50 gm	387.1±87.06 gm

RIGHT AND LEFT PLEURA

In the present study, of the 116 right lung specimens/portions studied, the pleura was normal in 114 cases (95 %) and thickened in 2 cases (1.7 %). Of the 111 left lung specimens/portions, the pleura was normal in 109 cases (90.8%) and thickened in 2 cases (1.7 %). One case was a 45 year male victim of RTA and other case was a 28 year male victim of poison.

RIGHT AND LEFT LUNGS

All 116 (96.7 %) right and 111 (92.5 %) left lung specimens/portions were non-collapsed in the present study.

EXTERNAL FINDINGS OF RIGHT LUNG

In this study, 60 lungs were unremarkable, 41 lungs had anthracotic changes, 7 lungs had emphysematous changes and 2 cases had absence of the right horizontal fissure.

Table 27: Comparative Incidence of Variation of Right Horizontal Fissure

Right Horizontal Fissure	Lukose et al[87] (1999)	IEHAV[88] (2002)	Meenakshi et al[21]	Present Study
ABSENT	10.50%	21%	16.60%	1.70%

IEHAV: Illustrated Encyclopaedia of Human Anatomic Variation

EXTERNAL FINDINGS OF LEFT LUNG

In this study, 61 lungs were unremarkable, 40 lungs had anthracotic changes, 6 lungs had emphysematous changes and 1 lung had lacerations in the lower lobe. This was an 8 year female victim of RTA who developed fractures of the ribs and hemothorax before succumbing to her injuries. The gross findings of tears in the lower lobe with pleural cavity showing blood in the present case correlated with the findings of the study of Moghissi.[61] Laceration of the lung was

found in 4.4% of cases of chest injury caused by blunt trauma.[61] In the present study, this was the only case (0.8%).

Table 28: Distribution of Cases with Gross Emphysematous changes in males and females

Cases	Male	Female	Total
Total	5	2	7
Percent (%)	5.8	5.7	5.8

It is estimated that there are around 14.9 million chronic cases of COPD in India in the age group of 30 years and above.[46] The prevalence of COPD is reported to be around 5% among males and 2.7% among females.[48]

From the above tabulated data, the overall percentage of cases of emphysema in the current study was 5.8% (7 cases). Percentage of males having emphysema among the 85 males in this study was 5.8 % (5/85) and that of females among all the 35 females in this study was 5.7 %(2/35). The high percentage of emphysema (COPD) in this study both overall as well as in females suggests the increased exposure to indoor air pollution from biomass fuels during cooking in and around the rural areas of Kolar.

CONSISTENCY OF RIGHT AND LEFT LUNGS

All 116 (96.7 %) right and 111 (92.5 %) left lung specimens/portions were spongy in consistency in this study.

CUT SECTION FINDINGS OF RIGHT AND LEFT LUNGS

Right – In this study, 73 lungs were unremarkable, 26 lungs had gray-white areas, 3 lungs had bronchiectatic changes and 2 lungs had clot/thromboembolus in the pulmonary artery and its branches.

Left- In this study, 72 lungs were unremarkable, 20 lungs had gray-white areas, 2 lungs had bronchiectatic changes and 3 lungs had clot/thromboembolus in the pulmonary artery and its branches.

Blood clots that occlude the large pulmonary arteries are almost always embolic in origin. Large-vessel in situ thromboses are rare and develop only in the presence of pulmonary hypertension, pulmonary atherosclerosis, and heart failure. The usual source of pulmonary emboli: Thrombi in the deep veins of the leg in more than 95% of cases. Its incidence at autopsy has varied from 1% in the general population of hospital patients to 30% in patients dying after severe burns, trauma, or fractures to 65% of hospitalized patients in one study in which special techniques were applied to discover emboli at autopsy. It is the sole or a major contributing cause of death in about 10% of adults who die acutely in hospitals. Large emboli lodge in the main pulmonary artery or its major branches or at the bifurcation as a saddle embolus.[14,18]

In the present study, thromboembolus in the lungs was seen in 3 cases (1.67 %). In one case, it was seen in a patient of organophosphorus poisoning who had a month long immobilized stay in the hospital. In this case, a saddle thromboembolus was seen at the bifurcation of the main pulmonary artery and also smaller thromboemboli in the distal smaller branches.

Remaining 2 cases were victims of RTA and had thromboemboli in the smaller branches of the pulmonary artery.

MICROSCOPY

PULMONARY CONGESTION

In a study done by Pathak et al, Pulmonary congestion was observed in maximum number of cases (80 % of right lungs and 57.7 % of left lungs) during autopsy.[15] In the present study, it was also observed in maximum number of cases (77.7 % of right lungs and 73.8 % of left lungs).

ALVEOLAR HEMORRHAGE

All cases of Diffuse Alveolar Haemorrhage have the common denominator of an injury to the alveolar microcirculation.[41] In a study done by Soeiro et al, it was observed in 9.2 % of the cases. In the present study, it was observed in 37.6% of right lungs and 39.6% of left lungs. The high incidence in the present study could be attributed to the circulatory failure associated with inciting causes like RTAs, Burns, chemicals and snake bites. Diffuse Alveolar Damage from a respiratory insult like Poison could also have contributed to the microcirculation injury.

PULMONARY EDEMA

In a study done by Pathak et al, it was observed in 37.7 % of right lungs and 33.3 % of left lungs. In the present study, it was observed in 47% of right lungs and 47.7% of left lungs. This high percentage in the present study could be attributed to the microvascular injury from circulatory failure/shock due to RTA, Burns, Trauma, Snake bites and chemicals.

HEMOSIDEROSIS

Most of the time, it could be due to recurrent alveolar haemorrhage.[32] In the present study, it was observed in 32.5 % of right lungs and 34.2 % of left lungs. Grade III changes were seen in 7 right lungs and 4 left lungs.

DIFFUSE ALVEOLAR DAMAGE (DAD)

In a study done by Yazdy et al, it was observed in 10.1% of the adult autopsies.[39] In a study done by Soeiro et al which was performed in all cases of acute respiratory failure, DAD was observed in 45.3 % of the cases. In the present study, it was observed in 13.6 % of right lungs and 13.5% of left lungs. When compared to Soeiro et al study, the lower rate of DAD in the present study could be due to the fact that most of the cases (86.5 %) did not die of acute respiratory failure. Instead these cases could have died due to circulatory failure from inciting causes of RTA, Burns, Chemicals, Trauma and snake bite.

REGIONAL ALVEOLAR DAMAGE (RAD)

In a study done by Yazdy et al, out of 827 adult autopsies, RAD was observed in 10 cases and most frequently involved the upper lobe.[39]

In the present study, it was observed in 5% of the right lung cases (1 in upper lobe and 5 in lower lobe) and 2 % of the left lung cases (both in lower lobe).

PNEUMONIA CHANGES

In the present study, it was observed in 12.8 % of right lungs and 13.5 % of left lungs.

Table 29: Comparison of a few Microscopic findings

S No	FEATURE	Pathak et al Study[15]		Present Study	
		Right Lung(%)	Left Lung(%)	Right Lung(%)	Left Lung(%)
1	Pulmonary Congestion	80	57.7	77.7	73.8
2	Pulmonary Oedema	37.7	33.3	47	47.7
3	Pneumonia	31.1	24.4	12.8	13.5
4	Tuberculosis	8.89	13.3	0	0

Table 30: Comparison of other Microscopic findings

S No	FEATURE	OVERALL CASES (%)	
		Soeiro et al Study[77]	Present Study
1	Diffuse Alveolar Damage	45.3	13.6
2	Pulmonary Oedema	23.3	47.7
3	Lymphocytic Interstitial Pneumonia	22.1	0
4	Alveolar Hemorrhage	9.2	39.6

MACROTHROMBOEMBOLUS AND INFARCT

Pulmonary embolus can be distinguished from a post-mortem clot by the presence of the Lines of Zahn in the thrombus.[18] In the present study, thromboembolus was observed in 1.8 % of left lungs. These cases showed well defined thrombi with Lines of Zahn inside the pulmonary arterial branches.

Only about 10 % of emboli actually cause infarction which occurs when the circulation is already inadequate, as in patients with heart or lung diseases. The diagnostic feature is the ischemic necrosis of the lung substance within the area of haemorrhage, affecting the alveolar walls, bronchioles and vessels.[18] In the present study, one case of Organophosphorus poisoning with pulmonary embolism had infarct changes in the lung lobes.

PULMONARY VESSEL THICKENING

The morphologic features described, such as changes in small arteries (medial hypertrophy, intimal proliferation, concentric intimal fibrosis, necrotizing arteritis) and changes in arterioles (muscularization, plexiform lesions, angiomatoid lesions) are useful in identifying the range of pathologic conditions encountered.[32] Increases in intimal thickness with longitudinal muscle formation are a common feature in lungs of patients with COPD.[54] In the present study, it was observed in 13.6 % of right lungs and 10.8 % of left lungs. All cases were that of obstructive pulmonary disorders (Emphysema, Chronic Bronchitis and Bronchiectasis).

One case of pulmonary vessel thickening was seen in a RTA male victim who was HIV positive by ELISA serology titres. The association between Primary Pulmonary Hypertension and HIV infection is well established.[89] In 1991, the prevalence of HIV-PAH in developed countries was estimated to be 0.5% and this prevalence remains the same regardless of HAART.[90] The pathogenic mechanisms how HIV infection leads to the development of PAH remains incompletely understood. The concentric-obliterative intimal changes, plexiform vascular lesions are the end result of common pathways leading to endothelial cell dysfunction, angiogenesis and vascular proliferative changes. However, how HIV infection triggers the pathway remains unknown.[91]

In evaluation of HIV-infected patients with pulmonary hypertension, other contributing factors must be looked for: left heart failure secondary to dilated cardiomyopathy, advanced liver disease (secondary to Hepatitis B and C virus infections), thromboembolic disease and chronic lung disease secondary to recurrent infections.[91]

The clinical classification of pulmonary hypertension includes Pulmonary Arterial hypertension, Pulmonary hypertension with left heart disease, Pulmonary Hypertension

associated with lung diseases/hypoxemia, Pulmonary Hypertension due to chronic thromboembolic disease and miscellaneous causes.[92]

BRONCHIOLAR CHANGES OF FIBROSIS/DILATATION

Fibrosis of the bronchial and bronchiolar walls and peribronchiolar fibrosis develop in the more chronic cases of Obstructive pulmonary diseases. In Chronic Bronchitis and Bronchiectasis, there is atrophy of the bronchial wall leading to weakening and ultimately dilatation.[18] In the present study, they were observed in 8.5 % of right lungs and 5.4 % of left lungs.

OBSTRUCTIVE PULMONARY DISEASES

In the present study, number of cases with Emphysema/ COPD is shown below:

Table 31: Distribution of Lungs with Microscopic Emphysematous changes

Cases	Male	Female	Total
TOTAL	11	5	16
PERCENT (%)	13	14	13

From the above tabulated data, the overall percentage of cases of emphysema in the current study was 13% (16 cases). Percentage of males having emphysema among the 85 males in this study was 13 % (13/85) and that of females among all the 35 females in this study was 14 % (14/35). The high percentage of emphysema (COPD) in this study both overall as well as in females suggests the increased exposure to indoor air pollution from biomass fuels during cooking in and around the rural areas of Kolar when compared to national statistics of COPD.[46,48]

Table 32: Distribution of total cases of Emphysema diagnosed on gross and microscopy

Findings	Molina et al Study[81]	Current study
Gross	3	7
Microscopy/Total	5	16

Table 33: Showing Discrepancy between Gross Anatomic and Microscopic findings

Findings	Molina et al Study[81]	Percent (%)	Current Study	Percent (%)
Grossly correct	3	60	7	44
Grossly missed	2	40	9	56
Total	5	100	16	100

From Tables 32 and 33, it shows that all cases of Emphysema (COPD) cannot be diagnosed on gross and the cases of mild emphysematous changes are missed on gross examination. On microscopy, these mild emphysematous cases were diagnosed. In Molina et al study, grossly correct cases comprised of 60% whereas the grossly correct ones in the present study was 44%.

SQUAMOUS METAPLASIA OF BRONCHIAL LINING

In the present study, it was observed in 2.5 % of right lungs (3 lungs). All these were cases of Obstructive Pulmonary Diseases.

REID'S INDEX

In the present study, it was increased in 3.4 % of right lungs and 5.4 % of left lungs. All these were cases of Obstructive Pulmonary Diseases which had other changes like Emphysema, Pulmonary vessel thickening, Bronchiectasis and Chronic Bronchitis.

MICRO-ORGANISMS

The fungal spores of Aspergillus species are released into the ambient air and viable organism can survive extreme climatic conditions.[23] In the present study, fungal hyphae were observed in 5 % of right lungs and 1.8 % of left lungs. This could be due to the normal anatomic structure of the right bronchus which is much wider, shorter and vertical than the left one. Periodic acid

Schiff special stain was done in all these cases and turned out to be positive. In all these cases, none of these hyphae were associated with host immune reaction in the lungs. In all these cases, they were situated right under the pleura. They could have been an asymptomatic infection or contamination from the atmosphere.

In the present study, Bacteria were observed in 6.8 % of right lungs and 3.6 % of left lungs. This could be due to the normal anatomical structure of right bronchus. Gram's stain was done and few cases showed gram positive organisms while few others showed gram negative organisms. This occurrence of coccobacilli/bacilli/cocci in the lung parenchyma could have been due to the aspiration of the normal oropharyngeal flora during the traumatic event.

BRONCHIOLITIS WITH STARCH/VEGETABLE MATTER

In the present study, foreign material probably starch/vegetable matter was seen inside the bronchioles in 3.4 % of right lungs (4 lungs) and 1 % of left lungs (1 lung). This again could be due to the normal anatomical structure of the right bronchus. All these cases had Bronchiolitis and changes of Pneumonia (Aspiration Pneumonitis). These changes were seen in all the lobes. All were cases of Poisoning. One case had clusters of cocci inside the alveolar spaces. They were probably due to aspiration of the normal oropharyngeal flora. Aspiration Pneumonitis occurs in approximately 10 % of patients who are hospitalized after a drug overdose.[68]

Aspirated food is usually identified by the presence of vegetable matter, which is classically characterized by large, usually non-polarizable, multi-septate elongate structures with thick cell walls, and occasional pigmentation. On cross-section, these may appear round with honeycomb like internal septation, dividing the structure into compartments.[69] Such structures were also seen in the present study.

CALCIFICATION OF BRONCHIAL CARTILAGINOUS PLATES

Airway calcification is usually restricted to the cartilaginous conducting portion of the bronchial tree. Alternatively, calcification of the alveoli is a relatively common consequence of calcium and phosphate imbalance. Localized areas of calcification within the bronchial tree can be seen in a variety of conditions – Old Age, Reaction to inflammation or trauma, Relapsing perichondritis, Tracheopathia osteoplastica, Chronic renal disease and recent transplantations.[93]

In the present study, it was observed in 1 % of left lungs (1 case). It was a poison case of a 25 year old male which showed calcification of the left sided bronchial cartilaginous plates. The etiologic factors like renal failure, transplantations, time duration etc could not be ascertained.

OTHER CHANGES:

- Septal thickening and Hyperplasia were observed in 6.8 % of right lungs and 8 % of left lungs. Type 2 Pneumocyte hyperplasia is a universal reaction in injured lung.[25,26,27]
- Microthrombi were observed in 2.5 % of right lungs and 5.4 % of left lungs.
- Smoker's macrophages were observed in 5 % of right lungs and 4.5 % of left lungs. These pigmented alveolar macrophages are seen in the lungs of smokers.[44]
- Anthracosis was observed in 52 % of right lungs and 45 % of left lungs.
- Vasculitis was observed in 1.7 % of right lungs and 1.8 % of left lungs. It was seen in a case of Poison and Fall from a tree. In both cases, Diffuse alveolar Damage was seen in the lungs.
- Bronchiolitis was observed in 9 % of right lungs and 7 % of left lungs.
- Bronchial congestion was observed in 58 % of right lungs and 60 % of left lungs.
- Bronchitis was observed in 2.5 % of right lungs and 3.6 % of left lungs.

PATHOLOGIC CAUSES OF DEATH IN THE PRESENT STUDY:

In 86.5 % of the cases, the cause of death was not because of acute respiratory failure or DAD. It was due to circulatory failure arising from Shocks. The inciting agent for the shock could have been due to RTA, Burns, Snake bites or Trauma.

Circulatory failure or Hypovolemic shock could have lead to hypoxic injuries to the other organs like Brain (Hypoxic intra-cerebral haemorrhage), Kidney (Renal Failure), and Liver (Liver Failure).

Poisoning from Agrochemical agents like organophosphates, organochlorine compounds, paraquat and aluminium phosphides can cause death by many mechanisms. Death in case of organophosphorus poisoning is caused by paralysis of respiratory muscles, respiratory arrest due to failure of respiratory centre, or intense bronchoconstriction. Organophosphorus compounds are powerful inhibitors of carboxylic esterase enzymes, including acetyl cholinesterase (found in the red cell, nervous tissue, skeletal muscle etc) and pseudo cholinesterase (found in plasma, liver, heart, pancreas, and brain). [94] Organophosphates can also cause death by Acute Respiratory Distress Syndrome (DAD).

Organochlorine compounds can cause death by CNS toxicity.[95] Rat poison (Aluminium Phosphide) can cause death by cardiovascular toxicity like arrhythmias, cardiogenic shock and ARDS. [95]

In the present study, 9 out of 44 poison cases had DAD (20 %). So the remaining cases could have died due to the reasons mentioned above. Out of 44 poison cases, 10 were due to Organophosphates, 1 was due to rat poison, 1 was due to paraquat poison and in remaining cases, the poison was unknown.

The temporal sequence of microvascular lung injury could be Pulmonary congestion, Pulmonary edema, Alveolar haemorrhage with/without hemosiderotic changes and finally Diffuse Alveolar Damage. So if the patient had acute lung injury due to any cause and died before the stage of hyaline membrane formation, DAD would not be observed in his/her lung parenchyma.

LIMITATIONS OF THE STUDY:

1. In few of the cases, only one lung was received.
2. In a few cases, only a portion of the lungs were sent.
3. The time interval between time of death and autopsy was not known.
4. Other confounding factors in the study interfered with the correlation of cause of death to the histomorphological findings.

SUMMARY & CONCLUSION

SUMMARY:

- This is a study on the histomorphological lung changes seen at autopsy undertaken in Sri Devaraj Urs Medical College, Kolar, Karnataka.
- A total of 120 cases were studied.
- Majority of patients belonged to the 3rd decade of life (27%), followed by 5th decade (20%) and 4th decade (17%).
- Out of 120 cases in this study, number of males were 85 (71%) and number of females were 35 (29%).
- The most common cause of death was Road Traffic Accidents (RTA) (44%), followed by Poisoning (36%) and Burns (7%).
- Maximum number of RTAs were seen in the 20-29 age group (13%) and 40-49 age group (13%) whereas highest frequency of poisoning was seen in the 10-19 age group (9%) and 20-29 age group (9%).
- Maximum victims of RTAs were males (40 %) and maximum victims of Burns were females (6.67 %).
- Maximum number of male victims were seen in the 20-29 age group (20 %) whereas maximum number of female victims were seen in the 20-29 age group (6.67 %) and 30-39 age group (6.67%).
- The most frequent manner of deaths were accidents (49 %), followed by suicides (45%) and sudden death (3 %).
- The overall percentage of cases of gross emphysema was 5.8% (7 cases).
- Pulmonary Congestion was observed in maximum number of cases (77.7 %).
- Pulmonary Edema was observed in 47.7 % of the cases.

- Alveolar Haemorrhage was observed in 39.6 % of the cases.
- Diffuse Alveolar Damage was observed in 13.6 % of right lungs and 13.5% of left lungs.
- The overall percentage of cases of microscopic emphysema/COPD was 13% (16 cases).
- Foreign material like starch/vegetable matter was seen inside the bronchioles in 3.4 % of right lungs (4 lungs) and 1 % of left lungs (1 lung).
- Squamous Metaplasia of Bronchial lining was observed in 2.5 % of right lungs (3 lungs).
- The main histological findings seen in the RTA cases were Pulmonary Congestion, Pulmonary Edema, Alveolar Haemorrhage, Hemosiderotic changes and coincidental Obstructive Pulmonary Disease changes.
- The main histological findings seen in the cases of Poison were Pulmonary Congestion, Pulmonary Edema, Alveolar Haemorrhage, Hemosiderotic changes, Diffuse Alveolar Damage and Pneumonia.

CONCLUSION:

- The objectives of studying the histomorphological changes in the lungs in this present study was achieved and showed significant findings.
- There was a gross and microscopic discrepancy of observing Emphysematous changes in the lungs.
- Acute Respiratory Failure should be strongly associated with Diffuse Alveolar Damage in the lungs, which in turn, is an important pathologic cause of death in such patients.
- The main histological findings seen in the RTA cases were Pulmonary Congestion, Pulmonary Edema, Alveolar Haemorrhage and Hemosiderotic changes. All these findings suggest that the pathologic cause of death in most of the cases was not Acute Respiratory Failure (DAD). It was due to hypovolemic circulatory failure leading on to microvascular damage and multi-organ injury.
- The main histological findings seen in the cases of Poison were Pulmonary Congestion, Pulmonary Edema, Alveolar Haemorrhage, Hemosiderotic changes, Diffuse Alveolar Damage and Pneumonia. All these findings suggest microvascular injury from the effects of the poison.
- In the present study, the main pathologic cause of death (86.5%) could be due to circulatory failure from inciting causes like RTA, Trauma, Burns, Snake bites and Chemicals. This could have had multi-organ effects in addition to lung microvascular injury.
- If the patient had acute lung injury due to any cause and died before the stage of hyaline membrane formation, DAD would not be observed in his/her lung parenchyma.

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ANNEXURES

ANNEXURE A

KEYS TO MASTER CHART

Medical Hx:

S No – Serial Number

RTA-Road Traffic Accident

OP-Organophosphorus Poison

CT-CT Scan

H'age-Haemorrhage

HTN-Hypertension

- Fracture

Gross Examination:

U/R- Unremarkable

UL-Upper Lobe

ML-Middle Lobe

LL-Lower Lobe

Anth- Anthracosis

G/W-Grey white Areas

G/Y-Grey Yellow Areas

G/B-Grey Brown Areas

G/Bl-Grey Black (Hemorrhagic) Areas

Emp- Emphysematous changes

Emp B – Emphysematous Bulla

Fix Art- Fixation Artefacts

Lac-Lacerations

Ab Hor fissure-Absence of Horizontal Fissure

DB-Dilated bronchioles

BE-Bronchiectatic changes

Microscopic Examination:

NA- Not Available

UL-Upper Lobe

ML-Middle Lobe

LL-Lower Lobe

C/ Pul Cong – Pulmonary congestion

ACE/Eng – Alveolar Capillary Engorgement

AH/Alv H'age/ Intra Alv H'age – Intra-Alveolar Haemorrhage

HF/Hemosid – Hemosiderotic changes (I, II, III)

PE/Pul Edema – Pulmonary Edema

HM-Hyaline Membrane

DAD – Diffuse Alveolar Damage

Lobar Pn – Lobar Pneumonic changes

LP – Lobar Pneumonia

P-Pneumonia

RH-Red Hepatization

GH-gray Hepatization

Aspiration P – Aspiration Pneumonia

IE-Inflammatory Exudate in alveoli

II-Interstitial Inflammation

Inflamm – Inflammation

BA/Bacilli/Cocci/CB-Bacterial organisms: Bacilli, Cocci, Coccobacilli

F – Fungal hyphae

GC-Giant cells

GI – Granulomatous Inflammation

B-S/V M – Bronchiolitis with starch/vegetable matter

Vegetable matt – vegetable matter

FB-Foreign Body inside Bronchiole

B- Bronchiolitis

Br-Bronchitis

Bronchial H'age – Bronchial haemorrhage

S-Smoker's macrophages

CM-Carbon Laden Macrophages

AM-Alveolar macrophages

PVT – Pulmonary vessel thickening

E/Emp – Emphysematous changes

ST/Septal Thick – Septal Thickening

SH/Septal Hyp-Septal Hyperplasia

IF/Int Fibrosis – Interstitial Fibrosis

FF- Fibroblast Foci

IO-Interstitial Oedema

IAF-Intra-alveolar fibrinous exudate

FN-Fibrinoid Necrosis

IV/ Inf Vasculitis- Vasculitis

Actino cont - Actinomycotic contaminant

DB-Dilated Bronchioles

BF-Peribronchiolar fibrosis

DAD org – DAD Organising phase

PA – Pulmonary artery

MT-Microthrombi

MAT-Macro thromboembolus

RI- Reid's Index increased

SM-Squamous Metaplasia

CC/Calci of Bl Cartilage-Calcification of Bronchial Cartilage

ANNEXURE B

PROFORMA

DEPARTMENT OF PATHOLOGY

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR

AUTOPSY REPORT

Name: Autopsy No:

Age: Forensic Post Mortem No:

Sex:

Hospital No:

Date of Death:

Medical History:

Cause of Death:

Organ for Autopsy Study: Lung

Weight:

Dimensions:

Gross – **E/S**: Pleura – Present/Absent

Normal/Thickened/Any other abnormality

Lung – Collapse/Non-Collapse

Other Findings –

C/S: Consistency – soft/spongy/firm/hard

Dilated Bronchi –

Other Findings -

Bits Taken (7):
A_2: Right Upper Lobe; B_2: Right Middle Lobe; C_2: Right Lower Lobe; D: Right Bronchus; E: Left Bronchus; F_2: Left Upper Lobe; G_2: Left Lower Lobe

Microscopy –

FEATURE	RUL	RML	RLL	RB	LB	LUL	LLL
Alveolar Wall Congestion							
Alveolar Wall Haemorrhage							
Alveolar Wall Capillary Engorgement							
Pulmonary Haemorrhage							
Septal Thickening							
Septal Hyperplasia							
Interstitial Oedema							
Interstitial Inflammation							
Interstitial fibrosis							
Alveolar Oedema							
Intra-alveolar Haemorrhage							
Heart failure cells							
Carbon-laden macrophages							
Inflammatory Exudate in alveoli							
Red Hepatization							
Grey Hepatization							
Other Findings							
Congestion							
Bronchioles							

IMPRESSION:

RT LUNG LT LUNG

ANNEXURE C

DEPARTMENT OF PATHOLOGY

CONSENT FORM

Date:

Autopsy No:

Name of Deceased:

I hereby consent to allow the Department of Pathology, SDUMC to take the following organs for Histomorphological diagnosis in relation to the Cause of Death.

Organs – 1) Heart with whole aorta

2) Bilateral lungs with intact Bronchi at level of carina

Name:

Signature:

Relation:

ANNEXURE D

MASTER CHART

- DEMOGRAPHIC DETAILS
- GROSS FINDINGS
- MICROSCOPIC FINDINGS