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A CLINICAL STUDY OF ADULT PATIENTS OF PLEURAL EFFUSION IN A TERTIARY CARE CENTER: A CROSS SECTIONAL OBSERVASTIONAL STUDY

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ABSTRACT

Background: accumulation of fluid in the pleural cavity is known as pleural effusion. It is the most common pleural disease and also one of the major cause of pulmonary morbidity and mortality. Most common cause in india is tuberculosis. It may be benign or malignant with rise in malignant effusion cases in recent. This study was done to evaluate clinical profile of new adult onset pleural effusion cases. **Objective**: To study recent trends in clinical profile of pleural effusion of adult patients in tertiary care unit. **Material and Method:** A cross sectional study which included all the patients of more than 18 years age admitted with pleural effusion in the department of General medicine at tertiary care center between January 2020 to June 2021. **Results:** the spectrum of etiology ranges from tb to nephrotic syndrome, tb being the leading cause followed by pneumonia. Peak age of incidence between 20-50 years and Male predominace. **Conclusion**: clinical profile tend of pleural effusion in adults appears to be similar to past in developing country like india with infectious diseases especially tb still being leading cause indicating need for extra efforts and programmes to control tb.

KEYWORDS: Predominace.

INTRODUCION

Pleural effusion is an abnormal accumulation of fluid in between the parietal and visceral pleura, called the pleural cavity. It results from either excess accumulation or decreased absorption of fluid. The pleural space normally contains a very thin layer of fluid which is around 0.1 ml/kg to 0.3 ml/kg and is constantly exchanged. Excess fluid results from the disruption of the equilibrium that exists across pleural membranes. Pleural effusion indicates presence of the disease which may be pulmonary, pleural or extra pulmonary. Pleural effusion is the most common disease among all the pleural diseases. It can also be classified as inflammatory and noninflammatory. The pleural fluid can be classified as either transudative or exudative.

The etiological distribution of pleural effusions in various series depends on the geographical area, patients age, advances in the diagnostic methods and treatment of the underlying causes. These always pose a common diagnostic problem in clinical practice, as the list of causes is quite exhaustive. The difficulty in determining the cause of pleural effusion is shown by the fact that in many studies unknown etiology constitutes 20% of effusions.

Most common causes of pleural effusions are infections and malignancy. India has the highest prevalence of tuberculosis in the world. Tuberculosis is the most common cause of effusion in India when compared to the west where malignancy and parapneumonic effusions are more common. The clinical, biochemical and cytological parameters of tubercular effusion are shared by malignancy, both being exudates and predominantly lymphocytic effusions. This can pose a significant diagnostic dilemma. ADA activity, gamma interferon, PCR various tumor markers like CA15-3, squamous cell carcinoma ag have been used to differentiate TB from nonTB. In upto 20% cases, the cause remains unknown despite a detailed diagnostic workup.

Pleural effusion may occur in the setting of acute or chronic disease and is not a diagnosis in itself. Diagnosing the etiology of pleural effusions clinically with certainty is a challenging task. The advancements in the field of medicine and with the advent of various diagnostic aids like pleural fluid analysis, pleural fluid cytology, pleural biopsy, ultrasonography, bronchoscopy, biopsy of scalene lymph node, serological tests like ANA, ADA, Rheumatoid factor, Pleural fluid Amylase, CT thorax help the physician to arrive at the diagnosis at an earlier course of the disease.

In a country like India with highest burden of tb and thus tubercular pleural effusion, the early etiological diagnosis can change the therapeutic dilemma and thus

early initiation of treatment. Considering the increasing incidence of pleural effusion in India as well worldwide, this study is done to make better understanding of the etiological, clinical, biochemical, cytological and radiological profile of pleural effusion in adult patients.

REVIEW OF LITERTURE

DEFINITION

Pleura is a serous membrane that covers the lung parenchyma. It has 2 layers, parietal pleura and visceral pleura. A thin film of fluid is normally present which acts as lubricant. Pleural effusion is abnormal accumulation of fluid in the pleural space.[1] It is either due to excessive production or decreased absorption of pleural fluid. They can be caused by several mechanisms including increased permeability of the pleural membrane, increased pulmonary capillary pressure, decreased negative intrapleural pressure, decreased oncotic pressure, and obstructed lymphatic flow. Pleural effusion indicates the presence of disease which may be pulmonary, pleural or extra pulmonary.

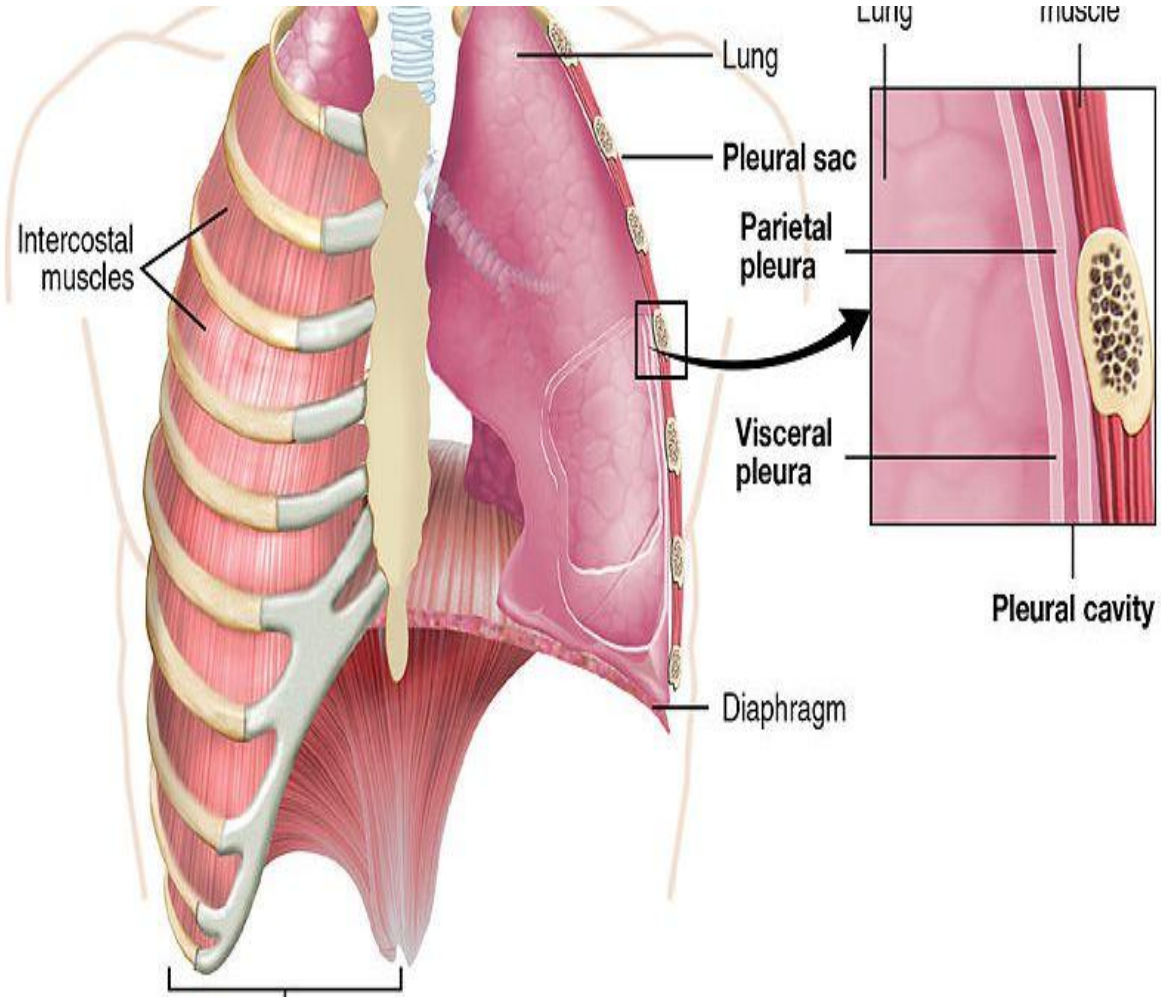
In the course of embryonic development the pleural membrane is formed from mesenchyme to line the space that will separate the lungs from mediastinum, diaphragm and chest wall.[1]

NORMAL COMPOSITION OF PLEURAL FLUID[2]

Volume - 0.2 ml/kg
Cells/cmm - 1000-5000
Mesothelial cells - 60%
Macrophages - 30%
Lymphocytes - 5%
PMN - 5%
Protein - 1-2 g/dl
Glucose - = Plasma level
LDH - <50 % of plasma level
pH - 7.60-7.64

ANATOMY OF THE PLEURA[3,4]

Each Lung is invested by a delicate serous membrane which is arranged in the form of a closed invaginated sac and is termed the pleura. The portion that covers the surface of lung and lines the tissues in-between the lobes is called the visceral pleura. The rest of the membrane lining the inner half of the chest wall is reflected over the structures occupying the middle part of the thorax is termed the parietal pleura. The visceral and parietal pleura are continuous with each other around and below the rootof the lung. In healthy they are in actual contact with each other in all phases of respiration. The potential space between them is called the Pleural cavity.



The right pleural cavity is wider than the left because the heart extends furtherto the left than to the right. The pleura covers the apices of the lung one inch above the medial third of the clavicle. The anterior margin found to converge, as they pass behind the sternoclavicular joints and come into apposition at the lower border of the manubrium sterni. It may be noticed that the anterior margin remains in apposition up to the level of the 4th costal cartilage. Right Pleura continues vertically, but the left arches out and descend lateral to the border of the sternum, half way to the apex of the heart. Each turn laterally at the 6th costal cartilage and passes around the chest wall crossing the midclavicular line at 8th rib and the mid axillary line at 10th rib. This lower border forms the costophrenic recess, falls somewhat short of the costal margin. It crosses the 12th rib at the lower border of the sacrospinalis muscle and passes in horizontally to the lower border of the 12th thoracic vertebra.

The arterial supply and lymphatic drainage of the parietal pleura are intercostals, internal thoracic and musculophrenic arteries and nodes respectively. The nerve supply is from the intercostals and phrenic nerves. The arterial supply of the visceral pleura is by the branches of Pulmonary arteries and the capillaries drain into both systemic and pulmonary venous system. Its lymphatics join with those of the lung and the nerve supply is derived from the autonomic system. It is insensitive to sensory stimuli.

PHYSIOLOGY OF PLEURA

During normal inspiration there is negative pressure in relation to the atmosphere (about -0.66kpa at functional residual capacity) within the pleural space.[2,5] This would tend to suck capillary fluid and gas from the surrounding tissue into the space. The pleura transmits the force generated by the respiratory muscles of the lung.[6] There is a regular transfer of low protein fluid from parietal to pleural space. Protein and particles are turned over much less rapidly, being absorbed by lymphatics opening into the parietal pleura Pleural surface pressure increased approximately 0.5cms of H_2O of vertical distance from the apex to the base of the lung.[6] The pleural fluid is in a dynamic state 30-75% of water being turned over every hour on normal respiration.[7,8]

Pleural space is lubricated by a thin film of few milliliters of serous fluid. For this lubrication surfactant would be more effective, have been identified in the fluid.[9,10]

PATHOPHYSIOLOGY[11]

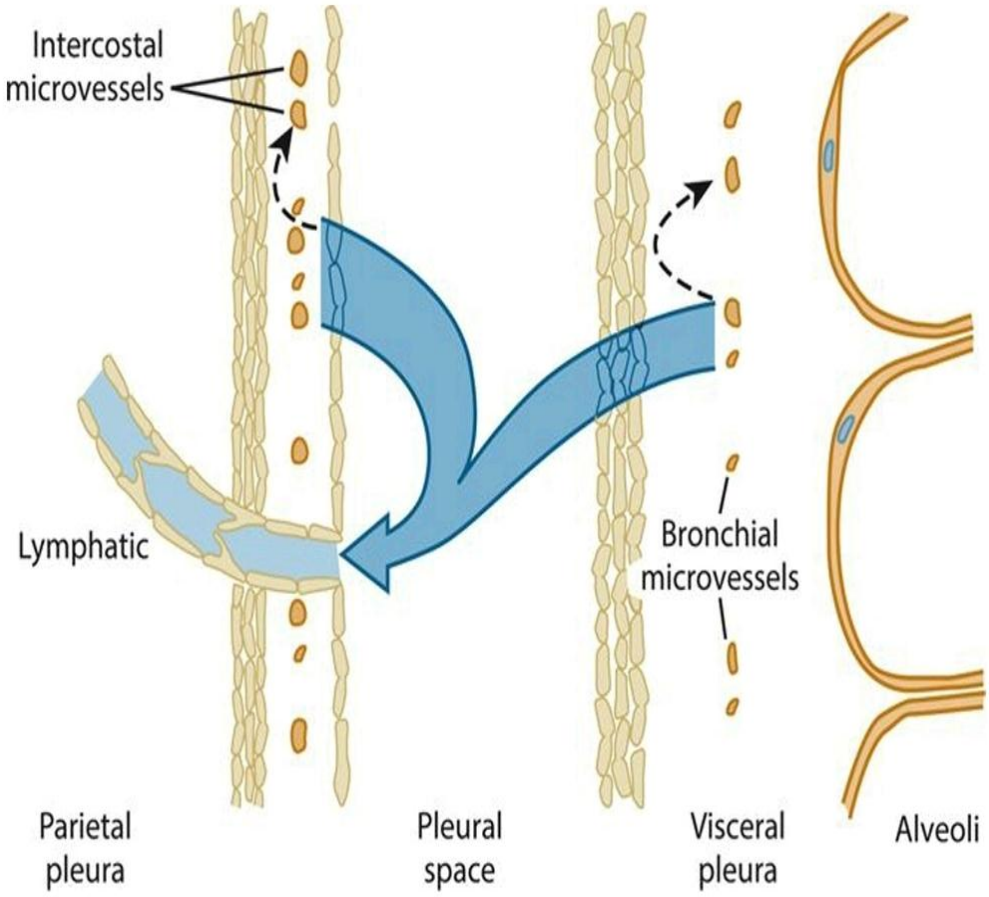
Normal interstitial fluid is filtered from the arterial end of the capillary, up to 90% is absorbed at the venous end of the capillary bed and the rest is removed by the lymphatics. Three main factors involved in the fluid movement are.

1. Capillary permeability 2. Hydrostatic pressure 3. Colloid osmotic pressure.

The potential pleural space has very close proximity to both the systemic and pulmonary circulation. Thus, the parietal pleura is supplied by the systemic circulation via the intercostals arteries and its venous drainage is mainly through the azygous system into superior venacava. In contrast, the arterial supply of the visceral pleura isby branches of the pulmonary artery and their capillaries drain into both systemic and pulmonary venous system. The intravascular hydrostatic pressure within the venousend of the visceral pleural capillaries is less than hydrostatic pressure in the capillaries of parietal pleura. Thus considering the pleural surfaces in isolation, the two separate circulatory system could presumably cope with filtrate, however, because of their closer proximity the visceral pleura is able to apply a sucking force to the pleural space which not only keep the later virtually free of fluid but also keeps the visceral and parietal surfaces apposed against the forces of lung elastic recoil inwards and chest wall outwards.

The visceral pleural capillary bed has a large capacity to absorb protein free fluid. Protein removal is by the lymphatic system. Normally, the pleural space contains small amount of fluid in protein content but in pleural effusion the later is increased. However, the capacity of the lymphatic system to deal with protein is small.

The factors affecting the pleural fluid transport system have been reviewed in detail by Brook (1972). When equilibrium between formation and absorption of pleural fluid is altered due to either one of the following reasons, abnormal accumulation of pleural fluid occurs.



Scheme of pleural fluid entry and exit in the normal state. The microvascular filtrate of the arterial blood supply flows across the leaky mesothelial layer into the lower pressure pleural space (with reabsorption as shown y dashed arrows). From the pleural space, pleural fluid exits via the parietal pleural lymphatics.

MECHANISM THAT LEADS TO ACCUMULATION OF PLEURAL FLUID[11,12]

1. Increased permeability of the pleural membrane (Inflammatory process)
2. Increased Hydrostatic pressure in the microvascular circulation
3. Decreased Oncotic pressure in the microvascular circulation
4. Decreased pressure in the pleural space
5. Decreased Lymphatic drainage from the pleural space
6. Movement of fluid from the peritoneum

Small pleural tumor implants are common findings. Such metastatic deposits can cause capillary and lymphatic obstruction resulting in increased pleural fluid production and decreased resorption. In addition secondary infections associated with the tumor deposits results in further inflammation and increased capillary permeability. Occasionally erosion of small vessels by tumor implants may cause hemorrhage into pleural space.

Major mediastinal lymph node involvement, which occurs commonly in conditions like lymphoma and small cell carcinoma of the bronchus, may interfere with lymphatic drainage and results in pleural effusion with negative cytology. Protein is unable to enter the vascular space and causes increase in pleural osmotic pressure and secondary accumulation of fluid. Obstruction of the superior venacava occurs with bronchial carcinoma and lymphoma elevates the systemic venous pressure causing a decrease in parietal pleural resorption and lymphatic flow.

PATHOGENESIS OF EFFUSION IN VARIOUS DISEASES[2,13]

Primary pathologic involvement of pleura is very rare. Primary disorders that reasonably common are:

1. Primary intrapleural bacterial infection
2. A primary neoplasm of the pleura, a mesothelioma.

Except these exceptions, usually pleural disease follows some underlying disorder, most often pulmonary and usually the pleural involvement is only an inconspicuous feature of the primary process. Secondary infections are extremely common, occasionally: secondary pleural disease assumes a dominant role in theclinical problem, as occurs in bacterial pneumonia, with development of

empyema.

The disease of the pleura can be divided into[11]

a. Inflammatory
b. Non-inflammatory

A. INFLAMMATION

Inflammation of the pleura can be divided according to the character of resultant exudates into serous, fibrinous, serofibrinous, suppurative and hemorrhagic pleuritis.

Serous, fibrinous, sero fibrinous essentially caused by the same process but the amount of fibrinous component depends largely on the stage and severity of inflammation. Common causes within the lungs are Tuberculosis, Pneumonia, Pulmonary infarction, Lung abscess, Bronchiectasis, Rheumatic fever, Disseminated lupus erythematosis, Uremia, systemic infections like Typhoid fever, Tularemia, Ornithosis, Blastomycosis, Coccidiodomycosis. The pleura is almost invariably affected by tuberculosis and the pleural reaction in the early stage tends to remain as a serous or copious serofibrinous exudation, commonly designated as pleurisy with effusion. Radiation used in therapy for tumors of lung or mediastinum often causes a serofibrinous exudates.

Suppurative Pleuritis is designated as frank, purulent exudates usually imply bacterial or mycotic seeding of the pleural space. Rarely, suppurative infection of the pleura leads on to fibrosis and markedly affects the lung expansion. Calcification can occur. Massive calcification is a feature of tuberculous empyema.

Hemorrhagic pleuritic exudates are infrequent and are usually found only in hemorrhagic diathesis, rickettsial disease, malignancy and very rarely in tuberculosis.

B. NON INFLAMMATORY PLEURAL COLLECTION

Hydrothorax is a non-inflammatory collection of serous fluid within the pleural cavity. Hydrothorax may be unilateral or bilateral depending upon the underlying cause.

Common cause of hydrothorax are

1. Congestive cardiac failure – Most common cause
2. Renal failure
3. cirrhosis of liver with ascites.
4. Meig's Syndrome-Ovarian tumor (fibroma) with ascites and right sided hydro thorax.

If the underlying cause is alleviated the hydrothorax get reabsorbed completely.

Hemothorax is the escape of blood into the pleural cavity. It is almost invariably a fatal complication of aortic aneurysm or a vascular trauma. Rarely non fatal leakage of smaller amounts can provide a stimulus to organization and pleural adhesions.

Chylothorax designates an accumulation of milky fluid, usually of lymphatic origin; chyle is milky white because it contains finely emulsified fat which should be differentiated from turbid serous fluid. It is most often encountered in malignancies arising within the thoracic cavity, which often cause obstruction to the major lymphatic ducts. However, more distant cancer metastasizes via the lymphatics and grows within the thoracic duct causing obstruction and resulting in chylothorax. Less commonly it may accompany traumatic rupture or perforation of the thoracic duct.

CAUSES OF PLEURAL EFFUSION

Pleural effusions are classified into transudates and exudates. A transudative pleural effusion occurs when the balance of hydrostatic forces influencing the formation and resorption of the pleural fluid is altered to favour pleural fluid accumulation. The permeability of the capillaries is normal.[14] In contrast, an exudative pleural effusion develops when the pleural surface and/or the local capillarypermeability are altered.[15]

ETIOLOGY[16]

Transudate

A. Increased Hydrostatic pressure:
- Left ventricular failure

B. Decreased Osmotic pressure:
- Liver cirrhosis
- Hypoalbuminemia
- Peritoneal dialysis
- Hypothyroidism
- Nephrotic syndrome
- Mitral stenosis

- Pulmonary embolism
- Constrictive pericarditis
- Urinothorax
- Superior venacaval obstruction

Exudate

A. Inflammatory conditions of the pleura
- Tuberculosis
- Parapneumonic effusion (bacterial, viral, parasitic, fungus)
- Pulmonary infections
- Pulmonary embolism

B. Malignancy
- Mesothelioma
- Malignancy of lung,

C. Connective tissue disorders
- Rheumatoid arthritis
- Autoimmune diseases (SLE)
- Immunoblastic lymphadenopathy
- Sjogren's syndrome
- Wegener's granulomatosis

- Churg-Strauss syndrome

D. Disorders of contiguous structures.
- Esophageal rupture
- Diaphragmatic hernia
- Liver abscess
- Subphrenic abscess
- Pancreatitis

Endoscopic variceal Sclerotherapy
- After Liver Transplant

E. Rare Causes
- Post Myocardial infarction syndrome
- Meig's Syndrome
- Yellow nail syndrome
- Benign asbestos effusion
- Uremia
- Post radiation therapy
- Sarcoidosis
- Trapped Lung
- Radiation therapy
- Post-coronary artery bypass surgery
- Ovarian hyperstimulation syndrome

F. Drugs known to cause Pleural effusion:
- Amiodarone
- Nitrofurantoin
- Methotrexate
- Methysergide
- Practolol
- Dantrolene
- Procarbazine
- Procainamide
- Penicillamine
- GCSF
- Cyclophosphamide
- Bromocriptine

Mycobacterium Tuberculosis and Pleural effusion[17]
Character of the fluid.
Serous exudates, very rarely Hemorrhagic or pus

Pathogenesis.
Most of the cases it spreads from underlying pulmonary focus. The effusion is always in the side of pulmonary lesion. Sometimes pleural effusion may be due to rupture of sub pleural focus or pleural involvement in Milliary tuberculosis.

Clinical Features.
- 1/3rd of patients will have acute illness less than one week duration.
- 2/3rd seek medical attention within a month, after the onset of symptoms.
- common symptoms are - Non Productive cough, Pleuritic type of chest pain, Fever – in 50% cases. Patients with chronic illness will have loss of weight, appetite, malaise and dyspnoea.

Tuberculous effusion is usually moderate and unilateral. In 1/3rd of patients tuberculous effusion will have co-existing parenchymal disease which is evident radiologically. 30% of patients with Tuberculous effusion will have negative tuberculin test. It will become positive after 8 weeks of development of symptoms. Mycobacterium is demonstrable in pleural fluid only in 10% cases. Culture will be positive in 25% cases. 50% cells in pleural fluid is mature lymphocytes. Eosinophil count rarely exceeds 10%.

Neoplasms
Malignant pleural effusions secondary to metastatic disease are the second most common type of exudative pleural effusion. These are the commonest cause of exudative effusion more than 60 years of age. The three tumors that cause approximately 75% of all malignant pleural effusions are lung carcinoma, breast carcinoma, and lymphoma.[16] Others include spread from liver metastasis, rarely an Ovarian or a gastric cancer. 7% cases show unknown primary. Mediastinal invasion with lymphatic blockage presenting with effusion is suggestive of Hodgkin's Lymphoma. Very rarely few cases of Multiple myeloma presenting as bilateral pleural effusion have also been noticed. It is usually a late complication and is associated with a poor prognosis.[18]

Most patients complain of dyspnoea, which is frequently out of proportion to the size of the effusion. The exudates may be serous, serosanguinous or hemorrhagic. Obstructive Pneumonitis with pleural effusion have a very strong presumptive evidence per se for diagnosis. Recovery of cells from pleural fluid or sputum, positive pleural biopsy, Bronchoscopy or Mediastinal node Biopsy, Fine needle aspiration cytology (FNAC) of secondary lymph node or from metastatic secondaries is helpfulin diagnosis.

Mesothelioma[16]
Malignant mesotheliomas are primary tumors that arise from the mesothelial cells that line the pleural cavities. Most are related to asbestos exposure. Patients with mesothelioma present with chest pain and shortness of breath. The chest radiograph reveals a pleural effusion, generalized pleural thickening, and a shrunken hemithorax. Thoracoscopy or open pleural biopsy is usually necessary to establish the diagnosis.[2]

Parapneumonic effusion
Parapneumonic effusions are associated with bacterial pneumonia, lung abscess or bronchiectasis. Patients with aerobic bacterial pneumonia and pleural effusion present with an acute febrile illness consisting of chest pain, sputum production, and leukocytosis. Patients with anaerobic infections present with a subacute illness with weight loss, a brisk leukocytosis, mild anemia, and a history of some factor that predisposes them to

aspiration. If the free fluid separates the lung from the chest wall by more than 10 mm on radiological examinations, a therapeutic thoracentesis should be performed.[16] The concentration of pleural-fluid myeloperoxidase helps to differentiate between nonpurulent complicated and noncomplicated parapneumonic pleural effusions.[19] Pleural fluid IL-8 is also an accurate marker for the identification of non-purulent complicated parapneumonic pleural effusion.[20]

Empyema[2]

Refers to a grossly purulent effusion. Clinically features include – High grade remittent fever with rigors and weight loss. Pleural Pain associated with cough and sputum production. Pleural fluid cytology reveals Polymorphonuclear leucocytosis. Organisms resulting in empyema: (75 % - single organisms) Mycobacterium tuberculosis, Streptococcus milleri, Streptococcus pneumonia, Staphylococcus aureus, E.coli, Klebsiella Proteus, B.melaninogenicus, Fusobacterium, Candida.[21] 25% multiple organisms: Streptococcus milleri and anareobes.

HIV Infection[16]

Pleural effusions are uncommon in such patients. The most common cause is Kaposi's sarcoma. Followed by parapneumonic effusion. Other common causes are tuberculosis, cryptococcosis and primary effusion lymphoma. Pleural effusions are very uncommon with Pneumocystis carnii infection. A pleural effusion is seen in 7-27 % of hospitalized patients with HIV infection.

Pancreatitis[2]

Usually serous exudates but may be serosanguinous. Pleural fluid amylase levels are higher than serum. Normal glucose, leucocytes 1000-50,000 cells/cmm, predominant polymorphs and rarely eosinophils are the characteristic feature of a pancreatic effusion in pleural fluid. Patients presents with history of acute abdominal pain, nausea, vomiting, rarely chest pain and dyspnoea. Usually pancreatic effusion is painless. 20% of patients with acute pancreatitis develop Pleural effusion, usually left sided sometimes bilateral occasionally right sided. Contact of the pleura with enzyme rich peripancreatic fluid occurs through the transdiaphragmatic lymphatics and less commonly through sinus between pancreatic pseudocyst and pleural space.

Diagnosis of pancreatic disease complications can be done by the pleural fluid pancreatic enzyme activity, and by computed tomography, Ultrasonography, Endoscopic Retrograde Cholangiopancreatography (ERCP).

Pulmonary Embolization

One of the rare cause of pleural effusion, which is usually exudative but can be transudative. Dyspnea is the most common symptom. The diagnosis is established by spiral CT scan or pulmonary arteriography.[16]

Effusion due to Heart Failure[16]

The most common cause of pleural effusion is left ventricular failure. The effusion occurs because the increased amounts of fluid in the lung interstitial spaces exit in part across the visceral pleura. This overwhelms the capacity of the lymphatics in the parietal pleura to remove fluid. A diagnostic thoracentesis should be performed if the effusions are not bilateral and comparable in size, if the patient is febrile, or ifthe patient has pleuritic chest pain to verify that the patient has a transudative effusion. Otherwise the patient is best treated with diuretics. If the effusion persists despite diuretic therapy, a diagnostic thoracentesis should be performed.

Hepatic Hydrothorax[16]

Pleural effusions occur in approximately 5% of patients with cirrhosis and ascites. The predominant mechanism is by the direct movement of peritoneal fluid through small holes in the diaphragm into the pleural space. The effusion is usually right-sided and frequently is large enough to produce severe dyspnoea. If medical management does not control the ascites and the effusion, the best treatment is a liver transplant. If the patient is not a candidate for this, the best alternative is insertion of a transjugular intrahepatic portal systemic shunt.

CLINICAL FEATURES OF PLEURAL EFFUSION

The onset of symptoms depends upon the quantity of the effusion and the mode of onset. Pleuritic pain and dry cough are usually the earliest symptoms but there may be preceding period of fever, loss of appetite and loss of weight. If the effusion accumulates rapidly dyspnoea, cyanosis and mediastinal flutter may be evident.

Pleural effusion may be: Generalised in the pleural space, Loculated in the pleural space, Interlobular, Intrapulmonary.

Pleural effusion can be diagnosed clinically when the pleural is more than 300 ml and it can be diagnosed radiologically in lateral view when it is 200 ml, in lateral decubitus view <200 ml and in PA view 500 – 600 ml.

If the effusion is generalised and is sufficiently large, the physical signs are.

1) Restriction of respiratory movements on the affected side
2) Stony dullness on percussion
3) Diminished or absent breath sounds
4) Diminished or absent vocal resonance and fremitus
5) Mediastinal displacement to the opposite side >1000 ml

Massive pleural effusion without mediastinal shift suggests fixation of the mediastinum and the following possibilities should be considered.

a) Carcinoma of the main stem bronchus with atelectasis of the ipsilateral lung

b) Fixed mediastinum due to neoplastic lymph nodes
c) Malignant mesothelioma

At the upper level of the dullness, which sweeps upwards towards axilla, it is saidthat the air conducted through the relaxed or collapsed lung produces tubular breathing, egophony (E- to- A change) and whispering pectoriloquy. Sometimes pleural friction rub may also be heard if there is associated pleurisy. With small effusion the signs are best elicited at the base posteriorly. Effusion located at the fissures may not be detectable on physical examination. Intrapulmonary effusion (subpulmonic effusion) may be clinically indistinguishable from fixed elevation of hemi–diaphragm with blunting of posterior costo-phrenic angle on lateral chest radiograph and other hint to diagnosis is widening of the distance between the top of the gastric bubble and the top of the Left hemi-diaphragm (2cms). Also, an effusion on the Right side causes the minor fissure to appear close to the diaphragm than usual.

PHYSICAL SIGNS OF PLEURAL EFFUSION

Findings of pleural effusion according to size

FINDING	SIZE OF EFFUSION		
	< 300 mL	300–1,500 mL	> 1,500 mL
Tachypnea	No	Present	Significant
Chest expansion	Normal	Decreased[a]	Significantly decreased[a]
Tactile fremitus	Normal	Decreased	Absent
Breath sounds	Vesicular	Decreased	Absent or bronchial
Contralateral tracheal or mediastinal shift[b]	Absent	Absent	Present
Bulging intercostal spaces	No	Sometimes	Present
Egophony[c]	No	Yes	Yes

[a]On the affected side or, in cases of bilateral effusions, both hemithoraces
[b]Mediastinal shift opposite to the side of the effusion, typically detected on chest radiography
[c]At the upper part of the effusion

DIAGNOSTIC ALGORITHM OF PLEURAL EFFUSION

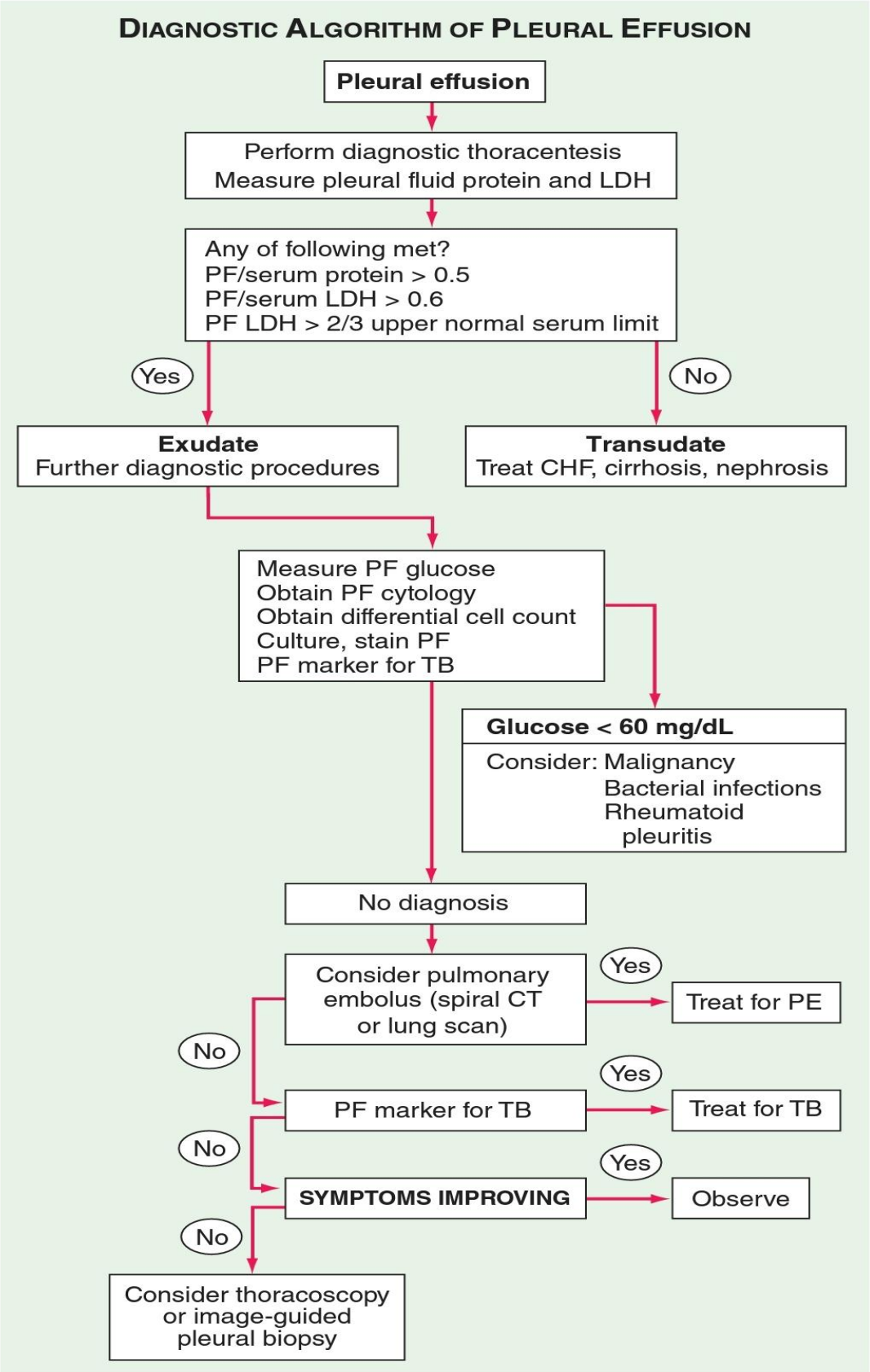


FIGURE 288-1 Approach to the diagnosis of pleural effusions. CHF, congestive heart failure; CT, computed tomography; LDH, lactate dehydrogenase; PE, pulmonary embolism; PF, pleural fluid; TB, tuberculosis.

INVESTIGATION OF PLEURAL EFFUSION

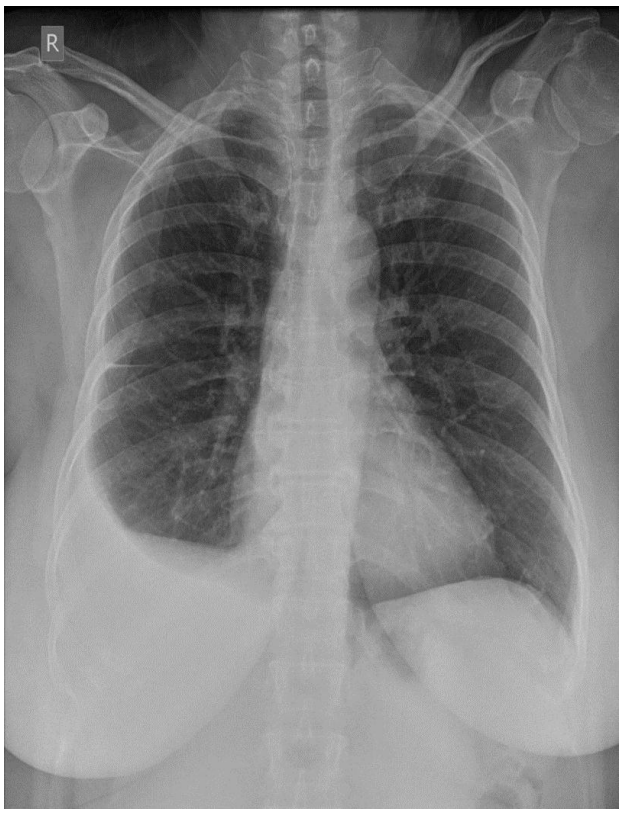
The initial step in assessing a pleural effusion is to ascertain whether it is a transudate or a exudate. The detailed clinical assessment alone is often capable of identifying a transudative effusion. Approximately 75% of patients with pulmonary embolism and pleural effusion have a history of pleuritic pain. These effusions tend to occupy less than a third of the hemithorax and the dyspnoea is often out of proportion to its size. The patient drug history is also important.

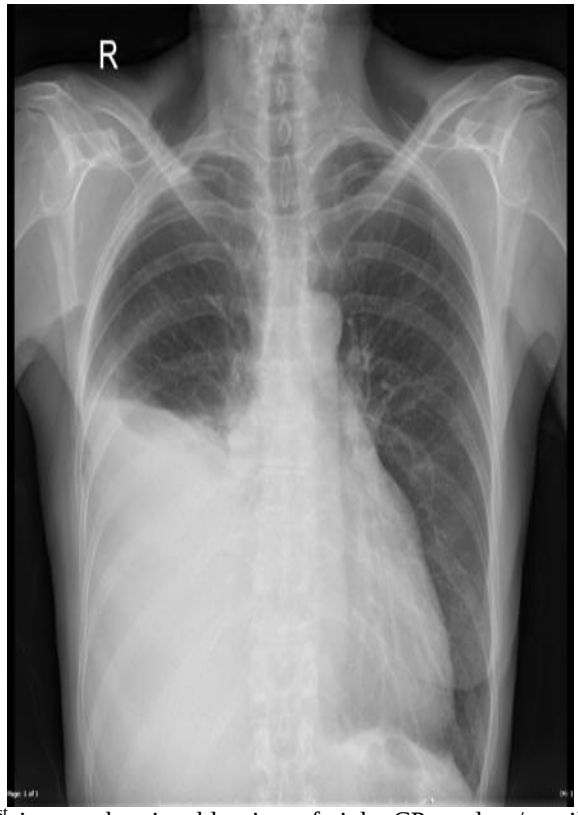
RADIOLOGY

The most sensitive method of detection of pleural fluid is by roentgenogram.

PA and Lateral chest radiographs should be taken in suspected pleural effusion.

The plain chest radiographic features of pleural effusion are usually characteristic. The PA chest radiograph is abnormal in the presence of about 200 ml of pleural fluid. However only 50 ml of pleural fluid can produce detectable posterior costophrenic angle blunting on a lateral chest radiograph.[23] Lateral decubitus film is occasionally useful as the free fluid gravitates to the most dependant part of the chest wall differentiating between pleural thickening and free fluid.[24]





1st image showing blunting of right CP angle s/o mild pleural effusion.

2nd image shows left sided moderate pleural effusion

Interlobar effusion may mimic tumor, occur partially in cardiac failure and their clearance following diuretic treatment has given rise to the term vanishing tumour.[25] Subpulmonic effusion occurs when pleural fluid accumulates in a subpulmonic location. They occur beneath the lung and are often transudates and can be difficult to diagnose on the PA radiograph and may requires a lateral decubitus view or ultrasonogram. The PA radiograph will often show a lateral peaking of apparently raised hemi- diaphragm which has a steep lateral slope with gradual medial slope. The lateral radiograph may have a flat appearance on the posterior aspect of the hemi- diaphragm with a steep downward at the major fissure.[26]

PLEURAL FLUID ASPIRATION (THORACOCENTESIS)

A diagnostic pleural fluid sample should be collected with a fine bore (21G) needle and a 50 ml syringe. The sample should be placed in sterile vials and blood culture bottles and analyzed for glucose, protein, LDH, gram stain, AFB stain, cytology, microbiological culture.

This is the primary means of evaluating pleural fluid and its findings are used to guide further investigations. Diagnostic taps are often performed in the clinic or by the bed side (if necessary under ultrasound guidance).

Microscopic examination of gram stain pleural fluid sediment is necessary forall fluids and particularly when

a parapneumonic effusion is suspected. If some of the microbiological specimen is sent in blood culture bottles the yield is greater, especially for anaerobic organisms.[27]

20 ml pleural fluid is adequate for cytological examination and the fresher the sample when it arrives at the laboratory the better is the yield. If the part of the sample is clotted, the cytologist must fix and section this and treat it as a histological section as it will increase the yield. Sending the cytological sample in a citrate bottle will prevent clots and is preferred by some cytologists. If delay is anticipated, the sample can be stored at 4^{o}C for up to 4 days.[28]

PERCUTANEOUS PLEURAL BIOPSY

Pleural tissue should always be sent for tuberculosis culture and for histological examination whenever a biopsy is performed. Smears for acid fast bacilli are only positive in 10 – 20 % of tuberculous effusion and only 25 – 50 % are positive on the pleural fluid culture.[27,29] The addition of pleural biopsy histology and culture improves the diagnostic rate to about 90%.[29]

Percutaneous pleural biopsies are of greatest value in the diagnosis of granulomatous and malignant disease of the pleura. They are performed on patients with undiagnosed exudative effusion, with non diagnostic cytology, and clinical suspicion of tuberculosis or malignancy.

Blind percutaneous pleural biopsy is done using an Abram's needle. The Abram's pleural biopsy needle is most commonly used in the UK while the Cope needle is being less commonly used. At least four samples should be taken from a single site to optimize diagnostic accuracy,[30] and these should be taken from one site as dual biopsy sites do not increase positivity.[31,32] The Biopsy specimens should be placed in 10% Formaldehyde for histological examination and sterile saline for tuberculosis culture.

Complications of Abram's needle pleural biopsy includes, site pain (1-15%), pneumothorax (3-15%), vasovagal reactions (1-5%), hemothorax (<2%), Site hematoma (<1%), transient fever (<1%) and very rarely death secondary to hemorrhage. If a pneumothorax is caused only 1% requires chest drainage.[32, 33, 34-37]

In case of mesothelioma, the biopsy site should be irradiated to stop biopsy site invasion by the tumour.

PLEURAL FLUID ANALYSIS

Key facts when investigating undiagnosed pleural effusion[38]

1. If the pleural protein is between 25 and 35 g/L then Light's criteria are used to differentiate accurately exudates from transudates.
2. Pleural fluid pH should be performed in all non purulent effusions if an infectionis suspected.
3. When sending the pleural fluid specimen for microbiological examination, it should be sent in both a sterile tube (for Gram Stain, AFB stain and TB culture) and in blood culture bottles to increase the diagnostic yield.
4. Only 60% of malignant effusions can be diagnosed by cytological examination. A contrast enhanced CT scan of the thorax is best performed in suspected cases for better visualization of pleura and identifying the best site for pleural biopsy.
5. Grossly bloody pleural fluid is usually due to malignancy, Pulmonary embolus with infection, trauma, or Post-cardiac injury syndrome(PCIS).

Typical characteristics of the pleural fluid[39]

After performing pleural aspiration the appearance and odour of the pleural fluid should be noted. The unpleasant aroma of anaerobic infection may guide the antibiotic choice. The appearance can be divided into serous, blood tinged, frank blood, or purulent. If the pleural fluid is turbid or milky it should be centrifuged. If the supernatant is clear, the turbid fluid was due to cell debris and empyema is likely. If itis still turbid, this is because of high lipid content and a Chylothorax or Pseudo-chylothorax is likely.[42]

A pleural fluid hematocrit is helpful in the diagnosis of Hemothorax.

Appearance of pleural fluid

Straw colored
Clear
Milky fluid – chylothorax
Bile stained – cholothorax {biliary fistula}
Food particles – esophageal perforation
Anchovy brown fluid – ruptured amoebic abscess
Black fluid – aspergillus infection
Putrid odor – anaerobic empyema
Urine – urinothorax

Straw colored appearance of Pleural fluid

Differentiating between a pleural fluid exudates and transudates

The pleural fluid protein should be measured to differentiate between a transudative and exudative pleural effusion. This will usually be suffice if the patients serum protein is normal and pleural protein is less than 25 g/L or more than 35 g/L. If not, Light's criteria should be used.

LIGHT'S CRITERIA[40]

The pleural fluid is an exudates if one or more of the following criteria are met:

1. Pleural fluid protein / Serum Protein > 0.5
2. Pleural fluid LDH / Serum LDH > 0.6
3. Pleural fluid LDH more than 2/3rd the upper limits of normal Serum LDH

The classical way of separating a trasudate from an exudates is by pleural fluid protein, with exudates having a protein level of > 30 g/L and transudate a proteinlevel of < 30 g/L. A considerable number of other biochemical markers have been compared with Light's criteria. These include measuring Pleural fluid cholesterol albumin gradient[42-45] and Serum/Pleural fluid Bilirubin ratio.[46] Valdes et al described the ratio between pleural cholesterol to serum cholesterol is more than 0.3 (sensitivity 92.5%, specificity 87.6%). It is found with 0.4 as the cutoff point the specificity was 100% and sensitivity 86.04%.[41]

A cut off value of LDH levels in pleural fluid of >0.66, the upper limits of the laboratory normal might be a better discriminator ("Modified Light's Criteria").[47]

The weakness of this criteria is that they occasionally identify an effusion in a patient with left ventricular failure on diuretics as an exudate. In this circumstance, clinical judgement is warranted.

Differential cell count on the pleural fluid[48]

When polymorphonuclear cells predominate, the patient has an acute process affecting the pleural surfaces. If there is concomitant parenchymal shadowing, the most likely diagnoses are parapneumonic effusion and pulmonary embolism with infarction. If there is no parenchymal shadowing, then diagnoses are pulmonary embolism, viral infection, acute tuberculosis, or benign asbestos pleural effusion.[39]

An eosinophilic pleural effusion is defined as the presence of 10% or more eosinophils in pleural fluid. Eosinophilic pleural effusions are not always benign.

The presence of pleural fluid eosinophilia is of little use in the differential diagnosis of pleural effusions. Benign etiologies include parapneumonic effusion, tuberculosis, drug induced pleurisy, benign asbestos pleural effusions, Churg-Strauss syndrome, pulmonary infarction, and parasitic disease.[49-51] It is often the result of air or blood in the pleural cavity.[50]

If the pleural fluid differential count shows a predominant lymphocytosis, the most likely diagnoses are tuberculosis and malignancy. Although high lymphocyte counts in pleural fluid raise the possibility of tuberculous pleurisy,[39] as many as 10% of tuberculous pleural effusions are predominantly neutrophilic.[48] Lymphoma, sarcoidosis, rheumatoid disease, chylothorax can cause a lymphocytic pleural effusion.[53]

pH of Pleural fluid

pH should be performed in all cases of purulent effusions. In an infected effusion a pH <7.2 indicates the need for tube drainage.[54-55]

Glucose

A pleural glucose level of less than 3.3 mmol/L is found in exudative effusions secondary to empyema, rheumatoid disease, lupus erythematosis, tuberculosis, malignancy, or esophageal rupture.[56] The lowest glucose concentrations are found in rheumatoid effusions and empyema.[56-58] In pleural infection, pH discriminates better than glucose.[55,57] Rheumatoid arthritis is unlikely to be the cause of an effusion if the glucose level in the fluid is above 1.6 mmol/L.[58]

Amylase

Amylase measurement should be requested if acute pancreatitis or rupture of the esophagus is suspected. Pleural fluid amylase levels are elevated if they are higher than the upper limits of normal for serum or the pleural fluid/ serum ratio is >1.0.[59] This suggests acute pancreatitis, Pseudo cyst of pancreas, esophageal rupture, ruptured ectopic pregnancy, or pleural malignancy (especially Adenocarcinoma).[39] Approximately 10% of malignant effusions have a raised pleural amylase levels.[60] Iso- enzyme analysis is useful in differentiating high, amylase levels secondary to malignancy or ruptured oesophagus from those raised in association with abdominalpathology.

Cytology

Malignant effusions can be diagnosed by pleural fluid cytology alone in 60% of cases. If the pleural fluid cytology specimen is negative, this should be repeated a second time. If the malignancy is suspected the cytological examination of the pleural fluid is a quick and minimally invasive way to obtain a diagnosis.[61-64]

SENSITIVITY OF PLEURAL FLUID CYTOLOGY IN MALIGNANT PLEURAL EFFUSION

The yield depends on the skill and interest of the cytologist and on tumourtype, with a diagnostic rate for adenocarcinoma is more than for mesothelioma, squamous cell carcinoma, lymphoma and sarcoma.

Staining of pleural fluid

A Gram stain of centrifuged pleural fluid should be obtained routinely. Smears of pleural fluid for AFB are

positive in approximately in 20-30% of patients with tuberculous pleurisy (American Thoracic society).

Adenosine deaminase levels

The Adenosine deaminase (ADA) level in pleural fluid tends to be higher with tuberculosis than in other exudates.[65-66] However, ADA levels are also raised in empyema, rheumatoid pleurisy, and malignancy which make the test less useful in countries with a low prevalence of tuberculosis. ADA analysis is a sensitive marker of tuberculous pleuritis even in HIV patients with very low CD4 counts in a high TB endemic region. The ADA assay is inexpensive, rapid, and simple to perform and is of great value for the immediate diagnosis of tuberculous pleuritis while waiting for culture result and this has a positive impact on patient outcome.

ADA levels more than 73 IU/L has a sensitivity of 98%, specificity of 96% in tuberculous pleural effusion.[66]

Other investigations used in the diagnosis of Tuberculous etiology:

a. Needle biopsy shows 80% cases with demonstration of granuloma.
b. The level of ADA, Lysozyme, Leukocyte count, lymphocytes in tuberculous effusion is higher than that of carcinomatous effusion.
c. Interferon γ production in tuberculous pleurisy is higher than that of malignant effusion. Levels > 140 pg/ml are more in favour of tuberculosis.[16] Interleukin-1, TNF-α also increased in tuberculous pleural effusion.
d. Tuberculous Pleural effusion, detected by tuberculo-stearic acid in pleural aspirates has a sensitivity of 71% (Grantham Hospital, Aberdin, Hong-kong).
e. PCR in the diagnosis of tuberculous pleural effusion is a G-C rich repetitive sequence (G=C RS) of mycobacterium tuberculosis that displayed a high homology with amplification of the proximal 150 bp of G=C RS and its detection by non-radioactive hybridization was developed. The accuracy of G=C RS based PCR assay was evaluated in a clinical setting for the detection of mycobacterial DNA in pleural fluid for the diagnosis of tuberculosis using clinical criteria and pleural biopsy histology as gold standard test.

ULTRASONOGRAM

Ultrasound guided pleural aspiration should be used as a safe and accurate method of obtaining fluid if the effusion is small or loculated.
Fibrinous septations are better visualized on ultrasound than on CT Scans.

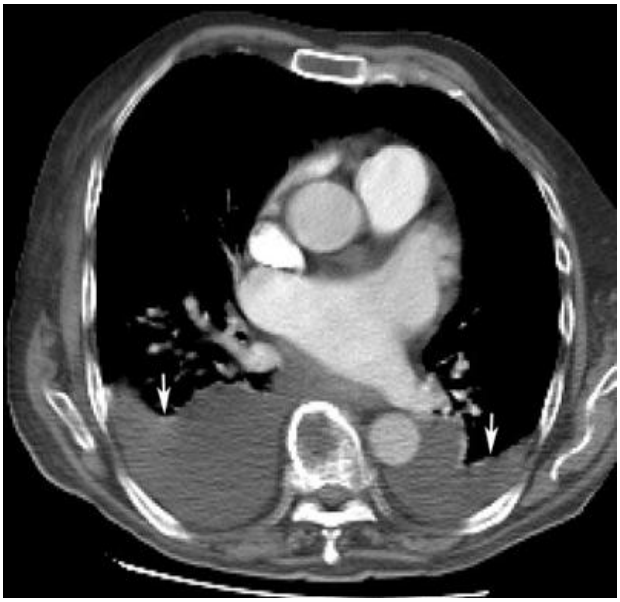
Ultrasound is more accurate than plain chest radiography for estimating pleural fluid volume and aids thoracocentesis.[68] Ultrasound is also useful in demonstrating fibrinous loculation and readily differentiates between pleural fluid and pleural thickening.[71]

Recently by using color Doppler it was observed that numerous echogenic floating particles within the pleural effusion (color signal), which is swirled in response to respiratory and cardiac cycle (this is Fluid color sign)[71] - is a sign of pleural effusion. None of the pleural thickening does not show Fluid color sign (specificity 100%).

CT SCAN THORAX

CT Scan for pleural effusion can be performed with or contrast enhancement. CT scan can usually differntiate between benign and malignant pleural thickening.

In case of difficult drainage, CT scanning should be used to delineate the size and position of loculated effusions.
These are the features of contrast enhanced thoracic CT scanning which can help differentiating in benign and malignant disease *Leung et al*[73] showed that malignant disease is favoured by nodular pleural thickening, mediastinal pleural thickening, Parietal pleural thickening greater than 1 cm, and circumferential pleural thickening. These features have specificities of 94%, 94%, 88% and 100% and sensitivities of 51%, 36%, 56%, and 41% respectively. When investigating a pleural effusion a contrast enhanced thoracic CT scan should be performed before full drainage of the fluid as pleural abnormalities will be better visualised.[74]



THORACOSCOPY

Thoracoscopy should be considered when less invasive tests failed to give a diagnosis. *Harris et al*[76] Thoracoscopy over a 5 year period and showed it to have a diagnostic sensitivity of 95% for malignancy.

BRONCHOSCOPY

Routine diagnostic bronchoscopy should not be performed for undiagnosed Pleural effusion.

Bronchoscopy is considered if there is hemoptysis or clinical features suggestive of bronchial obstruction.

Heaton and Roberts[77] bronchoscopy for undiagnosed pleural effusion has a limited role in patients with an undiagnosed pleural effusion. It should be reserved for patients whose radiology suggests the presence of a mass, loss of volume or when there is a history of hemoptysis or possible aspiration of a foreign body.

CONNECTIVE TISSUE DISEASES AND PLEURAL EFFUSION:

Rheumatoid arthritis

Suspected cases should have a pleural fluid pH, Glucose and complement measured. Rheumatoid arthritis is unlikely to be the cause of an effusion if the glucose level in the fluid is above 1.6 mmol/L (29mg/dL). Measurement of C4 complement in pleural fluid may be of additional help, with levels below 0.04 g/L in all cases of rheumatoid pleural disease.[78] Rheumatoid factor can be measured in the pleural fluid and often has a titer of >1:320.

Systemic lupus erythematosis

The pleural fluid ANA level should not be measured as it mirrors serum levels and is therefore is unhelpful. The presence of LE cells in pleural fluid is diagnostic of SLE,[78,79] *Khare et al.*

MATERIALS AND METHODS

STUDY DESIGN: This is a cross sectional study which done for a duration of 18 months, from 1/1/2020 to 30/6/2021 and data is systematically analyzed.

PLACE OF STUDY: department of general medicine, tertiary care center, Government medical college and hospital.

DURATION OF STUDY: The study is conducted for duration of 18 months – Janaury 2020 to June 2021.

SAMPLING METHOD AND SAMPLE SIZE: All patients fulfilling the inclusion criteria and willing to give written informed consent during specified 18 months duration of the study.

INCLUSION CRITERIA

- Age of subjects =/>18 years.
- Pleural effusion patients giving written informed consent.
- Both male and female participants are included.

EXCLUSION CRITERIA

- Pleural effusion patients not willing to give consent
- Age less than 18 years.

DATA COLLECTION

All the patients of more than 18 years age admitted with pleural effusion in the department of General medicine at tertiary care center between January 2020 to June 2021 were included in the study.

DATA COLLECTION AND DETAILED PROCEDURE OF STUDY CONDUCT

All the patients of 18 or more than 18 years age admitted with pleural effusion in the department of General medicine were included in the study. All patients were subjected to detailed clinical history regarding their presenting complaints like breathlessness, chest pain, cough with sputum production, fever, chest pain, hemoptysis, weight loss, loss of appetite, night sweats were enquired. Other symptoms of cardiac, liver or renal failure like swelling of feet, abdominal distension, oliguria were also enquired. Past history of any pulmonary tuberculosis, any history of previous intake of anti tuberculosis treatment, history of diabetes or any other significant illnesses like IHD, CKD, HIV, COPD, DCLD, contact history with tuberculosis were obtained. Detailed clinical examination was carried out and routine investigations like CBC, RFT, LFT, LDH testing were done for all patients. Chest X ray PA view, if needed Lateral decubitus view were also taken.

All the patients were subjected to Diagnostic Pleurocentesis. Under aseptic precautions about 10 ml of fluid was aspirated and subjected to pleural fluid analysis – Biochemical, Microbiological, Pathological analyses were done. Pleural fluid Sugar, Protein, LDH, ADA was measured for all patients. Pleural fluid cell count and cytology were done in all patients. Pleural fluid gram staining, AFB staining, CBNAAT, Culture and sensitivity tests were carried out in all patients. Other investigations like Pleural fluid Amylase levels, ANA, Rheumatoid factor, Hematocrit were done in those patients with high degree of clinical suspicion with the particular disease to support the diagnosis.

CT scan thorax was also taken for those affordable patients with clinical suspicion of parenchymal lesions or other associated diseases of the lung. Other investigations like Echocardiography, Ultra sonogram abdomen were done in relevant cases only. Special investigations like Serum ANA, RA factor, CRP, Thyroid function tests were done for relevant cases with strong clinical suspicion. All the patients were subjected to HIV screening by ELISA technique after consent. All the patients were studied in every possible way and an appropriate etiological diagnosis was made out in a systematic way.

Statistical analysis

Data was entered into Microsoft excel data sheet. Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and standard deviation.

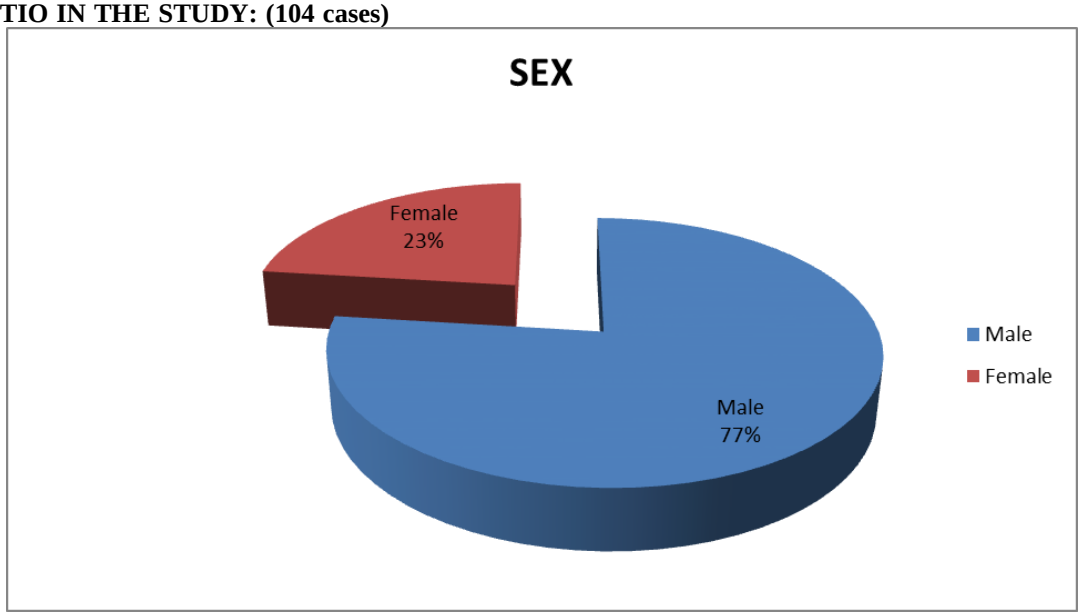
Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram.

ETHICAL CONSIDERATION

The protocol was reviewed and approved by Ethics Committee for Academic Research Projects. Informed consent was obtained from all the patients. The researcher did not record patients name for purpose of data collection. No external funding was used for this analysis.

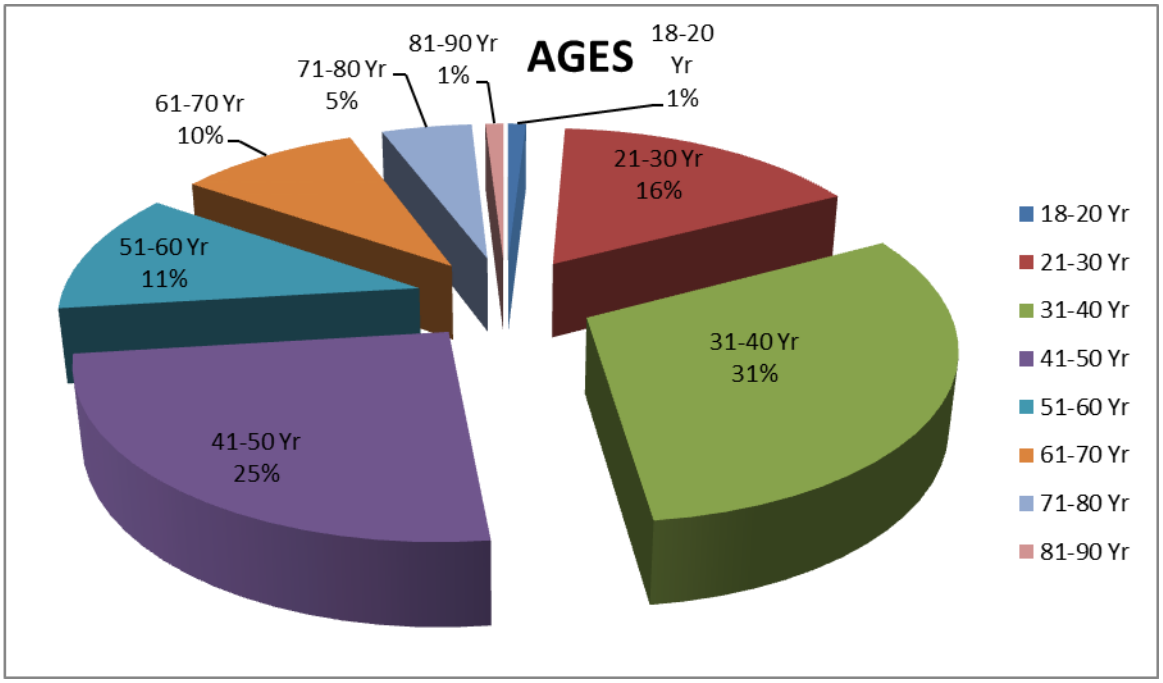
RESULTS

SEX RATIO IN THE STUDY: (104 cases)



Sex	Total cases	Percentage
Male	80	77
Female	24	23

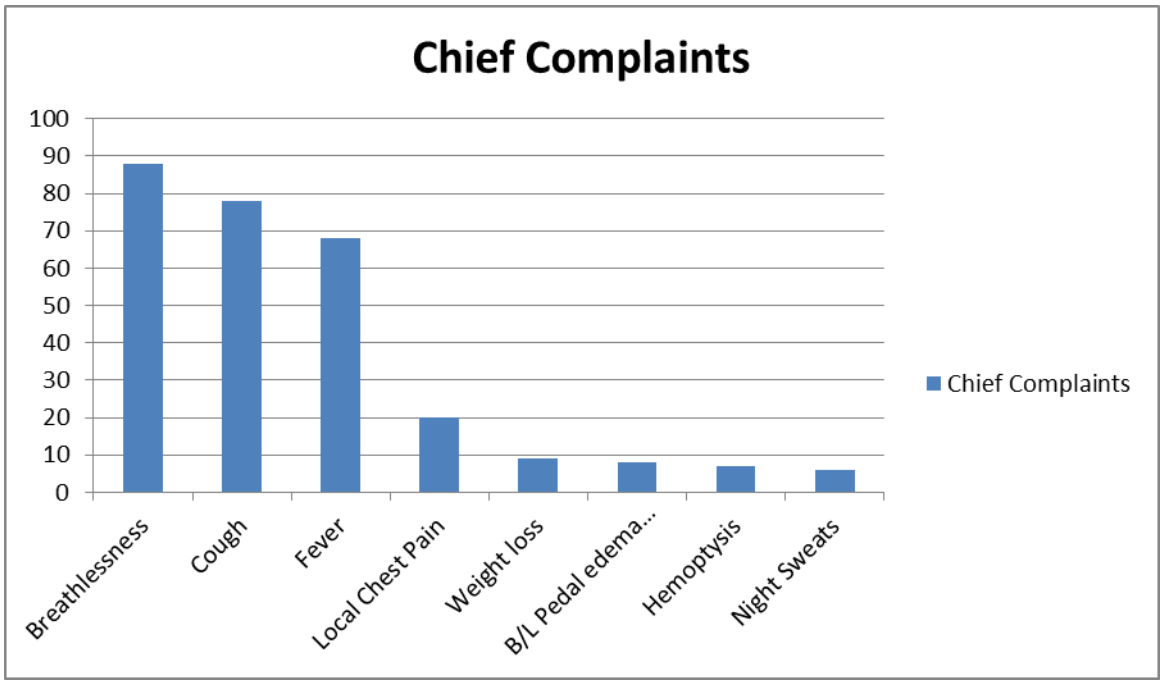
AGE DISTRIBUTION OF PATIENTS



AGE (YEARS)	PATIENTS	PERCENTAGE
18-20	1	1
21-30	17	16
31-40	32	31
41-50	26	25
51-60	12	11
61-70	10	10
71-80	5	5
81-90	1	1

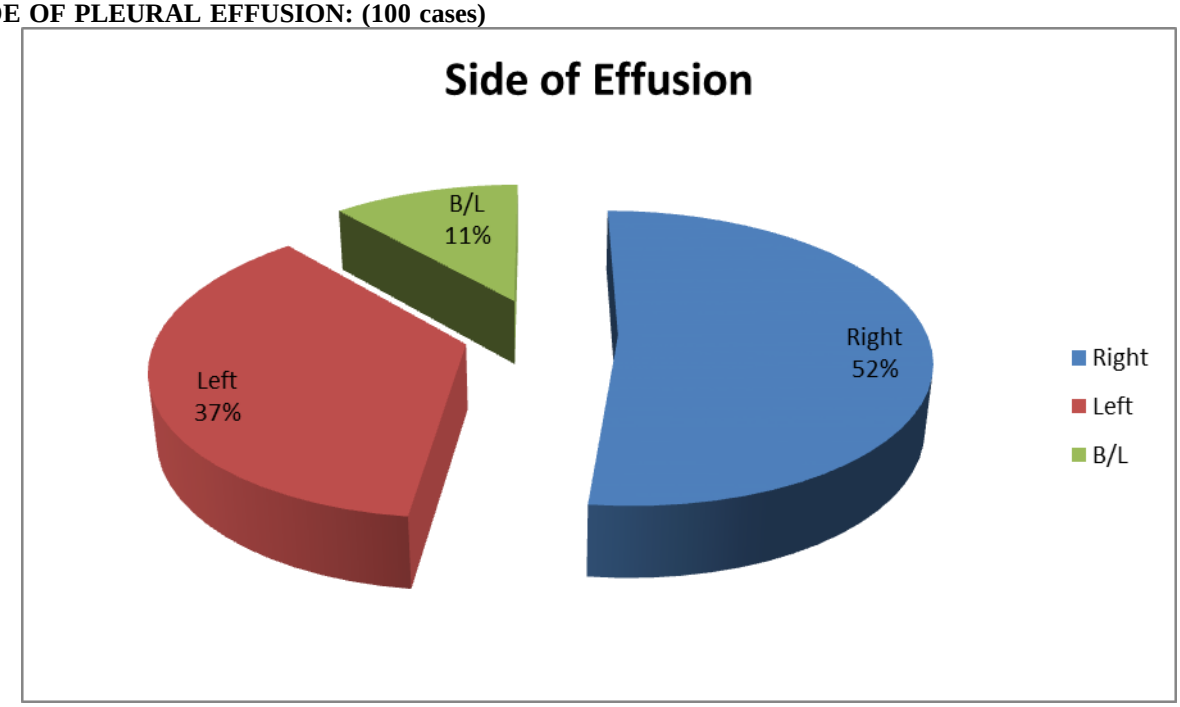
Peak age of incidence of Pleural effusion is between 20-50 y of age.

CLINICAL SYMPTOMATOLGY



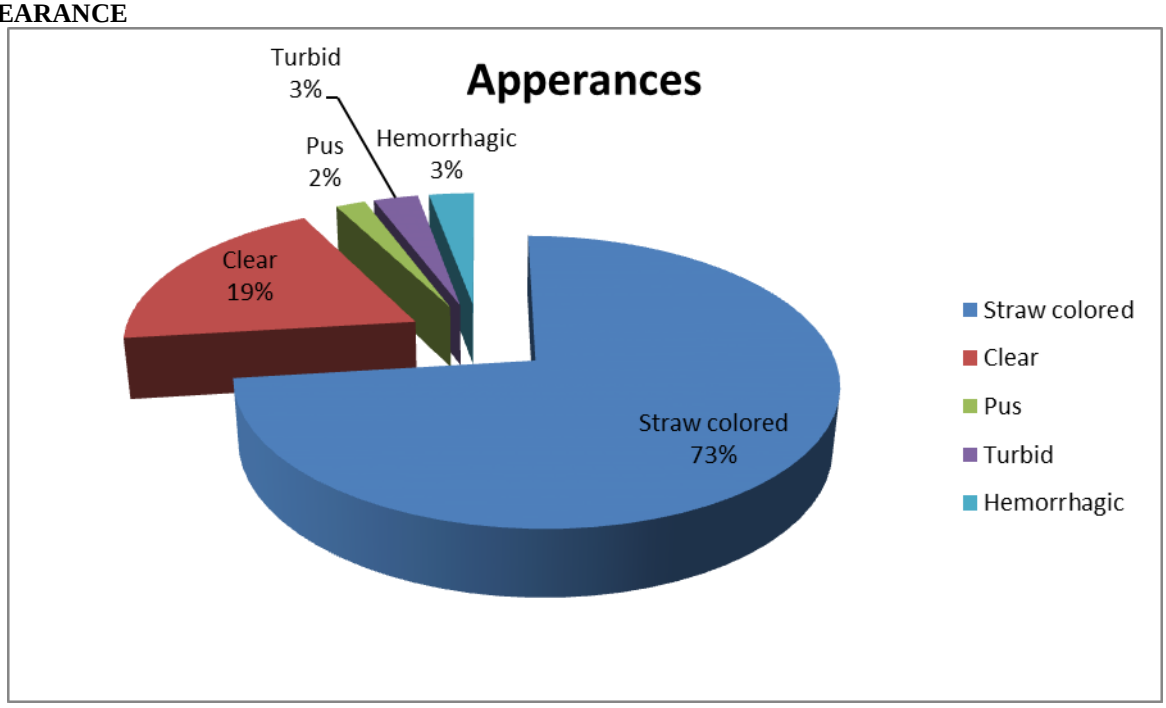
SYMPTOMS	FREQUENCY (Cases)	PERCENTAGE
Dyspnoea	88	84.6
Cough	78	75
Fever	68	65.4
Pleuritic chest pain	20	19.2
Weight Loss	9	8.65
Night sweats	6	5.8
Hemoptysis	6	5.8
Pedal edema	5	4.8
Icterus	5	4.8
Abdominal distension	3	2.9
Loss of appetite	3	2.9
Anasarca	3	2.9

SIDE OF PLEURAL EFFUSION: (100 cases)



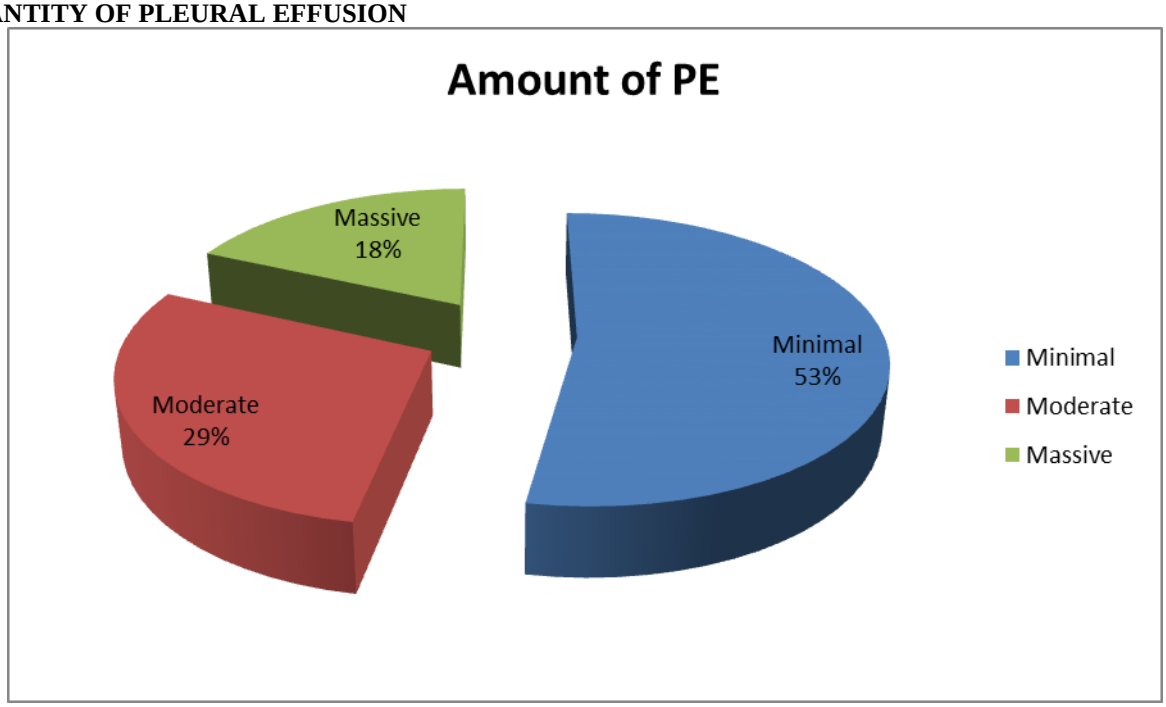
SIDE	TOTAL	PERCENTAGE
Right	54	52
Left	38	37
Bi lateral	12	11

EXAMINATION & ANALYSIS OF THE PLEURAL FLUID
APPEARANCE



Appearance of pleural Fluid	No of cases:	Percentage
Straw coloured	76	73
Clear	20	19
Hemorrhagic	3	3
Turbid	3	3
Pus	2	2

QUANTITY OF PLEURAL EFFUSION

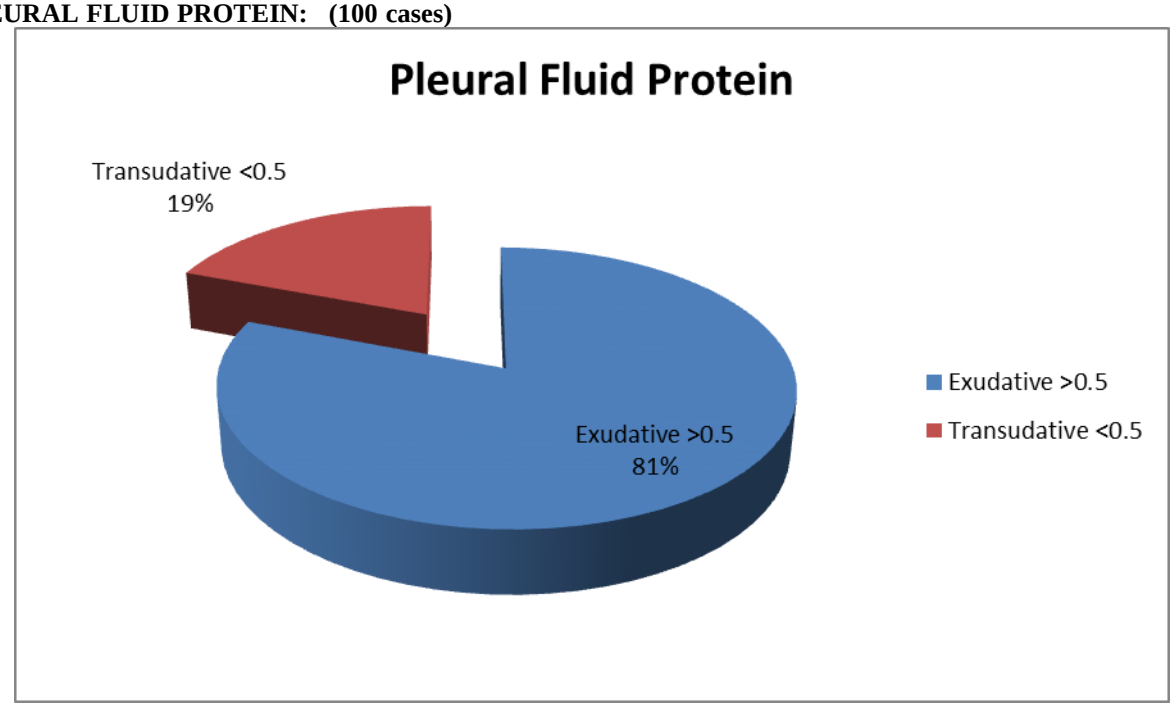


Quantity	No of cases	Percentage
Minimal	55	53
Moderate	30	29
Massive	19	18

PLEURAL FLUID GLUCOSE

The mean value of pleural fluid glucose is 133.05 mg/dL and extremely low sugar were seen in patients with malignancy and pyogenic infections.

PLEURAL FLUID PROTEIN: (100 cases)



TYPE	CASES	PERCENTAGE
Exudates	84	81
Transudates	20	19

In all the 20 transudative effusions, the pleural fluid protein/serum protein ratiowas found to be < 0.5.
In all the 84 exudative effusions, the pleural fluid protein/serum protein ratiowas found to be > 0.5

GRAM STAINING AND AFB STAINING
None of the cases showed positive results for gram stain and AFB stain.

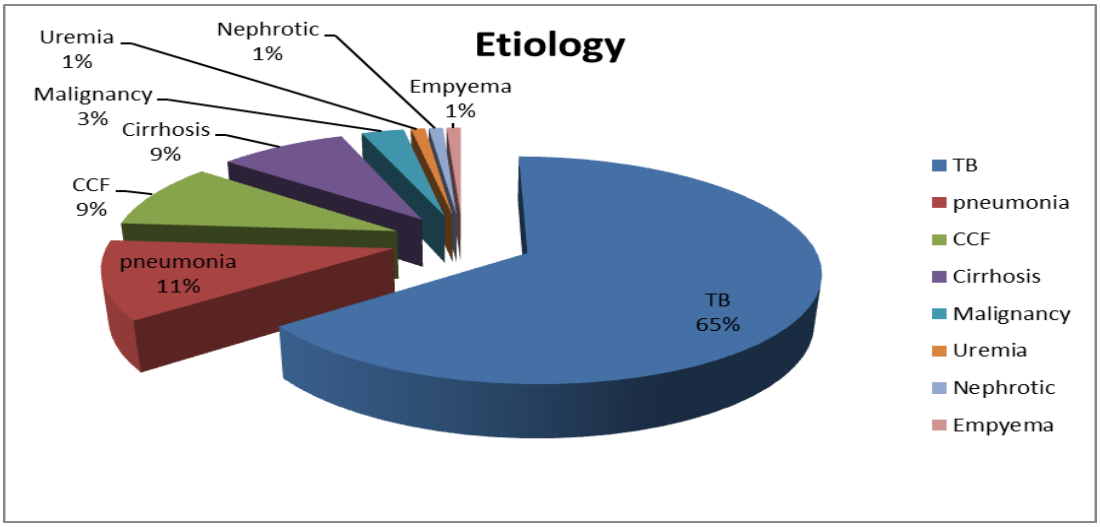
PLEURAL FLUID CYTOLOGY
The cell count varied from 560 to 13,300 cells/cmm in transudative effusion and tubercular effusion respectively. 3 cases had cytology positive for malignant cells. Lymphocyte predominance was seen in tubercular PE and polymorphonuclear predominant effusion were more common in pneumonia.

PLEURAL FLUID CULTURE
In 2 cases of pleural effusion bacterial culture was positive.

DIAGNOSIS	ORGANISM GROWN IN CULTURE
1. Parapneumonic PE	Pseudomonas
2. Empyema	Klebsiella

PLEURAL FLUID ADENOSINE DEAMINASE LEVELS
ADA levels were elevated (>43) in 66 cases (65 exudative and 1 transudative). The mean ADA level was 86.2 IU/L. of these 66, 59 were tubercular in origin. In Tuberculous effusions the values ranges from 25 – 168 IU/L. The mean ADA level in TB effusion was 66.64 IU/L. Only 9 cases of TB effusion had their values less than 43 IU/L.

ETIOLOGY OF PLEURAL EFFUSION



ETIOLOGY	CASES	PERCENTAGE
Tubercular PE	68	65
Pneumonia	11	11
CCF	10	9
DCLD	9	9
Malignancy	3	3
Empyema	1	1
Nephrotic syndrome	1	1
Uremia	1	1

CAUSES OF EXUDATIVE EFFUSION: 84 cases

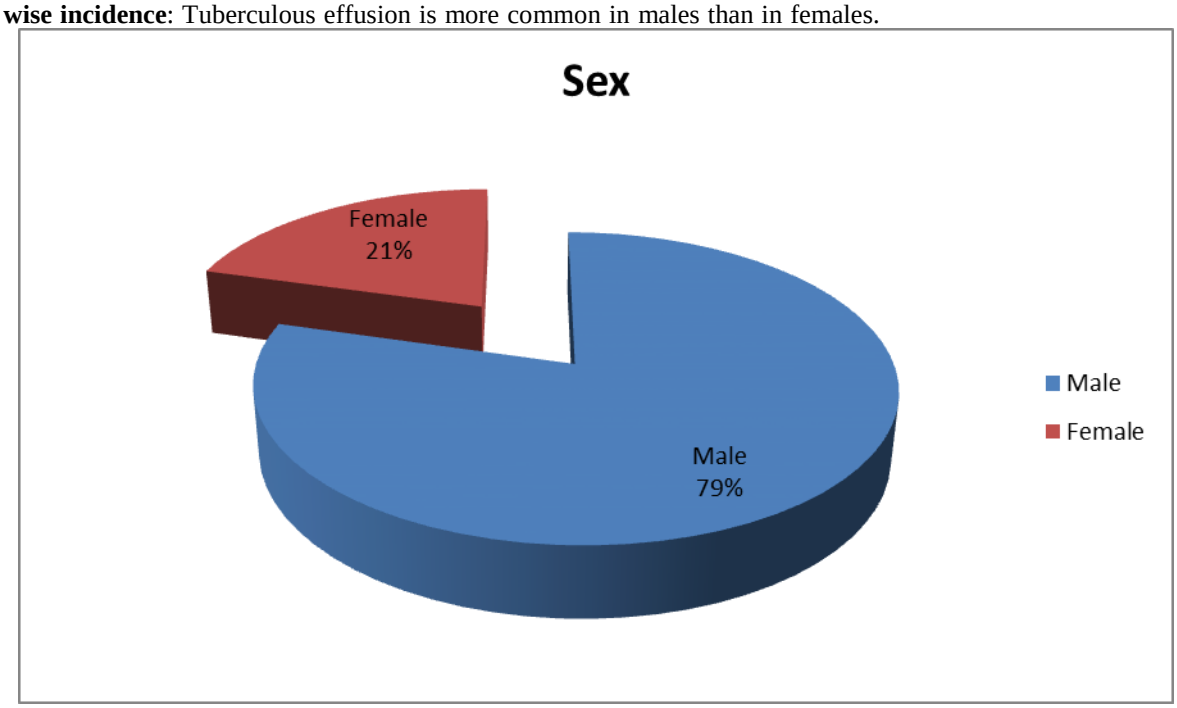
DISEASES	No OF CASES	PERCENTAGE
Tuberculous Pleural effusion	67	79.8
Tuberculous empyema	1	1.2
Pneumonia	11	13.1
Bacterial Empyema	1	1.2
Malignancy	3	3.5
Uremia	1	1.2

TRANSUDATIVE PLEURAL EFUSION: 20 cases

Transudative causes	No of cases	PERCENTAGE
Cardiac causes-CCF	10	50
Liver diseases- DCLD	9	45
Nephrotic syndrome	1	5

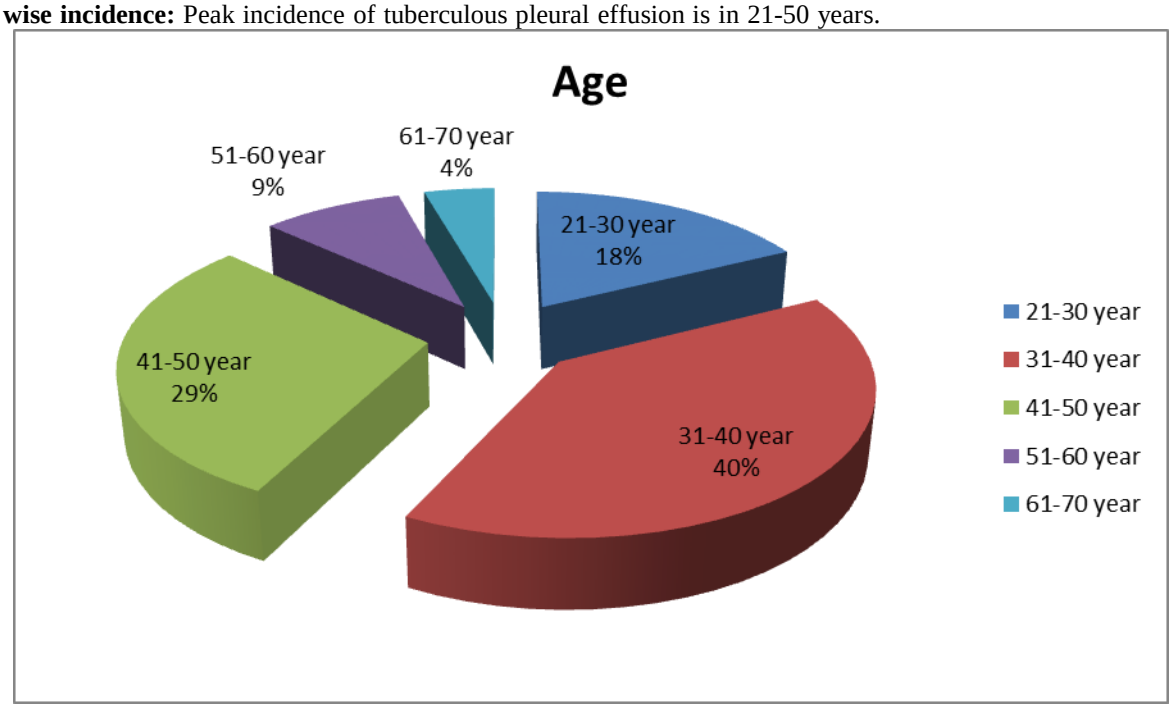
TUBERCULOUS PLEURAL EFFUSION

Sex wise incidence: Tuberculous effusion is more common in males than in females.



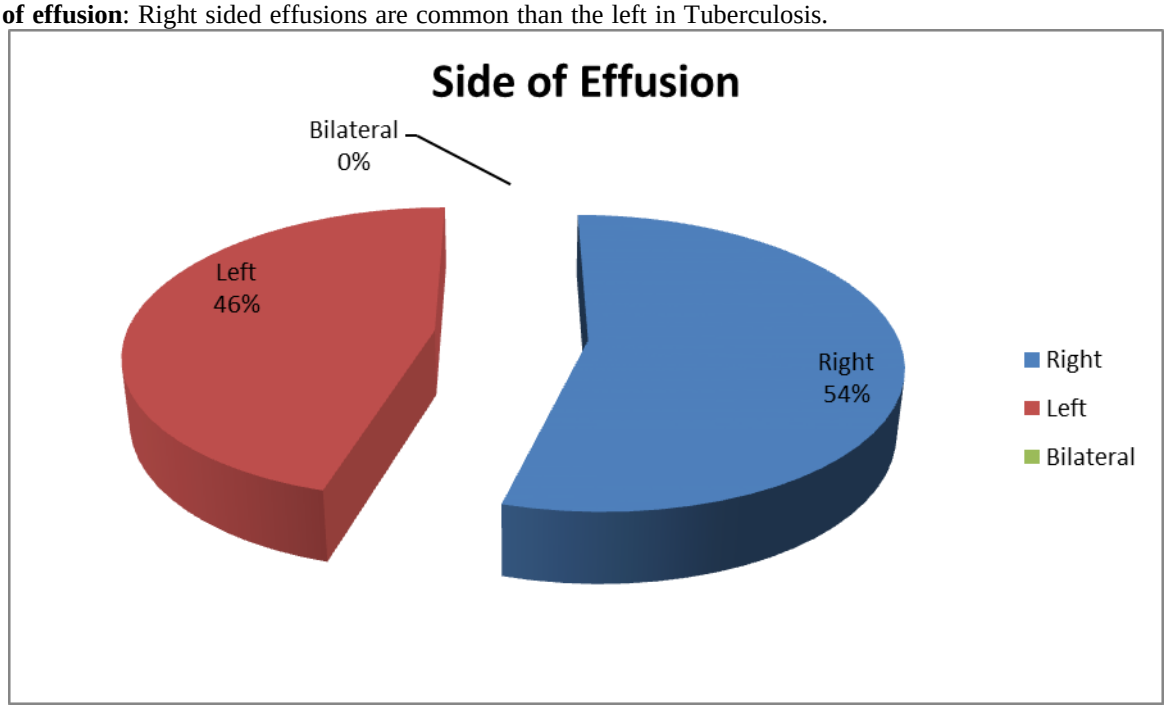
Sex	Total cases	Percentage
Male	54	79
Female	14	21

Age wise incidence: Peak incidence of tuberculous pleural effusion is in 21-50 years.



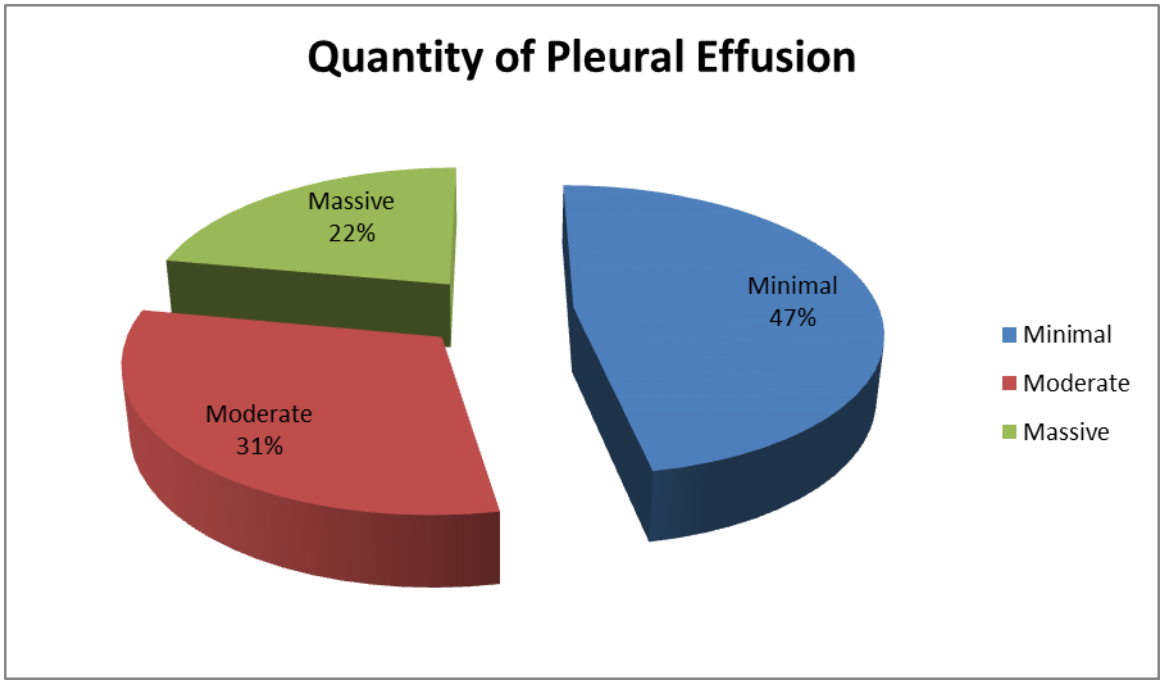
Age (yr)	Total cases	Percentage
21-30	12	18
31-40	27	40
41-50	20	29
51-60	6	9
61-70	3	4

Side of effusion: Right sided effusions are common than the left in Tuberculosis.



Side	Total cases	Percentage
Right	37	54
Left	31	46
Bilateral	0	0

QUANTITY OF PLEURAL EFFUSION

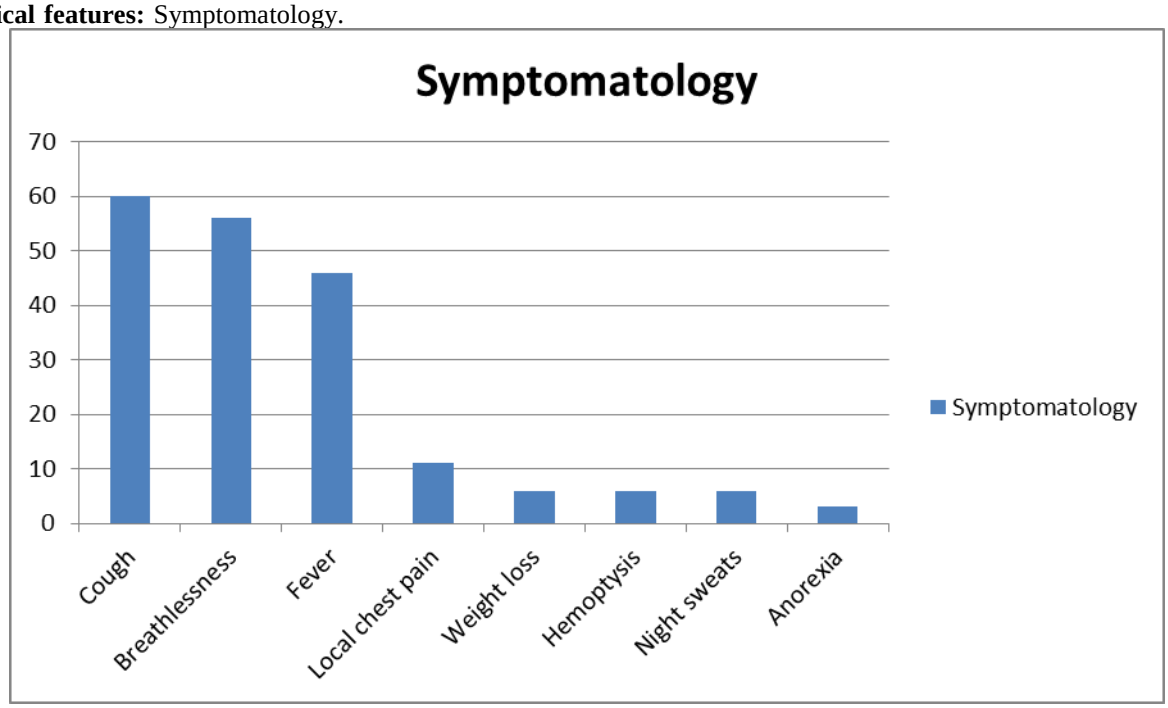


Quantity	No of cases	Percentage
Minimal	32	47
Moderate	21	31
Massive	15	22

PREVIOUS HISTORY OF TUBERCULOSIS

TYPE OF TUBERCULOSIS	TOTAL
Pulmonary Tb	7
Pleural effusion	1

Clinical features: Symptomatology.



Symptom	Cases	Percentage
Cough	60	88.2
Breathlessness	56	82.3
Fever	46	67.6
Local chest pain	11	16.1
Weight loss	6	8.8
Hemoptysis	6	8.8
Night sweats	6	8.8
Anorexia	3	4.4

DISCUSSION

In our study of 104 cases of pleural effusion, there were 80 (77%) males and 24 (23%) fe males. The patients were in the age group between 19 to 82 years. The mean age of the patients was 44.15 years. The peak age of incidence of overall pleural effusion was between 20-50 years, 72% patients belonged to this age group. A study in Qatar by Khan et al[81] showed that the mean age of the study population was 47 years with male to female ration was 3:1. Similarly in a study by Arya Shashikant and Archana[82] from India showed that the mean age of their 100 study population was 38.10 years with most of the study population were between 21 and 60 years of age and male to female ratio was 2.3:1 . Another study from India by Raghavan et al[83], included 100 patients of which majority of male patients with an age group of 30-60 years with a mean of 46 years.

The most common symptom in our series is Dyspnea presented by 88 patients (84.6 %), followed by cough in 78 (75 %), fever in 68 (65.4 %), and Pleuritic type of chest pain in 20 (19.2% cases). Weight loss was present in 9 cases of which 6 were due to tubercular origin and 3 were malignant origin. Hemoptysis was present in about 7 cases of which 4 were due to Pneumonia, 3 cases were due tubercular origin. 8 patients which presented with B/L pedal edema or anasarca were having CCF, DCLD, nephrotic syndrome

or uremia as underlying etiology. Similar study by Al-Alusi[84] included 100 patients in their study, of which most common symptoms were dyspnea (87%), followed by cough (86%), fever (79%), chest pain (67%). In a similar study done by Mbata Godwin ey al[85], the major symptoms were breathlessness (79%) followed by cough (78.4%). Desalew et al[86], in their study of 110 patients, cough, breathlessness and fever were present in 90%, 77.3% and 77.3% of cases respectively.

Previous history of tuberculosis was elicited in 8 cases. Of which 7 were pulmonary tuberculosis and 1 was recurrent tubercular PE. All of them took full course of anti-tuberculous therapy,

The mean Hemoglobin was 11.9 g/dl. The nutritional status of the patients in this series was fairly well. only 3 cases had their Hemoglobin levels below 8 g/dL, 1 was tubercular empyema and other 2 were malignant PE.. 3 patients were HIV positive.

Overall right sided effusions (52%) were more common in our study. Followed by left sided effusion in 37% cases and bilateral effusion in 11% cases. Pleural fluid analysis showed that straw colored fluids were common in 73 % cases followed by clear fluid in 19 % cases. Hemorrhagic fluid was seen in 3 % cases of pleural effusion, all 3 were of malignant etiology, 3 had turbid and 2 had purulent. Presence of straw colored effusion in tubercular effusion and hemorrhagic effusions in malignant effusions is a well established fact.[87]

The cell count varied widely between 560 and 13,300 cells/cmm in transudative effusion and tubercular effusion respectively. 3 cases had cytology positive for malignant cells. 61 (58%) cases showed a Lymphocyte predominant effusion, all were having tubercular effusion. Polymorphonuclear predominant effusions were more common in pneumonia. This is similar to Light[88] observation. These results are also similar to study done by Valdes L et al where they have encountered lymphocyte predominant tuberculous effusion in 93.3 % of patients.

None of the cases either tuberculous or pyogenic effusions showed any positivity for gram staining or AFB staining. Only two cases showed a positive bacterial culture, one Pseudomonas in case of right parapneumonic effusion and a Klebsiella induced left sided empyema.

The mean value of pleural fluid glucose was 133.05 mg/dl and extremely low sugars were seen in patients with malignancy and pyogenic infections, consistent with the earlier observation by Light[88] and study done by Rodriguez-Panadero et al.[89]

Presence of low pleural fluid glucose in malignant effusion indicates a poor prognosis, as it reflects a greater tumor burden.[90]

There were about 84 cases of exudative effusion and 20 cases of transudative effusion. The pleural fluid protein values ranged from 1.5 g/dl to 6.8 g/dl in transudative to exudative effusion. The mean value of Pleural fluid protein was 3.6 g/dl. All the 84 exudative cases had pleural fluid to serum protein ratio more than 0.5 and so also the ratio of Pleural fluid LDH to serum LDH was also more than 0.6. Transudative effusions had a protein value less than 2.3 g/dl, with pleural fluid to serum protein level less than 0.5 and the ratio of pleural fluid to serum LDH was less than 0.6. These observations are concurrent with observations done by Lights.[88]

Pleural fluid ADA was raised mainly in tubercular, pneumonic and malignant effusions. The level in Tuberculous effusions ranged from 25 – 239 IU/L. 59 cases (87%) had ADA >43 IU/L. The mean ADA level in TB effusionis 86.2 IU/L. In a similar study by Valdes et al[91], the mean ADA concentration in the patients with tubercular effusion was 111 IU/L and in empyema it was 139.7 IU/l. Shenoy et al[90] conducted a retrospective study on patients who were diagnosed to have tuberculous pleural effusion and empyema of non tubercular origin and results showed that pleural fluid ADA levels among tuberculous pleural effusion and empyema were 109.38 IU/L and 141 IU/L respectively, they concluded that apart from ADA, other parameters like lymphocyte to neutrophil ratio and glucose levels should be used to diagnose tubercular pleural effusion.

The most common cause of was effusion is tuberculous pleural effusion (65 %), followed by pneumonia (11 %), CCF (10 %), DCLD (9%), malignancy (3%), empyema (1%), uremia (1%), nephrotic syndrome (1%). This is similar to the observation in the study from India by Maldhure et al[91] where they showed that tubercular effusion constitute 66% of the effusions. This observation is different from that of the west where the incidence of parapneumonic and malignant effusions are much higher compared to that of pleural effusion. This is consistent with the fact that India has a high prevalence of tuberculosis in the general population.

Most common cause of exudative pleural effusion is tubercular pleural effusion accounting for 81% cases followed by pneumonia (13%), malignancy (3%) and 1 each case of bacterial empyema and uremia.

TUBERCULOUS PLEURAL EFFUSION: (81%, 68 cases)

Of the 68 cases (67 tubercular PE and 1 tubercular empyema), 54 (79%) were males and 14 (21%) were females. Most (59 cases, 58%) of them were between 21-50 years of age. The most common symptom at presentation is cough (60 cases, 40%), followed by dyspnea (56 cases, 30%), fever (46 cases, 20%), pleuritic chest pain (11 cases, %), hemoptysis (6 cases), weight loss (6 cases), night sweats (6 cases), anorexia (3 cases). One patient presented with seizures and was

found to have tuberculoma brain with incidental tuberculous pleural effusion.8 cases of tuberculous pleural effusion had a definite past history of tuberculosis, 1 was recurrent tubercular pleural effusion and the rest all had pulmonary tuberculosis. All of them took complete treatment. 11 cases gave positive contact history with tuberculosis with their family members and friends. Out of 68 cases, 13 were chronic smokers.

Out of the 68 cases only 2 cases were found to be sputum AFB positive, 2 cases sputum CBNAAT positive and 2 were positive for both AFB and CBNAAT. 46 (68%) patients had pleural fluid CBNAAT positive. Right sided (37 cases, 54%) effusion is common than left sided effusion (31 cases, 46%). 32 (47%) had minimal effusion, 21 (31%) had moderate and 15 (22%) had massive effusion. All of them had straw coloured pleural fluid on aspiration. All the patients had pleural fluid protein level >2.3 g/dl, pleural fluid to serum protein ratio >0.5 and pleural fluid to serum LDH ratio >0.6.

Pleural fluid ADA level in Tuberculous effusions the values ranged from 25 – 239 IU/L. 59 cases (87%) had ADA >43 IU/L. The mean ADA level in TB effusionis 86.2 IU/L.

In rest of the 12 cases (other than with sputum/pleural fluid positive for AFB/CBNAAT) the diagnosis was made on clinical, radiological evidence and pleural fluid analysis. Since our resources and facilities are limited, we have not done culture for Tubercule bacilli, Gamma interferon test or pleural biopsy. Tuberculosis is the commonest and more prevalent communicable disease in India, a straw coloured fluid clots on standing with lymphocytes predominance itself will speak about the tuberculous origin.

SYNPNEUMONIC PLEURAL EFFUSION :(11%, 11 cases)

11 Cases of pleural effusion occurred secondary to pneumonia. Most of the patients were middle aged persons -6 male and 5 women. Most common presenting complaint was cough with sputum production, fever followed by breathlessness. Radiological evidence of consolidation on the right side (8 cases) more when compared to the left (3 cases). 7 cases had a positive sputum culture. Most common organisms were klebsiella and alpha hemolytic streptococci. All of them had a high polymorphs count in pleural fluid. Only one had positive pleural fluid culture for pseudomonas.

EMPYEMA: (1 case)

60y male presented with cough, breathlessness, local left sided chest pain. Xray showed left sided massive effusion without mediastinal shifting. Thoracocentesis was purulent in nature, analysis showed cell count of 22000 with neutrophil predominance (95%). On culture showed klebsiella. He was treated with ICD and antibiotics.

MALIGNANT EFFUSION: (4%)

Out of 104 cases of pleural effusion malignant effusion was found in 3 cases only.all 3 cases were had pleural fluid analysis showing presence of malignant cells. 2 had adenocarcinoma and 1 had squamous cell carcinoma.

a. A 80 year old male presented with cough, dyspnoea, hemoptysis. Left lower lobe heterogeneous mass lesion in CT thorax and a left sided moderate pleural effusion. Her pleural fluid was hemorrhagic in appearance and showed positive cytology for malignant cells. CT guided mass biopsy showed squamous cell carcinoma.
b. A 60 year old male, with history of chronic smoking presented with cough with sputum production, weightloss and left sided chest pain was evaluated to have Left massive hemorrhagic pleural effusion with a left lower lobe mass lesion with mediatinal shift to right. CT guided Lung biopsy of mass revealed the lesion as moderately differentiated Grade III Adenocarcinoma.
c. A 62 year old female presented with cough, breathlessness, weight loss, right sided chest pain. CECT thorax showed heterogenous mass of 5*6cm in right upper lobe with multiple enhancing right pleural deposits along costal pleura with massive effusion. CT guided biopsy showed poorly differentiated adenocarcinoma.

UREMIA: (2%)

One case of left sided moderate pleural effusion due to CKD seen in82 year old male. He was a known case of CKD on routine hemodialysis since last 12 years, presented with dyspnea and volume overload signs. He had exudative effusion with few lymphocytes.

Transudative causes

The most common cause of transudative effusion is congestive cardiac failure followed by decompensated chronic liver disease and nephrotic syndrome.

CARDIAC DISEASES: (10%)

The commonest cause of transudative effusion in our study is due to cardiac failure. 10 cases presented with features of cardiac failure and pleural effusion. Most cases were above 35 yrs of age. Out of 10 cases 8 were male and 2 were female. 5 cases had a bilateral pleural effusion and remaining 5 cases presented with right sided effusion. Out of 10, 8 were minimal and 2 were moderate effusion. Out of the 10 cases, 9 cases were due to Coronary artery Heart disease in whom the ECG changes were consistent with an old Ischemia and Echocardiographically proven hypokinesia with poor ejection fraction. 1 case was due to Dilated Cardiomyopathy. 5 patients had presented with b/l pedal edema which was the most common presenting feature.

DECOMPENSATED LIVER DISEASE/CIRHOSIS OF LIVER: (3%)

Hepatic hydrothorax was present 9 cases of which 8 were males and 1 was female. Common age of

presentation was middle to old age. Most of them were bilateral minimal effusion only one patient had unilateral right sided minimal effusion. Abdominal distension, dyspnea and pedal edema/anasarca, icterus were common presenting complaints. All of them had ascites with cirrhotic liver. The causes for cirrhosis include alcoholic liver disease and cryptogenic.

NEPHROTIC SYNDROME: (2%)

One case of nephrotic syndrome 19 year female presented with anasarca, breathlessness, cough. Chest xray showed bilateral minimal pleural effusion. She was a known case of nephrotic syndrome since 6 months on frusemide. She had a nephrotic range of proteinuria 4.2 g/day, with a normal urea and creatinine levels.

CONCLUSION

108 cases of pleural effusion admitted in the medical wards of in our tertiary care center were investigated and the following conclusions were made.

1. The spectrum of etiological causes ranges from Tuberculosis to nephrotic syndrome.
2. The most common cause of pleural effusion is Tuberculosis (65%) followed by pneumonia (11%), CCF (10%).
3. The peak age of incidence of overall pleural effusion is between 20-50 Years with mean age 44.15 years. The peak age of Tubercular effusion is between 21-50 years of age.
4. Male predominance was seen with 77% Patients being male, remaining 23% Female.
5. Most common symptom of overall pleural effusion is Dyspnea (84.6%), followed by cough (75%) Most common symptom of tuberculous pleural effusion is cough (40 %) followed by Dyspnea (30%).
6. Right sided effusions (52%) are more common, followed by left (37%), bilateral (11%).
7. Pleural fluid with low glucose was seen predominantly in patients with malignancy and pyogenic infections.
8. pleural fluid ADA more than 43 IU/L increases the chances of tubercular Effusion. Mean ADA level in tubercular pleural effusion is 86.2 IU/L.
9. out of 68 cases of tubercular pleural effusion, 8 were having previous history of pulmonary TB.

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