AN ANALYTICAL STUDY OF CLINICAL PROFILE OF PLEURAL EFFUSION

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CERTIFICATE

This is to certify that the dissertation titled "A STUDY OF CLINICAL PROFILE OF PLEURAL EFFUSION" is a bonafide original work of DR**. S. EZHILNILAVAN** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in MARCH 2009. The Period of study was from JANUARY 2007 to JUNE 2008.

Prof.S.Sundar, M.D.
Additional Professor,
Dept. of Medicine,
Govt. Stanley Medical College
& Hospital, Chennai-600001

Prof.V.Ruckmani,M.D.
Head of the Dept. of Medicine,
Govt. Stanley Medical College &
Hospital, Chennai-600001.

DEAN
Prof.J.Mohanasundaram.MD., Ph.D., D.N.B.
Govt. Stanley Medical College & Hospital,
Chennai-600001.

DECLARATION

I, DR**.S.EZHILNILAVAN** solemnly declare that the dissertation titled **"A STUDY OF CLINICAL PROFILE OF PLEURAL EFFUSION"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital during 2007-2008 under guidance and supervision of my unit chief **Prof.S.SUNDAR**. Additional Professor, department of medicine.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

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Date :

(DR.S.EZHILNILAVAN)

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CONTENTS

INTRODUCION

Pleural effusion is an abnormal accumulation of fluid in the Pleural space. The pleural space lies between the lung and chest wall and normally contains a very thin layer of fluid, which serves as a coupling system. Excess fluid results from the disruption of the equilibrium that exists across pleural membranes. Pleural effusion is an indicator of a pathologic process that may be of primary pulmonary origin or of an origin related to another organ system or occasionally the first evidence of some other systemic disease.

It 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 for physicians.

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.

Here I have made an attempt to arrive at the etiological diagnosis of 100 cases of pleural effusion by collecting relevant clinical as well as laboratory data using the recent modalities available in our hospital.

AIM OF THE STUDY

1. To study about the clinical presentation of various causes of pleural effusions.

2. To identify the spectrum of pleural effusion in 100 cases of pleural effusion admitted in Govt.S.M.C.H between 2007-2008.

3. To study about the rare causes of pleural effusion in our hospital.

REVIEW OF LITERTURE

DEFINITION:

Pleural effusion is the result of accumulation of fluid in the pleural space, is a common medical problem.[1] 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	-	0.1-0.2 ml/Kg
Cells/cmm	-	1000-5000
Mesothelial cells	-	3 – 70 %
Macrophages	-	30 –75%
Lymphocytes	-	2 – 30%
Granulocytes	-	10 %
Protein	-	1 – 2 g/ dL
% Albumin	-	~ plasma level
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 root of 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 further to the left than to the right. The pleura cover 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 4^{th} 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 6^{th} costal cartilage and passes around the chest wall crossing the midclavicular line at 8^{th} rib and the mid axillary line at 10^{th} rib. This lower border forms the costophrenic recess, falls somewhat short of the costal margin. It crosses the 12^{th} rib at the lower border of the sacrospinalis muscle and passes in horizontally to the lower border of the 12^{th} 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: [2]

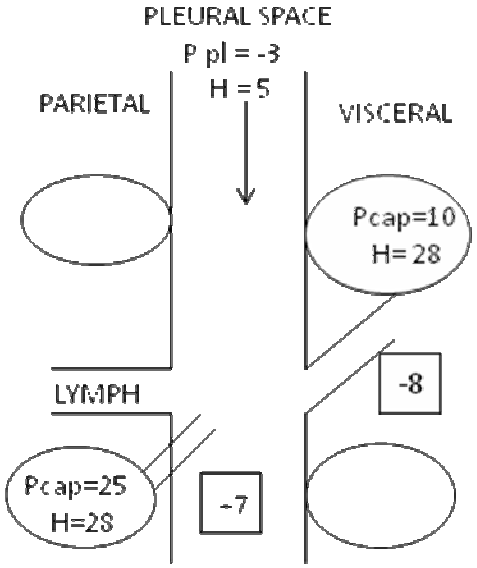

FIG 1. Distribution of Hydrostatic (P) and Oncotic (H) pressure across the parietal and visceral pleura. The numbers in the open arrow indicate the net magnitude of pressure gradient between the hydrostatic and oncotic pressure across the visceral and parietal pleura.

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.[5, 7, 8, and 9]

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 is by branches of the pulmonary artery and their capillaries drain into both systemic and pulmonary venous system. The intravascular hydrostatic pressure within the venous end 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.

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

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

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 that imply seeding of space as an isolated focus in the course of a transient bacteremia.
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 the clinical 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

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, serofibrinous 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.

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. The most common cause of hydrothorax is Congestive cardiac failure. Other conditions that produce transudative effusion are:

1. Renal failure
2. Liver disease, particularly cirrhosis of liver with ascites. It is generally believed that the fluid reaches the pleural cavity via the transdiaphragmatic lymphatics.
3. Meig's Syndrome-Ovarian tumor (fibroma) with ascites and right sided hydro thorax. It is now studied that any type of ovarian tumor may cause this syndrome.

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 capillary permeability 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

Collagen vascular diseases:

- Rheumatoid arthritis
- Autoimmune diseases (SLE)
- Immunoblastic lymphadenopathy
- Sjogren's syndrome
- Wegener's granulomatosis
- Churg-Strauss syndrome

Disorders of contiguous structures:

- Esophageal rupture
- Diaphragmatic hernia
- Liver abscess
- Subphrenic abscess
- Pancreatitis
- Endoscopic variceal Sclerotherapy
- After Liver Transplant

Malignancy:

- Mesothelioma
- Malignancy of lung, breast, ovary. (Primary and metastatic disease)

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

Drugs known to cause Pleural effusion:

- Amiodarone
- Nitrofurantoin
- Methotrexate
- Methysergide
- Practolol
- Dantrolene
- Procarbazine

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- Procainamide
- Penicillamine
- GCSF
- Cyclophosphamide
- Bromocriptine

Mycobacterium Tuberculosis and Pleural effusion: [17]

Character of the fluid:

Serous exudates, very rarely Hemorrhagic.

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%.

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).

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 helpful in 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.

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 if the 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

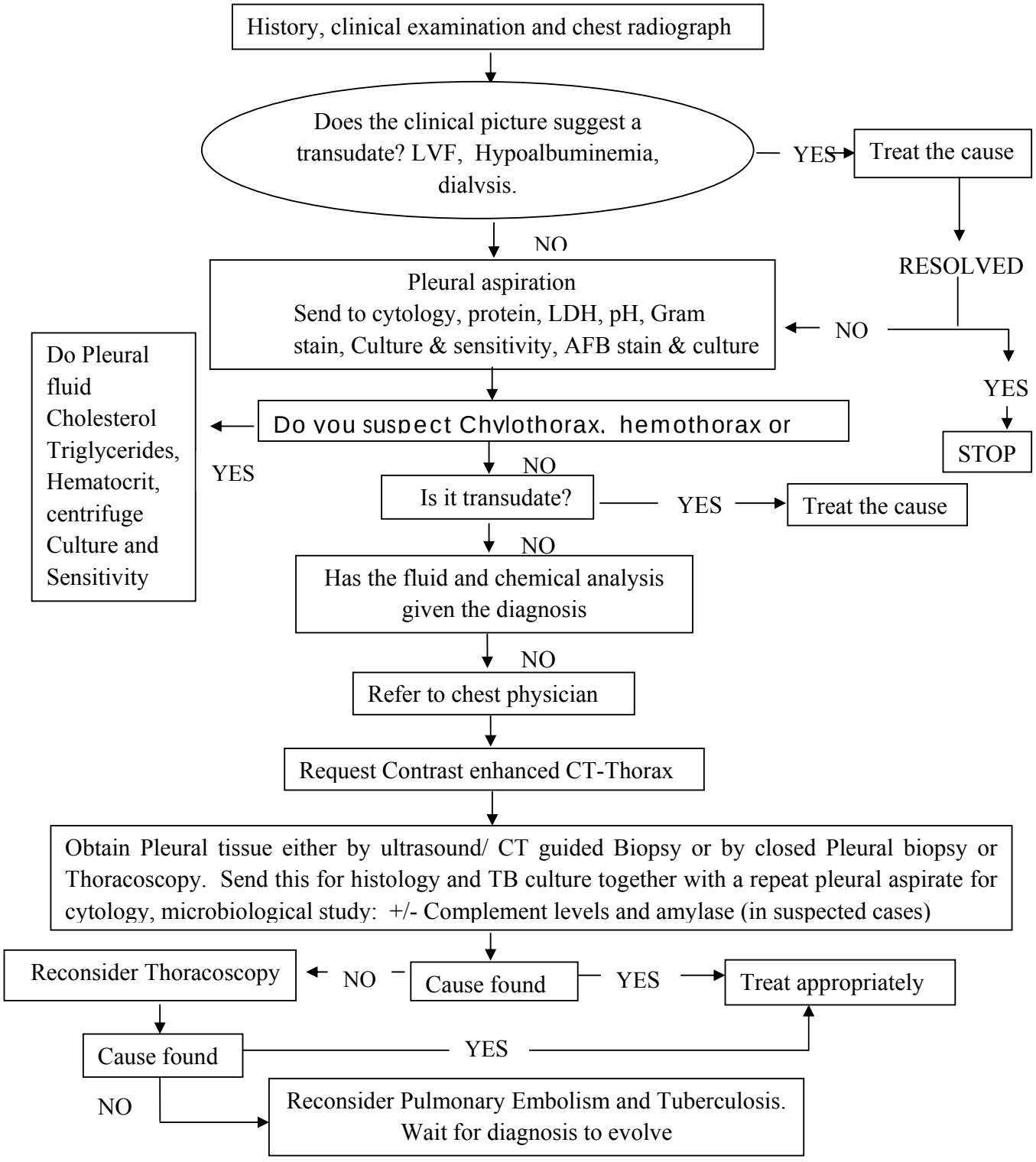
At the upper level of the dullness, which sweeps upwards towards axilla, it is said that the air conducted through the relaxed or collapsed lung produces tubular

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

Amount of Effusion	**Expansion**	**Fremitus**	**Percussion**	**Breath sounds**	**Contralateral mediastinal shift**
Small	N	N	N	Vesicular	No
300-1000ml	Decreased	Decreased	Stony dull	Decreased Vesicular	No
1000-2000ml	Moderately Decreased	Decreased	Stony dull	Moderately decreased	+
>2000 ml	Severely Decreased	Moderately Decreased	Stony dull	Severely Decreased	++

DIAGNOSTIC ALGORITHM FOR INVESTIGATION OF PLEURAL EFFUSION



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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]

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 for all 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 infection is 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 it is 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:

PLEURAL FLUID	SUSPECTED DISEASE
Putrid odour	Anaerobic Empyema
Food particles	Esophageal rupture
Bile stained	Biliary fistula
Milky	Chylothorax/Pseudochylothorax
‘ Anchovy’ sauce like fluid	Ruptured amoebic abscess

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 protein level 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 polymophonuclear 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 abdominal pathology.

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:

Reference	**No.of patients**	**No. Of cases caused By malignancy**	**% diagnosed by cytology**
Salyer et al[62]	271	95	72.6
Prakash et al[64]	414	162	57.6
Nancy et al [63]	385	109	71.0
Hirsch[61]	300	117	53.8
TOTAL	1370	371	61.6

The yield depends on the skill and interest of the cytologist and on tumour type, 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 70 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.

In a blind study, a total of 67 Pleural fluid samples (38 Tuberculous and 29 non Tuberculous) were analyzed by PCR and the results were compared with pleural biopsy, Zeihl-Neihlson Staining and culture. Mycobacteria could not be detected by either smear or culture techniques in any of the pleural fluid samples. Out of 38 Tuberculous pleural effusion, 24 were positive by PCR (63.2%) histology, an increased sensitivity of 73.3% was obtained. Out of the obtained accounting for an overall specificity of 93.1 %. G=C RS based PCR assays has a definite role in the diagnosis of Tuberculous Pleural effusion in contrast to smear/culture techniques. (AIIMS)

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, 69]

Yang et al [70] found that pleural effusions with complex septations, complex non-septations, or homogenously echogenic patterns are always exudates, whereas hypo echoic effusions can be either transudates or exudates. Ultrasound is also useful in demonstrating fibrinous loculation and readily differentiates between pleural fluid and pleural thickening.[71]

Recently by using colour 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 should be performed with contrast enhancement. CT scan can usually diferntiate 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 PLACE:

Stanley Medical College & Hospital, Department of Medicine.

STUDY DURATION:

Study was done over a period of 18 months, from January 2007 to June2008.

STUDY POPULATION:

Patients admitted with pleural effusion in the department of medicine were included in the study.

STUDY DESIGN:

Cross-sectional study.

INCLUSION CRITERIA:

1. Any case of Pleural effusion
2. Age 13-85 years.

EXCLUSION CRITERIA:

1. Age < 13 years
2. Hemodynamically unstable patients
3. Pregnant women
4. Patients with bleeding tendencies.

METHODOLGY:

All patients admitted with pleural effusion in the department of medicine were included in the study. All these patients were subjected to detailed clinical history

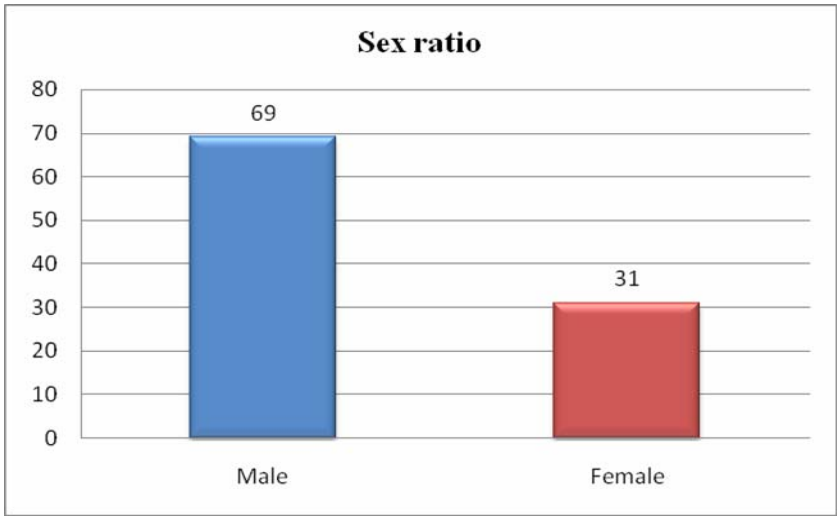
regarding their presenting complaints, other symptoms like breathlessness, chest pain, cough with sputum production, fever, weight loss, loss of appetite were enquired. Other symptoms of cardiac, liver or renal failure like swelling of feet, abdominal distension, oliguria were also enquired. Past history of any pulmonary tuberculosis, any history of previous intake of anti tuberculosis treatment, history of diabetes or any other significant illnesses, contact history with tuberculosis were obtained. Detailed clinical examination was carried out and routine investigations like Hemoglobin, ESR, Mantoux testing were done for all patients. Chest X ray PA view, 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, was measured for all patients. Pleural fluid ADA levels were estimated for exudative effusions in affordable patients. Pleural fluid cell count and cytology were done in all patients. Pleural fluid gram staining, AFB staining, Culture and sensitivity tests were carried out in all patients. For doubtful cases the Pleural fluid biopsy was done and histopathological analysis is carried out. Informed consent was obtained for all the invasive procedures prior to it. Pleural Biopsy was done for few patients only, due to practical difficulties and many patients deferred to give the consent. In our series we used Abram's pleural biopsy needle for obtaining the pleural tissue. 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. All the patients were studied in a every possible way and an appropriate etiological diagnosis was made out in a systematic way.

OBSERVATION AND RESULTS

SEX RATIO IN THE STUDY: (100 cases)



INCIDENCE – AGE/ SEX WISE: (100 cases)

Age (years)	Total no. of cases-100	Male	Female
13-20	7 (7%)	4	3
21-30	23 (23%)	16	7
31-40	22 (22%)	14	8
41-50	19 (19%)	15	4
51-60	14 (14%)	10	4
61-70	13 (13%)	9	4
71-80	2 (2%)	2	0

Peak age of incidence of Pleural effusion is between 20-40 y of age.

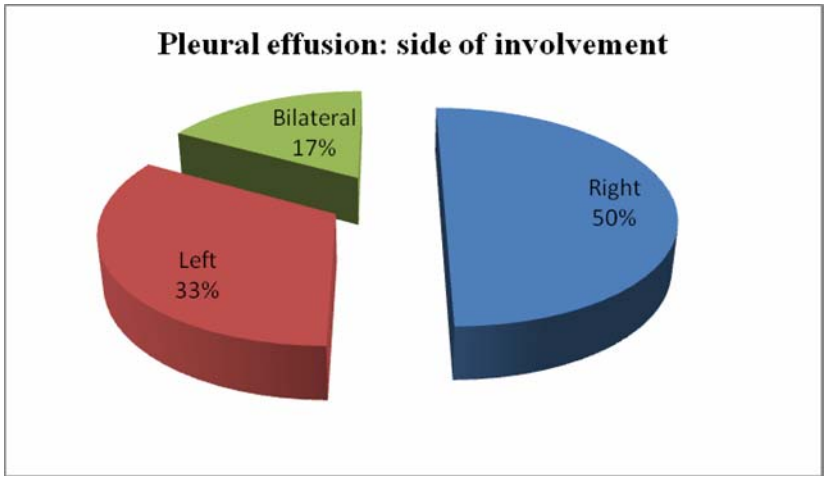
CLINICAL SYMPTOMATOLGY (100 Cases):

SYMPTOMS	**FREQUENCY (Cases)**
Dyspnoea	70
Cough	55
Fever	54
Pleuritic chest pain	50
Anorexia	44
Weight Loss	37
Pedal edema	20
Night sweats	19
Abdominal distension	12
Hemoptysis	9
Abdominal pain	4
Anasarca	3
Jaundice	1

PREVIOUS HISTORY OF TUBERCULOSIS: (100 cases)

TYPE OF TUBERCULOSIS	**TOTAL**	**MALE**	**FEMALE**
Pleural effusion	2	1	1
Pulmonary Tb	11	6	5
Tuberculous abdomen	1	1	

SIDE OF PLEURAL EFFUSION: (100 cases)



EXAMINATION & ANALYSIS OF THE PLEURAL FLUID

APPEARANCE: (100 cases)

Appearance of pleural Fluid	**No of cases:**
Straw coloured	52
Clear	20
High coloured	17
Pus	5
Turbid	3
Hemorrhagic	3

PLEURAL FLUID GLUCOSE:

The mean value of pleural fluid glucose is 69.85 mg/dL and extremely low sugar was seen in patients with malignancy and pyogenic infections.

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PLEURAL FLUID PROTEIN: (100 cases)

Exudates	80
Transudates	20

In all the 20 transudative effusions, the pleural fluid protein/serum protein ratio was found to be < 0.5

In all the 80 exudative effusions, the pleural fluid protein/serum protein ratio was 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 5-120000 cells/cmm in transudative effusion and tubercular effusion respectively.

In 4 cases of malignant pleural effusion the cytology for malignant effusion was positive for 2 cases only.

PLEURAL FLUID CULTURE:

In 2 cases of pleural effusion bacterial culture was positive-

DIAGNOSIS	ORGANISM GROWN IN CULTURE
1. Pyopneumothorax	Pseudomonas
2. Pneumonia/Synpnemonic effusion	Klebsiella

PLEURAL FLUID ADENOSINE DEAMINASE LEVELS:

ADA levels were estimated in 44 cases (41 exudative cases and 3 trasudative cases). In Tuberculous effusions the values ranges from 25 – 239 IU/L. The mean

ADA level in TB effusion was 123.213 IU/L. Only 3 cases of TB effusion had their values less than 45 IU/L. Only one case of Rheumatoid arthritis had ADA levels of 65 IU/L.

PLEURAL BIOPSY:

Total No. of Pleural Biopsy done	12
Tuberculous granuloma	6
Non specific inflammation	5
Normal study	1

CAUSES OF EXUDATIVE EFFUSION:

DISEASES	**No OF CASES**
Tuberculous Pleural effusion	50
Tuberculous empyema	2
Tuberculous hydropneumothorax	1
Pneumonia	8
Pyogenic pyopneumothorax	2
Liver abscess	4
Collagen vascular diseases	4
Malignancy	4
Uremia	2
Pulmonary embolism	1
Aortic aneurysm	1

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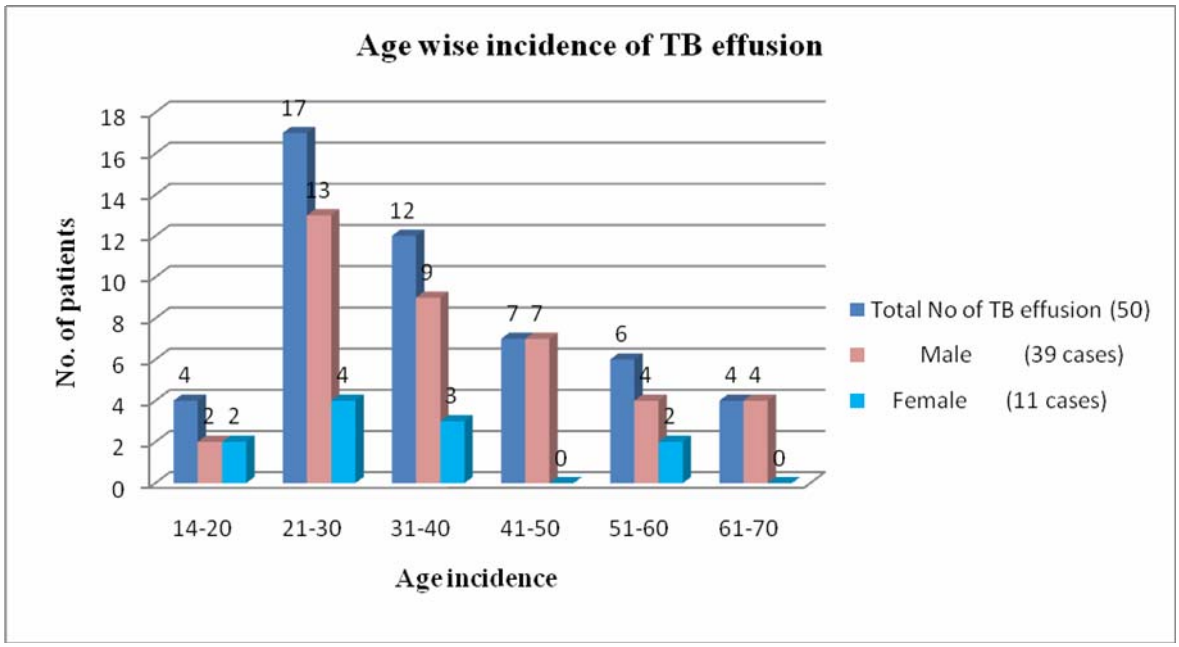
TUBERCULOUS PLEURAL EFFUSION:

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

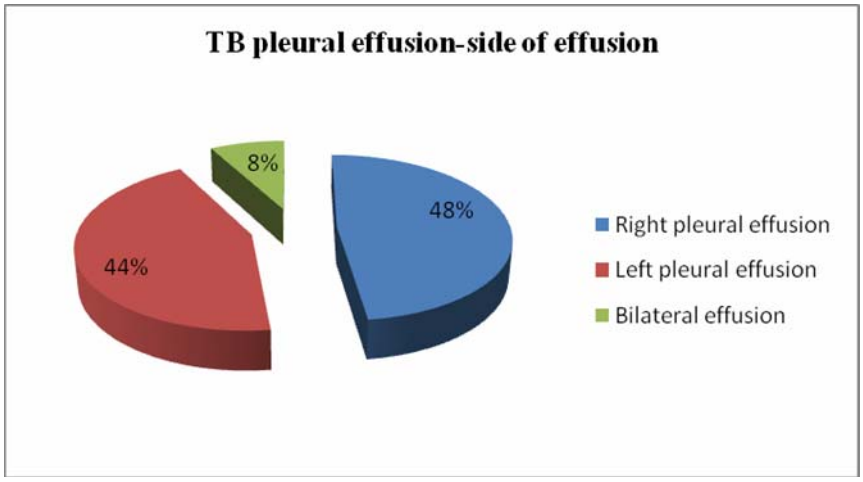
Total no of cases	Male	Female
50	39	11

Age wise incidence: Peak incidence of tuberculous pleural effusion is in 21-40 years.

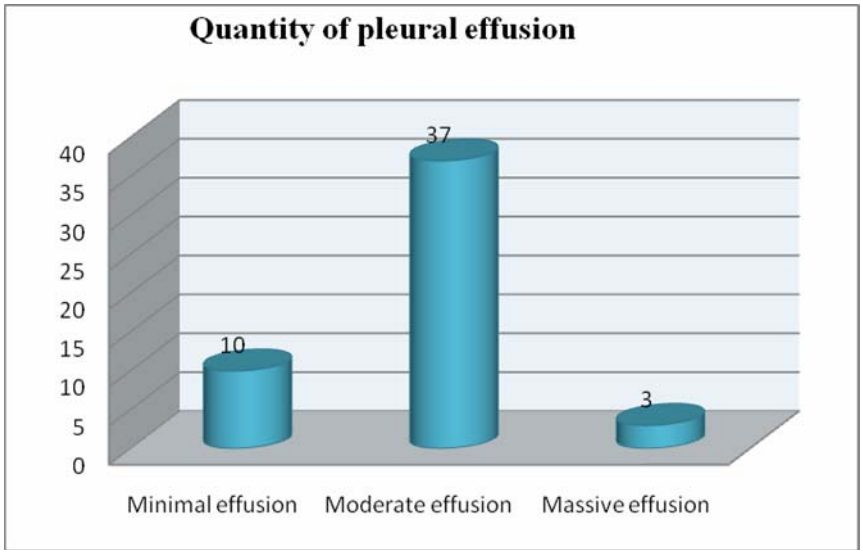
Age (yr)	Total No of TB effusion-50cases	Male (39)	Female (11)
14-20	4	2	2
21-30	17	13	4
31-40	12	9	3
41-50	7	7	0
51-60	6	4	2
61-70	4	4	0



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



Quantity of pleural effusion: 37 cases had moderate effusion.



Risk factors: related to Tuberculous effusion: (total 50 cases)

Past history of pulmonary tuberculosis	8
Smoking	22
Contact with Pulmonary Tuberculosis	11
Diabetes mellitus	3
Low socio-economic group	46

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Clinical features: Symptomatology

Presenting complaints: Most common symptom at presentation is Pleuritc chest pain.

Chest pain	20
Fever	15
Dyspnoea	10
Productive cough	2
Dry cough	1
Anorexia	1
Seizures	1

Frequency of symptoms:(50 cases) Most common symptom is Pleuritic chest pain

Pleuritic chest pain	35
Dyspnoea	33
Fever	32
Productive cough	25
Weight loss	25
Anorexia	25
Night sweats	15
Dry cough	9

Radiological presentation (associated pulmonary parenchymal lesion):

TB infiltrates			Fibrosis/fibrocavity			Cavity		
R	L	B/L	R	L	B/L	R	L	B/L
-	2	1	-	1	-	-	1	-

TRANSUDATIVE PLEURAL EFUSION: 20 cases

Transudative causes	**No of cases**
Cardiac causes-CCF	11
Liver diseases- DCLD	3
Nephrotic syndrome	2
Hypothyroidism	2
Dengue	1
Hypoalbuminemia (malabsorption)	1

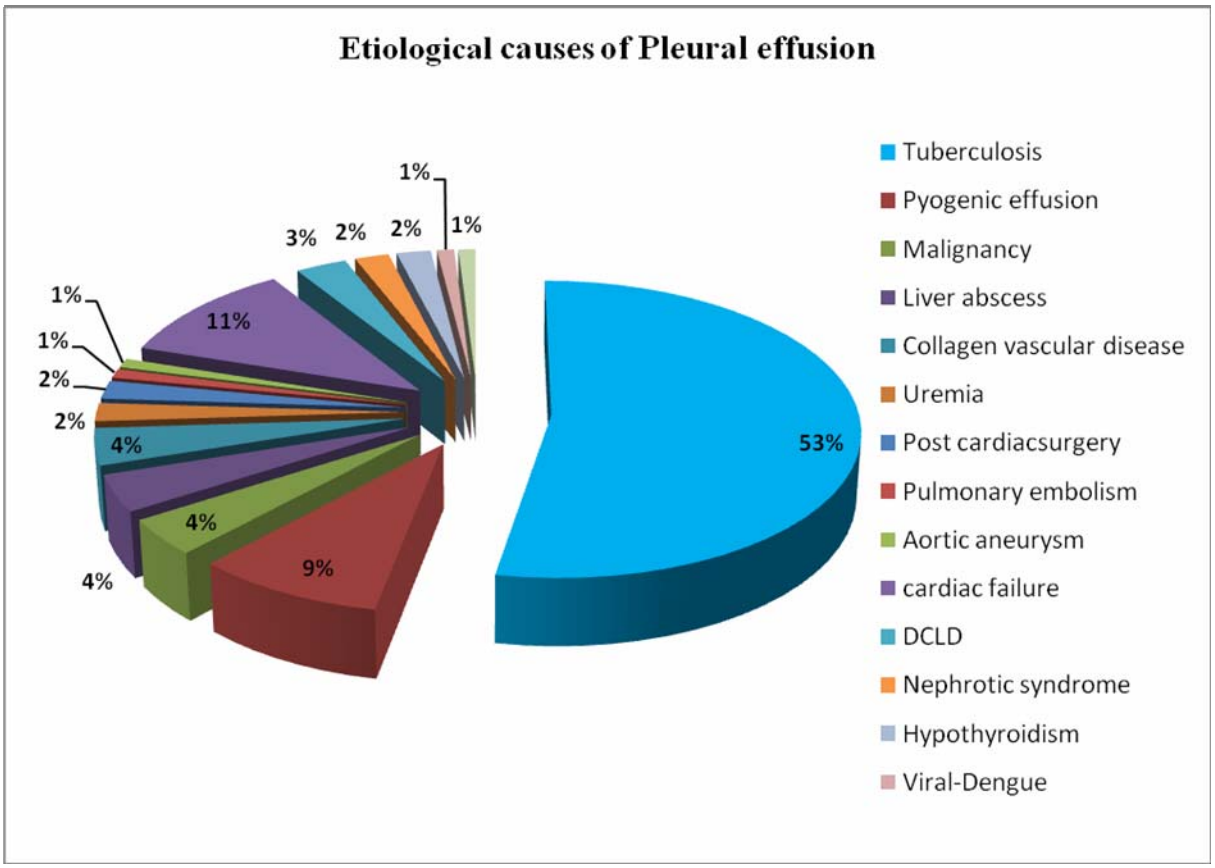
CARDIAC CAUSES OF PLEURAL EFFUSION: (11 cases)

Causes	**No of cases**
Dilated Cardiomyopathy	4
Coronary artery heart disease	4
Rheumatic heart disease/Mitral valve disease	2
Constrictive pericarditis	1

ETIOLOGICAL CAUSES OF PLEURAL EFFUSION in (100 cases):

Tuberculosis	53%
Pyogenic effusion	9%
Liver abscess	4%
Collagen vascular diseases	4%
Malignancy	4%
Uremia	2%
Post-cardiac surgery	2%
Pulmonary embolism	1%
Aortic aneurysm	1%
CCF	11%
DCLD	3%
Nephrotic syndrome	2%
Hypothyroidism	2%
Dengue	1%
Hypoalbuminemia (Nutritional)	1%

ETIOLOGICAL CAUSES OF PLEURAL EFFUSION in (100 cases):



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DISCUSSION

In our study of 100 cases of pleural effusion, there were 69 males and 31 females. The patients were in the age group between 13 to 75 years. The mean age of the patients was 42 years. The peak age of incidence of overall pleural effusion was between 20-40 years.

The most common symptom in our series is Dyspnoea (70 %), followed by cough (55%), fever (54%), and Pleuritic type of chest pain (in 50% cases). Hemoptysis was present in about 9 cases of which 4 were due to Pneumonia, 3 cases were due to bronchogenic carcinoma, one case was due to pulmonary infarction and one in CCF due to pulmonary congestion. None of the tuberculous pleural effusion did not manifest with hemoptysis.

Previous history of tuberculosis was elicited in 14 cases. Of which two cases were recurrent pleural effusion, 11 were pulmonary tuberculosis and the other one was a known Tuberculous abdomen patient. One patient among them was a treatment defaulter. The rest took full course of anti-tuberculous therapy,

The mean Hemoglobin was 10.833 and about 48 cases had their Hemoglobin levels below 11g/dL. The nutritional status of the patients in this series was fairly well. ESR levels were not much informative in this series and it varied widely from and even normal in 10 cases of tuberculous effusion. None of the patients showed positivity for HIV ELISA in this study.

Overall right sided effusions (50%) were more common in our study. Followed by left sided effusion in 33% cases and bilateral effusion in 17% cases. Pleural fluid

analysis showed that straw coloured fluids were common in 52 % cases followed by clear fluid in 20% cases. Hemorrhagic fluid was seen in 3 % cases of pleural effusion (hydropneumothorax, carcinoma lung and pulmonary infarction due to pulmonary thromboembolism). The cell count varied widely between 5-120000 cells/cmm in transudative effusion and tubercular effusion respectively. In 4 cases of malignant pleural effusion the cytology was positive in 2 cases only. Most of the cases showed a Lymphocyte predominant effusion, in nearly 85 % cases. Polymorphonuclear predominant effusions were more common in pyogenic infections. 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 a Pseudomonas Pyopneumothorax in an emphysematous patient and a Klebsiella induced syn-pneumonic pleural effusion. The mean value of pleural fluid glucose was 69.85 mg/dl and extremely low sugars were seen in patients with malignancy and pyogenic infections. In Rheumatoid arthritis the sugar values were around 30 mg/dl.

There were about 80 cases of exudative effusion and 20 cases of transudative effusion. The pleural fluid protein values ranged from 1.9 g/dl to 8.2 g/dl in exudative effusion. About 11 cases had protein values less than 3 g/dl. The mean value of Pleural fluid protein was 4.392 g/dl. All these 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. The rest of the transudative effusions had a protein value less than 2.3 g/dl.

The most common cause of exudative effusion is tuberculous pleural effusion (50% cases in our study)

TUBERCULOUS PLEURAL EFFUSION: (50%, 50 cases)

Of the 50 cases, 39 were males and 11 were females. Most of them were between 21-40 years of age (29 cases, 58%). The most common symptom at presentation is pleuritic chest pain (20 cases, 40%), followed by fever (15 cases, 30%), dyspnoea (10 cases, 20%). One patient presented with seizures and was found to have tuberculoma brain with incidental tuberculous pleural effusion. The most common symptoms perceived by the patients were Pleuritic chest pain (70% cases), followed by dyspnoea (66%), fever (64%), weight loss and anorexia in 50% cases. Night sweats were present in only 30 % cases.

8 cases of tuberculous pleural effusion had a definite past history of tuberculosis, One with TB abdomen, 2 cases with pleural effusion, and the rest all had pulmonary tuberculosis. All of them took complete treatment except one defaulter. 11 cases gave positive contact history with tuberculosis with their family members and friends. Out of 50 cases, 22 were chronic smokers.

Only two patients had an associated bronchial breath sound (cavernous type) clinically with end inspiratory crackles. Other three cases had radiologically identifiable radio dense infiltrates in the chest X ray.

Out of the 50 cases only 3 cases were found to be sputum AFB positive and 3 cases were found to show reactivity for Mantoux test. Right sided (24 cases) effusion is common than left sided effusion (22 cases). Most of them had moderate effusion and massive effusion was seen in 3 cases (6%) only. Most of them had straw coloured pleural fluid on aspiration. The mean protein was about 4.633 g/dl. 49 cases had pleural fluid protein >3 g/dl only one patient had a value of about 1.9 g/dl. Pleural

fluid ADA levels were estimated in 35 cases of tuberculous effusion. In Tuberculous effusions the values ranged from 25 – 239 IU/L. The mean ADA level in TB effusion is 123.213 IU/L. Only 3 cases of TB effusion had their values less than 45 IU/L.

Pleural Biopsy was done only in 6 patients with suspected tuberculous effusion. All of them showed caseating tuberculous granuloma with surrounding area of epitheloid cells and lymphocytes.

In rest of the cases 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, PCR and Gamma interferon. 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.

Other associated conditions observed with Tuberculous effusion:

a. 3 cases of pleural effusion had associated pericardial effusion. One case of tuberculous empyema had tuberculous pericarditis. The ECG of whom showed changes consistent with pericarditis, ST elevation in all the leads & PR segment depression.
b. One case presented with convulsions and later he was evaluated to have tuberculoma brain with incidental TB pleural effusion.
c. 2 cases had associated Tuberculous ascites and one case of cirrhosis of liver had a tuberculous effusion.
d. One case of Liver abscess had biopsy proven tuberculous pleural effusion.

e. One case had tuberculous meningoencephalitis presented with alterd sensorium and high grade fever along with tuberculous pleural effusion.

EMPYEMA: (4 cases)

Empyema secondary to tuberculosis- 2 cases of which one had a tuberculous pericarditis with pericardial effusion a 13 year old girl with sputum positive pulmonary tuberculosis.

Other two cases were secondary to liver abscess, probably secondary to rupture into thoracic cavity.

All of them had an acute presentation with classical signs and symptoms.

SYNPNEUMONIC PLEURAL EFFUSION :(8%)

8 Cases of pleural effusion occurred secondary to pneumonia. All the patients were middle aged persons -7 men and one women. All of them had cough with sputum production, fever and radiological evidence of consolidation on the right side (5 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 klebsiella. One patient had a Lung abscess in the left lower lobe for which he presented with foul smelling sputum and halitosis.

PYOGENIC PYOPNEUMOTHORAX: (1%)

One case of pyopneumothorax was present. He is a 55 year old male. His pleural fluid culture was positive for Pseudomonas. He had associated Emphysema which may responsible for the development of pneumothorax.

MALIGNANT EFFUSION: (4%)

Out of 100 cases of pleural effusion malignant effusion was found in 4 cases only 3 cases were associated with Carcinoma Lung- two being squamous cell carcinoma.

a. A 50 year old female presented with chest pain, dyspnoea, hemoptysis, weight loss and anorexia. She had a left cervical Lymphadenopathy, L lower lobe heterogeneous mass lesion in CT thorax and a left sided moderate pleural effusion. Her pleural fluid showed positive cytology for malignant cells. Lymph node excision biopsy revealed Metastatic squamous cell carcinoma from the lung.

b. A 75 year old chronic smoker presented with dyspnoea, hemoptysis, weight loss , anorexia ,left massive Hydropnuemothorax with right upper lobe Mass lesion, Mediastinal mass lesion and mediastinal emphysema. CT guided Lung biopsy revealed a poorly differentiated squamous cell carcinoma.

c. A 69 year old female presented with cough with sputum production, weight loss and hemoptysis was evaluated to have Left hemorrhagic pleural effusion with a left lower lobe mass lesion invading into the pericardium and presenting with large hemorrhagic pericardial effusion. CT guided Lung biopsy of mass revealed the lesion as moderately differentiated Grade III Adenocarcinoma.

d. One another case was an ovarian tumor, a 47 year old female presenting with abdominal pain and hypogastric mass. She was found to have ascites, Right pleural effusion secondary metastatis to the right side 10^{th} and 11^{th} ribs. USG abdomen revealed a mixed echogenic mass in Right adnexa and ascites. Biopsy of the abdominal mass revealed a Papillary serous cystadenocarcinoma.

LIVER ABSCESS : (4%)

Four cases of Pleural effusion secondary to liver abscess were seen. Of which two were frank empyema. All the four had fever and abdominal pain. Presented with an exudative effusion. Only one had a positive pleural fluid culture for Pseudomonas.

UREMIA: (2%)

Two cases of pleural effusion, one due to ARF and other due to CKD seen in 40 year old females. Both of them presented with dyspnoea and volume overload signs. Both had exudative effusion with few lymphocytes.

COLLAGEN VASCULAR DISEASES: (4%)

Two cases of Rheumatoid arthritis and two cases of SLE were seen. All the four persons were middle aged females. All the four patients had exudative effusion and one patient with rheumatoid arthritis had elevated ADA levels and positive RA factor in the pleural fluid.Pleural fluid glucose levels were low~30 mg/dl. Right side effusions were seen in Rheumatoid arthritis patients whereas bilateral pleural effusion. was seen in SLE patients.

POST CARDIAC SURGERY STATUS: (2 %)

Two cases of post-thoracostomy status were seen. A 37 year old female, a known Rheumatic Heart disease underwent a closed mitral commisurotomy 1 month before the date of admission, was found to have an incidental pleural effusion when she was admitted for malarial fever.

Other one is 55 year old male, who underwent a CABG 3 months before the present admission, admitted for abdominal distension, found to have a minimal left pleural effusion, a minimal pericardial effusion.

PULMONARY EMBOLISM WITH INFARCTION: (1%)

A 30 year old female admitted with sudden onset dyspnoea and chest pain, supraventricular tachycardia was found to have a large pulmonary embolism occluding the Right main pulmonary artery to lower lobe. Later she developed pulmonary infarction with hemorrhagic pleural effusion and hemoptysis. (fig 6 & 7)

AORTIC ANEURYSM: (1%)

A 60 year old male, known Hypertensive with left sided chest pain, palpitations and neck pain, was found to have superior mediastinum widening and further investigations revealed a large saccular aortic aneurysm of 10.6-6.4 cm size, involving the arch of aorta and descending thoracic aorta and eroding the adjacent vertebrae is visualized in the CT and MRI study of the thorax.(fig 8 & 9)

Transudative causes:

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

CARDIAC DISEASES: (11%)

The commonest cause of transudative effusion in our study is due to cardiac failure. 11 cases presented with features of cardiac failure and pleural effusion. All the cases were above 45 yrs of age except one, a rheumatic heart disease patient who was about 19 years of age. Out of 11 cases 8 were male and 3 were female. 6 cases had a bilateral pleural effusion, 3 cases presented with right sided effusion and two with left sided effusion. Out of the 11 cases, 4 cases were due to Coronary artery Heart disease in whom the ECG changes were consistent with an old Ischemia and

Echocardiograohically proven global Hypokinesia with poor ejection fraction. The rest 4 cases were due to Dilated Cardiomyopathy, two cases were due to Rheumatic Heart disease and one case was due constrictive pericarditis presenting with congestive cardiac failure. All the patients had the following common features:

1. Dyspnoea was present in all the cases. Other common symptoms include orthopnea and paroxysmal nocturnal dyspnoea.
2. Pedal edema was present in all the cases
3. JVP was elevated in all the cases, and there were absent a wave in RHD cases with Atrial fibrillation and a prominent y descent in Constrictive pericarditis.
4. Atrial fibrillation was present in 2 cases of Rheumatic heart disease.
4. Cardiomegaly was present in 10 cases and pulmonary congestion in 4 cases only.
5. Congestive hepatomegaly in 6 cases and ascites was present in two cases.
6. Mild pericardial effusion was present in 2 cases and moderate effusion in one case of constrictive pericarditis.
7. MR murmur due to LV dysfunction and DCMP was seen in 4 cases, RHD in one case. TR murmur due RVF was seen in 3 cases.

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

Hepatic hydrothorax was present 3 cases of which 2 were middle aged males and the other is a middle aged female. All of them presented with abdominal distension, dyspnoea and pedal edema. One patient had Jaundice at the time of presentation. All of them had ascites with splenomegaly. SAAG values were>1.1 mg/dL in all the patients. All of them had cirrhosis of liver with portal hypertension and ascites. The causes for cirrhosis include alcoholic liver disease and cryptogenic

cirrhosis of liver. One case had a massive pleural effusion and other two had a minimal left sided and bilateral effusion respectively.

NEPHROTIC SYNDROME: (2%)

Two cases of nephrotic syndrome presented with facial puffines, pedal edema and abdominal distension. One was a 13 year old male and other a 19 year old female. Both of them had a nephrotic range of proteinuria > 3.5 g/day, with a normal urea and creatinine levels, with hypercholesterolemia. One patient had a right minimal effusion whereas the other had a bilateral pleural effusion.

HYPOTHYROIDISM: (2%)

Two cases of hypothyroidism, one a 57 year old female and other 61 year old male, presented with dyspnoea, obesity, constipation were found to have pericardial and pleural effusion. In both the cases the TSH levels were elevated > 100mIU/L and free T4 and T3 levels were low.

HYPOALBUMINEMIA: (1%)

One case of Hypoalbuminemia was recorded with pleural effusion and ascites in a 55 year old female, in whom the serum albumin were 2.1 g/dL and associated rheumatic heart disease without any evidence of congestive cardiac failure. She had features of abdominal wall edema, pedal edema malabsorption and her stool microscopy revealed Giardia trophozoites.

DENGUE: (1%)

One case of dengue fever (24 year, Male) developed a minimal pleural effusion and mild ascites which recovered spontaneously without any intervention.

RESOLUTION OF PLEURAL EFFUSION[80]

Diseases	Incidence	Therapy	Resolution time
Parapneumonic effusion [a]			
Non HIV	40-90 %	Antibiotics	2-3 weeks
HIV positive	21 %	Antibiotics	2-3 weeks
Tuberculosis			
Non-HIV	3-23%	No therapy	2-4 months
		ATT	1-2 months
		ATT + Steroids	1-2 months
HIV positive	3-40%	ATT	1-2 months
Congestive cardiac failure	40-60%	Diuretics, ACE-I, Digoxin	< 1 month
PCIS:			
Post Myocardial infarction	40-68%	NSAIDS, Prednisone	1-5 wk (1 wk-4 mo)
Post pericardiotomy	41-85%	NSAIDS, Prednisone	1-3 wk (1 wk-4 mo)
Post CABG	40- 90%	Self limited	8 wk (6 wk-20 mo)
RA	4-7%	NSAIDS, Prednisone	3-4 mo (1mo- 5 yr)
SLE	16-37%	Corticosteroids	2 wk (1-6 wk)
Sarcoidosis	0-7.5%	Self limited, Prednisone	1-3 mo (2 wk- 6 mo)
Pulmonary embolism	10-50%	Heparin, LMWH	< 1 wk (3-7 days)
Uremia	2-3%	Hemodialysis	4-6 wk
Pancreatitis			
Acute	4-20%	Treat acute pancreatitis	2 wk (1-8 wk)
Chronic	5%	TPN, Thoracocentesis	2-3 wk (1-8 wk)
Benign asbestos effusion	1-9%	Self limited	3-4 mo (1-17 mo)
After organ transplantation			
Lung and heart-lung	100%	Self-limited	2-3 wk (3d –7 mo)
Liver	50-100%	Self-limited	2-3 wk (3d – 7 mo)

a- Uncomplicated, ATT- anti tuberculous therapy, TPN-Total perenteral nutrition

CONCLUSION

100 cases of pleural effusion admitted in the medical wards of Stanley Medical college, Chennai were investigated and the following conclusions were made.

1. The spectrum of etiological causes ranges from Tuberculosis to Hypoalbuminemia
2. The most common cause of pleural effusion is Tuberculosis (50%) followed by congestive cardiac failure (11%)
3. The peak age of incidence of overall pleural effusion is between 21-40 years. The peak age of Tuberculous effusion is between 21-40 years of age.
4. Most common symptom of overall pleural effusion is Dyspnoea (70%)
5. Most common symptom of tuberculous pleural effusion is Pleuritic chest pain (70 %) followed by Dyspnoea (66%)
6. Right sided effusions (50%) are more common.
7. Rare causes of Pleural effusions noted in this study are:
    - Papillary serous cystadenocarcinoma of ovary
    - Pulmonary thromboembolism
    - Collagen vascular diseases-RA and SLE
    - Post cardiac surgery
    - Aortic aneurysm
    - Hypothyroidism

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NAME : I.P. NO:
AGE :
SEX:
OCCUPATION:
ADDRESS:

CLINICAL HISTORY:
CHEST PAIN : DUR: TYPE: PLEURITIC/ CONTINUOUS
BREATHLESSNESS: DUR: CLASS:
FEVER: DUR: LOW GRADE / HIGH GRADE
COUGH DUR: DRY / PRODUCTIVE
SPUTUM PRODUCTION: QUANTITY / PURULENT
HEMOPTYSIS:
WEIGHT LOSS:
LOSS OF APPETITE:
NIGHT SWEATS:
ORTHOPNEA: PND:
SWELLING OF FEETS / FACE:
ABDOMINAL DISTENSION:
OLIGURIA:
JAUNDICE:
ABDOMINAL PAIN:
JOINT PAINS / JOINT SWELLING:
MORNING STIIFNESS:
RASHES- PHOTOSENSITIVITY:
TRAUMA TO THE CHEST:

PAST HISTORY:
TB: DM:
ALD/DCLD: HT:
CKD: CAHD:
THYROID DISORDERS: CONTACT TB :
OTHERS: ASPIRATION/ GENERAL ANESTHESIA/ EPILEPSY/ COMA

PERSONAL HISTORY:
SMOKER : DUR:
ALCOHOLIC: DUR:
EXPOSURE TO STI:
MENSTRUAL HISTORY: MENSTRUAL IRREGULARITY:

DRUG INTAKE:
NITROFURANTOIN/AMIODARONE/ PHENYTION/ METHOTREXATE

CLINICAL EXAMINATION:
BUILD & NUTRITION:
FEBRILE / AFEBRILE:
PALLOR: ICTERUS:
LYMPHADENOPATHY: CLUBBING:
PEDAL EDEMA:
THYROID:

EXTERNAL MARKERS OF TUBERCULOSIS:
EXTERNAL MARKERS OF LIVER DISEASE:
JVP: `PULSE: BP: R.R.:

EXAMINATION OF RESPIRATORY SYSTEM:

POSITION OF TRACHEA:
APICAL IMPULSE:
CHEST WALL MOVEMENTS:
VOCAL FREMITUS/VOCAL RESONANCE:
PERCUSSION: KRONIG ISTHMUS/ TRAUBE'S SPACE OBLITERATION
SHIFTING DULLNESS:
AUSCULTATION: BREATH SOUNDS / ADDEDSOUNDS
COIN PERCUSSION/ SUCCUSSION SPLASH
PLEURAL RUB /

EXAMINATION OF OTHER ASYSTEMS:

C.V.S.: S_3
ABDOMEN: HEPATOMEGALY/ ASCITES / SPLENOMEGALY
C.N.S.:

INVESTIGATIONS:

1. HB g/dl :
   T.C.
   D.C.
   ESR:
   PLATELET COUNT:
2. URINE : ALBUMIN:
   SUGAR :
   DEPOSITS:
3. R.B.S:
   BLOOD UREA:
   SERUM CREATININE:
   SERUM ELECTROLYTES: Na K
4. MANTOUX TEST:
5. CHEST X RAY : EFFUSION: MILD / MODERATE / MASSIVE
   PA VIEW:
   LATERAL VIEW:
   DECUBITUS VIEW:
6. ECG:
7. SPUTUM CULTURE & SENSITIVITY:
8. SPUTUM AFB STAINING:
9. LIVER FUNCTION TEST
   TOTAL BILIRUBIN: DIRECT: INDIRECT:

SGOT: SGPT: ALP:
TOTAL PROTEIN:
SERUM ALBUMIN:

10. PLEURAL FLIUD ANALYSIS:

COLOUR: STRAW / HEMORRHAGIC/ PUS
CELL COUNT: TOTAL & DIFFERENTIAL COUNT
CYTOLOGY :
BIOCHEMICAL: SUGAR:
PROTEIN:
LDH:
PLEURAL FLIUD/ SERUM PROTEIN RATIO:
GRAM STAINING:
ZN STAINING :
CULTURE & SENSITIVITY:
ADA:
SPECIAL INVESTIGATIONS: HEMATOCRIT/TGL/ANA/RA / AMYLASE

11. PLEURAL BIOPSY:

12. USG: CHEST & ABDOMEN:

13. CT SCAN THORAX / BRAIN (IF NEEDED):
:

14. ECHOCARDIOGRAPHY:

15. SPECIAL INVESTIGATIONS:
PERICARDIAL FLUID ANALYSIS:
ASCITIC FLUID ANALYSIS:
THYROID FUNCTION TESTS:
SERUM ANA / RA FCTOR / AMYLASE
24 HR URINE PROTEINS:
SPUTUM MALIGNANT CELL CYTOLOGY:

16. .ELISA:

FINAL DIAGNOSIS: -

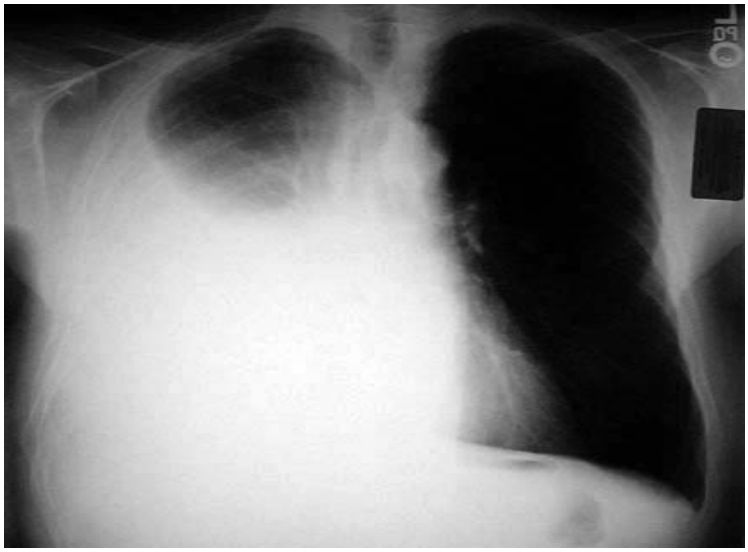

Fig 1.Right sided Malignant pleural effusion

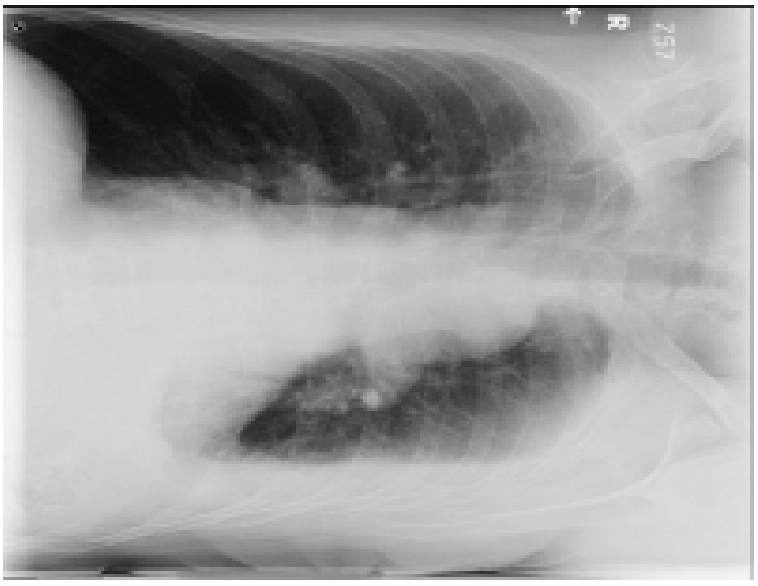

Fig 2. Left lateral decubitus view, Moderat left sided Pleural effusion

ABRAM' PLEURAL BIOPSY NEEDLE:

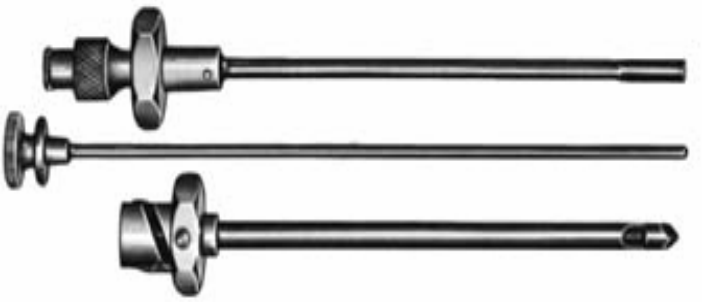

Fig 3. 3 piece instrument comprises 8G x 3 1/2" outer cannula with trocar point and cutting window which can be closed with a turning action of the inner tube, thus catching severed tissue.

COPE'S PLEURAL BIOPSY NEEDLE

Fig 4. Consists of 5 parts, including an 11G outer needle with tapered end and an adjustable needle stop. Inner 13G needle has beveled point and fitted stylet. Inner 13G biopsy snare has hook shape for sample collection.

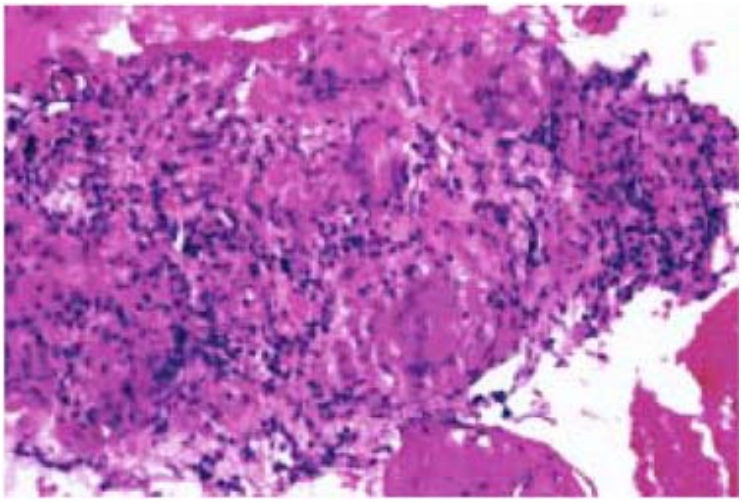

Fig 5. Pleural biopsy specimen of a Tuberculous pleural effusion patient demonstrating granulomatous inflammation with central caseation.

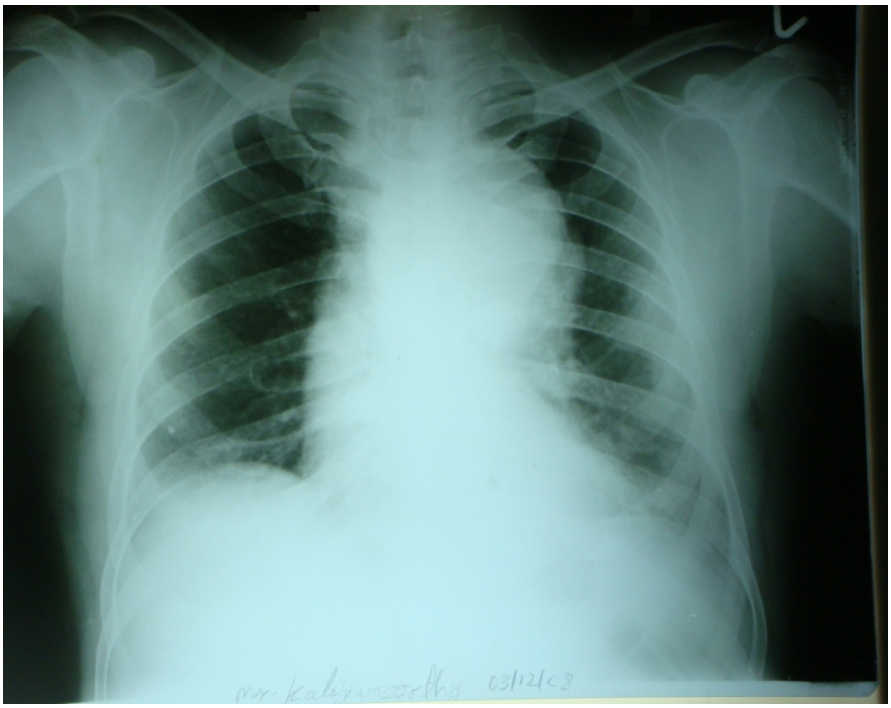

Fig 8: Aortic aneurysm with Left minimal pleural effusion

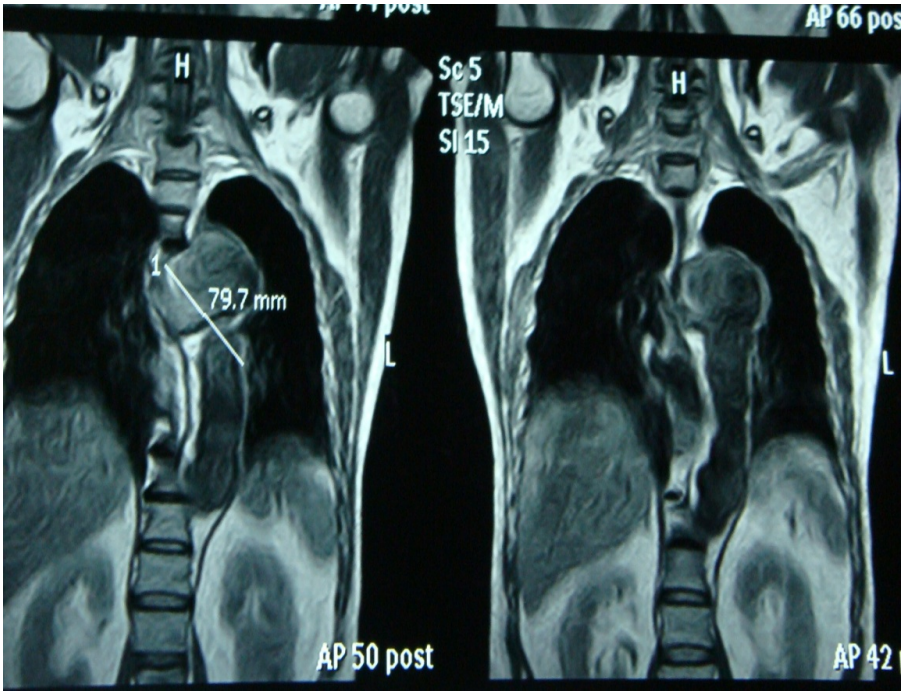

Fig 9: Large saccular aneurysm 10.6-6.4 cm arch of aorta and Descending thoracic aorta aneurysm eroding into the adjacent vertebrae With left minimal pleural effusion (MRI thorax)

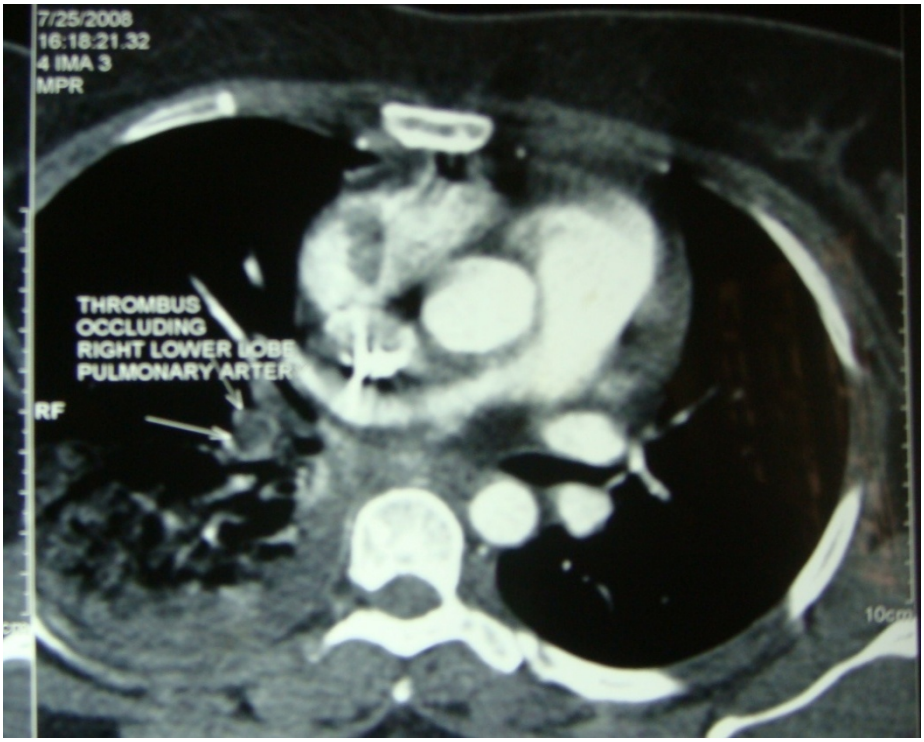

Fig 6 : CT Pulmonary angiography: revealing a Large thrombus occluding Rt lower lobe pulmonary artery with Lower lobe pulmonary infarction and Rt pleural effusion.

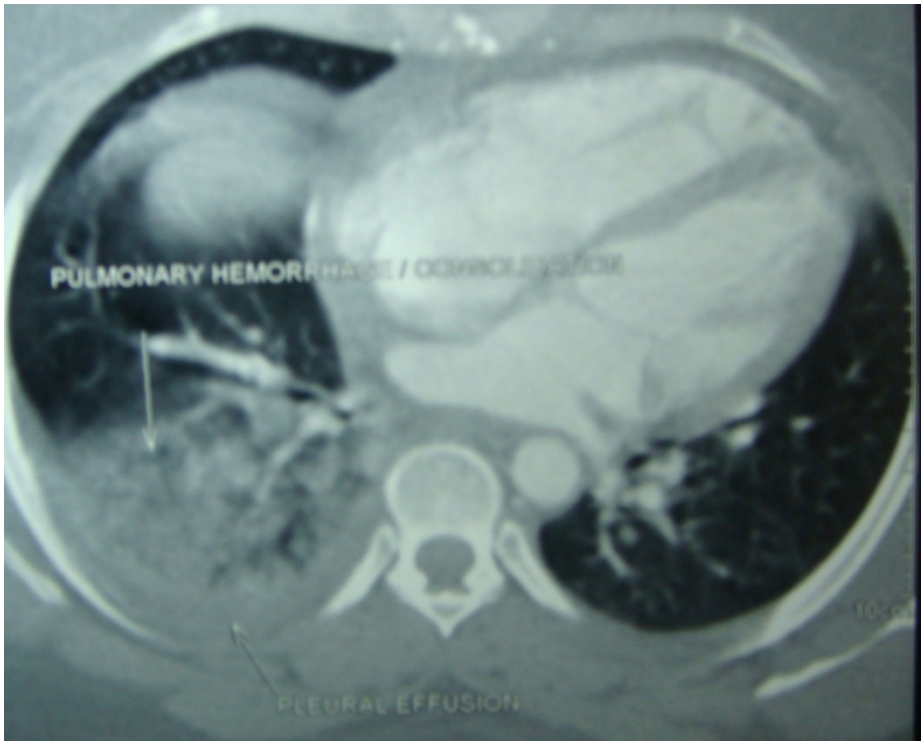

Fig 7 : CT thorax of same patient with pulmonary hemorrhagic infarction and Rt pleural effusion.