“Efficacy of Total Pleural fluid Bilirubin and ratio to serum levels , Pleural fluid Cholesterol and Total Protein level in diagnosing Pleural Effusion Exudates and Transudates and its correlation with Light’s criteria”

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This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the rules and regulations for the award of **M.D Degree General Medicine Branch- I**; examination to be held in **April 2015.**

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ABSTRACT

INTRODUCTION

Pleural effusion is a very common clinical presentation of diseases. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. Therefore, the first step is to classify them as transudates or exudates. Light's criteria is the most commonly used method . It was found that even Light's criteria misclassified a large number of effusions , 25% of transudates as exudates.

Hence, there is a need to investigate into new parameters which will prove to be superior or supportive to the present available array of tests. Hence, this study is being done to evaluate the Efficacy of Total Pleural fluid Bilirubin and its ratio to serum Bilirubin levels, Pleural fluid Cholesterol and Pleural fluid total Protein level in classifying the Pleural Effusion as Exudates and Transudates and its correlation with Light's criteria.

AIMS AND OBJECTIVES

To evaluate the usefulness of Total Pleural fluid Bilirubin and its ratio to serum Bilirubin levels, Pleural fluid Cholesterol and Pleural fluid Total Protein level in classifying pleural effusions as exudates and transudates.

MATERIALS AND METHODS :

STUDY POPULATION :

This study is to be conducted among 50 patients with pleural Effusion , attending the Department of Medicine & Department of Thoracic Medicine in Govt. Rajaji Hospital, Madurai

STUDY PROTOCOL:

- Patients with clinical and radiological evidence of pleural effusion are to be included in the study.Then they are classified in to exudates and transudates on the basis of the clinical , radiological and biochemical evaluation .
- Pleural fluid bilirubin & Serum Bilirubin , Pleural fluid cholesterol, Pleural fluid total protein are estimated and the patients are classified in to exudates and transudates. Then the patients are classified in to exudates and transudates on the basis of Light's criteria.
- Now the classification of exudates and transudates done on the basis of Total Pleural fluid bilirubin and its ratio to serum bilirubin , Pleural fluid cholesterol , Pleural fluid Total protein are compared with results of the classification of exudates and transudates done on the basis of Light's criteria.
- Sensitivity , specificity , Positive predictive value , negative predictive value , diagnostic accuracy of each testsare calculated .

RESULTS :

From our study we came to known that there was no statistically significant difference among various criterias in classifying pleural effusion as exudates and transudates. The misclassification of exudates and transudates by various criteria when compared to Light's criteria is not statistically significant as p value is <0.05.

CONCLUSION :

From our study we came to a conclusion that to classify an exudative pleural effusion from a transudative pleural effusion

- most specific test is pleural fluid total protein and
- most sensitive test is pleural fluid / serum bilirubin ratio .

The positive predictive value, negative predictive value and diagnostic accuracy is higher for pleural fluid total protein .

To conclude, though Light's criteria remains as gold standard to differentiate transudates and exudates, in cases where there is a mismatch between clinical diagnosis and the outcome from Light's criteria, pleural fluid bilirubin / serum bilirubin ratio and pleural fluid total protein evaluation may add to the diagnostic accuracy.

KEYWORDS : Pleural fluid , bilirubin ,cholesterol , pleural fluid total protein, Light's criteria ,exudates , transudates

INTRODUCTION

Pleural effusion is a very common clinical presentation of diseases. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. A limited number of diseases causes transudative pleural effusions, whereas exudative effusions require more extensive diagnostic investigations. Therefore, the first step is to classify them as transudates or exudates, even if this differentiation does not contribute to the etiological diagnosis.

Many criteria have been used to distinguish them, but none of them have been found to be satisfactory. Light's criteria is the most commonly used method

The criteria is one or more of the following for diagnosing exudates.

1.pleural fluid protein /serum protein >0.5

2.pleural fluid LDH/serum LDH >0.6

3.pleural fluid LDH more than 2/3 rd of the upper limit of serum.

It was found that even Light's criteria misclassified a large number of effusions , 25% of transudates as exudates.

Hence, there is a need to investigate into new parameters which will prove to be superior or supportive to the present available array of tests. Many other biochemical markers like bilirubin, cholesterol, and albumin are there.

Hence, this study is being done to evaluate the Efficacy of Total Pleural fluid Bilirubin and its ratio to serum Bilirubin levels, Pleural fluid Cholesterol and Pleural fluid total Protein level in classifyingthe Pleural Effusion as Exudates and Transudates and its correlation with Light's criteria.

AIMS AND OBJECTIVES

To evaluate the usefulness of Total Pleural fluid Bilirubin and its ratio to serum Bilirubin levels, Pleural fluid Cholesterol and Pleural fluid Total Protein level in classifying pleural effusions as exudates and transudates.

REVIEW OF LITERATURE

Definition

Pleural effusion is defined as the abnormal accumulation of pleural fluid within the pleural cavity. Crucial feature of the breathing apparatus is the pleural space. This is a potential space between the parietal pleura and the visceral pleura It is the coupling system between the lung and the chest wall .

ANATOMY OF PLEURA

The lung parenchyma, the diaphragm , the mediastinum and the rib cage are covered by a serous membrane called the pleura. Pleura is divided into visceral pleura and parietal pleura. At the lung root , the visceral and parietal pleura meet.

Visceral pleura :

It covers the lung parenchyma in its points of contact with the diaphragm , the mediastinum and the chest wall and also in the interlobar fissures.

Parietal pleura :

It lines inside of the thoracic cavities.

It is subdivided on the basis of intrathoracic structures that it lines in to

1. Costal parietal pleura ,
2. Mediastinal parietal pleura,
3. Diaphragmatic parietal pleura.

Pulmonary ligament :

This is a thin double fold of pleura formed due to the downward extension of the pleura , posterior to the lung root.

Pleural space :

This is a potential space between the the visceral pleura and parietal pleura.

Pleural fluid :

This is a thin film of fluid normally present in between the visceral pleura and parietal pleura ie., pleural space

Functions of pleural fluid - acts as a lubricant . During the respiratory movements the pleural fluid allows the visceral pleura which is covering the lung to slide along the parietal pleura which is lining the thoracic cavity.

HISTOLOGY OF PLEURA :

Parietal pleura - composed of loose , irregular connective tissue which is covered by a single layer of mesothelial cells. Within the pleura there are blood vessels , mainly capillaries and lymphatic lacunas. Endothoracic fascia is situated deeper to parietal pleura. This is a continuous dense band of irregular connective tissue. This is mainly composed of elastin and collagen and it covers ribs and intercostal spaces.

Visceral pleura – composed of two layers namely the mesothelium and the connective tissue.

Connective tissue layer functions :

1. Contributes to elastic recoil of lung ,helps in expelling air from the lung
2. Restricts the volume of lung to which the lung can be inflated , and thereby protecting the lung

Mesothelialcells functions :

It forms a monolayer of pavement like cells lining the pleural surfaces.

1. Movement and transport of particulate matter and fluid across the pleural surfaces .

2. Migration of leucocytes in response to inflammation .
3. Synthesis of cytokines , growth factors , EC matrix proteins .
4. Antigen presentation and transformation to myofibroblasts .

Blood supply :

Parietal pleura receives blood supply from systemic capillaries such as intercostal artery ,pericardiophrenic artery , superior phrenic and musculophrenic artery and drained by intercostal veins , phrenic veins.

Visceral pleura : Blood supply of thin pleura is derived from pulmonary circulation , and that of thick pleura is derived from bronchial arteries. Venous drainage is through the pulmonary veins.

Lymphatic drainage :

Lymphatic plexus in the parietal pleura drains in to intercostal ,mediastinal, tracheobronchial , parasternal and phrenic nodes.

In the parietal pleura the lymphatic vessels are in communication with the stomas, the diameter of which ranges between 2 to 6 microns. The main pathways for the elimination of particulate matter is the stomas with lacuna and lymphaticsvessels .

In the visceral pleura there are abundant lymph vessels which joins bronchial lymph vessels.

Nerve supply :

Intercostal nerves supply the costal and peripheral part of diaphragmatic pleura. So the pain sensation due to inflammation of this pleura is perceived in the chest wall.

Phrenic nerve supplies the central part of diaphragmatic pleura . So when this part of pleura is irritated or inflamed the pain is felt in the ipsilateral shoulder.

PHYSIOLOGY OF PLEURA

Formation of the Pleural Fluid :

Pleural fluid can originate in the

- pleural capillaries,
- the intra-thoracic lymphatics,
- the intrathoracic blood vessels,
- the peritoneal cavity , or
- the interstitial spaces of the lung,

Pleural Capillaries

Starling's law of transcapillary exchange governs the movement of fluid between the pleural capillaries and the pleural space .

Hydrostatic pressure :

In the parietal pleura , the hydrostatic pressure is approximately 30 cm H_2O,but the pleural pressure is approximately -5 cm H_2O. The net hydrostatic pressure is therefore 30 - (-5) = 35 cm H_2O .This pressure favors the movement of fluid from the capillaries in the parietal pleura to the pleural space.

Oncotic pressure :

This hydrostatic pressure gradient is opposed by oncotic pressure gradient. Plasma oncotic pressure is approximately 34 cm H_2O.

Normally, the pleural fluid has an oncotic pressure of approximately 5 cm H_2O, as it contains a small amount of protein .The net oncotic pressure gradient is 34 - 5 = 29 cm H_2O. Thus, the net gradient is 35 - 29 = 6 cm H_2O. It favours the movement of fluid to the pleural space from the capillaries in the parietal pleura.

The net gradient for fluid movement across the visceral pleura in humans is probably close to zero, which has not been demonstrated. The pressure in the parietal pleural capillaries is approximately 6 cm H_2O more than that in the visceral pleural capillaries.

This is because the visceral pleural capillaries is drained by the pulmonary veins**.** Also this is the only pressure that differs from those

pressure affecting fluid movement across the parietal pleura. The net gradient for the parietal pleura is 6 cm H_2O. So the net gradient is approximately zero for the fluid movement across the visceral pleura.

The capillaries in the visceral pleura when compared to those in the parietal pleura , are much farther from the pleural space .So the filtration coefficient (L^p) for the visceral pleura is substantially less than that for the parietal pleura .

When compared with the intercostal spaces ,the fluid formation is more across the parietal pleura over the ribs. Also fluid formation was more over the caudal ribs than over the cranial ribs. But in contrast, pleural liquid absorption was more primarily in the parietal pleura adjacent to the intercostal space rather than in the parietal pleura overlying the ribs. The formation of pleural fluid was more, if the breathing frequency was increased.

Interstitial Origin

It has been demonstrated that the interstitial spaces of the lungs, is the origin of much of the fluid that enters the pleural space. Pleural fluid accumulates if there is either high-pressure or high-permeability pulmonary edema.The elevation in the wedge pressure is directly related to the amount of pleural fluid formed. But only after the development of pulmonary edema, increases in pleural fluid accumulation occur.

In patients with congestive heart failure , the origin of the pleural effusion is probably the pulmonary interstitial space.

It is likely that many conditions associated with lung injury, such as lung transplantation and pulmonary embolization , the origin of the pleural fluid is also the interstitial spaces of the lung.

It has been shown that the subpleural interstitial pressure increases, with increasing levels of interstitial fluid. Even though the visceral pleura is thin, the barrier to the movement of fluid across the visceral pleura appears to be weak. Therefore, once there is increase in subpleural interstitial pressure, the fluid will enter to the pleural space through the visceral pleura.

Peritoneal Cavity

If there is free fluid in the peritoneal cavity, pleural fluid accumulation can occur. Peritoneal fluid enters the pleural space through the openings in the diaphragm. Since the pressure in the pleural cavity is less than the pressure in the peritoneal cavity the fluid will flow from the peritoneal space to the pleural space. In the following conditions like hepatic hydrothorax, Meigs' syndrome, and peritoneal dialysis, the peritoneal cavity is the origin of the pleuralfluid.

Thoracic Duct or Blood Vessel Disruption

If there is disruption of thoracic duct, there is accumulation of lymph in the pleural space.Thiswill produce a chylothorax. With chylothorax the rate of fluid accumulation can be more than 1,000 mL/day.

Origin of Normal Pleural Fluid

It is believed that the fluid that normally enters the pleural space originates in the capillaries in the parietal pleura.

The amount of pleural fluid formed daily is approximately 15 mL in a 50-kg individual. Since in the interstitial spaces the protein level is normally approximately 4.5 g/dL, and the protein level in normal pleural fluid is only approximately 1 to 1.5 g/dL, the origin of the fluid does not appear to be the interstitial spaces of the lung . Pleural fluid with lower protein levels are produced by higher vascular pressures . Evans blue dyed albumin studies with rabbits have demonstrated that most fluid originates in the parietal pleura over the ribs .

Pleural Fluid Absorption

Lymphatic Clearance

The lack of fluid accumulation in normal individuals is due to the clearance of fluid through the pleural lymphatics. By means of stomas in the parietal pleura , the pleural space is in communication with the lymphatic vessels in the parietal pleura. Visceral pleura lacks such stomas. The lymphatics in the parietal pleura, removes proteins**,** cells, and all other particulate matter from the pleural space. The carbon particles exit the pleural space through the stomas ,where the mesothelial cells are small and not flattened . These stoma increases in diameter in response to increased levels of nitric oxide in the pleural space.

In a 60-kg individual the lymphatic drainage from each pleural space is on the order of 20 mL/hr or 500 mL/day.

Once the volume of the pleural liquid exceeds a certainthreshold, the lymphatics operate at maximum capacity. The capacity for lymphatic clearance is 28 times as high as the normal rate of pleural fluid formation.

Clearance through Capillaries in Visceral Pleura

Until the mid-1980s, it was thought that the capillaries in the visceral pleura in humans is the primary route for the exit of fluid from the pleural space.

Through the lymphatics in the parietal pleura almost all the pleural fluid is removed. Several hundred milliliters of water probably traverse the pleural membranes each day. Since the osmolarity is nearly identical on each side of the membrane , the net movement is of only a few milliliters.

Alternative Mechanisms for Pleural Fluid Removal

In the removal of protein from the pleural space , transcytosis plays a role and there is some evidence for that. Only 29% of the overall removal of albumin occurred through the stoma with small hydrothoraces, while 64% of the albumin from large hydrothoraces was removed through the stoma

Pathogenesis of Pleural Effusions

Whenever the rate of pleural fluid formation exceeds the rate of pleural fluid absorption, there is accumulation of pleural fluid.

Normally, from the capillaries in the parietal pleura, a small amount (0.01 mL/kg/hour) of fluid constantly enters the pleural space. The lymphatics in the parietal pleura removes almost all of this fluid . Lymphatics have a capacity to remove at least 0.20 mL/kg/hour. The lymphatics remove the fluid exceeding the normal rate of fluid formation by a factor of 20.

GENERAL CAUSES OF PLEURAL EFFUSION :

A.Increased pleural fluid formation :

1.Increased interstitial fluid in lungs

- Left ventricular failure ,
- Pneumonia ,
- Pulmonary embolism

2. Decreased pleural pressure

- Lung atelectasis
- Lung elastic recoil is increased

3.Increased permeability of pleural capillaries

- Pleural inflammation ,
- Elevated vascular endothelial growth factor levels

4.Increased levels of protein in the pleural fluid

5. Increased intravascular pressure in pleura

- Right or left ventricular pressure ,
- Superior vena cava syndrome

6.Distruption of thoracic blood vessels

7.Thoracic duct distruption

8.Increased fluid in the peritoneal cavity

- Peritoneal dialysis
- Ascites

B.Decreased pleural fluid absorption

1.Obstruction of pleural lymphatic drainage

2.Distruption of aquaporin system in the pleura

3. Elevated systemic vascular pressure

- Superior vena caval syndrome

- Right ventricular failure

1.Increased Pleural Fluid Formation

Whenever there is increased pulmonary interstitial fluid or when one of the terms in Starling's equation is changed , there is increased pleural fluid formation .

a) Increased Interstitial Fluid

Increased interstitial fluid in the lungs is the most common cause of increased pleural fluid formation . As mentioned earlier, irrespective of whether the edema is due to low-protein fluid or high-protein fluid, pleural fluid accumulates, whenever the amount of edema in the lung exceeds 5 g/gram of dry lung weight. In conditions like congestive heart failure, parapneumonic effusions, acute respiratory distress syndrome, and in those who have undergone lung transplantation , this appears to be the predominant mechanism for the accumulation of pleural fluid.

b) Increased Hydrostatic Pressure Gradient

Through Starling's equation ,there will be an increase in the rate of pleural fluid formation , if there is an increase in the gradient between the intravascular pressure and the pleural pressure.

In conditions like right ventricular failure, left ventricular failure, pericardial effusions, or superior vena cava syndrome, there is increase in the intravascular pressure. Atelectasis of the lower lobe or complete lung due to bronchial obstruction is the most common situation producing a decrease in the pleural pressure. When the visceral pleura becomes coated with a collagenous peel and the lung becomes trapped, a decrease in the pleural pressure also occurs. The pleural pressure can become very negative, in these instances ie.,it goes below -50 cm H_2O . Diseases in which the elastic recoil of the lung is increased, the decreased pleural pressures can also contribute to pleural fluid accumulation.

c) Increased Capillary Permeability

If the pleural surfaces become inflamed, the permeability of the capillaries may be increased . The permeability of the capillaries is increased by increased levels of vascular endothelial growth factor (VEGF) .This may be at least partially responsible for the accumulation of pleural fluid. Mesothelial cells have VEGF receptors on their surface which have been demonstrated. In exudative effusions the levels of VEGF are higher when compared to transudative pleural effusions .

d) Decreased Oncotic Pressure Gradient

In conditions likehemothorax, increased - permeability pulmonary edemaand with conditions in which the pleural capillary permeability is increased, the levels of pleural fluid protein is increased. The capacity to remove pleural fluid by the lymphatics is approximately equal to the rate of formation of pleural fluid. Moreover, a very uncommon cause of pleural effusionis hypoproteinemia.

e) Presence of Free Peritoneal Fluid, or Disruption of the Thoracic Duct or anIntrathoracic Blood Vessel :

The free fluid in the peritoneal cavity traverse through the holes in the diaphragm and it will lead to pleural fluid accumulation and pleural effusion. In a similar manner, if there is a disruption in the thoracic duct, chyle will accumulate in the pleural space . And if there is a disruption of a blood vessel in the thorax , blood will accumulate in the pleural space .

2.Decreased Pleural Fluid Absorption

a) Normal Pleural fluid absorption by lymphatics

Normally, the lymphatic flow from the pleural space is approximately 0.01 mL/kg/hour or 15 mL/day because this is the amount of pleural fluid formed.

However, the capacity of the lymphatics is approximately 0.20 mL/kg/hour or 300 mL/day.

b) Obstruction of Lymphatics

Obstruction of the lymphatics draining the parietal pleura is the most common cause of decrease in pleural fluid absorption .In the development of a malignant pleural effusion , lymphatic blockade is an important factor .

c) Elevation of Systemic Venous Pressures

When there is elevation of the pressures in the central veins , lymphatic flow will be decreased. This is because the lymphatics drain into the systemic venous circulation .

The pleural effusions developed because of (a) leakage of lymph out of the lymphatics that pass through the chest (these include the diaphragmatic and pulmonary lymphatics and thoracic duct) ; or (b) leakage of interstitial fluid into the pleural space due to obstruction of lung or chest wall lymphatics .

CLINICAL MANIFESTATIONS OF PLEURAL EFFUSION :

Normally, only a few milliliters of pleural fluid is present in the pleural space. If fluid in the pleural space is detected on a radiologic examination, it is abnormal. Pleural fluid accumulation is associated with many conditions . When pleural fluid is detected, an effort should be made to determine the etiology .

1. Symptoms

In a patient with pleural effusion , symptoms mainly depends on the underlying process causing the effusion . Many patients have no symptoms referable to the effusion. When symptoms are related to the effusion, they arise either from inflammation of the pleura, from compromise of pulmonary mechanics, from interference with gas exchange, or on rare occasions, from decreased cardiac output.

a) Pleuritic chest pain

Normally visceral pleura does not have pain fibers , only the parietal pleura contains pain fibers . In a patient with pleural effusion , pleuritic chest pain always indicates inflammation of the pleura, specifically parietal pleura . Some patients with pleural effusions experience a dull, aching chest pain rather than pleuritic chest pain.

The parietal pleura is innervated mostly by the intercostal nerves. So, the pain associated with pleural disease is well localized and it coincides with

the area of the pleura which is affected by disease . Since the intercostal nerves are also distributed to the abdomen ,pleuritic pain is referred to the abdomen .When the central portion of the diaphragmatic pleura is involved, there are exceptions to the localization of the pain . Phrenic nerve is the nerve supply to this portion of the parietal pleura . Pain is referred to the tip of the ipsilateral shoulder , if the central portion of the diaphragm is inflammed.

Pathognomonic of diaphragmatic involvement is pleuritic pain felt simultaneously in the lower chest and ipsilateral shoulder.

b) Cough

A dry, nonproductive cough is the second symptom of pleural effusion. Although it may be related to pleural inflammation ,the exact mechanism producing the cough is not clear. Alternately, cough reflex is stimulated by the pleural fluid compressing the lung , bringing the opposing bronchial walls into contact.

c) **Dyspnea**

Dyspnea is the third symptom of pleural effusion . As pleural effusion acts as a space-occupying process in the thoracic cavity , it cause dyspnea by reducing all subdivisions of lung volumes.

This explains the small increase in pulmonary function following therapeutic thoracentesis if pleural effusion is associated with parenchymal disease . The

degree of dyspnea is frequently out of proportion to the size of the pleural effusion. Due to the weight of fluid on the diaphragm , the diaphragmatic function is compromised and this results in dyspnea .

2. Physical Examination

a) Inspection

When the chest of a patient with pleural effusion, or who is suspected of having a pleural effusion is examined, particular attention should be paid to the relative sizes of the hemithoraces and the intercostal spaces.

Depending upon the pleural pressure clinical findings vary . The ipsilateralhemithorax will be larger, and the usual concavity of the intercostal spaces will be blunted or even convex, if the pleural pressure on the side of the effusion is increased. In contrast, the ipsilateralhemithorax will be smaller, and the normal concavity of the intercostal spaces will be exaggerated , if the pleural pressure on the side of the effusion is decreased.This occurs with obstruction of a major bronchus or a trapped lung. In addition, the intercostal spaces retract, with inspiratory efforts.

An indication of therapeutic thoracentesis is enlargement of the hemithorax with bulging of the intercostal spaces. This is done to relieve the increased pleural pressure. Of course, the hemithoraces are equal in size and the intercostal spaces are normal, in many patients with pleural effusions.

b) Palpation

To delineate the extent of the effusion , palpation of the chest in patients with pleural effusions is useful. Tactile fremitus is absent or attenuated, in areas of the chest where pleural fluid separates the lung from the chest wall.This is because the vibrations emanating from the lung are absorbed by the fluid .

To identify the upper border of the pleural fluid , tactile fremitus is much more reliable than percussion. It is also useful to identify a proper site to attempt a thoracentesis. Tactile fremitus is much more reliable than percussion , because with a thin rim of fluid, the tactile fremitus is diminished, but the percussion note may still be resonant.

Apical impulse

Palpation may also reveal that the apical impulse is shifted to one side or the other. The apical impulse may not be palpable, in patients with large left pleural effusions.

Position of trachea

The position of the trachea in patients with pleural effusions, always indicates the relationship between the pleural pressures in the two hemithoraces.

c) Percussion

In a patient with pleural effusion the percussion note over the area of involvement is dull or flat. At the lung bases where the thickness of the fluid is the greatest, the dullness is maximum. As mentioned earlier, if only a thin

rim of fluid is present, the percussion note may not be duller. For identifying small amounts of pleural fluid, light percussion is better than heavy percussion.

d) Auscultation

Auscultation over the area of pleural effusion characteristically reveals decreased or absent breath sounds. However,breath sounds may be accentuated and take on a bronchial characteristic, near the superior border of the fluid.

This accentuation of breath sounds does not mean that an associated parenchymal infiltrate is present.

Pleural rub

Auscultation may also reveal a pleural rub. Pleural rubs are most commonly heard during the latter part of inspiration and the early part of expiration, and are characterized by coarse, leathery, creaking sounds producing a to-and-fro pattern of sound. The rubbing together of the roughened pleural surfaces during respiration, causes pleural rubs. Pleural rubs are often associated with local pain on breathing that subsides with breath-holding. Pleural rubs often appear as pleural effusions diminish in size, either spontaneously or as a result of treatment, because the pleural fluid is no longer present between the roughened pleural surfaces.

It is important to realize that , all the classic physical findings associated with a pleural effusion can be produced by an elevated hemidiaphragm.

Obviously, while evaluating a patient with a pleural effusion ,the chest is not the only structure that should be examined. Because clues to the origin of the effusion are often present elsewhere.

Here are some of the causes of pleural effusion and their clinical findings that are helpful in the diagnosing the patient.

Systemic cause and clinical findings :

1. If the patient has cardiomegaly, neck vein distension, or peripheral edema, the effusion is probably due to congestive heart failure (CHF) .
2. The pleural effusion is due to rheumatoid disease or lupus erythematosus (LE) if the patient has signs of joint disease or subcutaneous nodules .
3. Metastatic disease, as do breast masses is suspected as the cause of pleural effusion if there is an enlarged, nontender nodular liver or the presence of hypertrophic osteoarthropathy.
4. In patients with subdiaphragmatic pathology there will be abdominal tenderness.
5. Tense ascites suggests cirrhosis and a hepato thorax.
6. Lymphoma, sarcoidosis or metastatic disease should be suspected if there is lymphadenopathy.

DIFFERENTIAL DIAGNOSIS OF PLEURAL EFFUSION :

I. Transudative pleural effusions

A. Congestive heart failure

B. Cirrhosis

C. Nephrotic syndrome

D. Cerebrospinal fluid leaks to pleura

E. Hypoalbuminemia

F. Sarcoidosis

G. Peritoneal dialysis

H. Glomerulonephritis

I. Myxedema

J. Superior vena caval obstruction

K. Fontan procedure

L. Urinothorax

II. Exudative pleural effusions

A. Neoplastic diseases

1. Metastatic disease
2. Mesothelioma
3. Pyothorax-associated lymphoma

4. Body cavity lymphoma

B. Infectious diseases

1. Bacterial infections
2. Tuberculosis
3. Viral infections
4. Parasitic infections
5. Fungal infections

C. Pulmonary embolization

D. Gastrointestinal disease

1. Pancreatic disease
2. Subphrenic abscess
3. Intrahepatic abscess
4. Heart diseases Postcoronary artery bypass graft surgery
5. Postcardiac injury (Dressler's) syndrome
6. Pericardial disease
7. Diaphragmatic hernia
8. Endoscopic variceal sclerosis
9. Postliver transplant
10. Pulmonary vein stenosis postcatheter ablation of atrial fibrillation
11. Intrasplenic abscess
12. Esophageal perforation

13.Postabdominal surgery

E.Obstetric and gynecologic disease

1. Ovarian hyperstimulation syndrome
2. Fetal pleural effusion
3. Endometriosis
4. Postpartum pleural effusion
5. Meigs' syndrome

F.Collagen vascular diseases

1. Rheumatoid pleuritis
2. Systemic lupus erythematosus
3. Familial Mediterranean fever
4. Churg-Strauss syndrome
5. Wegener's granulomatosis
6. Drug-induced lupus
7. Immunoblastic lymphadenopathy
8. Sjogren's syndrome

G.Drug-induced pleural disease

1. Ergot drugs
2. Amiodarone

3. Interleukin 2
4. Nitrofurantoin
5. Dantrolene
6. Methysergide
7. Procarbazine
8. Clozapine
9. Methotrexate

H.Miscellaneous diseases and conditions

1. Sarcoidosis
2. Uremia
3. Trapped lung
4. Acute respiratory distress syndrome
5. Whipple's disease
6. Iatrogenic pleural effusions
7. Asbestos exposure
8. Postlung transplant
9. Postbone marrow transplant
10. Yellow nail syndrome
11. Electrical burns

12.Extramedullaryhematopoiesis

13.Rupture of mediastinal cyst

14.Therapeutic radiation exposure

15.Drowning

16.Amyloidosis

17.Milk of calcium pleural effusion

I.Hemothorax

J. Chylothorax

GENERAL TESTS TO DIFFERENTIATE THE CAUSES OF EXUDATIVE PLEURAL EFFUSION :

1.Appearance of the fluid :

Mostly transudative and many exudative pleural effusions are clear , straw colored , nonviscid and odourless.

The red colour of the fluid indicates the presence of blood. To confirm hemothorax we have to do a hematocrit. If the hematocrit of the pleural fluid was more than 50 % of the peripheral blood hematocrit , then it is a hemothorax. When the pleural fluid is blood tinged the RBC count is 5000 to 10000 / mm3 . If the pleural fluid macrophages contain haemoglobin inclusions , then it indicates that the blood was present before thoracentesis and the blood is not due to traumatic tap.

Increased lipid content or increased cellular content both can make pleural fluid to appear turbid . If after centrifuge the supernatant fluid remains turbid then it is due to lipid content. But if the supernatant fluid is clear , then the turbidity is due to cellular debris .

Amebiasis with a hepatopleural fistula – chocolate sauce or anchovy paste. The mixture of blood ,cytolysed and normal liver tissue make this appearance.

Malignant mesothelioma – high viscocity due to elevated hyaluronic acid .

Anaerobic bacterial infection – feculent odour

Urinothorax – smell of urine

2.WBC count :

Most transudates have WBC count below 1,000/mm3 and exudates have more than 1,000/mm3.

WBC count > 10,000/mm3 – parapneumonic effusions

WBC count > 50,000/mm3 – pancreatic disease and pulmonary embolism

Neutrophils predominate – suggests acute inflammation . It is seen in pneumonia , pancreatitis , pulmonary embolisation ,subphrenic abscess , early tuberculosis .

Eosinophils predominate – indicates air or fluid in the pleural space. It is seen in patients with spontaneous pneumothorax who undergone thoracotomy , introduction of air during thoracentesis into pleural space , traumatic hemothorax , pulmonary embolization , CABG , asbestos related effusion , drugs like dantrolene , bromocriptine , parasitic disease like amebiasis , ascariasis .

Basophils predominate – pneumothorax , pneumonia , leukemic pleural involvement .

Pleural fluid lymphocytosis - malignancy , TB , CABG , leukemia or lymphomas .

Mesothelial cells – Tuberculosis in HIV patients . Whereas it is absent in complicated parapneumoniceffusions , malignancy after pleurodesis.

3.Glucose levels :

Glucose level < 60 mg / dL – malignancy ,parapneumonic effusions,rheumatoid disease , tuberculosis . Other causes include hemothorax , lupus pleuritis ,paragonimiasis , churg – strauss syndrome .

4.Amylase level :

It is elevated in pancreatic disease , malignancy , esophageal rupture . In later two cases the amylase is of salivary type.

5.Lactate dehydrogenase level :

LDH in the pleural fluid is a reliable indicator of degree of inflammation of the pleura. More the inflamed surfaces , higher the LDH levels . The most common causes of elevated LDH levels are parapneumonic effusions and malignancy . These two conditions mostly meet the light's criteria on the basis of levels of LDH than the protein levels .The isoenzymes elevated in these conditions are LDH – 4 and LDH – 5. They are thought to arise from the inflammatory WBC .

Usually LDH isoenzyme is not used routinely . This is done in conditions where there is a bloody pleural fluid tap in a patient who is having transudative pleural effusion clinically .The pleural fluid protein meets the criteria for transudative pleural effusion but LDH levels meets the criteria for exudative pleural effusion. In these conditions isoenzyme LDH – 1 , confirms that the rise in LDH was due to blood .

6.Pleural fluid pH :

If the pleural fluid pH is less than 7.2 then we have to consider the following causes : complicated parapneumonic effusions , esophageal rupture , rheumatoid pleuritis , tuberculouspleuritis malignant pleural disease , hemothorax , systemic acidosis , lupus pleuritis , paragonimiasis , urinothorax .

7.AdenosineDeaminase :

ADA has two isoenzymes – ADA 1 and ADA 2

ADA 1 is produced by lymphocytes , neutrophils , monocytes , macrophages

ADA 2 is produced by macrophages and monocytes .

The cut off level for ADA level to diagnose tuberculous pleural effusion is 40 to 45 U/L . The diagnosis of TB pleural effusion is more likely if the level is higher ie., more than 70 U/L .

Other conditions with elevated ADA levels areempyema , rheumatoid pleuritis, neoplasms , Q fever , brucellosis . If the ADA 1 to ADA ratio is less than 0.42 the diagnosis of TB pleuritis is increased .

8.Interferon gamma :

In patients with tuberculouspleuritis CD 4 lymphocytes produce interferon gamma . It enhances the elimination of intracellular parasites by increasing the production of polymyristate acetate induced hydrogen peroxide in macrophages. In monocytes this inhibits the mycobacterial growth . If the interferon gamma level is more than 200 pg / ml then the diagnosis of tuberculouspleuritis is made.

9.Polymerase chain reaction :

It is used in patients with low numbers of tubercle bacilli in pleural fluid . It is also used on pleural biopsy specimens .

10. **C – Reactive proteins** more than 50 mg /L , high levels of **lysozyme** are also used to diagnose tuberculous pleuritis .

10.Lipids :

Chylothorax – Accumulation of chyle in the pleural space due to distruption of the thoracic duct. In these situations the triglyceride levels are increased .

Chyliform pleural effusions – This is characterised by high levels of lecithin globulin levels .

Pseudo chylous effusions – There is increased levels of cholesterols crystals .

Triglyceride levels more than 110 mg / dL – Chylothorax is confirmed . But if the levels are less than 50 mg / dL then the patient is not having chylothorax .

If triglyceride level is between 50 to 110 mg / dL then we need to perform a lipoprotein analysis .Chylothorax is diagnosed if there is presence of chylomicrons in the lipoprotein analysis of pleural fluid.

11.Bilirubin

Bilirubin has a high molecular weight (584) .With respect to its concentration between serum and protein it behaves in a manner identical to that of the high molecular weight proteins . Any serous membrane

inflammation often leads to increased capillary permeability and this enables the diffusion of high molecular weight bilirubin .

A pleural fluid bilirubin of more than 0.48 mg / dL and a pleural fluid bilirubin to serum bilirubin ratio of more than 0.62 is considered as exudates.

12.Cholesterol

The mechanism of increased concentration of cholesterol in

Exudative pleural effusion is not known clearly.

The permeability of pleura is increased due to “serum leakage” and this leads to the accumulation of cholesterol in exudative pleural effusion .

A pleural fluid cholesterol of more than 60 mg / dL is used in diagnosing exudates.

RADIOGRAPHIC EXAMINATIONS OF PLEURAL EFFUSIONS

Typical Arrangement of Free Pleural Fluid

In the pleural space the distribution of free fluid is influenced by two main factors.

First, since the lung is less dense than pleural fluid, accumulation of the pleural fluid occurs in the most dependent part of the thoracic cavity.

The distribution of fluid within the free pleural space obeys the law of gravity. The lung also maintains its shape when compressed. Bearing, these 2 factors in mind it is easy to predict the distribution of excess pleural fluid.

The fluid first gravitates to the base of the hemithorax and comes to rest between the inferior surface of the lung and the diaphragm, where the pleural sinus is the most inferior, particularly posteriorly. The fluid spills out into the costophrenic sinuses posteriorly, laterally, and anteriorly, when the fluid accumulation is higher. Additional fluid assumes a higher position in the thorax as it spreads upward in a mantle-like manner around the convexity of the lung and gradually tapers .

The lateral costophrenic angle is obliterated, in the posteroanterior projection.The density of the fluid is high laterally and curves gently medially and downward , to terminate at the mediastinum with a smooth,

meniscus-shaped upper border. At the mediastinal border the layer of fluid is narrower than at the costal border.

The upper surface of the pleural fluid density is semicircular in the lateral projection. It is high in the anterior and posterior regions. It curves smoothly downward to its lowest point approximately midway between the posterior chest walland the sternum .

Frequently, in the lateral chest radiograph a middle lobe step is observed . The explanation for the middle lobe step is that the most dependent and the the first affected lobe is the lower lobe , the pleural fluid starts to accumulates here. Therefore, it starts to float and shrink but maintains its shape. So the middle lobe is unaffected and its full volume is maintained . Accordingly, the result is a a middle lobe that retains its usual size and shrunken lower lobe . The fluid accumulation is mostly in the posterior part of the chest ,radiographically. The height of the pleural fluid is greater laterally , based on the radiologic appearance. When viewed en face ,this layer of fluid is of insufficient depth to cast a discernible shadow, so it assumes a meniscus shape.

Radiologic Signs

The fluid first accumulates between the inferior surface of the lower lobe and the diaphragm, when the patient is in the upright position. The pleural fluid occupies this position , if the amount of fluid is small (approximately 75 mL) and without spilling into the costophrenic sinuses. The normal configuration of the diaphragm is maintained, with this small amount of fluid.

The chest radiograph does not demonstrate that pleural fluid is present.

When viewed in the lateral projection , accumulation of more fluid obliterates the costophrenic angle as it spills over into the posterior costophrenic angle . The posterior costophrenic angle is normally sharp . It is obliterated by a homogeneous , shallow shadow with a meniscus-shaped upper surface . There is also widening of the pleura that lines the posterior thoracic wall .

If the posterior part of one or both diaphragms is obscured or the posterior costophrenic angle is obliterated, this indicates the presence of pleural fluid.

Then we should be do further diagnostic tests .

Moreover, the presence of clinically significant amounts of free pleural fluid can be nearly excluded , if both posterior costophrenic angles are clear and sharp. In the postero - anterior chest radiograph , lateral costophrenic angle is blunted with increasing amounts of fluid . The entire outline of the

diaphragm is lost on the affected side, as more fluid accumulates . The fluid then extends upwards around the posterior , anterior and lateral thoracic walls. At the lung base , this fluid produces opacification which is the typical meniscus shape .

Supine Position

There are three characteristics that serve to differentiate the increased density due to parenchymal infiltrate from that due to a pleural fluid.

First, in a properly exposed film , the vascular structures of the lung will be readily visible through the density, if the density is caused by pleural fluid. However, vascular structures are obliterated by the silhouette effect, if a similar density is produced by any intrapulmonary process.•

Secondly , the density is usually completely homogenous, if it is due to pleural fluid. Whereas, the infiltrates are usually less homogenous, if it is caused by an intrapulmonary processes.

Third, the presence of air bronchograms . They are are present only if the increased density is due to a parenchymal infiltrate and not due to a pleural fluid.

Ultrasound

In a patient with pleural effusion , the ultrasound can be used for the following purposes. They are

(a) to determine the presence of pleural fluid;

(b) to identify an appropriate location for the attempted thoracentesis, chest tube placement, or pleural biopsy;

(c) to identify loculated pleural effusion;

(d) to distinguish pleural thickening from pleural fluid;

(e) tosemiquantify the amount of pleural fluid;

(f) to differentiate a lung abscess from a pyopneumothorax;

(g) to assess a whether a pleurodesis is present; and

(h) to evaluate the trauma patient for the presence of a pneumothorax or a hemothorax.

FIGURE 1

ULTRASOUND OF LEFT LUNG AND SURROUNDING STRUCTURES

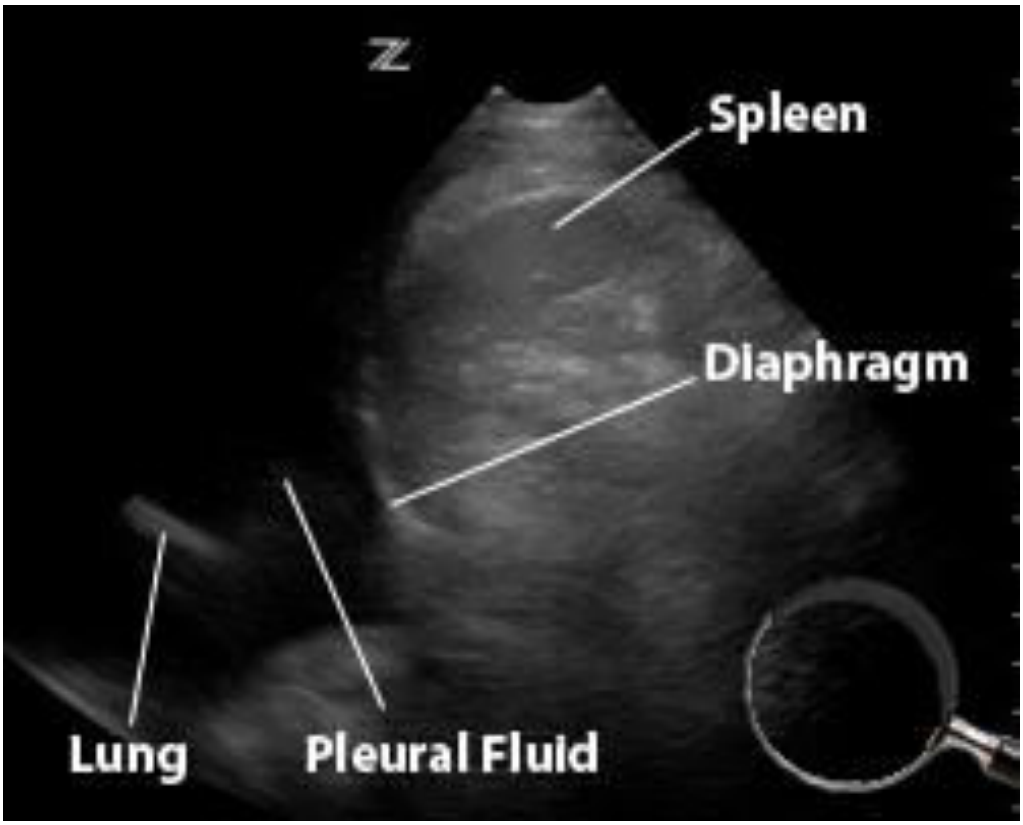


FIGURE 2.

ULTRASOUND OF RIGHT LUNG AND SURROUNDING STRUCTURES

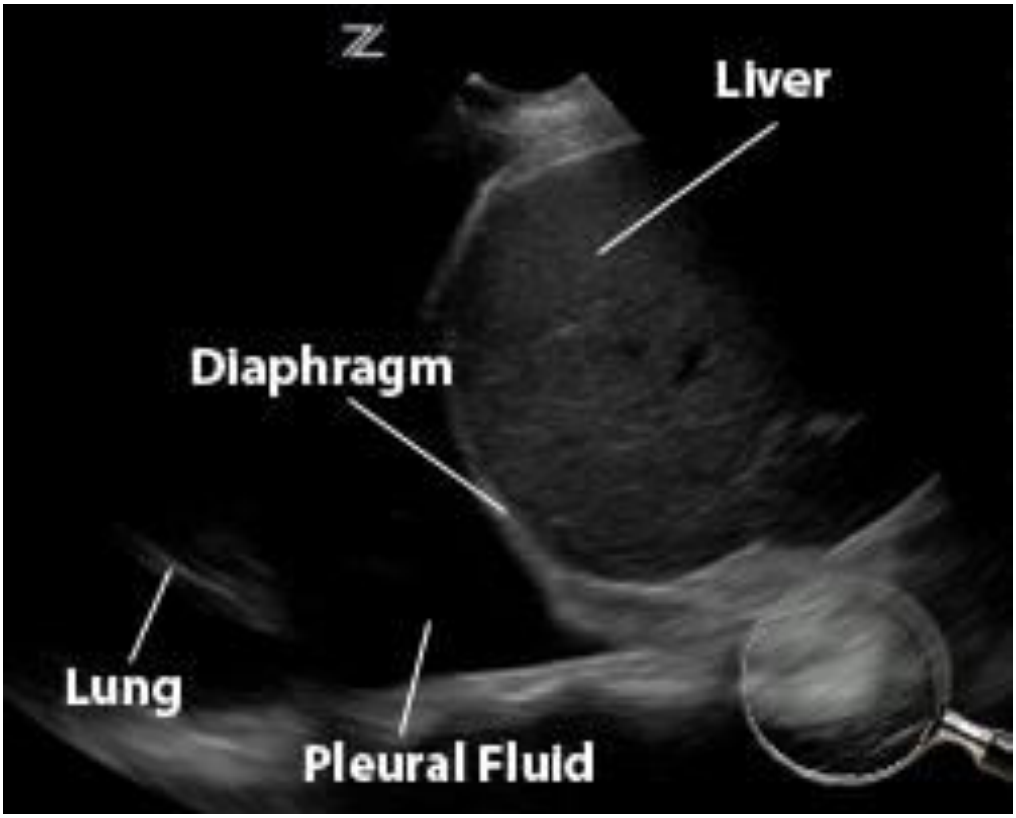


FIGURE 3

CHEST X RAY – POSTERIOR ANTERIOR VIEW SHOWING RIGHT SIDED PLEURAL EFFUSION .

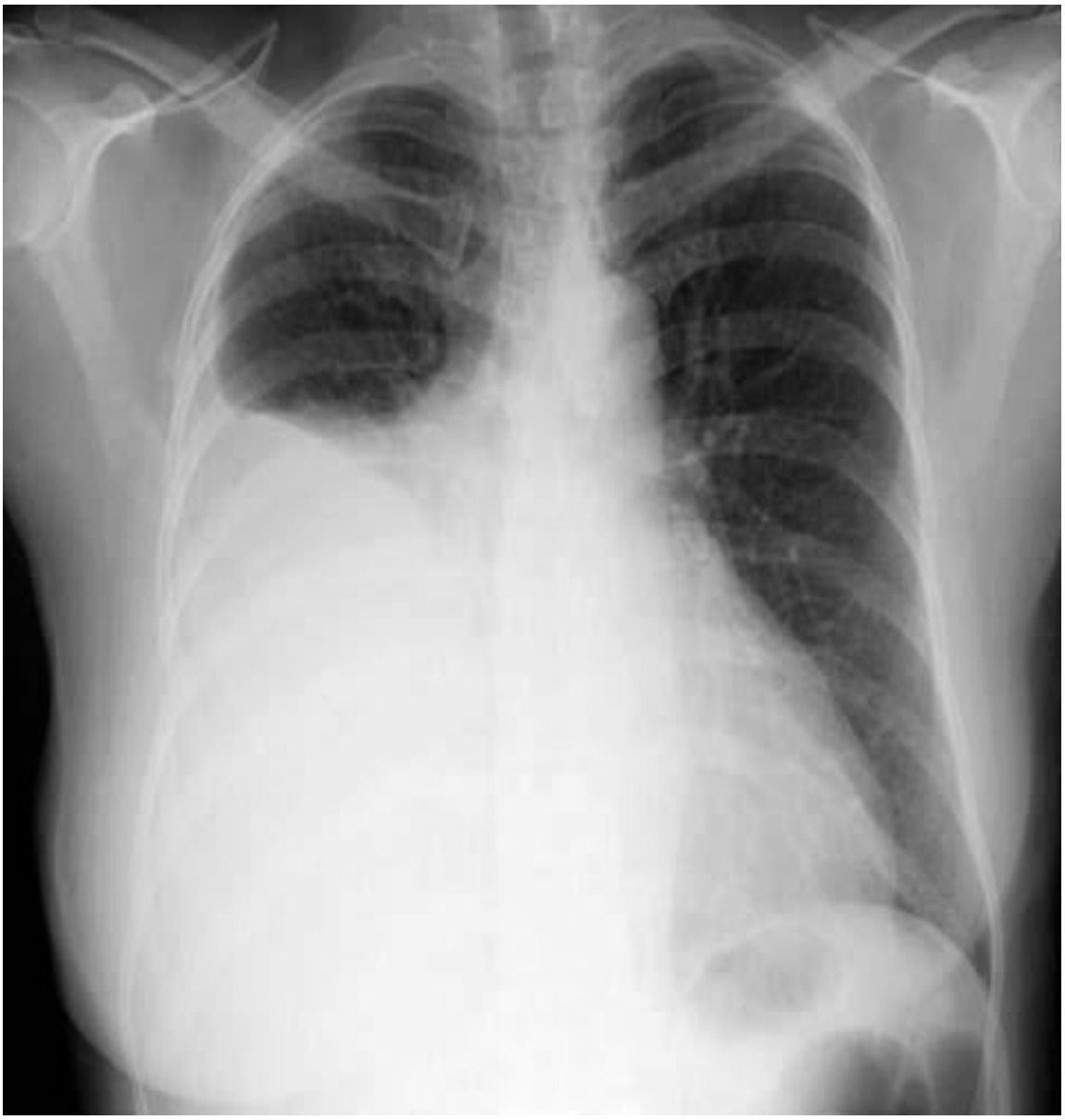


FIGURE 4

DIAGNOSTIC OR THERAPEUTIC THORACENTESIS

- **RECOMMENDED POSITION OF THE PATIENT**

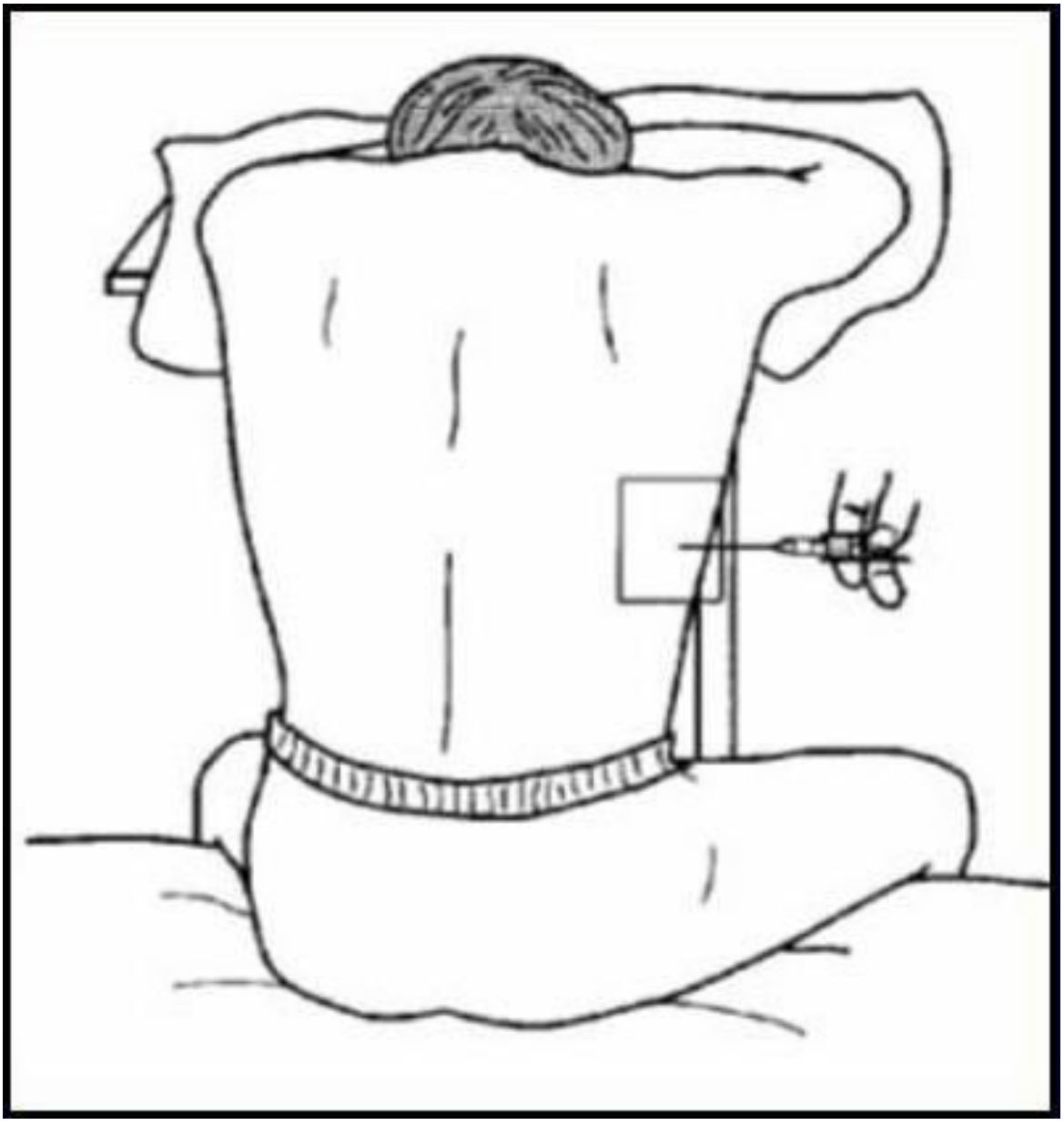


FIGURE 5

DIAGNOSTIC THORACENTESIS : THE PLEURAL SPACE IS ENTERED AND PLEURAL FLUID IS OBTAINED.

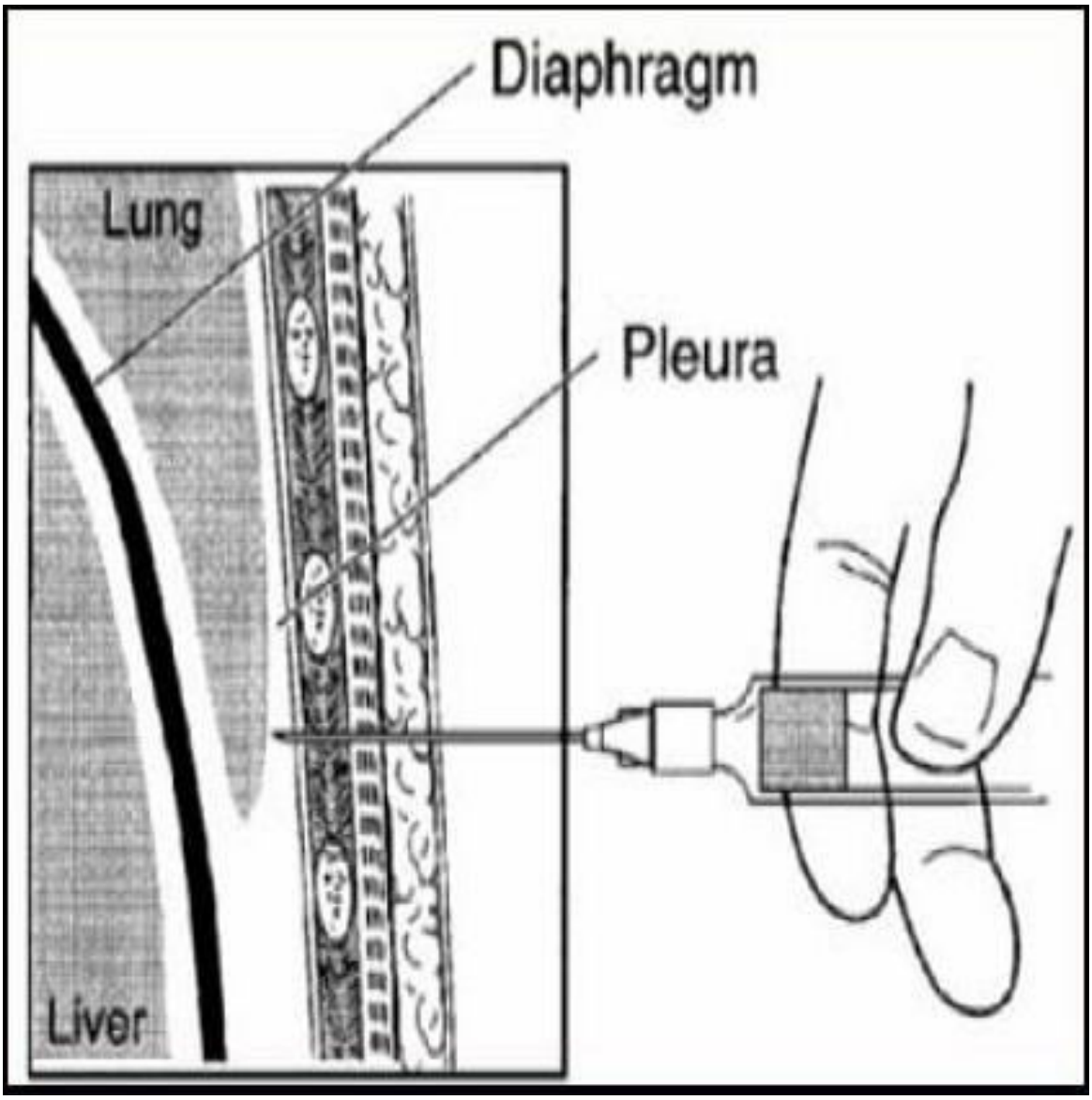
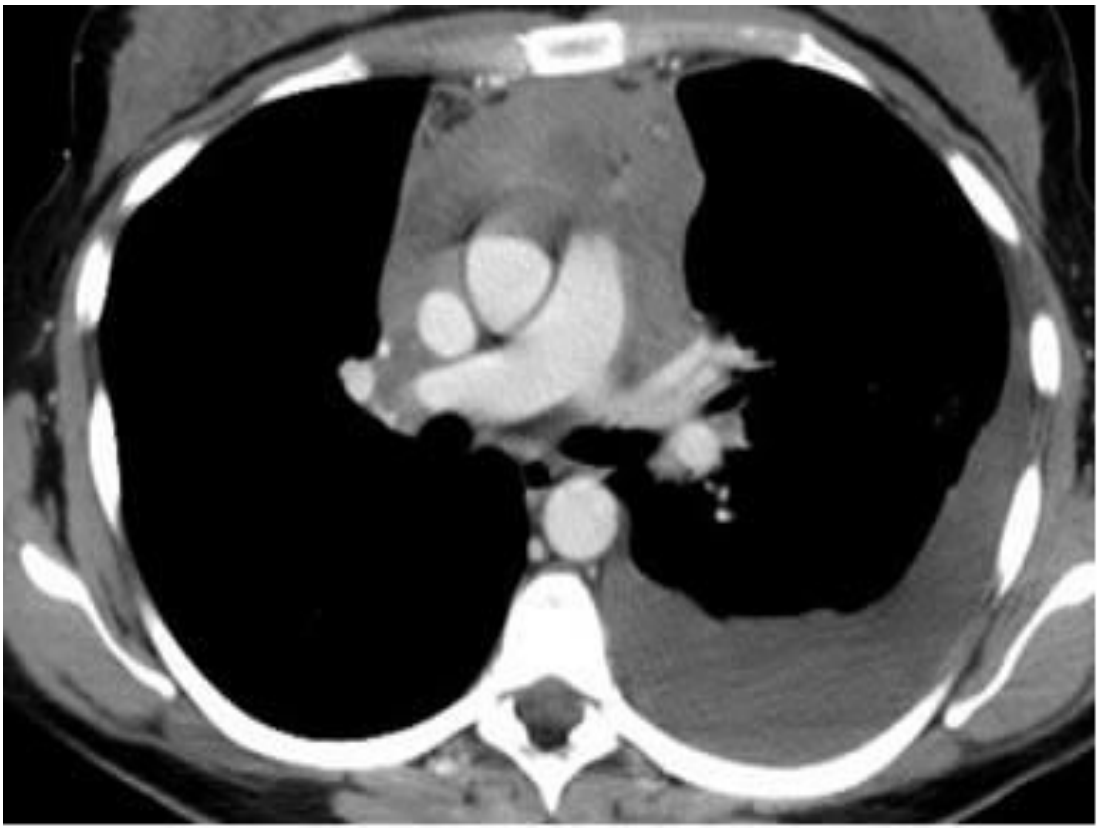


FIGURE 6

CT CHEST PLAIN SHOWING PLEURAL EFFUSION



SEPARATION OF TRANSUDATIVE FROM EXUDATIVE EFFUSIONS

The accumulation of clinically detectable quantities of pleural fluid is distinctly abnormal.

Indications of diagnosticthoracentesis:

1. Whenever the thickness of pleural fluid on ultrasound or the decubitus radiograph is greater than 10 mm or
2. Whenever loculated pleural fluid is demonstrated with ultrasound
3. Etiology of the effusion is unknown.

A diagnostic thoracentesis when properly done takes less than 10 minutes.It should not cause any morbidity more than a venipuncture. In the management of the patient with pleural effusion , the information available from examination of the pleural fluid is invaluable.

Transudative pleural effusion :

If the systemic factors influencing the absorption or formation of pleural fluid are altered, transudative pleural effusion develops.

The permeability of the capillaries to proteins,bilirubin,cholesterol is normal in the area where the fluid is formed.

Examples of conditions producing transudative pleural effusions :

1. Increased pulmonary interstitial fluid and a resulting pleural effusion - left ventricular failure .
2. Movement of fluid through the diaphragm from ascites due to cirrhosis .
3. Decreased serum oncotic pressure with hypoproteinemia.

Exudative pleural effusion

In contrast, when the pleural surfaces or the capillaries in the location where the fluid originates are altered such that fluid accumulates , and an exudative pleural effusion develops.

The common causes of exudative pleural effusions are :

1.Pleural malignancy,

2.Parapneumonic effusions,

3.Tuberculosis and

4.Pulmonary embolism.

In assessing a patient with a pleural effusion, the first question to ask is whether that effusion is an exudates or a transudate. If the pleural effusion is a transudate, then no further diagnostic pleural procedures are necessary. Now therapy is directed to the underlying CHF, cirrhosis, or nephrotic syndrome.

Alternately, a more extensive diagnostic investigation is indicated , if the effusion proves to be an exudate, to delineate the cause of the effusion.

Total protein :

Earlier to separate between transudate and exudates , a pleural fluid protein of 3gms was used. This test misclassified about 10% of pleural effusions.

Light's criteria:

Light demonstrated the following criteria for diagnosing exudate.

Exudative pleural effusions meet at least one of the following criteria

- Pleural fluid protein divided by serum protein greater than 0.5
- Pleural fluid LDH divided by serum LDH greater than 0.6
- Pleural fluid LDH greater than two thirds of the upper limit of normal serum LDH

Other tests to differentiate exudates and transudate

In recent years, following are the other tests for the separation of transudates from exudates.

1.pleural fluid cholesterol >60mg,

2.pleural fluid cholesterol>45mg,

3.pleural fluid serum albumin gradient of <1.2,

4. pleural fluid protein gradient <3.1,

5.pleural fluid serum bilirubin ratio >0.6

When a pleural fluid shows above findings on analysis then it indicates it is an exudates.

Light's criteria identify approximately 20% of transudative effusions as exudates. This mislabeling occurs most commonly in patients with CHF. When they are treated with diuretics before thoracentesis is performed. These mislabeled transudates barely meet the exudative criteria. The mislabeled transudate can be identified by examining the gradient between the serum and the pleural fluid protein levels. If this gradient is greater than 3.1 g/dL, one can presume that the fluid is actually a transudate. An albumin gradient of 1.2 g/dL rather than the protein gradient of 3.1 g/dL be used. However, the protein gradient is equally effective as the albumin gradient. Also the pleural fluid bilirubin and cholesterol can be used to correctly identify the transudates and exudates .

And if the pleural fluid bilirubin is more than 0.48 mg/dl and pleural fluid to serum bilirubin ratio is more than 0.60 mg/dl , pleural fluid cholesterol more than 60 mg/dl then it is an exudates.

Approach to diagnose a transudative or exudative pleural effusion

To determine whether a pleural effusion is a transudate or an exudate , the following approach is recommended.

First assess the fluid for Light's criteria. The fluid more likely an exudate if there is higher the value for the protein ratio, the LDH ratio, and the absolute value of the LDH. If the fluid meets the criteria for a transudative effusion, it is a transudate.

If the fluid meets the criteria for an exudative effusion by only a small margin and the clinical picture is compatible with a transudative effusion, measure the protein gradient between the serum and pleural fluid . If this value is greater than 3.1 g/dL, then the fluid can be relabeled a transudate.

And if the pleural fluid bilirubin is more than 0.48 mg/dl and pleural fluid to serum bilirubin ratio is more than 0.60, pleural fluid cholesterol more than60 mg/dl then it is an exudates.

Other Characteristics of Transudates

Most transudates are clear, straw coloured, non - viscid, and odourless. The discovery of blood-tinged pleural fluid does not mean that the fluid is not a transudate.To give the pleural fluid a pinkish tinge , pleural fluid red blood cell (RBC) count should be more than 10,000/mm^3 . Approximately 15% have RBC counts above this level. RBC ‘s contain a large amount of LDH . So elevated LDH level in a blood-tinged or bloody transudative pleural effusion would meet the criteria for an exudative pleural effusion.

White blood cell (WBC) count

White blood cell (WBC) count in the pleural fluid of most transudates is less than 1,000/mm^3, but approximately 20% have WBC counts that exceed 1,000/mm^3. In transudative pleural effusions , WBC counts in pleural fluid above 10,000/mm^3 are rare . The differential WBC count may be dominated by polymorphonuclear leukocytes, small lymphocytes, or other mononuclear cells in transudative pleural effusions.

In a series of 51 transudative effusions, 7 (13%) had more than 50% polymorphonuclear leukocytes, whereas 17 (34%) had predominantly small lymphocytes, 23 (47%) had predominantly other mononuclear cells, and 4(6%) had no single predominant cell type .

The glucose level in pleural fluid is similar to the serum glucose level, but the level of pleural fluid amylase is low. Because of active transport of bicarbonate from the blood into the pleural space ,there is always higher the pleural fluid pH in patients with transudative pleural effusions than the pH in simultaneously obtained blood .

Diagnostic Thoracentesis :

If the decubitus film demonstrates presence of free pleural fluid, then one should consider performing a diagnostic thoracentesis with the aid of ultrasound or with a CT scan. The thickness of the fluid is important in performing the diagnostic thoracentesis . If the thickness of the fluid on the decubitus radiograph, ultrasound, or the CT scan is less than 10 mm , then performing a diagnostic thoracentesis is difficult. However , we have to consider performing a diagnostic thoracentesis, if the thickness of the fluid is greater than 10 mm.

There is no need to perform diagnostic thoracentesis , if the patient has congestive heart failure. But in a patient with congestive heart failure if any of the following three conditions are met: (a) the patient is febrile (b) the effusions are not bilateral and comparably sized (c) the patient has pleuritic chest pain. Otherwise, treatment of the congestive heart failure is initiated.

A diagnosticthoracentessis is done later, if the pleural effusions do not rapidly disappear.

To conclude the main aim of performing a diagnostic thoracentesis is determining whether the patient has an exudative or a transudative pleural effusion.

TRANSUDATIVE PLEURAL EFFUSIONS

Alternation in the systemic factors influencing the formation and absorption of the pleural fluids leads to accumulation of the pleural fluid and formation of transudative pleural effusions .

The major causes are :

1.Congestive Heart Failure :

The most common cause of pleural effusion is probably the congestive heart failure (CHF) .The researchers interested in pleural effusions usually do not see most patients with pleural effusions of this cardiac origin and this is the reason for the low incidence of pleural effusions secondary to heart failure in most of the studies . The incidence of pleural effusions in patients with CHF is high.

Pathophysiology :

In the concepts of pleural fluid formation and reabsorption in patients with heart failure , there are significant modifications in the recent years. It was believed in the past that the accumulation of the pleural fluid in patients with CHF was due to increased pressure in the parietal or the visceral pleural capillaries. According to Starling's equation, these increased pressures results in a decreased removal of fluid through the visceral pleura and an increased entry of fluid into the pleural space from the parietal pleura .

In patients with CHF , according to current theories on pleural fluid formation and reabsorption, there is a different entry pathway and a different exit pathway for pleural fluid.

It is believed that almost all fluid exits the pleural space through the lymphatics in the parietal pleura rather than by passively diffusing across the visceral pleura. In patients with CHF, accumulation of pleural fluid occurs when the rate of entry of fluid into the pleural space exceeds the capability of the lymphatics in the parietal pleura to remove the fluid .

Clinical Manifestations :

In patients with pleural effusions due to CHF they are usually associated with other manifestations of that disease. The patient has a history of increasing dyspnea on exertion, orthopnea or paroxysmal nocturnal dyspnea , increasing peripheral edema. The dyspnea is frequently out of proportion to the size of the effusion.

Physical examination :

Physical examination usually reveals signs of the pleural effusions as well as signs of both left-sided heart failure with an S_3 ventricular gallop and rales and right-sided heart failure with peripheral edema and distended neck veins.

Investigations :

The chest radiograph almost always reveals usually bilateral pleural effusions and cardiomegaly. The most common cause of bilateral pleural effusions is congestive heart failure . But only 88% of the patients studied had bilateral pleural effusions ,if cardiomegaly is not present.

The mean volume of pleural fluid in the right pleural space (1,084 mL) when compared to the mean volume of pleural fluid in the left pleural space (913 mL),was only slightly greater. Also mediastinal lymphadenopathy is common in patients with pleural effusions that are secondary to CHF.

Diagnosis :

If the patient has bilateral pleural effusions and cardiomegaly, not febrile, and no history of pleuritic chest pain, we have to first initiate treatment of the CHF. Then we have to observe the patient and determine whether the pleural fluid is reabsorbed. We then perform a diagnostic thoracentesis , if the effusions do not disappear within a few day.

One problem with this approach is that the characteristics of the pleural fluid may change from those of a transudate to those of an exudates , since the patients are with diuresis.

Serum pleural fluid albumin or protein gradient :

The serum to pleural fluid protein gradient should be examined , if the pleural fluid meets exudative criteria but the effusion is thought to be due to CHF. If this gradient is greater than 3.1 g/dL, additional diagnostic studies are not indicated because the pleural effusion is probably due to the CHF . Currently, as the protein gradient is already available when Light's criteria are measured , the protein gradient of 3.1 g/dL is preferred to the albumin gradient.

Pro-brain natriuretic peptide :

The measurement of the serum or pleural fluid pro-brain natriuretic peptide (pro-BNP) , is an another test that should be considered for establishing the diagnosis of CHF. The level NT pro-brain natriuretic peptide (NT pro-BNP) considereddiagnostic of CHF is 1500pg/mL

Treatment

In a patient with pleural effusion secondary to heart failure the preferred treatment is to treat the heart failure with the following drugs.,

- digitalis,
- diuretics – to reduce preload , and
- dilators - to reduce afterload .

The pleural effusion disappears , if we manage heart failure successfully. In most patients with heart failure , the pleural effusion is effectively managed only with above management .

Occasionally, the patients tends to be very dyspneic, if they are associated with large pleural effusions. Such persons may get rapid relief from the dyspnea , if about 0.5L to 1.0L of pleural fluid are removed . Sometimes therapeutic thoracentesis is indicated in patients with heart failure and large pleural effusions that are refractory to treatment, to get symptomatic relief . So consider interventions to control the pleural effusions , in such patients.

2. Hepatic Hydrothorax

One of the complication of hepatic cirrhosis is pleural effusion. But only when ascitic fluid is present, pleural effusions usually occur. They are usually called as hepatic hydrothorax.

Pathophysiology

It is evident from the foregoing studies, that the orgin of pleural fluid in these patients is from the ascitic fluid.

The fluid in the peritoneal cavity passes directly through the defects in the diaphragm to the pleural space . The diaphragm may be stretched in patients with tense ascites, causing microscopic defects. This is because of the increased intraabdominal pressure. There is always a one-way transfer of

fluid from the peritoneal to the pleural cavity ,in patients with ascites. The is because of increased hydrostatic pressure in the asciticfluid .

In some patients, the lymphatic vessels play an important role in the production of the pleural effusion. The mechanism behind this is the transfer of ascitic fluid across the diaphragm by the lymphatic vessels .

To conclude , the dominant mechanism of hepatic hydrothorax is the direct movement of fluid across the diaphragm. Because the placement of the chest tube results in diminution in the amount of ascites, within minutes.

Clinical Manifestations

The clinical pictures of cirrhosis and ascites dominate in patients with pleural effusions secondary to cirrhosis. At times, in association with large pleural effusions , these patients develop acute dyspnea. Although the pleural effusions may be small to moderate in size, they are frequently large and occupy the entire hemithorax. The diaphragmatic defect permits fluid to flow into the pleural cavity from the peritoneal cavity , until the pleural pressure approaches the peritoneal pressure and this results in development of large pleural effusion.

Diagnosis

It is usually easy to diagnose the pleural effusion that is secondary to cirrhosis with ascites. We should perform both a paracentesis and a thoracentesis. This is to confirm that the ascites and pleural fluid are

compatible with the diagnosis. Also to ascertain that they are not have high polymorphonuclear cell counts.

The pleural fluid is occasionally blood tinged or is frankly bloody. But due to the poor coagulation status of the patient , such findings have no significance. The differential cell count is dominated by polymorphonuclear leukocytes, small lymphocytes, or other mononuclear cells.

To rule out pancreatic ascites amylase levels should be determined. Also a cytologic examination should be performed to rule out malignant disease. This should be done in both pleural fluid and ascitic fluid.

Treatment

Since the hydrothorax is an extension of the peritoneal fluid in patients with cirrhosis and ascites , the management of pleural effusions always should be directed toward treatment of the ascites .

The patient should be put on a low-salt diet, and moderate fluid restriction. Then diuretics should be administered. The combination of furosemide and spironolactone , is the best diuretic therapy. The initial starting dose is 40 mg of furosemide and 100 mg of spironolactone and they can be titrated upto a maximum dose of 160 mg of furosemide and 400 mg of spironolactone. This combination appears to have the optimal ratio for the two diuretics.

3. Nephrotic Syndrome

The nephrotic syndrome is common in patients with the pleural effusion.

Mechanism of pleural fluid accumulation :

The combination of increased hydrostatic pressure and decreased plasma oncotic pressure , is the mechanism responsible for the transudative pleural effusion in patients associated with the nephrotic syndrome.

Diagnosis :

In the typical clinical situation to diagnose pleural effusion secondary to the nephrotic syndrome it is not difficult. But to confirm that the pleural fluid is indeed a transudate ,a diagnostic thoracentesis should be performed.

In patients with the pleural effusion and nephrotic syndrome, the possibility of pulmonary embolism should always be considered. In all patients with the pleural effusion and nephroticsyndrome , one should always obtain a lung scan or a CT angiogram. It is important that evidence of deep venous thrombosis should be sought with venograms, pulmonary arteriogram or a impedance plethysmograms, if the lung scan or spiral CT scan is equivocal.

Treatment :

The main aim of treatment is to decrease the protein loss in the urine of patients with pleural effusion and associated with the nephrotic syndrome. This is done to decrease the increased extracellular volume and to increase the plasma protein.

This is best accomplished by administering

- diuretics in conjunction with a low-sodium diet,
- angiotensin-converting enzyme inhibitors.

As serial therapeutic thoracentesesonly deplete the protein stores, they should not be performed . We should consider a pleurodesis with a sclerosingagent , in selected patients who are symptomatic from the pleural effusion.

EXUDATIVE PLEURAL EFFUSION

MOST COMMON CAUSES ARE :

1. Parapneumonic pleural effusion

2. Pleural effusion related to metastatic malignancies

3. Tuberculous pleural effusion

1.METASTAIC MALIGNANCIES AND PLEURAL EFFUSION :

The exudative pleural effusion secondary to malignant disease involving the pleura is the second leading cause of exudative pleural effusion. Parapneumonic effusion ranks first in this category.

Common carcinomas associated with malignant pleural effusions are :

1. Lung carcinoma ,
2. Breast carcinoma ,
3. Lymphoma ,
4. Ovarian carcinoma ,
5. Sarcoma

Rarely carcinoma of uterus , cervix , stomach , colon , pancreas , bladder

MECHANISMS BY WHICH MALIGNANT DISEASE LEADS TO PLEURAL EFFUSION

There are two types of mechanisms by which the malignant disease leads to the development of pleural effusions

1.Direct mechanism :

a) Increased permeability due to pleural metastasis
b) Obstruction of the pleural lymphatic vessels caused by pleural metastasis
c) Decreased pleural lymphatic drainage and mediastinal node involvement
d) Chylothorax – thoracic duct interruption
e) Decreased pleual pressure – bronchial obstruction
f) Due to involvement of pericardium

2.Indirect result :

a) Pulmonary embolism
b) Postobstructive pneumonitis
c) Hypoproteinemia
d) Postradiation therapy

CLINICAL MANIFESTATIONS :

The most common symptom in patients with malignant pleural effusion is dyspnea . Also the symptoms due to the underlying disease will predominate. The symptoms due to underlying malignancy are weight loss , malaise , anorexia .

The other manifestations are chest pain , hemoptysis, cough in patients with lung malignancy , breast mass in carcinoma breast , swelling in neck, axilla inguinal regions with mass in the abdomen in case lymphomas .

Chest radiograph :

Besides the pleural effusion , pulmonary abnormalities are demonstrated by the patients with pleural effusion secondary to carcinomas. Also there is involvement of mediastinallymphadenopathy .

The pulmonary abnormalities are :

a) pleural nodularity ,
b) pleural rind ,
c) mediastinal pleura involvement ,
d) pleural thickening > 1 cm

Pleural fluid analysis :

- Grossly bloody with RBC count > 100,000/mm3 .
- WBC count between 1,000 to 10,000 / mm3 with lymphocytes 45 % , other mononuclear cells > 40% , polymorphonuclear cells 15 % .
- Reduced pleural fluid glucose level less than 60 mg/ dl .
- Pleural fluid pH below 7.3 .
- Cytology : it is used to classify the histological subtype like adenocarcinoma but not the primary site of tumour.
- Immunohistochemicaltests :carcinoembryonic antigen stained by metastatic adenocarcinoma and also stains MOC 3,1,B72.3,Ber – EP4 and BG – 8. Malignant mesothelial cells stain positive for cytokeratin and calretin .
- Tumormarkers :carcinoembyronic antigen (CEA), carbohydrate antigen (CA) 15 – 3, 19 – 9 , 549 and 72.Neuron specific enolase ,SCC antigen , SSEA – sialyl state specific mouse embryonic antigen , cytokeratin 19 fragments .

Non invasive test :

This includes measurement of oncogenes, lectin binding, FISH, flow cytometry, proteomics , chromosomal analysis and hyaluronic acid.

But the only test that is advised is flow cytometry . This is done when a lymphoma is suspected . The diagnosis of lymphoma is done by showing the clonality of lymphocytes in pleural fluid .

Pleural biopsy – CT guided or via thoracoscopy

TREATMENT :

In the management of pleural effusion due to metastatic disease the important thing is to identify the site of primary. This is because to decide whether the primary tumor responds to systemic chemotherapy or not. Because some tumors like breast carcinoma , lymphoma , small cell carcinoma can responds to systemic chemotherapy very well.

Also intrapleural chemotherapy with cisplatin , staphylococcal aureus super antigen (SSAg) , rituximab , interferon – gamma ,tumor necrosis factor , interleukin IL -2 has been tried with varying results.

In patients with malignant pleural effusion and a chylothorax , malignancy usually involves the thoracic duct . So in these patients it is good to administer radiotherapy to the mediastinum.

We have to consider removal of the pleural fluid , if the tumor is not responding to chemotherapy or fails to respond to treatment . This is done mainly to relieve the dyspnea.

The procedures available for the treatment resistant pleural effusion are ;

1. Indwelling pleural catheter (pleur X)
2. Pleurodesis
3. Intercostal drainage
4. Pleuroperitoneal shunt
5. Repeated thoracentesis
6. Pleurectomy

2.TUBERCULOUS PLEURAL EFFUSION

The development of pleural effusion in a patient with absence of radiologically apparent TB indicates that it would be a sequelae to the primary infection that occurred 6 to 12 weeks before or it may be due to reactivation of TB .

Pathogenesis oftuberculous pleural effusion :

In tuberculous patients there are subpleuralcaseous focus. Tuberculous pleural effusion occurs due to rupture of the subpleuralcaseous focus in the lung to the pleural space.

In the development of tuberculous pleural effusion the delayed hypersensitivity plays a major role .There is clonal expansion of lymphocytes sensitised to the tuberculous protein . Initially the macrophages

predominate in the pleural fluid from day 2 to day 6 and then the lymphocytes predominate in the pleural fluid.

It is clear that the delated hypersensitivity increases the pleural capillaries permeability to protein. There is higher rate of pleural fluid formation due to the increased levels of pleural fluid protein. Also there is increased levels of VEGF, which also increases the permeability. This leads to the accumulation of pleural fluid and development of pleural effusion .

Also there is decrease in the clearance of proteins in the pleural space. This is because of the impedence to the clearance of proteins by the lymphatics as a result of delayed hypersensitivity reactions .

Clinical manifestation :

Patients with pleural TB have symptoms such as fever, dry cough ,pleuritic chest pain, and dyspnea.

Physical findings are those of pleural effusion such as dullness to percussion and absence of breath sounds.

In HIV individuals there will be longer duration of illness. The incidence of chest pain is low , but night sweats , fatigue , diarrhoea , hepatomegaly , lymphadenopathy , splenomegaly are more common.

They have associated parenchymal lesions , smear for acid fast bacilli positive and also culture positive for AFB.

DIAGNOSIS :

Tuberculin skin testing : Tuberculin skin testing is almost always positive if performed after 8 weeks of development of symptoms . So a negative skin testing after 8 weeks of development of symptoms can be used to rule out TB. However in malnourished individuals or HIV patients the test remains negative .

Pleural fluid analysis :

1. Pleural fluid protein elevated and usually above 5 g/dL
2. WBC count has more than 50% small lymphocytes . If there is eosinophils it suggests previous thoracentesis or associated pneumothorax .
3. Mesothelial cells not more than 5 % .
4. Adenosine deaminase levels more than 70 U/L
5. Interferon gamma levels more than 3.7IU/ml
6. Low pleural fluid pH and CRP levels more than 30 mg/dl
7. Pleual biopsy – demonstration of parietal pleura granuloma , AFB , caseous necrosis.
8. Pleual fluid AFB staining and culture for mycobacteria

3.Parapneumonic effusion :

When any pleural effusion is associated with bacterial pneumonia , lung abscess or bronchiectasis , it is called as parapneumonic effusion .

An empyema is defined as pus in the pleural space. Many complicated parapneumonic effusions are empyema .

According to Weese et al. empyema is charecterised by specific gravity greater than 1.018 , protein more than 2.5 g/dL , WBC count more than 500 cells/ mm3 But according to Vianna empyema is defined as pleural fluid protein more than 3.0 g/dL , WBC greater than 15000 / mm3 or positive bacterial cultures.

Pathogenesis :

1.Exudative stage :

This stage is characterised by rapid accumulation of sterile pleural fluid in pleural space. The fluid orginates from the interstitial spaces of lung and also from the visceral pleural capillaries due to increased capillary permeability. There is low WBC count , low LDH level and a normal glucose level in the pleural fluid at this stage. This stage resolves if appropriate antibiotics is instituted.

2.Fibropurulent stage

The pleural space is invaded by the bacteria , if antibiotics are not intiated. In this stage there is accumulation of large amounts of pleural fluids which is rich in bacteria ,polymorphonuclear leucocytes and cellular debris . The visceral and parietal pleura are covered by a continuos sheet of fibrin. This leads to the formation of loculation and prevents the spread of pus . But this makes the insertion of chest tube difficult. In this stage there is higher pleural fluid LDH and lower pleural fluid glucose and pH

3.Organisation stage

This stage is characterised by pleural peel. The fibroblasts grow in to the exudates and an inelastic membrane is produced . The lung is encased by this inelastic pleural peel and makes it functionless. The exudates is thick at this stage and it may spontaneously drain through the chest wall called as empyema necessitatis or into the lung producing a bronchopleuralfistula .

The most common organisms are Staphylococcal aureus , Escherichia coli and anaerobe Bacteroids .

Clinical features :

Fever , cough with expectoration , chest pain are the major symptoms .In immunocomprimised person fever may be absent . If the fever is present for more than 48 hours after the institution of antibiotics then it is called as parapneumonic effusion. The history of alcoholism , seizures or an episode of unconsciousness should be sought as it leads to aspiration.

Light's classification for parapneumonic effusions and empyema :

1.Nonsignificant pleural effusion

2.Typicalparapneumonic pleural effusion

3.Borderline complicated pleural effusion

4.Simple complicated pleural effusion

5.Complex complicated pleural effusion

6.Simple empyema

7.Complex empyema

Diagnosis :

1. During thoracocentesis , there is frank pus .
2. The pleural fluid will be positive for Gram stain , culture.

3. Pleural fluid glucose less than 40 mg / dL , pH < 7.0 , LDH > 3 times the upper limit.

Also the above findings along with loculations constitutes the bad prognostic factors for both empyema and parapneumonic effusions.

Management :

Antibiotics :

Community acquired pneumonias :

- Fluroquinolones such as levofloxacin , moxifloxacin ,gatifloxacin or a macrolide such as azithromycin , clarithromycin plus a beta lactams such as cefotaxime , ceftriaxone , ampicillin – sulbactam .
- If pseudomonas is suspected anti pseudomonas antibiotics like meropenam ,imipenam , piperacillintazobactam or cefepime is used.

Anaerobes – metronidazole or clindamycin .,

MRSA – vancommycin

Management for pleural effusions :

1.Therapeuticthoracentesis

2.Tubethoracostomy

3.Intrapleuralfibrinolytics like streptokinase , streptodornase , tissue plasminogen activator

4.Video assisted thoracoscopy with lysis of adhesions and / or decortications

5.Decortication

6.Open drinage

MATERIALS AND METHODS

STUDY POPULATION:

This study is to be conducted among 50 patients with pleural Effusion , attending the Department of Medicine & Department of Thoracic Medicine in Govt. Rajaji Hospital, Madurai.

Inclusion criteria:

- In Patients with clinical and radiological evidence of pleural effusion irrespective of etiology, both sex
- Age > 12 years

Exclusion criteria:

- Patients having jaundice , dyslipidemia , hypoproteinemia
- Age < 12 years

ANTICIPATED OUTCOME:

- Total Pleural fluid Bilirubin and ratio to serum levels, Pleural fluid Cholesterol and Pleural fluid Total Protein level is superior or supportive to Light's criteria in differentiating transudates and exudates.

DATA COLLECTION:

- A Brief history with clinical examination will be done.
- Detailed Clinical Examination ,
- Pleural fluid bilirubin , Serum Bilirubin , Pleural fluid cholesterol, Pleural fluid total protein, Serum total protein , Pleural & Serum LDH are estimated.

LABORATORY INVESTIGATIONS:

1. Pleural fluid bilirubin & Serum Bilirubin
2. Pleural fluid cholesterol
3. Pleural fluid total protein & Serum Protein
4. Pleural fluid LDH & Serum LDH

STUDY PROTOCOL:

- Patients with clinical and radiological evidence of pleural effusion are to be included in the study.
- Then they are classified in to exudates and transudates on the basis of the clinical , radiological and biochemical evaluation .

- In all the patients following investigation are done to classify them as exudates and transudates
- Pleural fluid bilirubin & Serum Bilirubin , Pleural fluid cholesterol, Pleural fluid total protein are estimated and the patients are classified in to exudates and transudates.
- Then the patients are classified in to exudates and transudates on the basis of Light's criteria.
- Now the classification of exudates and transudates done on the basis of Total Pleural fluid bilirubin and its ratio to serum bilirubin , Pleural fluid cholesterol , Pleural fluid Total protein are compared with results of the classification of exudates and transudates done on the basis of Light's criteria.
- Sensitivity , specificity , Positive predictive value , negative predictive value , diagnostic accuracy of each testsare calculated .

DESIGN OF STUDY:

Prospective analytical study

PERIOD OF STUDY:

JANUARY 2014 TO AUGUST 2014

CONSENT:

Individual written and informed consent.

ANALYSIS:

SIMPLE STATISTICAL ANALYSIS

CONFLICT OF INTEREST :

NIL

FINANCIAL SUPPORT:

NIL

RESULTS

Table 1 : Age distribution of the study population (n=50)

Age group	Frequency	Percent
<25 years	2	4
26 – 40 years	6	12
41 – 55 years	17	34
56– 70 years	24	48
>70 years	1	2
Total	50	100

Mean age (± S.D): 53.3 (11.65) years, minimum : 21 years, maximum : 75 years.

Comments: About 48% of the study subjects were in the age group of 56-70 years while the 34% were in the age group 41-55 years.

FIGURE 7

AGE DISTRIBUTION OF THE STUDY POPULATION

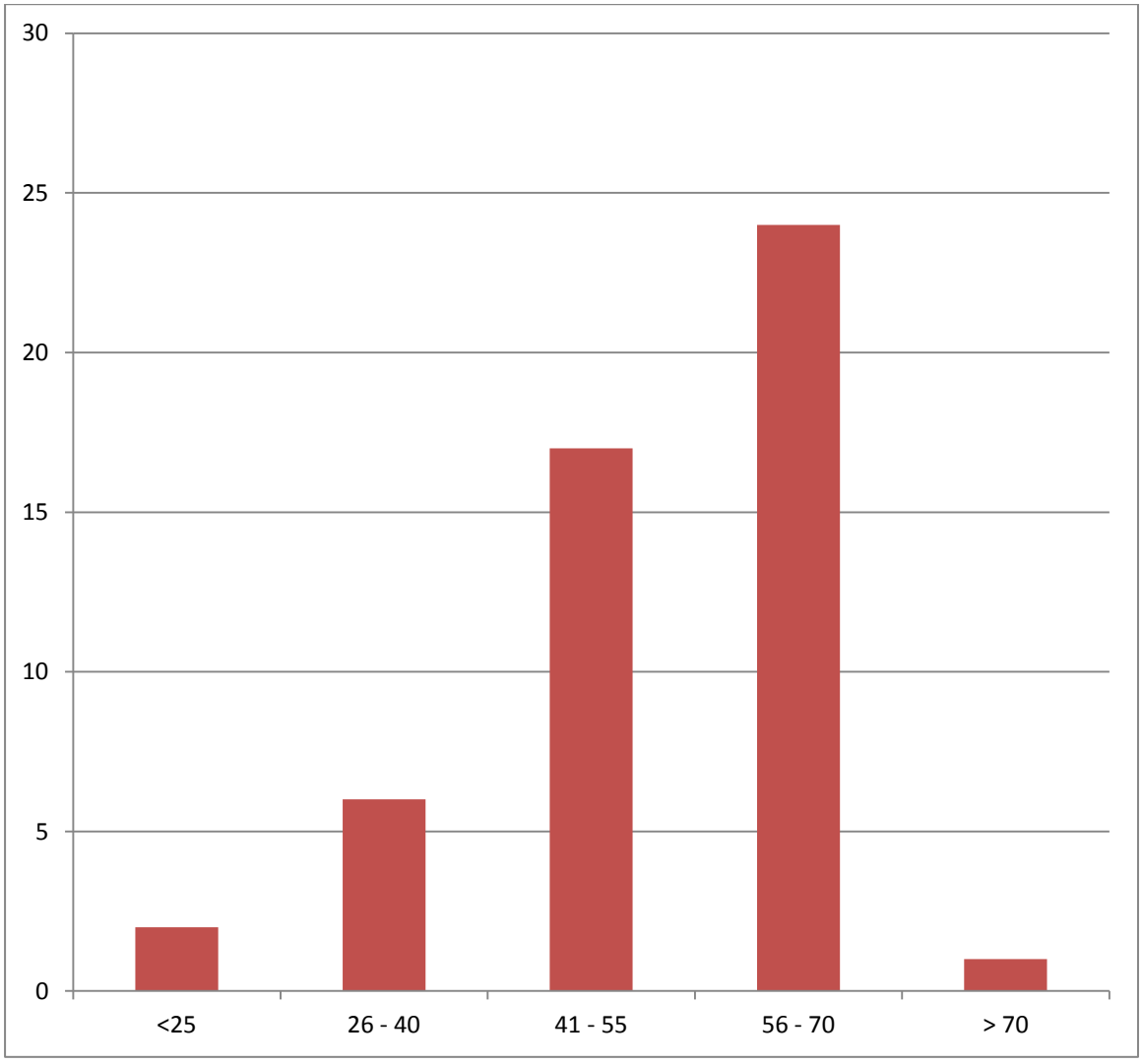


Table 2 : Gender distribution of the study population (n=50)

Gender	Frequency	Percent
Female	21	42
Male	29	58
Total	50	100.0

Comments: About 58 % of the study subjects were males while the remaining 42% were females.

FIGURE 8

GENDER DISTRIBUTION OF THE STUDY POPULATION

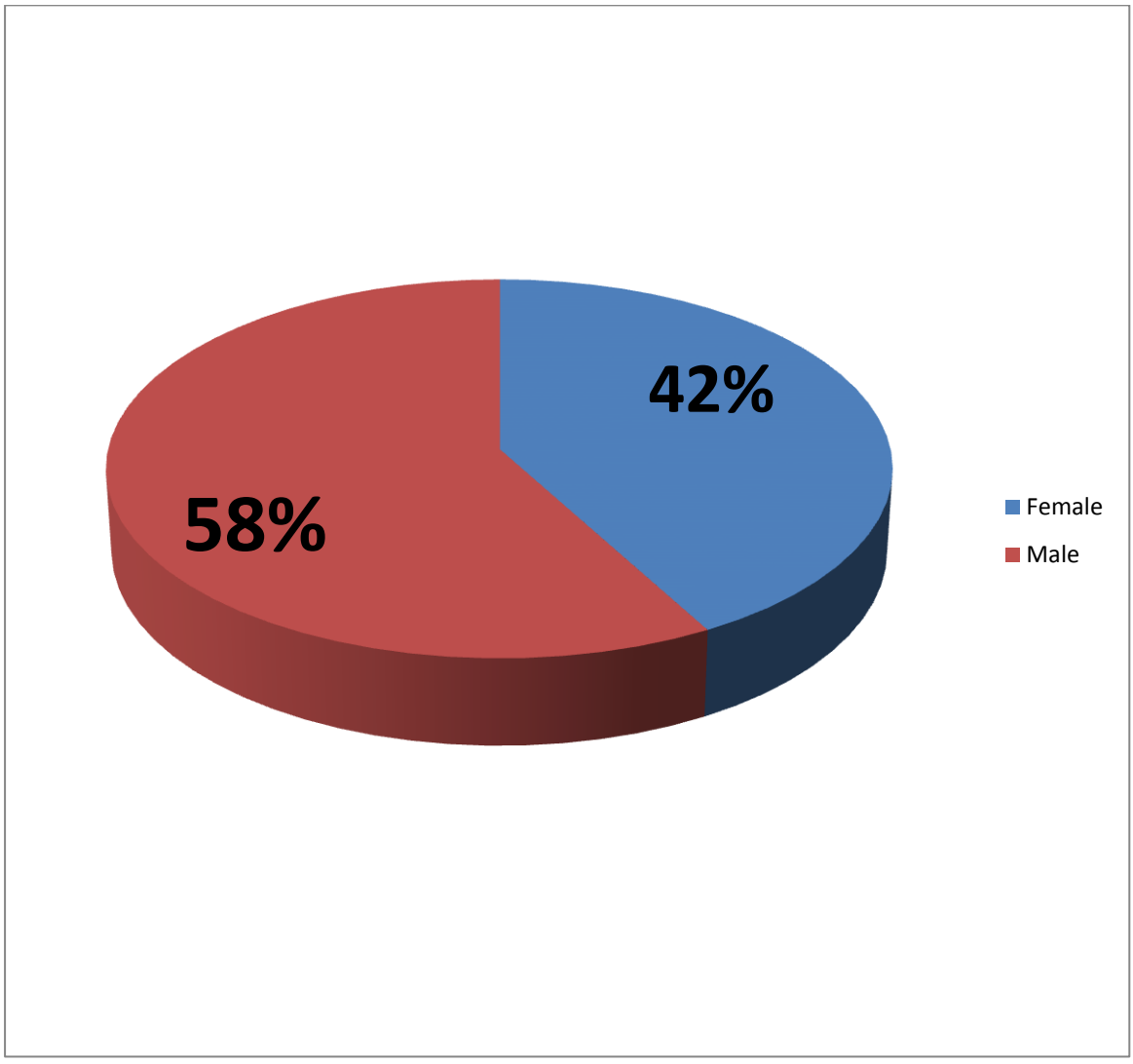


Table 3 : Clinical criteria for classifying pleural effusions as exudates and transudates

Diagnosis	Criteria
Tuberculosis	Clinically cough , fever with evening rise of temperature, loss of weight and appetite sputum showing AFB, ADA in pleural fluid , Chest x ray showing pleural effusion , Response to ATT.
Parapneumonic effusions	Clinically cough with expectoration, fever with chills & rigors, Chest x ray showing pleural effusion, Bacteria in pleural fluid/sputum.
Malignant pleural effusions	Pleural fluid cytology, Pleural biopsy, Demonstration of primary sites.
Congestive cardiac failure	Clinically pedal edema , ascites, elevated JVP , basal crepitations, Chest x ray , ECG, Echocardiography, Response to Diuretics
Chronic liver disaese	Signs of Liver cell failure , ascites , splenomegaly ,
Chronic kidney disease	Raised serum urea and creatinine, Contracted kidneys in ultrasonogram , along with signs and symptoms of volume overload.

Table 4 : Classification of the study population according to clinical criteria

Clinical classification	Frequency	Percent
Exudates	28	56
Transudates	22	44
Total	50	100

Comments: About 56% of the study subjects are exudates while 44% are transudates .

FIGURE 9

CLASSIFICATION OF THE STUDY POPULATION ACCORDING TO CLINICAL CRITERIA

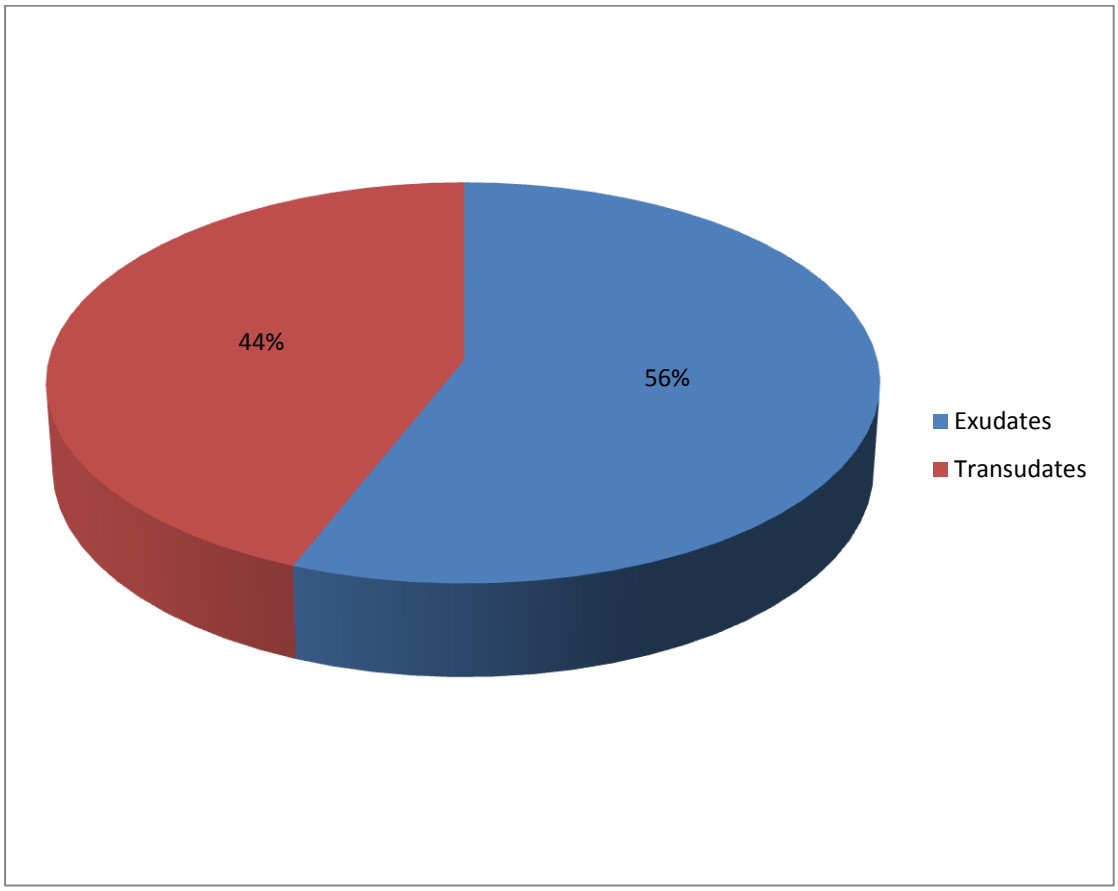


Table 5: Distribution of Exudates in the study group

Etiology	Frequency	Percent
Tuberculosis	14	50
Malignant pleural effusions	10	35.72
Parapneumonic effusions	4	14.28
Total	28	100

Comments : About 50 % of study group have tuberculosis , 35.72 % have malignancy and 14.28 % have parapneumonic effusions.

Table 6 : Distribution of Transudates in the study group

Etiology	Frequency	Percent
Congestive cardiac failure	10	45.46
Chronic liver disease	8	36.36
Chronic kidney disease	4	18.18
Total	22	100

Comments : About 45.46 % of study group have congestive cardiac failure , 36.36 % have chronic liver disease and 18.18 % have chronic kidney disease.

Table 7: Descriptive statistics of pleural fluid protein , serum and pleural fluid bilirubin and pleural fluid cholesterol levels of the study population (n=50)

Descriptive statistics	Pleural Fluid Protein (gm/dl)	Pleural Fluid Bilirubin (mg/dl)	Serum Fluid Bilirubin (mg/dl)	Pleural Fluid Cholesterol (mg/dl)
Mean	3.04	0.43	0.61	49.98
Standard Deviation	0.53	0.121	0.14	19.69
Minimum	2.10	0.20	0.32	16.00
Maximum	4.40	0.61	0.90	80

Comments:

1) The mean level of protein and cholesterol in pleural fluid is 3.04 gm/dl and 49.98 mg/dl .

2) The mean level of bilirubin in serum and pleural fluid is 0.61 mg/dl and 0.43 mg/dl .

Table 8 : Identififcation of exudates by various criteria (n=28)

Criteria	Correctly classified as exudate N (%)	Wrongly classified as transudate N (%)
Light 's criteria	24 (85.72%)	4 (14.28%)
Pleural fluid Bilirubin	23 (82.14%)	5 (17.86%)
Pleural fluid / Serum Bilirubin ratio	27 (96.42%)	1 (3.58%)
Pleural fluid cholesterol	21 (75.00%)	7 (25.00%)
Pleural fluid Total Protein	26 (92.85%)	2 (7.15%)

Comments:

1) According to the Lights criteria, 85.72 % of the cases were detected with exudative pleural effusion.

2) According to Pleural fluid Bilirubin, 82.14 % of the cases were detected with exudative pleural effusion.

3) According to Pleural fluid / Serum Bilirubin ratio, 96.42 % of the cases were detected with exudative pleural effusion.

4) According to Pleural fluid cholesterol, 75% of the cases were detected with exudative pleural effusion

5) According to Pleural fluid Total Protein, 92.85% of the cases were detected with exudative pleural effusion

Table 9 :Identifiifcation of transudate by various criteria (n=22)

Criteria	Correctly classified as transudate N (%)	Wrongly classified as exudate N (%)
Light 's criteria	20 (90.90%)	2 (9.10%)
Pleural fluid Bilirubin	19 (86.36%)	3 (13.64%)
Pleural fluid / Serum Bilirubin ratio	20 (90.90%)	2 (9.10%)
Pleural fluid cholesterol	19 (86.36%)	3 (13.64%)
Pleural fluid Total Protein	21 (95.45%)	1 (4.55%)

Comments:

1) According to the Lights criteria, 90.90 % of the cases were detected with transudative pleural effusion.

2) According to Pleural fluid Bilirubin, 86.36 % of the cases were detected with transudative pleural effusion.

3) According to Pleural fluid / Serum Bilirubin ratio, 90.90 % of the cases were detected with transudative pleural effusion.

4) According to Pleural fluid cholesterol, 86.36 % of the cases were detected with transudative pleural effusion

5) According to Pleural fluid Total Protein, 95.45 % of the cases were detected with transudative pleural effusion

Table 10 :Distribution of exudates in study population (n=28)

Criteria		Tuberculosis	Para pneumonic effusions	Malignant pleural effussion	P value
Light 's criteria	**Exudate**	12	9	3	0.003
	Transudate	2	1	1	
Pleural Fluid bilirubin	**Exudate >0.48 mg/dL**	13	7	3	0.009
	Transudate <0.48 mg/dL	1	3	1	
Pleural Fluid / Serum Bilirubin	**Exudate > 0.62**	13	10	4	<0.001
	Transudate < 0.62	1	0	0	
Pleural Fluid Cholesterol	**Exudate > 60 mg/dL**	10	8	3	0.050
	Transudate < 60 mg/dL	4	2	1	
Pleural Fluid Total Protein	**Exudate > 3 g/dL**	14	9	3	<0.001
	Transudate < 3.0g/dL	0	1	1	

FIGURE 10

IDENTIFIFCATION OF EXUDATE BY VARIOUS CRITERIA

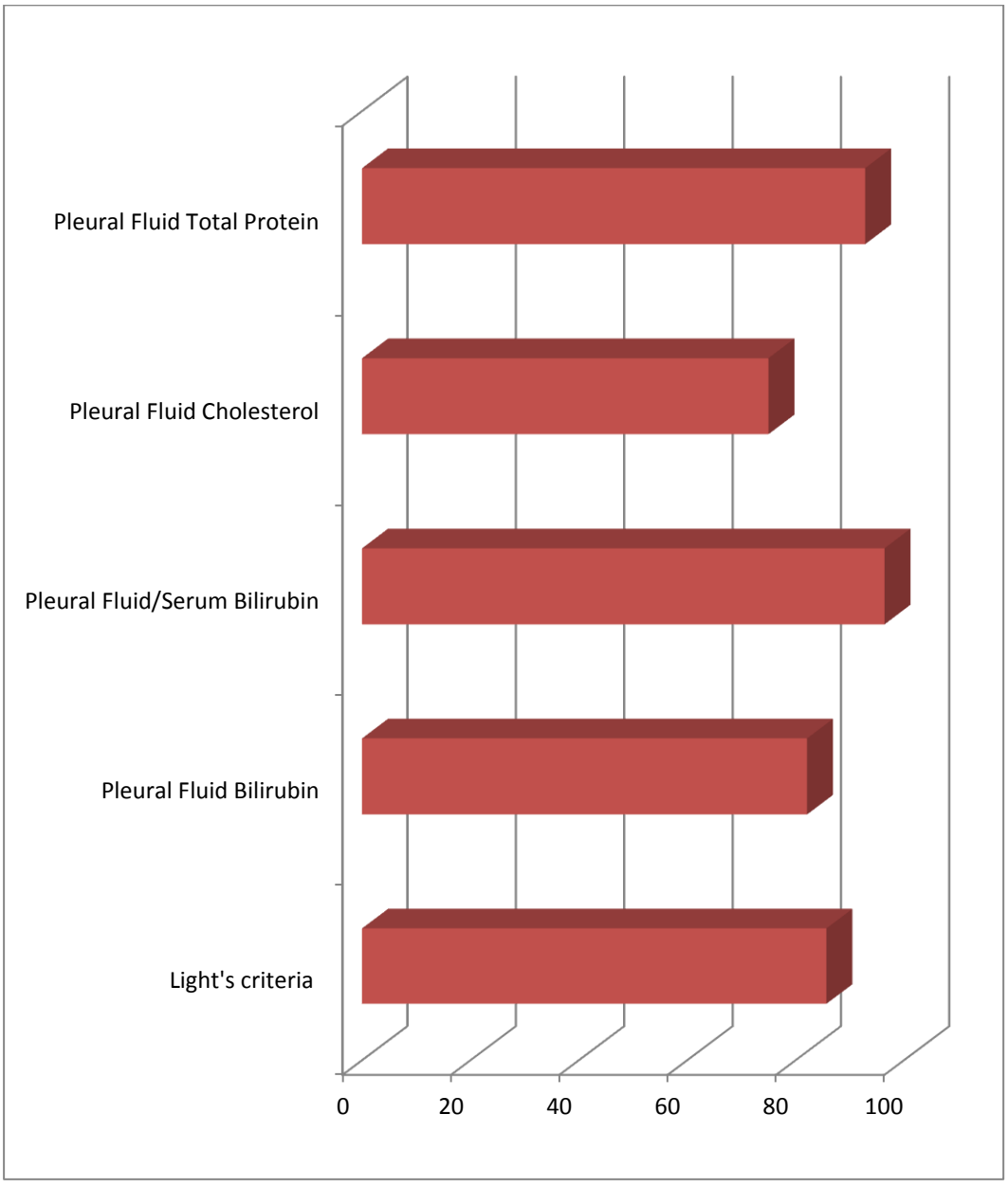


Table 11 :Distribution of transudates in study population (n=22)

Criteria		Congestive Cardiac Failure	Chronic Liver Disease	Chronic Kidney Disease	P value
Light 's criteria	**Transudate**	8	8	4	0.003
	Exudate	2	0	0	
Pleural Fluid bilirubin	**Transudate < 0.48 mg/dL**	8	8	3	0.009
	Exudate > 0.48 mg/dL	2	0	1	
Pleural Fluid / Serum Bilirubin	**Transudate < 0.62**	10	8	2	0.003
	Exudate > 0.62	0	0	2	
Pleural Fluid Cholesterol	**Transudate < 60 mg/dL**	9	6	4	0.009
	Exudate > 60 mg/dL	1	2	0	
Pleural Fluid Total Protein	**Transudate < 3.0g/dL**	10	7	4	<0.001
	Exudate > 3 g/dL	0	1	0	

FIGURE 11

IDENTIFIFCATION OF TRANSUDATE BY VARIOUS CRITERIA

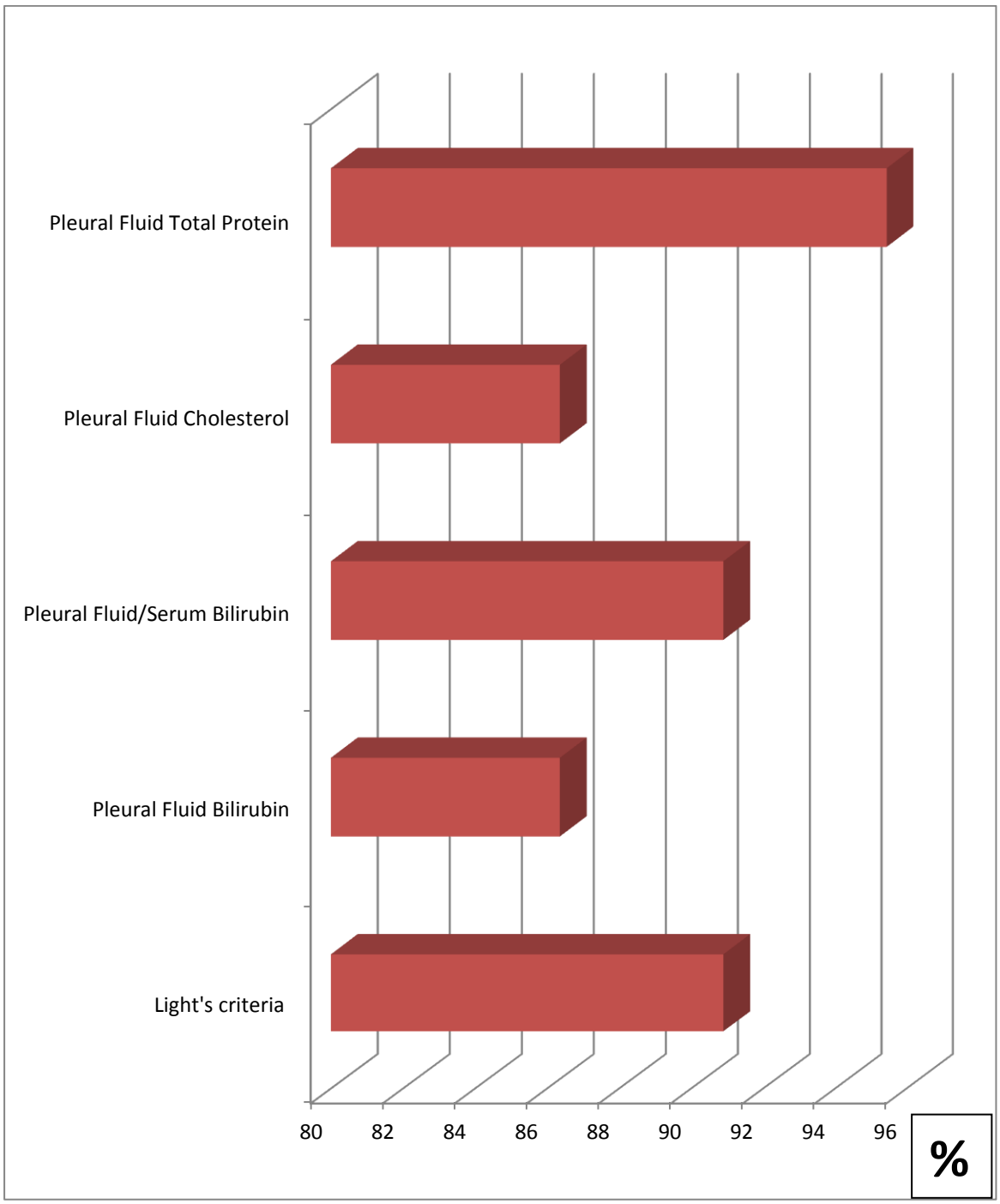


Table 12 : Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) , diagnostic accuracy of various criteria.

Criteria	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Light 's criteria	85.71 %	90.90%	92.30%	83.33%	88%
Pleural Fluid bilirubin	82.14 %	86.36%	88.46%	79.16%	84%
Pleural Fluid/ Serum Bilirubin	96.42%	90.90%	93.10%	95.23%	94%
Pleural Fluid Cholesterol	75.00%	86.36%	87.50%	73.07%	80%
Pleural Fluid Total Protein	92.85%	95.45%	96.29%	95.23%	94%

Comment :

The misclassification of exudates and transudates by various criteria when compared to Light's criteria is not statistically significant as p value is <0.05.

To classify an exudative pleural effusion from a transudative pleural effusion, the most specific test is pleural fluid total protein and the most sensitive test is pleural fluid / serum bilirubin ratio .

DISCUSSION

One of the most common disease entity encountered by physicians worldwide is pleural effusion . In a situation where undiagnosed pleural effusion has come upon, the first and foremost thing to be resolved is whether the fluid is a transudate or exudate. The most frequently used Light's criteria, though still considered as a gold standard, often misclassify a transudate as an exudates. The present study was undertaken to evaluate the efficacy of pleural fluid bilirubin and its ratio to serum levels , pleural fluid cholesterol and pleural fluid total protein in distinguishing pleural fluid transudates and exudates and its correlation with Light's criteria .

Method of study:

This study was conducted in Govt. Rajaji Hospital, Madurai which is affiliated to Madurai Medical College. This study subjects were selected from the patients admitted in Department of Medicine and Department of Medicine , Govt. Rajaji Hospital.

The study was conducted in 50 patients; the patients had pleural effusion with clinical background of congestive cardiac failure, chronic liver disease , chronic kidney disease ,tuberculosis , parapneumonic effusions , malignancy.

The patients are examined clinically with the following parameters and only 50 patients are taken for study.

Clinical criteria to classify patients as exudates and transudates :

If the patient had oedema legs, ascites, cardiac enlargement, radiological evidence of congested lungs and responded to treatment for congestive cardiac failure , then the diagnosis of congestive cardiac failure was made.

When there were raised serum urea and creatinine levels along with signs and symptoms indicating volume overload, chronic kidney disease was diagnosed.

If the patient had features of liver cell failure,ascites, spleenomegaly and evidence of volume overload status , chronic liver disease was diagnosed.

The diagnosis of tuberculosis was made if there is cough , fever with evening rise of temperature, loss of weight and appetite ,sputum showing AFB, ADA in pleural fluid ,chest x ray showing pleural effusion ,response to ATT.

The diagnosis of parapneumonic effusion was made if there is cough with expectoration, fever with chills & rigors, chest x-ray showing pleural effusion, bacteria in pleural fluid/sputum.

The diagnosis of malignant pleural effusion was made if there is Pleural fluid cytology, Pleural biopsy, demonstration of primary sites.

Study protocol :

- Patients with clinical and radiological evidence of pleural effusion are to be included in the study
- Then they are classified in to exudates and transudates on the basis of the clinical , radiological and biochemical evaluation .
- In all the patients following investigation are done to classify them as exudates and transudates
- Pleural fluid bilirubin & Serum Bilirubin , Pleural fluid cholesterol, Pleural fluid total protein are estimated and the patients are classified in to exudates and transudates.
- Then the patients are classified in to exudates and transudates on the basis of Light's criteria.
- Now the classification of exudates and transudates done on the basis of Total Pleural fluid bilirubin and its ratio to serum , Pleural fluid cholesterol , Pleural fluid Total protein are compared with results of the classification of exudates and transudates done on the basis of Light's criteria.
- Sensitivity , specificity , Positive predictive value , negative predictive value , diagnostic accuracy of each tests are calculated .

Age and sex distribution of the population in our study is as follows :

82% of the study subjects were in the age group of 51-70yrs while the 16% were in the age group of 41-50yrs.

Majority of the study subjects were males (58%) while remaining 42% were females.

Exudates and transudates distribution in our study is as follows :

In our study about 56% of the study subjects were exudates while 44% were transudates .

Among the exudates , about 50 % of study groups have tuberculosis , 35.72 % have malignancy and 14.28 % have parapneumonic effusions.

Among the transudates , about 50 % of study groups have tuberculosis , 35.72% have malignancy and 14.28 % have parapneumonic effusions.

Pleural fluid bilirubin , Serum Bilirubin , Pleural fluid cholesterol, Pleural fluid total protein , Serum total protein , Pleural fluid LDH , Serum LDH are estimated.

Pleural fluid Bilirubin , Cholesterol , Total protein :

Any serous membrane inflammation often leads to increased capillary permeability and this enables the diffusion of high molecular weight bilirubin , protein .

The permeability of pleura is increased due to “serum leakage” and this leads to the accumulation of cholesterol in exudative pleural effusion .

In our study to diagnose exudates the following parameters are used :

A pleural fluid bilirubin of more than 0.48 mg / dL ,

A pleural fluid bilirubin to serum bilirubin ratio of more than 0.62 ,

A pleural fluid cholesterol of more than 60 mg / dL ,

A pleural fluid total protein more than 3 g/dL .

Results :

By applying Light’s criteria in patients with exudative pleural effusion classified clinically , 85.72 % of the cases were correctly diagnosed as exudative pleural effusion.

By applying Pleural fluid Bilirubin in patients with exudative pleural effusion classified clinically , 82.14 % of the cases were correctly diagnosed as exudative pleural effusion.

According to Pleural fluid / Serum Bilirubin ratio , patients with exudative pleural effusion classified clinically, 96.42 % of the cases were correctly diagnosed as exudative pleural effusion.

By applying Pleural fluid cholesterol to patients with exudative pleural effusion classified clinically , 75% of the cases were correctly diagnosed as exudative pleural effusion

According to Pleural fluid Total Protein , patients with exudative pleural effusion classified clinically, 92.85% of the cases were correctly diagnosed as exudative pleural effusion.

In our study by applying the Lights criteria, about 14.28 % of exudative pleural effusion was misclassified as transudative, and by applying Pleural fluid Bilirubin and Pleural fluid cholesterol , the misclassification was 17.86 % and 25 % respectively . Whereas by Pleural fluid / Serum Bilirubin ratio , the misclassification was only 3.58 %. Also 7.15 % of exudates were misclassified as transudates , when Pleural fluid Total Protein was applied.

By applying Light's criteria in patients with transudative pleural effusion classified clinically , 90.90 % of the cases were correctly diagnosed as transudative pleural effusion.

By applying Pleural fluid Bilirubin in patients with transudative pleural effusion classified clinically , 86.36 % of the cases were correctly diagnosed as transudative pleural effusion.

According to Pleural fluid / Serum Bilirubin ratio , in patients with transudative pleural effusion classified clinically, 90.90 % of the cases were correctly diagnosed as transudative pleural effusion.

By applying Pleural fluid cholesterol to patients with transudative pleural effusion classified clinically , 86.36 % of the cases were correctly diagnosed as transudative pleural effusion .

According to Pleural fluid Total Protein to patients with transudative pleural effusion classified clinically, 95.45% of the cases were correctly diagnosed as transudative pleural effusion.

In our study by applying the Lights criteria, about 9.10 % of transudative pleural effusion was misclassified as exudative, and by applying Pleural fluid Bilirubin and Pleural fluid cholesterol , the misclassification was 13.64 % and 13.64 % respectively . Also 9.10 % of transudates were misclassified as exudates , when Pleural fluid / Serum Bilirubin ratio was applied. Whereas by Pleural fluid Total Protein, the misclassification was only 4.55 %.

Among the parameters used most specific test to classify an exudative pleural effusion from a transudative pleural effusion is pleural fluid total

protein which is 95.45 % and most sensitive test is pleural fluid / serum bilirubin ratio which is 95.45 %. The positive predictive value, negative predictive value and diagnostic accuracy to classify an exudative pleural effusion from a transudative pleural effusion is higher for pleural fluid total protein which is 96.29 % , 95.23 % , 94 % respectively .

The sensitivity , specificity , positive predictive value, negative predictive value and diagnostic accuracy of Light's criteria are 85.71 % , 90.90 % , 92.30 % , 83.33 % , 88 % respectively .

In a study conducted by Gupta K. B .,Depts.of Tuberculosis & Chest Diseases

Pt.B.D.Sharma Post Graduate institute of Medical Sciences, Rohtak, Haryana, A total of 80 patients were classified on the basis of clinical radiological and biochemical evaluation into transudates and exudates. Assessment of efficacy of pleural fluid bilirubin (P BIL) , pleural fluid bilirubin/serum bilirubin ratio (P/S BIL) and Light's criteria to correctly classify transudates and exudates were done. On the basis of pleural fluid bilirubin and pleural fluid bilirubin / serum bilirubin ratio, 78% of misclassified transudate by Light's criteria and 84% of misclassified exudates were accurately diagnosed. For Pleural fluid Bilirubin , a positive predictive value of 91% and a negative predictive value of 58% were found

by using a cut off value of 0.48mg%. Similarly, a positive predictive value of 91% and a negative predictive value of 57% was observed , using a cut off value of 0.62 for Pleural fluid /Serum Bilirubin.

In a study conducted by Anand K. Patel and SushmitaChoudhury ,Department of Respiratory Medicine, Shree M.P. Shah Medical College, Jamnagar (Gujarat), India, 60 patients with evidence of pleural effusion clinically and radiologically were classified 49 as exudates and 11 as transudates. To distinguish transudates and exudates they used a criteria of pleural fluid cholesterol levels at a cut-off point of greaterthan 60 mg/dL and/or total protein at a cut-off point of greater than 3 g/dL.The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), were 100 percent. Using Light's criteria for discriminating transudates and exudates, sensitivity, specificity, PPV and NPV were found to be 98%; 100%; 100% and 92%, respectively. The differences resulted from a mis-classification of one expected exudate as transudate
by Light's criteria.

DEFINITIONS

Diagnostic accuracy : This is the probability that a randomly selected subject is correctly diagnosed by the test .

Negative Predictive Value : The probability that a person who has tested negative on a diagnostic test (T−) actually does not have the disease (D−).

Positive Predictive Value : This is the probability that a person who has tested positive on a diagnostic test (T+) actually has the disease(D+).

Sensitivity : This is the probability that a person with disease (D+) will correctly test positive based on the diagnostic test (T+).

Specificity: This is the probability that a person without disease (D−) will correctly test negative based on the diagnostic test (T−).

D – Disease ., **T** – Test

CONCLUSION

Many decades Light ‘s criteria has been used widely to differentiate exudative from transudative pleural effusion. But it also misclassifies 25 % of transudates as exudates , so there is a need to identify new parameters which will prove to be superior or supportive to the present available array of tests.

From our study we came to known that there was no statistically significant difference among various criterias in classifying pleural effusion as exudates and transudates.

The misclassification of exudates and transudates by various criteria when compared to Light’s criteria is not statistically significant as p value is <0.05.

From our study we came to a conclusion that to classify an exudative pleural effusion from a transudative pleural effusion

- most specific test is pleural fluid total protein and
- most sensitive test is pleural fluid / serum bilirubin ratio .

The positive predictive value, negative predictive value and diagnostic accuracy is higher for pleural fluid total protein .

To conclude, though Light's criteria remains as gold standard to differentiate transudates and exudates, in cases where there is a mismatch between clinical diagnosis and the outcome from Light's criteria, pleural fluid bilirubin / serum bilirubin ratio and pleural fluid total protein evaluation may add to the diagnostic accuracy.

SUMMARY

The classic criteria of differentiating an exudate from a transudate is Light's criteria. Over the last few years, it has been noted that even Light's criteria may misclassify a significant percentage of pleural effusions.

The objective of the present study was to evaluate the usefulness of Total Pleural fluid Bilirubin and its ratio to serum levels , Pleural fluid Cholesterol and Pleural fluid Total Protein level in classifying pleural effusions as exudates and transudates with Light's criteria as the gold standard .

From our study it is evident that most specific test to classify an exudative pleural effusion from a transudative pleural effusion is pleural fluid total protein which is 95.45 % and most sensitive test is pleural fluid / serum bilirubin ratio which is 95.45 %. The positive predictive value, negative predictive value and diagnostic accuracy is higher for pleural fluid total protein which are 96.29 % , 95.23 % , 94 % respectively .

The sensitivity , specificity , positive predictive value, negative predictive value and diagnostic accuracy of pleural fluid bilirubin and pleural fluid cholesterol was not superior to Light 's criteria .

The pleural fluid /serum bilirubin ratio , pleural fluid total protein are very effective in differentiating exudative and transudative pleural effusion.

Limitations of the study :

1.Shorter study period and smaller study sample.

2.The various parameters studied are neither combined with others nor with the Light's criteria .

3.Different levels of the Pleural fluid bilirubin , Pleural fluid / Serum Bilirubin ratio, Pleural fluid cholesterol , Pleural fluid total protein are not tried in this study .

Further recommendations :

1. A longer study period and a larger study sample should be considered in the future .

2. Combination of Pleural fluid bilirubin , Pleural fluid / Serum Bilirubin ratio, Pleural fluid cholesterol , Pleural fluid total protein with other parameters of the Light's criteria .

3. Another study on varying levels of Pleural fluid bilirubin , Pleural fluid / Serum Bilirubin ratio, Pleural fluid cholesterol , Pleural fluid total protein which will give the highest accuracy in detecting exudative effusions .

ANNEXURES

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PROFORMA

Name : **Age/Sex/Occupation:**

Presenting complaints:

H/o Fever, chest pain , cough & expectoration, hemoptysis ,dyspnea, Loss of weight, Loss of Appetite. Etc.

Past history:

H/o Tuberculosis, Chronic liver disease, coronary artery disease, chronic kidney disease

Clinical examination:

General examination:

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy,

Vitals: PR, BP, RR, SpO2, Temperature

Systemic examination:

CVS:

RS:

Abdomen :

CNS:

LABORATORY INVESTIGATIONS :

1.Pleural fluid bilirubin & Serum Bilirubin

2.Pleural fluid cholesterol

3.Pleural fluid total protein & Serum Protein

4.Pleural fluid LDH & Serum LDH

ABBREVIATIONS

CHF – Congestive Heart Failure

Pro -BNP – Pro Brain Natriuretic Peptide

LDH-Lactate dehydrogenase

PF-pleural fluid

Sr-serum

Pro-protein

Alb-albumin

MASTER CHART

S.No	NAME	AGE	SEX	DIAGNOSIS	PLEURAL FLUID PROTEIN g/ dl	SERUM PROTEIN g/dl	PLEURAL FLUID PROTEIN / SERUM PROTEIN RATIO PLEURAL FLUID / SERUM PROTEIN RATIO	PLEURAL FLUID LDH	SERUM LDH	PLEURAL FLUID / SERUM LDH RATIO	PLEURAL FLUID BILIRUBIN mg/dl	SERUM BILIRUBIN mg/dl	PLEURAL FLUID / SERUM BILIRUBIN RATIO	PLEURAL FLUID CHOLESTEROL mg/dl
1	MOHAN	45	M	CCF	2.7	6.1	0.44	156	306	0.51	0.3	0.9	0.33	30
2	PANDIARAJAN	46	M	CCF	2.9	5.6	0.51	132	288	0.45	0.52	0.9	0.57	65
3	IYYAMMAL	43	F	CCF	2.9	6.4	0.45	45	159	0.28	0.32	0.8	0.4	41

4	AYYAVU	52	M	CCF	2.5	6.2	0.4	116	250	0.46	0.3	0.6	0.52	33
5	LAKSHMANAN	62	M	CCF	2.3	6.4	0.35	129	296	0.43	0.38	0.7	0.54	21
6	CHANDRAN	57	M	CCF	2.9	6.5	0.44	112	220	0.51	0.33	0.8	0.41	29
7	KANAGA VALLI	55	F	CCF	2.2	6.5	0.34	28	91	0.31	0.35	0.6	0.58	31
8	JAMUNA	53	F	CCF	2.6	6.2	0.42	59	146	0.4	0.26	0.6	0.43	18
9	SELVA RANI	49	F	CCF	2.8	5.2	0.53	98	189	0.51	0.27	0.6	0.45	30
10	NEHRU	65	M	CCF	2.6	6.1	0.42	57	110	0.51	0.5	0.7	0.71	25
11	BAGHAYA LAKSHMI	57	F	Hepatic hydrothorax	2.9	6.4	0.45	69	156	0.44	0.42	0.8	0.52	22
12	MUTHU MANI	38	M	Hepatic hydrothorax	2.8	6.5	0.43	116	216	0.53	0.28	0.7	0.4	36
13	JAYA LAKSHMI	63	F	Hepatic hydrothorax	3.2	6.5	0.49	97	193	0.5	0.41	0.7	0.58	26
14	SIVA SANKARI	49	F	Hepatic hydrothorax	2.6	6.7	0.38	149	320	0.46	0.26	0.8	0.32	73
15	BASHEER AHMEED	57	M	Hepatic hydrothorax	2.3	6.4	0.35	133	287	0.46	0.38	0.7	0.54	16

16	MANIKANDAN	58	M	Hepatic hydrothorax	2.6	5.9	0.44	41	142	0.28	0.28	0.6	0.46	34
17	IRULAYI	35	F	Hepatic hydrothorax	2.6	5.8	0.43	26	98	0.26	0.31	0.8	0.38	46
18	MARI MUTHU	63	M	Hepatic hydrothorax	2.5	5.7	0.44	35	116	0.31	0.26	0.8	0.32	69
19	SONAI MUTHU	59	M	CKD	2.5	5.9	0.45	19	85	0.22	0.52	0.8	0.65	32
20	ARJUNAN	60	M	CKD	2.1	6.5	0.31	56	132	0.42	0.27	0.5	0.54	40
21	ANGARYARKANNI	55	F	CKD	2.1	6.6	0.32	48	124	0.38	0.21	0.4	0.52	19
22	ESHWAR LAL	65	M	CKD	2.3	6.7	0.34	38	106	0.35	0.2	0.3	0.66	23
23	RAJAMMAL	63	F	Tuberculosis	3.8	6.1	0.62	79	165	0.47	0.42	0.8	0.52	55
24	PONAMBALAM	59	M	Tuberculosis	3.5	6.1	0.57	100	133	0.75	0.5	0.6	0.8	66
25	RAGHAVAN	54	M	Tuberculosis	4.4	6.1	0.72	45	95	0.47	0.52	0.7	0.74	60
26	MALAIKANI	64	M	Tuberculosis	3.2	5.9	0.54	106	190	0.55	0.51	0.7	0.6	72
27	JAYAKUMAR	21	M	Tuberculosis	3.6	6.1	0.59	98	172	0.56	0.49	0.6	0.81	63

28	PREMAVATHI	52	F	Tuberculosis	3.2	5.6	0.57	94	166	0.56	0.58	0.8	0.72	33
29	RAJENDRAN	56	M	Tuberculosis	3.3	5.5	0.6	69	124	0.55	0.6	0.8	0.75	76
30	GURUVAMMAL	53	F	Tuberculosis	4.1	5.9	0.69	71	137	0.51	0.51	0.7	0.72	65
31	KUMAR	25	M	Tuberculosis	3.2	6.8	0.47	58	101	0.57	0.55	0.9	0.61	66
32	RAMESH	65	M	Tuberculosis	3.1	5.2	0.59	66	86	0.76	0.53	0.8	0.66	45
33	PANJU	68	F	Tuberculosis	3.9	5.9	0.66	298	387	0.77	0.56	0.9	0.62	80
34	PALANIVEL	60	M	Tuberculosis	3.6	5.3	0.67	250	320	0.78	0.52	0.7	0.74	71
35	MEENAKSHI	61	F	Tuberculosis	4.1	6.1	0.65	114	235	0.48	0.6	0.8	0.75	61
36	RANJITHAM	30	F	Tuberculosis	3.1	6.4	0.48	99	219	0.45	0.5	0.6	0.83	49
37	ARUMUGAM	32	M	Pneumonia	3.5	6.5	0.53	306	421	0.72	0.61	0.9	0.67	69
38	GANESAN	57	M	Pneumonia	3.2	6.6	0.48	112	216	0.51	0.58	0.8	0.72	48
39	VIMALA	36	F	Pneumonia	3.4	6.1	0.56	341	487	0.71	0.55	0.6	0.9	78
40	SUMATHI	52	F	Pneumonia	2.9	6.5	0.58	221	362	0.61	0.44	0.6	0.73	66
41	KANNAN	52	M	Malignancy	3.2	5.9	0.54	74	116	0.63	0.33	0.5	0.66	66
42	SANTHA RAM	60	M	Malignancy	3.1	5.8	0.53	102	154	0.66	0.5	0.8	0.62	68
43	VASANTHA	39	M	Malignancy	2.7	5.9	0.45	82	198	0.41	0.33	0.5	0.72	61

44	INDRA	68	F	Malignancy	3.4	6.3	0.53	68	85	0.79	0.51	0.8	0.63	45
45	KASIRAJAN	75	M	Malignancy	3.3	6.1	0.54	41	79	0.51	0.41	0.6	0.68	78
46	THAVAMANI	47	F	Malignancy	3.1	5.9	0.52	95	166	0.57	0.53	0.7	0.75	71
47	MYTHILI	52	F	Malignancy	3.2	5.8	0.54	86	109	0.78	0.55	0.8	0.68	33
48	VASUDEVAN	49	M	Malignancy	3.5	5.6	0.62	56	141	0.39	0.51	0.7	0.72	62
49	NARAYANAN	62	M	Malignancy	3.2	5.8	0.54	112	163	0.68	0.59	0.9	0.65	70
50	KALAISELVI	67	F	Malignancy	3.4	6.2	0.54	59	92	0.64	0.54	0.7	0.77	63

Ref. No. 68/E4/2/2014

Govt. Rajaji Hospital,
Madurai.20. Dated: 02.2014

Institutional Review Board / Independent Ethics Committee.
Captian. Dr. B. Santhakumar, M.D., (F.M.,)
Dean, Madurai Medical College &
Govt Rajaji Hospital, Madurai 625020. **Convenor**

Sub: Establishment-Govt. Rajaji Hospital, Madurai-20-
Ethics committee-Meeting Minutes- for January 2014
Approved list -regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held on 20.1.2014, Monday at 10.00 am to 12.00.noon at the Anaesthesia Seminar Hall, Govt. Rajaji Hospital, Madurai. The following members of the committee have attended the meeting.

1.Dr. V. Nagarajan, M.D., D.M (Neuro) Ph: 0452-2629629 Cell.No 9843052029	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2. Dr.Mohan Prasad , M.S M.Ch Cell.No.9843050822 (Oncology)	Professor & H.O.D of Surgical Oncology(Retired) D.No.72, West Avani Moola Street, Madurai -1	Member Secretary
3. Dr. Parameswari M.D (Pharmacology) Cell.No.9994026056	Director of Pharmacology Madurai Medical College	Member
4. Dr.S. Vadivel Murugan, MD., (Gen.Medicine) Cell.No 9566543048	Professor of Medicine Madurai Medical College	Member
5. Dr.S. Meenakshi Sundaram, MS (Gen.Surgery) Cell.No 9842138031	Professor & H.O.D of Surgery Madurai Medical College	Member
6. Mrs. Mercy Immaculate Rubalatha, M.A., Med., Cell. No. 9367792650	50/5, Corporation Officer's quarters, Gandhi Museum Road, Thamukam, Madurai-20	Member
7. Thiru.Pala. Ramasamy , BA.,B.L., Cell.No 9842165127	Advocate, D.No.72.Palam Station Road, Sellur, Madurai -2	Member
8. Thiru. P.K.M. Chellah ,B.A Cell.No 9894349599	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20	Member

The following Project was approved by the committee

..2..

Name of P.G.	Course	Name of the Project	Remarks
Dr.B. Karthik	PG in M.D., (General Medicince) Madurai Medical College and Government Rajaji Hospital, Madurai.	Efficacy of total pleural fluid bilirubin and ratio to serum levels, pleural fluid cholesterol and total protein level in diagnosing pleural effusion exudates and transudates and its correlation with Light's criteria.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.
2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any Extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

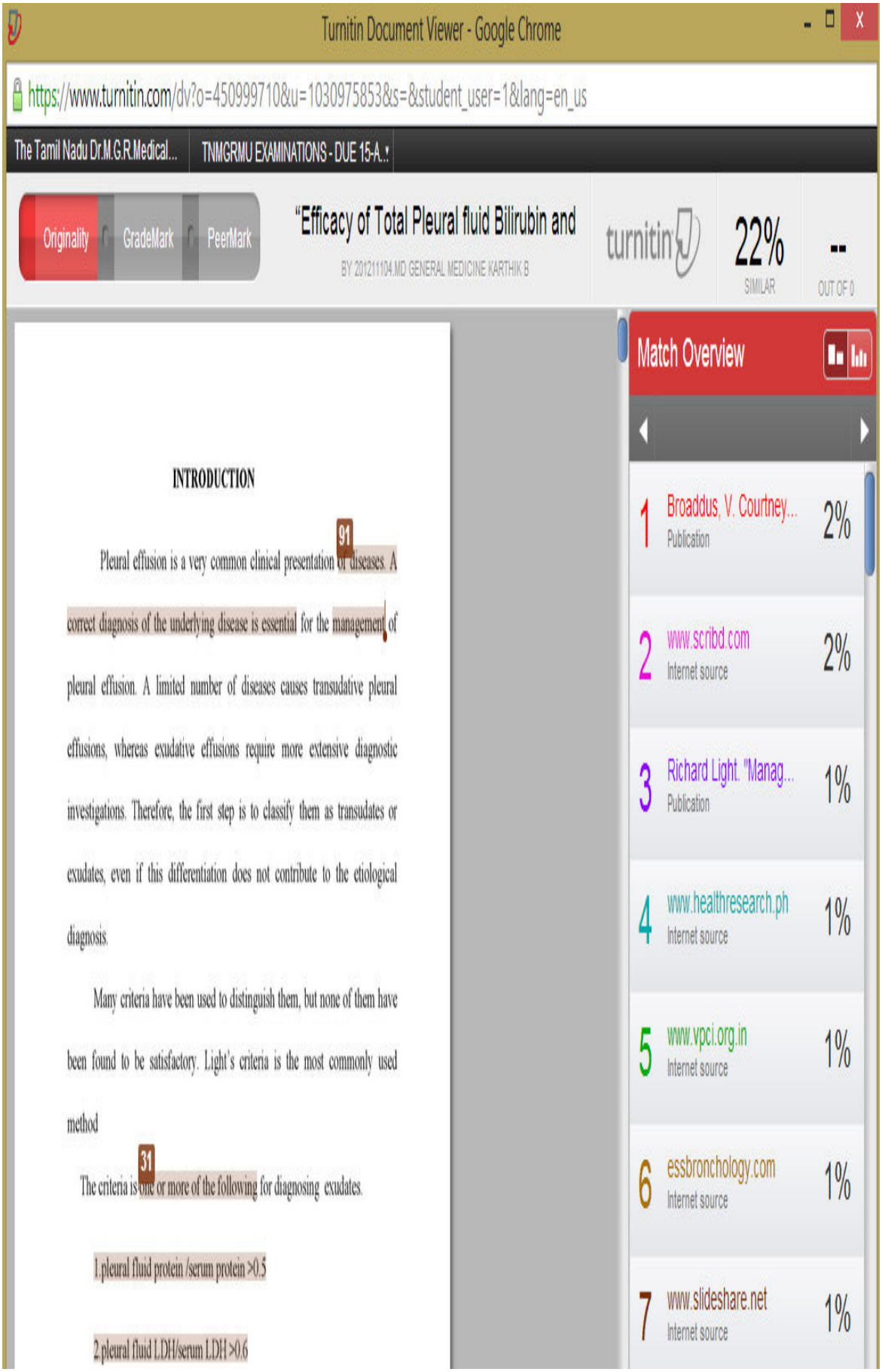
Member Secretary
Ethical Committee

Chairman

26.2.14
DEAN/Convenor
Govt. Rajaji Hospital,
Madurai- 20.

6/2/14

To
The above Applicant
-thro. Head of the Department concerned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INTRODUCTION
Pleural effusion is a very common clinical presentation of diseases. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. A limited number of diseases causes transudative pleural effusions, whereas exudative effusions require more extensive diagnostic investigations. Therefore, the first step is to classify them as transudates or exudates, even if this differentiation does not contribute to the etiological diagnosis.
Many criteria have been used to distinguish them, but none of them have been found to be satisfactory. Light's criteria is the most commonly used method
The criteria is one or more of the following for diagnosing exudates.
1.pleural fluid protein /serum protein >0.5
2.pleural fluid LDH/serum LDH >0.6
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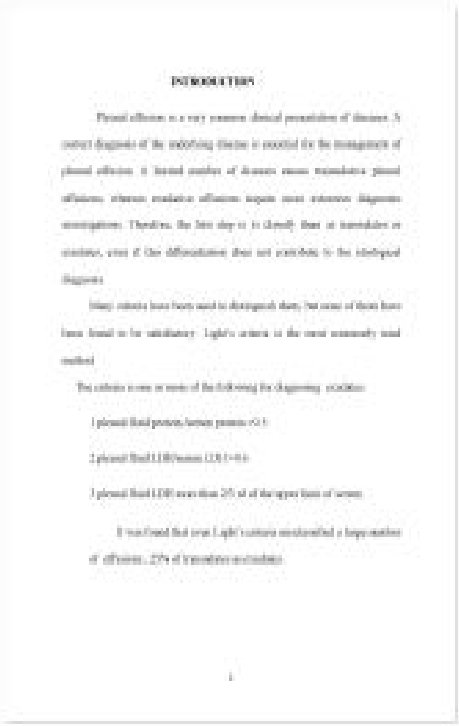

INTRODUCTION