"STUDY OF PLEURAL FLUID TO SERUM PSEUDOCHOLINESTERASE RATIO AND ITS CORRELATION WITH CLINICAL PROFILE AND LIGHT'S CRITERIA"

By

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DISSERTATION SUBMITTED TO THE SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

Under the guidance of

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APRIL 2018

DECLARATION BY THE CANDIDATE

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to be submitted to the

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ACKNOWLEDGEMENT

No academic work is single handedly accomplished. This work is no exception. Words fail me in expressing my heartfelt and humble gratitude to my guide ***Dr. VIDYASAGAR C.R.,*** *M.D., Professor, Department of General Medicine, for the guidance and encouragement all along in completing my study. His encouragement, sense of punctuality, research oriented approach, the painstaking effort to weed out errors and his affection during the entire course of study leaves me permanently indebted to him.*

It is with deep sense of gratitude and respect, I have taken an opportunity to thank my teacher ***Dr. PRABHAKAR K,*** *M.D, Professor and HOD, Department of General Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar, for his constant inspiration and valuable guidance at various stages of preparation of this dissertation.*

I express my deep sense of gratitude and humble thanks to ***Dr.Lakshmiaiah V, Dr. B.N.Raghavendra Prasad, Dr.P.N.Venkatarathnamma****,* ***Dr.Raveesha*** *Professors for their advice and constant encouragement throughout the present study.*

*I would like to thank all my teachers****, Dr.M.N.Chandrashekara****,* ***Dr.Srinivasa.S.V, Dr.Harish Kumar, Dr.Jagmohan, Dr.Reddy Prasad, Dr.Vishwanath Reddy, Dr.Niveditha, Dr.Prasanna, Dr.Anitha & Dr.Mahesh*** *from the Department of General Medicine for their heartfelt support at all times.*

I would like to acknowledge the opportune help and permission rendered by the Medical Director, Principal and Medical superintendent, SDUMC/RLJH, in conducting this study.

*I humbly thank **Dr.Rahul, Dr.Uphar Gupta, Dr.Sridhar, Dr Harish, Dr Surya** my senior postgraduates for their help and guidance to complete my dissertation.*

*I thank all my colleagues **Dr.Harsha, Dr.Prathap, Dr.Abhishek, Dr.Rakesh, Dr. Swetha, Dr.Dwarak, Dr.Maharaj, Dr.Raghvendra** for their timely suggestion throughout the preparation of this manuscript.*

*I thank **Dr.Mahesh,** Bio Statistician for his aid in Data interpretation & Statistical analysis of my Study which led to its successful completion.*

I am also thankful to all the Nursing Staff, Technical Staff and non-teaching staff for their invaluable help without which this study would not have been possible.

*I thank my father **Dr. K Suresh**, my mother **Mrs. Sumangali** and other family members for their constant source of encouragement, and support throughout the entire career.*

Last but not the least I am grateful to all those patients who were the subjects for the study, without whose cooperation this work would not have been possible.

Dr. SUHAS S AITHAL

ABSTRACT

Background:

Pleural effusion is a common clinical condition encountered in every day practice. It occurs in a large variety of pathological conditions, but the determination of cause of pleural effusion is not always easy. Lights et al developed criteria for differentiating between transudate and exudate using pleural and serum levels of protein and LDH with sensitivity and specificity of 99% and 98% respectively. Several prospective studies were unable to reproduce the excellent results obtained by Light et al. and have shown that the Light et al criteria misclassify a large number of effusions.

Pseudocholinesterase is found in plasma and most tissues. It is synthesized in the liver and its levels are remarkably constant. Measurement of serum ChE activity can serve as sensitive measure of synthetic capacity of the liver. Therefore measurement of its activity may serve as a useful diagnostic tool. Garcia and Padilla confirmed the importance of estimations of pseudocholinesterase activity in the diagnosis. Estimating the ratio of pleural fluid to serum pseudocholinesterase may serve as a useful diagnostic tool in a rural health setup compared to Lights criteria in terms of efficacy and cost. Hence this study was taken up to evaluate the same.

Objectives of the Study:

1. To estimate the pleural fluid to serum pseudocholinesterase ratio in patients with pleural effusion.
2. To compare the pleural fluid to serum pseudocholinesterase ratio with Lights criteria so as to identify as exudates or transudate.
3. To correlate the pleural fluid to serum pseudocholinesterase ratio with clinical profile of the patient.

Materials and Methods:

Patients with suspected pleural effusion was evaluated in detail, comprising of detailed history, clinical examination and relevant investigations. Patients with clinical evidence of pleural effusion was sent for chest X-ray PA and lateral view and ultrasound thorax if required. Then after informed written consent diagnostic thoracocentesis was done performed taking great care. Pleural fluid samples were sent for cytology, protein, LDH and pseudocholinesterase levels. Serum samples were sent for protein, LDH and pseudocholinesterase levels. Lights criteria and pleural fluid to serum pseudocholinesterse ratio was calculated and analysed with the clinical profile of the patient.

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data.

Results:

The study included 82 patients with pleural effusion among whom 56 were males (68.3%) and 26 were females (31.7%). The mean age of subjects was 50.21 ± 14.02 years and the majority of subjects were in the age group 61 to 70 years (29.3%). 37.8% patients with pleural effusion were diagnosed as Tubercular effusion, 19.5% had effusion due to CCF, 14.6% had syn-pneumonic effusion, 9.8% due to Carcinoma Lung, 6.1% due to Cirrhosis of Liver, 2.4% due to Carcinoma Breast and CKD respectively.

Pleural fluid to serum ratio of protein cut of value was taken as 0.5. The average value of pleural fluid to serum protein ratio was 0.8±0.2 in exudates and 0.5±0.1 in transudates.
In case of LDH, two-thirds of the upper limit of normal was used as the cut-off. The cut-off value for pleural fluid to serum LDH level was **0.6**[1] and the average value in this study was 0.4±0.1 in transudates and 2.1±2.6 in exudates and the difference between the two was statistically significant.(p=<0.001)

93% patients were diagnosed to have exudate and 7% were missed and classified as transudate according to Light's criteria and out of 25 subjects with transudate, 96% were diagnosed to have transudate and 4% were misclassified as Exudate. The average Pseudocholinesterase (PChE) levels in transudative effusions was 618.9±201.2U/L and in case of exudates it was 2259.1±654.6 U/L. 96.5% were diagnosed to have exudative effusion according to pseudocholinesterase levels and 3.5% were misclassified as transudate.

96% of ransudates were diagnosed to have transudative effusion and 4% were misclassified as Exudate. There was significant association between Pseudo cholinesterase criteria and diagnosis.

Light's criteria had a sensitivity of 92.98%, specificity of 96%, Pseudo cholinesterase criteria had a sensitivity of 96.49%, specificity of 96%. The mean pleural fluid pseudocholinesterase levels were highest in patients with tubercular pleural effusion (2326.8) and lowest in the cirrhosis of liver (568). There was significant difference in mean Pleural fluid parameters with respect to disease.

Conclusion:

Pleural effusion is a very common respiratory condition in clinical practice amount for morbidity due to the same. The average values of pleural fluid pseudocholinesterase was significantly higher in exudates than in transudates, highest being in tubercular effusions.

The ratio of pleural fluid to serum pseudocholinesterase was found to be superior to Light's criteria in differentiating between transudates and exudates. Limitations of this criteria being it cannot be interpreted in few conditions like acute hepatitis, cirrhosis, pulmonary embolism, chronic renal disease.

LIST OF ABBREVATIONS

WHO	**World Health Organisation**
API	**Association of Physicians of India**
LDH	**Lactate Dehydrogenase**
PChE	**PseudoCholinesterase**
AChE	**Acetylcholinesterase**
Ach	**Acetylcholine**
ESR	**Erythrocyte Sedimentation Rate**
ECG	**Electrocardiogram**
SPSS	**Statistical Package for Social Sciences**
ARF	**Acute Renal Failure**
MODS	**Multi Organ Dysfunction Syndrome**
DIC	**Disseminated Intravascular Coagulation**
CKD	**Chronic Kidney Disease**
CCF	**Congestive Cardiac Failure**

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INTRODUCTION

INTRODUCTION

Pleural effusion is a common clinical condition encountered in every day practice. It is defined as an abnormal, excessive collection of fluid in the pleural space. It occurs in a large variety of pathological conditions, but the determination of cause of pleural effusion is not always easy. Such effusion has been classified as transudate or exudate based on the etiology and the underlying pathology, and differentiating the two types of pleural effusion is critical for guiding the treatment.

Many criteria have been used to distinguish between exudate and transudate based on the pleural fluid, but none of them have been found to be satisfactory. In 1972, Lights et al[1] developed criteria for differentiating between transudate and exudate using pleural and serum levels of protein and LDH with sensitivity and specificity of 99% and 98% respectively. Several prospective studies were unable to reproduce the excellent results obtained by Light et al. and have shown that the Light et al criteria misclassify a large number of effusions[2].

Later on many modifications were done in Light's criteria by many researchers[3,4]. To differentiate the type of pleural effusion many parameters like pleural fluid cholesterol, bilirubin, albumin, alkaline phosphatase, adenosine deaminase[5-8], malondialdehyde (MDA) and their ratio with serum values have been used. However, most of these parameters also classified pleural effusions falsely.

Cabrer et al[9] were the first researchers who estimated pseudocholinesterase activity in pleural effusions and concluded that there exists difference in the activity of pseudocholinesterase among different types of pleural effusions and it was possible to differentiate them into transudates and exudates based on pseudocholinesterase levels. Garcia and Padilla[10] confirmed the importance of estimations of pseudocholinesterase

activity in the diagnosis. Estimating the pleural fluid pseudocholinesterase ratio would be more cost effective and more efficient parameter in differentiating between transudative and exudative pleural effusion in a rural setup. Hence this study was taken up to study of pleural fluid to serum pseudocholinesterase ratio and its correlation with clinical profile and light's criteria.

OBJECTIVES

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1. To estimate the pleural fluid to serum pseudocholinesterase ratio in patients with pleural effusion.

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REVIEW OF LITERATURE

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Pleural Anatomy:

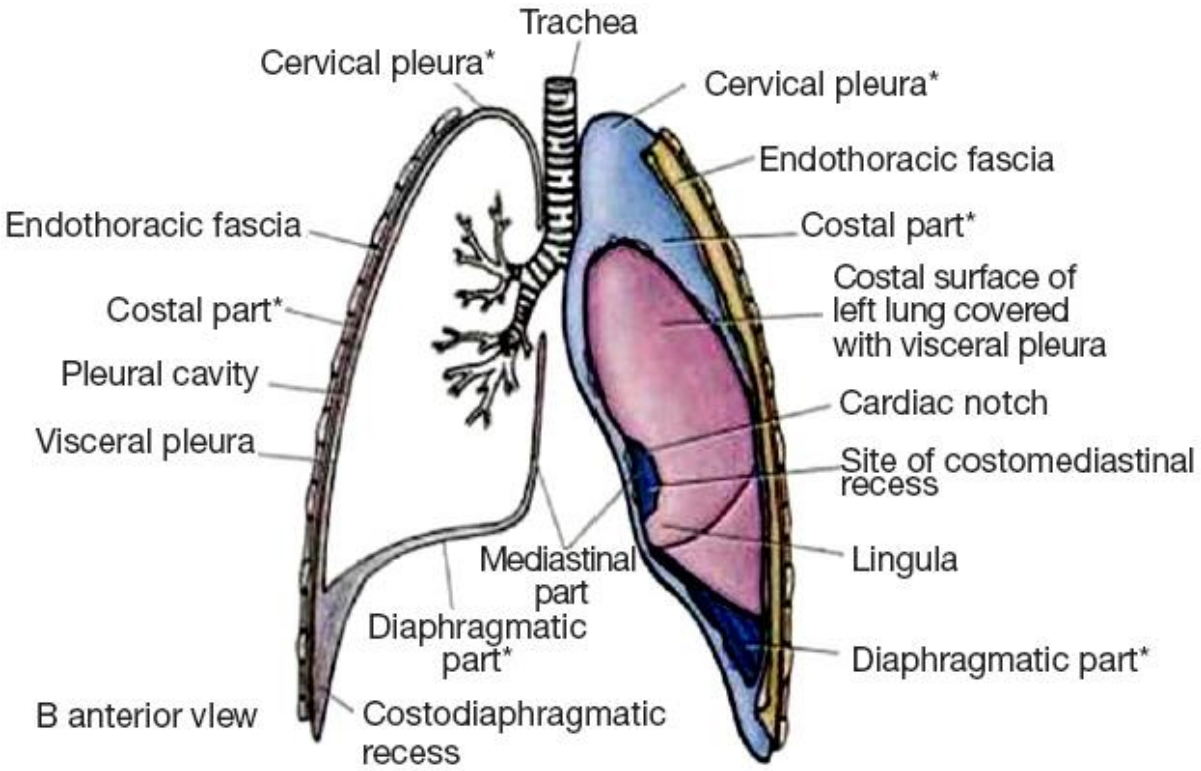


Figure 1: Normal Pleural Anatomy

The pleura is a serous membrane that covers the lung parenchyma, the mediastinum, the diaphragm and the rib cage. It is divided into parietal and visceral pleura. The visceral pleura covers the lung parenchyma, diaphragm, mediastinum and the interlobar fissures. The parietal pleura lines the inside of the thoracic cavity[11]. The pleural cavity is created between the 4-7 weeks of embryologic development and is lined by the splanchnopleurae and somatopleurae. These embryonic components of visceral and parietal pleurae develop different anatomic characteristics.

A thin film of fluid is normally present between the parietal and the visceral pleura, which acts as lubricant and allows the visceral pleura to slide over the parietal pleura. As only a thin layer of fluid is present in this space, it is a potential space rather than an actual space[12].

Histology of the pleura:

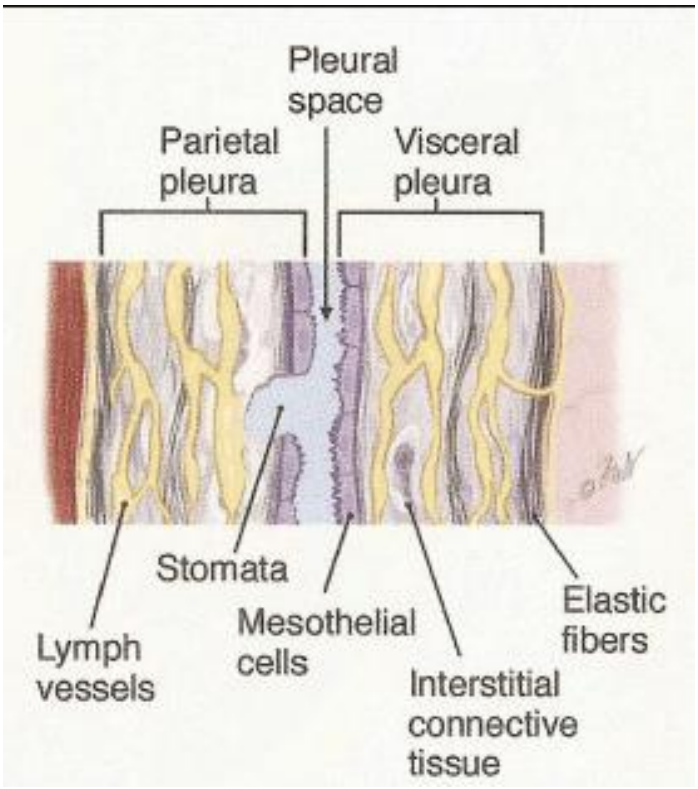


Figure 2: Normal Histology of Pleura

The parietal pleura is composed of loose irregular connective tissue with a single layer of the mesothelial cells. Within the pleura there are blood capillaries, and lymphatic lacunae. The visceral pleura has thick connective tissue, which has blood vessels, lymphatics and a single layer of mesothelial cells. It contributes to the elastic recoil of the lung, which is important in expelling the air from the lung. It also restricts the volume to which the lungs can be inflated thereby protecting the lungs.

The mesothelial layer is a fragile layer with active mesothelial cells sensitive to various stimuli. These cells can transform to macrophages and can express procoagulant activity due to tissue factor that binds the factor VII at the cell surface[13].

Pleural Fluid:

Normally, a small amount of pleural fluid is present in the pleural space. Noppen et al, have demonstrated that the mean amount of fluid in the right pleural space in normal individuals is 8.4 ± 4.3 mL. Normally, the volume of fluid in the right and left pleural spaces is quite similar. Expressed per kilogram of body mass, the total pleural fluid volume in normal, nonsmoking humans is 0.26 ± 0.1 mL/kg[14, 15].

The pleural fluid is distributed relatively evenly throughout the pleural space. Therefore, the pleural fluid behaves as a continuous system. The pleural space is slightly narrower near the top (18.5μm) than at the bottom (20.3 μm). Pleural space width in dependent recesses, such as the costo-diaphragmatic recess is 1 to 2 mm. Because the microvilli of the mesothelial cells in the visceral and parietal pleura do not interdigitate, the frictional forces between the lungs and chest wall are low.

The mean white blood cell count in pleural fluid is 1,716 cells/mm^3 and the mean red cell count is approximately 700 cells/mm^3. These numbers are similar to those recorded in animals. Approximately 75% of the cells are macrophages and 25% are lymphocytes, with mesothelial cells, neutrophils, and eosinophils accounting for less than 2% each[14].

A small amount of protein is present in the pleural fluid. Protein electrophoresis demonstrated that electrophoretic pattern of the pleural fluid is similar to that of plasma protein except that low-molecular weight proteins like albumin are present in large quantities[12]

Formation of Pleural Fluid:

Fluid that enters the pleural space can originate in the pleural capillaries, the interstitial spaces of the lung, the intrathoracic blood vessels, the intrathoracic lymphatics, or the peritoneal cavity[16,17].

Pleural capillaries -

The movement of the fluid between the pleural surface and capillaries is governed by Starling's law of transcapillary exchange[18]. The law states that the movement of fluid across capillaries is an equation of the hydrostatic and osmotic forces. The rate of filtration at any point along the capillary depends upon a balance of forces called the Starling's forces. One of these forces is the hydrostatic pressure gradient (the hydrostatic pressure in the capillary minus the hydrostatic pressure of the interstitial fluid). The other force is the osmotic pressure gradient across the capillary wall (colloid osmotic pressure of plasma minus colloid osmotic pressure of the interstitial fluid).

Fluid moves into the interstitial space at the arteriolar end of the capillary, where the filtration pressure across its wall exceeds the oncotic pressure and moves into the capillary at the venular end, where the oncotic pressure exceeds the filtration pressure. The hydrostatic pressure of the parietal pleura is 30 cm of water, where as that of the

pleural space is about –5cm of water. The net hydrostatic pressure gradient is 35 cm of water.

Opposing this is the oncotic pressure which is 34 cm of water. Thus a positive net gradient favours movement of fluid from capillaries to pleural space[18].

Interstitial origin -

In recent years it has been implicated that much of the fluid that enters the pleural space is from the interstitial space of the lung. Either high pressure or high permeability pulmonary edema can lead to the accumulation of the pleural fluid in this manner[19].

Thoracic duct or blood vessel disruption -

Disruption of the thoracic duct can lead to accumulation of lymph in the pleural space producing chylothorax. In a similar manner, trauma to the blood vessels or diseases of the blood vessels can lead to accumulation of blood in the pleural space producing haemothorax[19].

Increased pleural fluid formation takes place because of increased secretion or decreased absorption or both.

I. Increased pleural fluid formation

The various mechanisms by which increased pleural fluid formation occurs are:

a. Increased interstitial fluid formation

It occurs when the amount of fluid exceeds 5g per gram of lung dry weight; pleural fluid accumulates whether the edema is high protein or low protein. This occurs in

1. Congestive cardiac failure
2. Para pneumonic effusion
3. Acute respiratory distress syndrome
4. Lung transplantation

b. Increased hydrostatic pressure gradient

If there is an increased pressure gradient between the intravascular pressure and pleural pressure there will be an increase in the rate of pleural fluid formation. This occurs in,

1. Right ventricular failure
2. Left ventricular failure
3. Pericardial effusion
4. Superior venacaval obstruction

In the above mentioned conditions the intravascular pressure is increased.

c. Increased capillary permeability

Inflammation of the pleural surface causes increase in capillary permeability leading to pleural fluid formation.

d. Decreased oncotic pressure gradient

Decreased oncotic pressure gradient leads to the formation of pleural fluid through its influence on the Starling's equation. e.g. hypoproteinemic states

e. Disruption of the thoracic duct or intrathoracic blood vessel

Trauma to the thoracic duct and intercostals vessels can lead to formation of chyle or blood in the thoracic cavity respectively

f. Hole in the diaphragm

Excess pleural fluid formation occurs if there is a hole in the diaphragm with associated ascites.

II. Decreased pleural fluid absorption

a. Lymphatic obstruction

Lymphatics are responsible for the majority of pleural fluid absorption from the pleural space. Normally the lymphatic flow from the pleural space is about 0.01ml per kg per hour or 15 ml per day, but the capacity of the lymphatics is about 0.20mlper kg per hour or 300 ml per day. Obstruction to lymphatics is most commonly seen in malignant effusion where the lymphatics are obstructed by malignant cells.

b. Elevation of systemic venous pressure

Elevation of central venous pressure in turn impedes lymphatic flow, thereby causing pleural effusion. As the venous pressures increases, the pleural fluid accumulation increases exponentially. This occurs in superior venacaval obstruction[18].

CAUSES OF PLEURAL EFFUSION

I. Transudative pleural effusions

1. Congestive heart failure
2. Cirrhosis
3. Nephrotic syndrome
4. Superior Vena Caval obstruction
5. Fontan procedure
6. Urinothorax
7. Peritoneal dialysis
8. Glomerulonephritis
9. Myxoedema
10. Cerebrospinal fluid leaks to pleura
11. Hypoalbuminemia
12. Sarcoidosis

II. Exudative pleural effusions

A. Neoplastic diseases

1. Metastatic disease
2. Mesothelioma
3. Body cavity lymphoma
4. Pyothorax-associated lymphoma

B. Infectious diseases

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

5. Viral infections

C. Pulmonary embolization

D. Gastrointestinal disease

1. Pancreatic disease
2. Subphrenic abscess
3. Intrahepatic abscess
4. Intrasplenic abscess
5. Esophageal perforation
6. Postabdominal surgery
7. Diaphragmatic hernia
8. Endoscopic variceal sclerosis
9. Postliver transplant

E. Heart diseases

1. Postcoronary artery bypass graft surgery
2. Postcardiac injury (Dressler's) syndrome
3. Pericardial disease
4. Pulmonary vein stenosis postcatheter ablation of atrial fibrillation

F. Obstetric and gynecologic disease

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

G. Collagen vascular diseases

1. Rheumatoid pleuritis

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

H. Drug-induced pleural disease

1. Nitrofurantoin
2. Dantrolene
3. Methysergide
4. Ergot drugs- ergotamine
5. Amiodarone
6. Interleukin 2
7. Procarbazine
8. Methotrexate
9. Clozapine
10. Minoxidil
11. Imatinib

I. Miscellaneous diseases and conditions

1. Asbestos exposure
2. Postlung transplant
3. Postbone marrow transplant
4. Yellow nail syndrome

5. Sarcoidosis
6. Uremia
7. Trapped lung
8. Therapeutic radiation exposure
9. Drowning
10. Amyloidosis
11. Milk of calcium pleural effusion
12. Electrical burns
13. Extramedullary hematopoiesis
14. Rupture of mediastinal cyst
15. Acute respiratory distress syndrome
16. Whipple's disease
17. Iatrogenic pleural effusions

J. Hemothorax

K. Chylothorax

Pleural effusions are classically divided into transudates and exudates. This is first step in the management of effusions. A transudate occurs when the mechanical factors influencing the formation or reabsorption of pleural fluid are altered. An exudate results from inflammation or other diseases of the pleural surface.

Exudative pleural effusions are a common diagnostic problem in clinical practice, as the list of causes is quite exhaustive[12], although sometimes they can be inferred from the clinical picture. If an exudative effusion is present, further diagnostic procedures are imperative, such as cytopathology, pleural biopsy and sometimes even thoracotomy to achieve definitive diagnosis. The etiological distribution of pleural effusions in various series depends on the geographical area, patient's age, and advances in the diagnostic methods and treatment of the underlying causes. The difficulty in determining the cause of pleural effusion is shown by the fact that in many series "unknown etiology" constitutes nearly 15%[19]. It is generally admitted that defining a pleural effusion as a transudate limits the differential diagnosis to a small number of disorders. It also ends the need for further diagnostic workup of the pleural effusion itself.

Very early criteria include pleural fluid (PF) specific gravity, cell counts and the presence or absence of clotting in the fluid[1]. One of the first methods of differentiation was the pleural fluid protein level of 3g/dl. Carr and Power found that 8% of exudates and 15% of transudates were misclassified by this criterion[20]. Luetscher suggested that the ratio of pleural fluid to serum protein was more discriminating but there were misclassifications.

In 1972 Light et al[1] conducted a prospective study of 150 cases of pleural effusion and evaluated the efficacy of pleural fluid cell count, protein levels and LDH for the separation of transudates from exudates. From the characteristics of the fluids found in the study a new set of criteria was established.

Any fluid is an exudate if it has

(1) Pleural fluid-to-serum protein ratio greater than 0.5

(2) Pleural Fluid LDH greater than 200IU or

(3) Pleural fluid-to-serum LDH ratio greater than 0.6

These characteristics were found in all but one exudate and one transudate in their study.

In that study it was observed that most exudative effusions had a relatively high value of LDH. Previously it was believed that LDH was high only in malignant effusions. Kirkeby and Prydz concluded that raised LDH was a feature of all inflammatory conditions of the pleura. LDH is released from the lymphocytes and marcophages actively phagocytising. The PF LDH criterion was later modified to more than two thirds the upper limit of a laboratory's normal LDH range to account for variations in assay methods[23]. Light's criteria were considered the most superior among all the available tests. Possible modifications in the cut off values were analyzed and concluded to offer no advantage[24],[25].

However, several reports have shown later that the criteria of Light et al misclassified a larger number of effusions, most of them transudates[3,22-24]. Light's criteria was found to be inferior in patients on diuretics and in such patients alternative biochemical criteria need to be used[25,26]. It was found to misclassify 15-30% of

transudates as exudates. In patients receiving diuretic therapy, the accuracy of Light's criteria is 83% (60 of 72 cases), neither different to that of the albumin gradient (88%; 63 of 72 cases) nor to that of the protein gradient (86%; 62 of 72 cases) [2,27,28].

Therefore, different alternative parameters have been proposed and analyzed to improve the results of the classical criteria.

One of the parameters extensively analyzed was pleural fluid cholesterol. Suay et al concluded that a pleural fluid cholesterol of $\geq$ 54mg/dl and/or a pleural/serum cholesterol ratio of $\geq$ 0.32 had a sensitivity of 98% and specificity of 89.5% in differentiating between transudates and exudates. In the same study, Light's criteria had a sensitivity of 100% and specificity of 64.5%[8]. Cholesterol enters the fluid through increased vascular permeability in case of inflammation[29]. Pleural fluid cholesterol is independent of the serum cholesterol levels. Another explanation for the presence of cholesterol in pleural fluid is cellular degeneration, mainly of WBCs and RBCs[30].

Paramothayan et al[31] compared pleural fluid LDH levels and fluid to serum protein ratio and concluded that they are equally good with a sensitivity of 90% and specificity of 79% and their combination achieved higher efficiency than that of Light's criteria.

Other parameters that have been studied include albumin gradient and pleural fluid to serum bilirubin ratio. An albumin gradient of >1.2g/dl (serum minus pleural fluid albumin) is indicative of transudate and <1.2g/dl indicates an exudate. Pleural fluid to serum bilirubin ratio of $\geq$ 0.6 was found to be as good as Light's criteria[28].

In a review of available parameters the following values were obtained regarding the sensitivity and specificity[19].

Table showing Efficiency of Various Tests To Differentiate Into Transudates And Exudates

TEST	SENSITIVITY FOR EXUDATE	SPECIFICITY FOR EXUDATE
	%	
Light's criteria (one or more of the following three)	98	83
Ratio of pleural-fluid protein level to serum protein level >0.5	86	84
Ratio of pleural-fluid LDH level to serum LDH level >0.6	90	82
Pleural-fluid LDH level >two thirds the upper limit of normal for serum LDH level	82	89
Pleural-fluid cholesterol level >60 mg/dl (1.55 mmol/liter)	54	92
Pleural-fluid cholesterol level >43 mg/dl (1.10 mmol/liter)	75	80
Ratio of pleural-fluid cholesterol level to serum cholesterol level >0.3	89	81
Serum albumin level − pleural-fluid albumin level ≤1.2 g/dl	87	92

*LDH denotes lactate dehydrogenase.

In 1978, Cabrer et al[8] analyzed the pseudocholinesterase activity in pleural effusions of diverse causes and found significant differences in the average level between transudates and exudates.

Garcia-Pachon et al conducted a study on 153 cases of pleural effusion and evaluated Light's criteria, pleural fluid cholesterol, pleural fluid cholinesterase and pleural fluid to serum cholinesterase ratio in all the cases. Among the analyzed parameters, the pleural fluid to serum cholinesterase ratio obtained the best results by correctly classifying 98.7% of cases[10]. The pleural fluid cholinesterase level showed poorer results than the cholinesterase ratio. This finding is not surprising because

cholinesterase is synthesized in the liver and the levels can be influenced by different disorders. These include acute hepatitis, cirrhosis, acute infections, pulmonary embolism, chronic renal disease, and after surgical procedures. In the original study by Light et al[1], in a series of 150 patients, all but two of the pleural effusions, one transudate and one exudate were correctly classified.

Cholinesterase

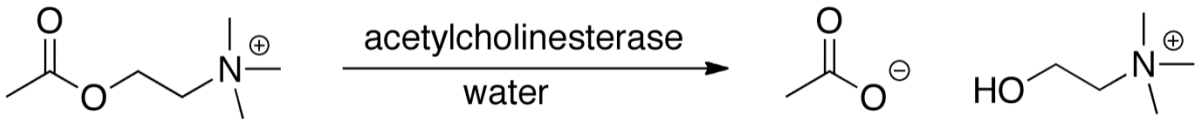


Figure 3: Action of Cholinesterase Enzyme

Cholinesterases are a family of enzymes that hyrdolyze acetylcholine into choline and acetic acid. These are serine hydrolases that belong to the esterases family. The enzyme family of cholinesterases includes

1. Acetylcholinesterase (AChE, EC 3.1.1.7), also known as true, specific, type I cholinesterase or RBC cholinesterase: It is found in nervous tissue, erythrocytes, lungs, spleen and grey matter. It is decreased in pernicious anemia and after anti-malarial therapy
2. Butyrylcholinesterase (BChE, EC 3.1.1.8), also known as plasma, nonspecific, type II cholinesterase or Pseudocholinesterase. It is found in plasma, liver, pancreas and intestinal mucosa, liver being the main organ. Variations occur due to liver disease, chronic inflammation, malnutrition, morphine, codeine, succinylcholine administration and hypersensitivity reactions.

BChE is normally found in plasma, liver, pancreas, intestinal mucosa and white matter of the brain. It is called so as it hydrolyzes butyrylcholine 4 times faster than AChE. It is synthesized by the liver, heart, lungs and brain but primarily by the liver. For a long time the physiological functions of BChE was vague. Now it has been found to have a role in lipoprotein metabolism, myelin maintenance, cellular adhesion, neurogenesis, as a scavenger of toxic molecules and in the processing of amyloid precursor. As an enzyme it hydrolyses acetylcholine (ACh) and other choline esters, and non-choline esters such as a number of local anaesthetics, muscle relaxants, aspirin, and cocaine[32.] Therefore, it may be useful for the treatment for cocaine addiction and toxicity. Its serum/plasma activity has been primarily used in clinical biochemistry to test diminished protein-synthesizing capacity of the liver and organophosphorus insecticide poisoning[33].

BChE is made up of four subunits of ChE which are identical and contain 574 amino acids each with 9 carbohydrate chains attached.

The cholinergic anti-inflammatory pathway mediated by the neurotransmitter ACh exerts a direct inhibitory effect on pro-inflammatory cytokine production[34]. Increased activities of AChE and BChE may lead to a greater hydrolytic destruction and diminished concentrations of ACh, and this fact could trigger and perpetuate systemic inflammation[35].

Several studies have addressed the association of chronic low-grade inflammation and cholinesterase activity[36-38] with obesity, metabolic syndrome, insulin resistance, and

cardiovascular risk. Consequently, it has been suggested that increased plasma and tissue activities of cholinesterase seen in various clinical conditions could serve as a marker of low-grade systemic inflammation[39].

SIGNS AND SYMPTOMS	SUGGESTED ETIOLOGY
Ascites	Cirrhosis
Distended neck veins	Heart failure, pericarditis
Dyspnoea on exertion	Heart failure
Fever	Abdominal abscess, empyema, malignancy, pneumonia, tuberculosis
Haemoptysis	Malignancy, Tuberculosis, pulmonary embolism
Hepatosplenomegaly	Malignancy
Lymphadenopathy	Malignancy
Orthopnoea	Heart failure, pericarditis
Peripheral edema	Heart failure
S3 gallop	Heart failure
Unilateral lower extremity swelling	Pulmonary embolism
Weight loss	Malignancy, tuberculosis

Table 1: Signs and Symptoms that Suggest an Etiology of Pleural Effusion [40-42]

FINDING	SENSITIVITY (%)	SPECIFICITY (%)
Pleural friction rub	5.3	99
Asymmetric chest expansion	74	91
Reduced vocal resonance	76	88
Reduced vocal fremitus	82	86
Auscultatory percussion	30 to 96	84 to 95
Diminished breath sounds	42 to 88	83 to 90
Dullness to percussion	30 to 90	81 to 98
Crackles	56	62

TABLE 2:Accuracy of Common Clinical Findings for Diagnosing Pleural Effusion [43]

FINDING	POTENTIAL ETIOLOGY
Anchovy brown fluid	Ruptured amoebic abscess
Bile staining	Cholothorax (i.e. biliary fistula)
Black fluid	Aspergillus infection
Food particles	Esophageal perforation
Milky fluid	Chylothorax
Putrid odour	Anaerobic empyema
Urine	Urinothorax

TABLE 3: Gross Pleural Fluid Findings and Potential Etiologies [41]

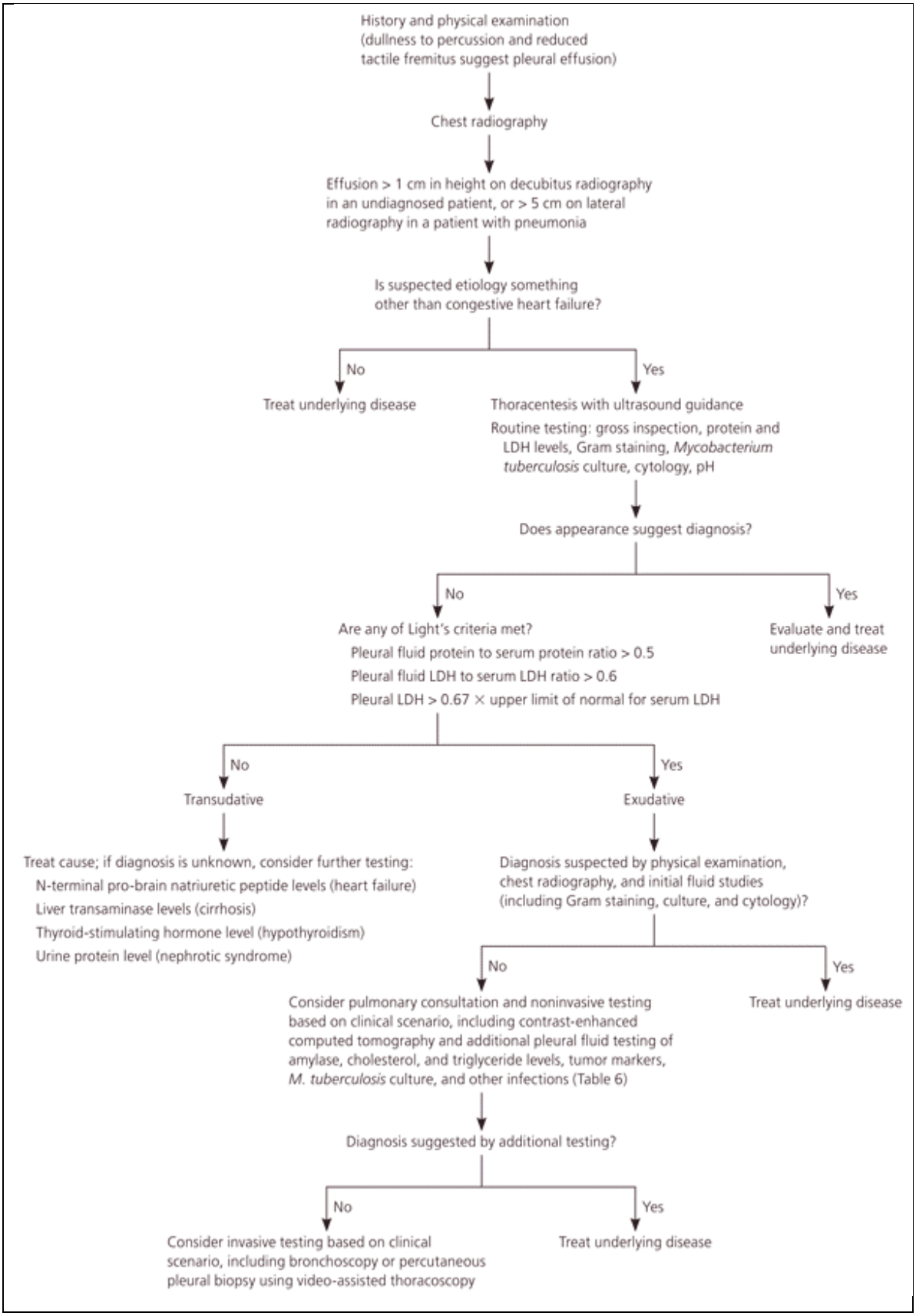


FIGURE 4: Algorithm for evaluating pleural effusion[41,43,44]

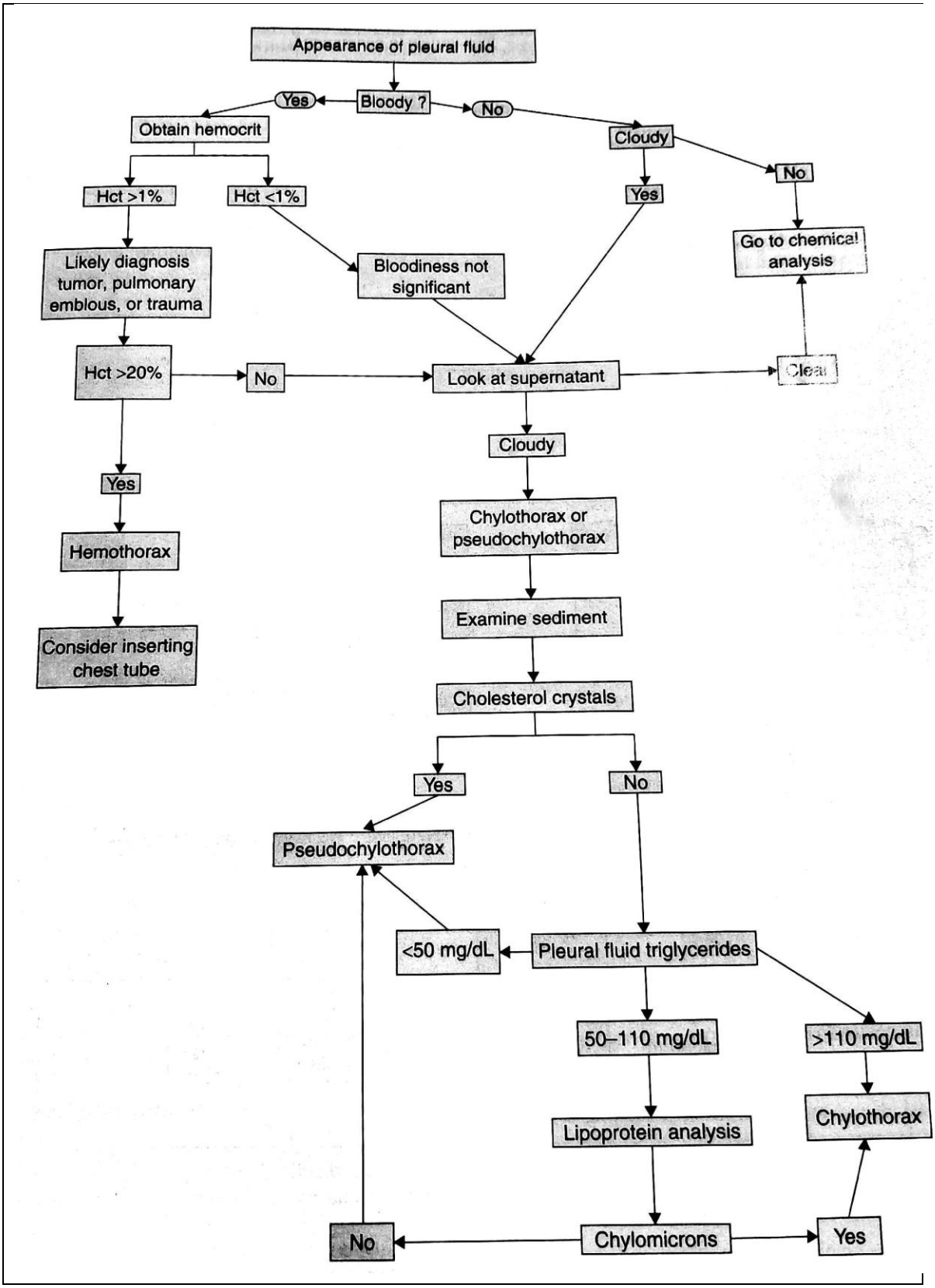


FIGURE 5: Algorithm for evaluating the appearance of pleural fluid [44].

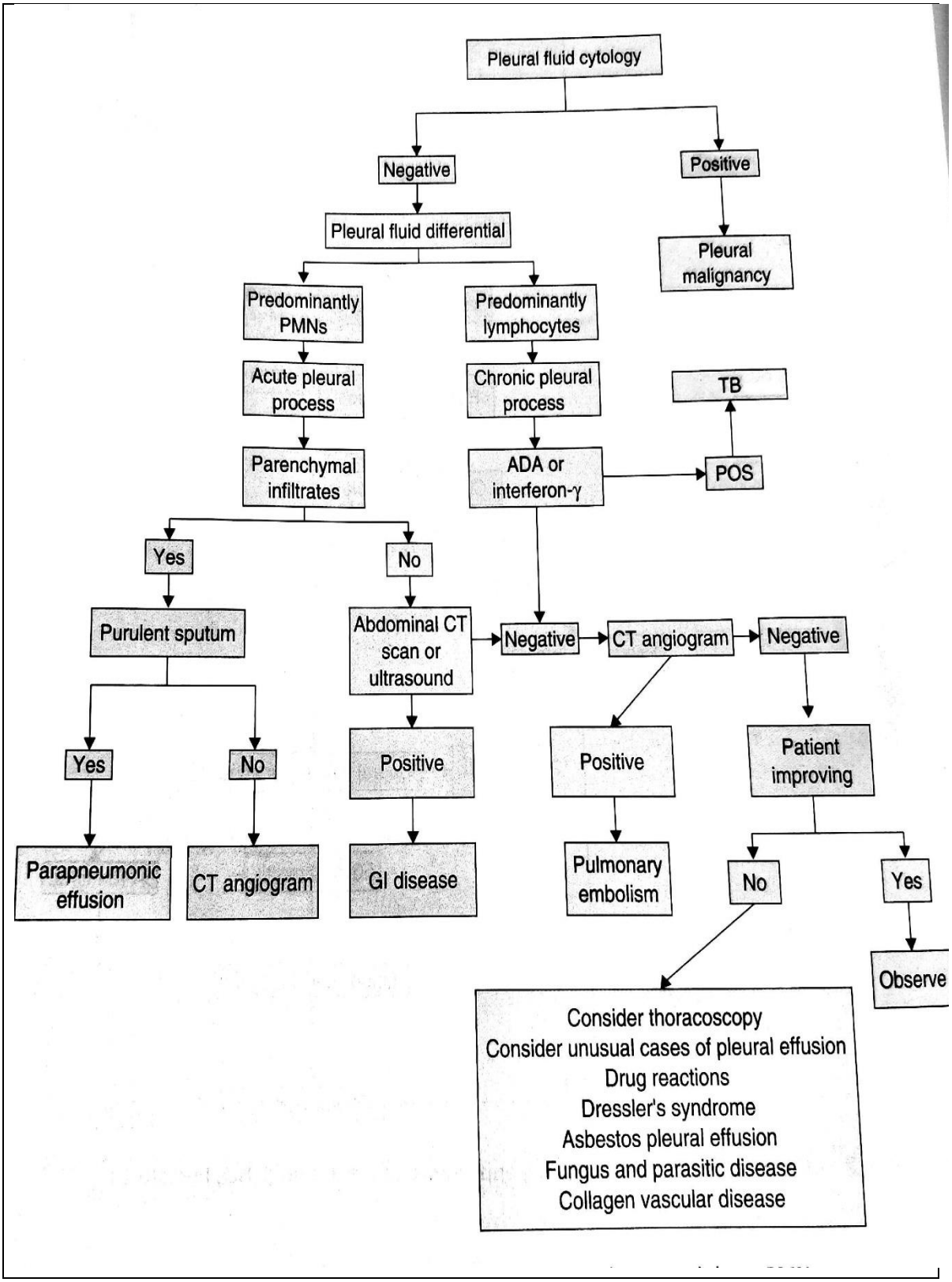


FIGURE 6: Algorithm for evaluating exudates with unknown etiology [44]

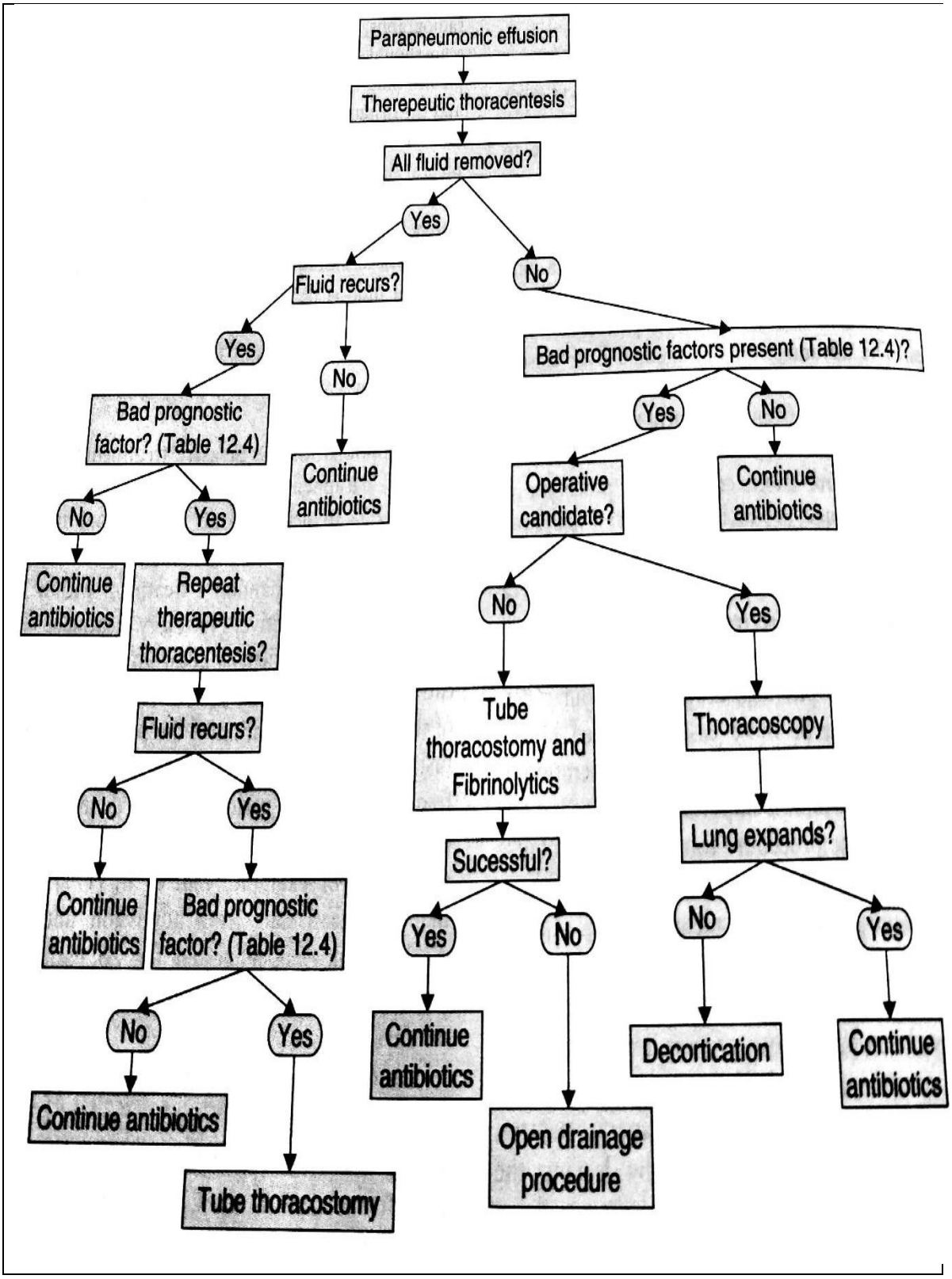


FIGURE 7: Algorithm for managing patients with parapneumonic effusions [44].

METHODOLOGY

METHODOLOGY

SOURCE OF DATA

The study was conducted in the Department of General Medicine at R L Jalappa hospital, Kolar. Both inpatients and outpatients were included in the study.

METHOD OF COLLECTION OF DATA:

Inclusion criteria:

1. Patients more than 18 years of age
2. Presence of pleural effusions proved by clinical/radiological examination

Exclusion criteria:

1. Patients having pleural effusion with suspected more than one possible cause.
2. Pregnant women
3. Patients with known hepatic disease.

SAMPLE SIZE AND DESIGN:

The study was a cross sectional study and included 82 patients with pleural effusion who met the inclusion and exclusion criteria. The study was conducted from January 2016 to June 2017.

STUDY METHODS:

Patients with suspected pleural effusion were evaluated in detail, comprising of detailed history, clinical examination and relevant investigations. Patients with clinical evidence of pleural effusion chest X-ray was done.

Following investigations was carried out on all the patients in the study group.

- Haemogram with ESR

- Random Blood Sugar
- Blood urea, serum creatinine
- Serum protein
- Serum LDH
- Serum pseudocholinesterase

Then after informed written consent diagnostic thoracocentesis was performed taking great care not to let the fluid mix with blood.

Pleural fluid was sent for the following investigations:

- Pleural fluid cytology including malignant cells
- Proteins, sugar
- Lactate dehydrogenase
- Pseudocholinesterase
- ADA (for suspected tubercular effusions)
- Amylase (for suspected pancreatic effusions)

Protein levels were estimated in serum and pleural fluid by Biuret method. LDH levels were estimated using Multipoint enzymatic method . Cholinesterase levels were measured using the butrylthiocholine method.

PROCEDURE FOR THORACOCENTESIS

Equipments required: 21G sterile needle, sterile gloves, iodine tincture, 10mL sterile syringe, 1 red top container, 1 purple top container.

Steps include:

1. Patients were positioned at the edge of the bed seated upright and slightly rotated to the opposite side to splay the ribs. Percussed for dullness to identify the superior and inferior margins of the effusion. Marked one-two rib spaces below the top of the effusion in the posterior axillary line using light pressure with a closed pen. Caution not to go below the 8th intercostal space was taken.

2. The area was cleaned with iodine tincture and allowed to dry for one minute.

3. A 21G sterile needle with a 10mL syringe attached was inserted perpendicular to the rib above the superior margin and continued until there was a little resistance.

4. Pleural fluid was then aspirated to confirm position of needle in pleural space.

5. When in pleural space, 10mLs of pleural fluid was drawn in the same syringe. The needle and syringe were removed and the site closed with a sterile dressing

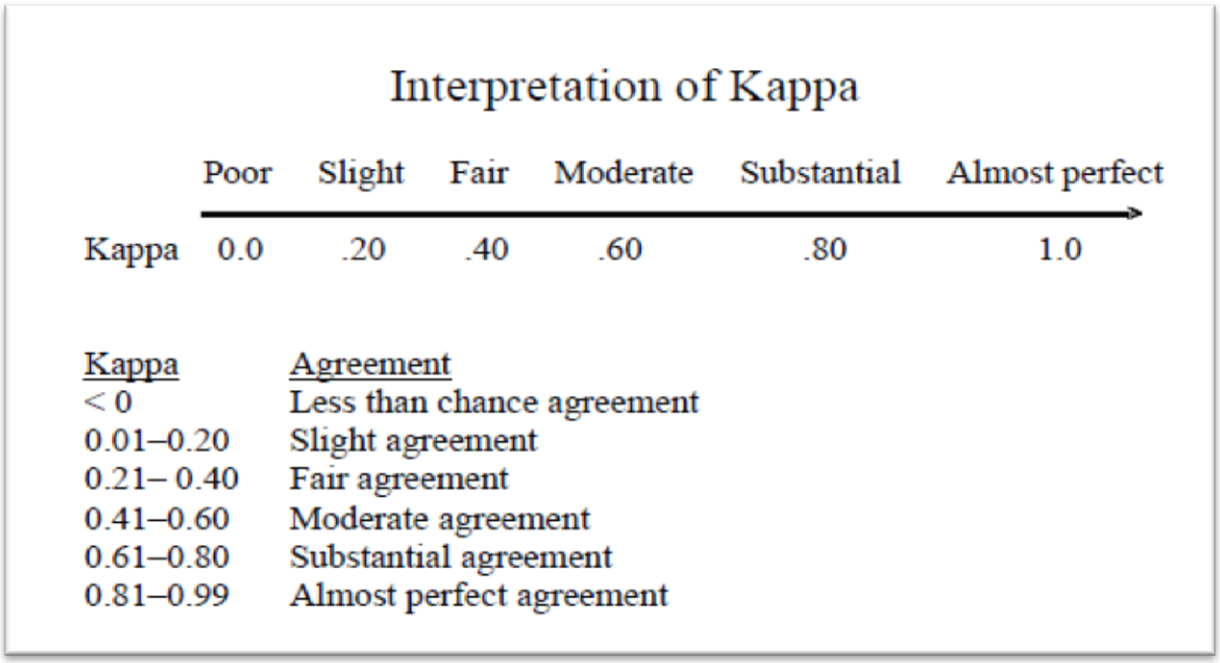
STATISTICAL METHODS:

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data.

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

Kappa Statistics: Agreement between two or more observers/ between two or more methods or instruments and equipments was assessed by using Kappa statistics.



Screening of Disease:

Screening test results	Diagnosis		Total
	Diseased	Healthy	
Positive	a (True postive)	b (False Postive)	a+b
Negative	c (False Negative)	d (True Negative)	c+d
Total	a + c	b + d	a+b+c+d

- ☐ Sensitivity = a/(a+c) x 100 = True positive / True positive + False Negative
- ☐ Specificity = d/(b+d) x 100 = True Negative / True Negative + False Postive
- ☐ Positive predictive value = a/ (a+b) x 100 = True Postive / True positive + False Postive
- ☐ Negative predictive value = d/ (c+d) x 100 = True Negative / True Negative + False Negative
- ☐ Diagnostic accuracy = a + d / a + b + c + d = True postive + True Negative / Total

Sensitivity: Defined as ability of a test to identify correctly all those who have the disease i.e. true positive

Specificity: It is the ability of test to identify correctly those who do not have the disease i.e. true negative.

Positive predictive value (PPV): The proportion of patients who test positive who actually have the disease.

Negative predictive value (NPV): The proportion of patients who test negative who are actually free of the disease.

Diagnostic accuracy: Is the ability of screening test to detect true positives and true negatives in the total population studied.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS

RESULTS

Study population:

The study included 82 patients with pleural effusion among whom 56 were males (68.3%) and 26 were females (31.7%) (Table 4; Chart 1)

Table 4: Gender distribution of subjects in the study

		COUNT	%
GENDER	FEMALE	26	31.7%
	MALE	56	68.3%
	TOTAL	82	100.0%

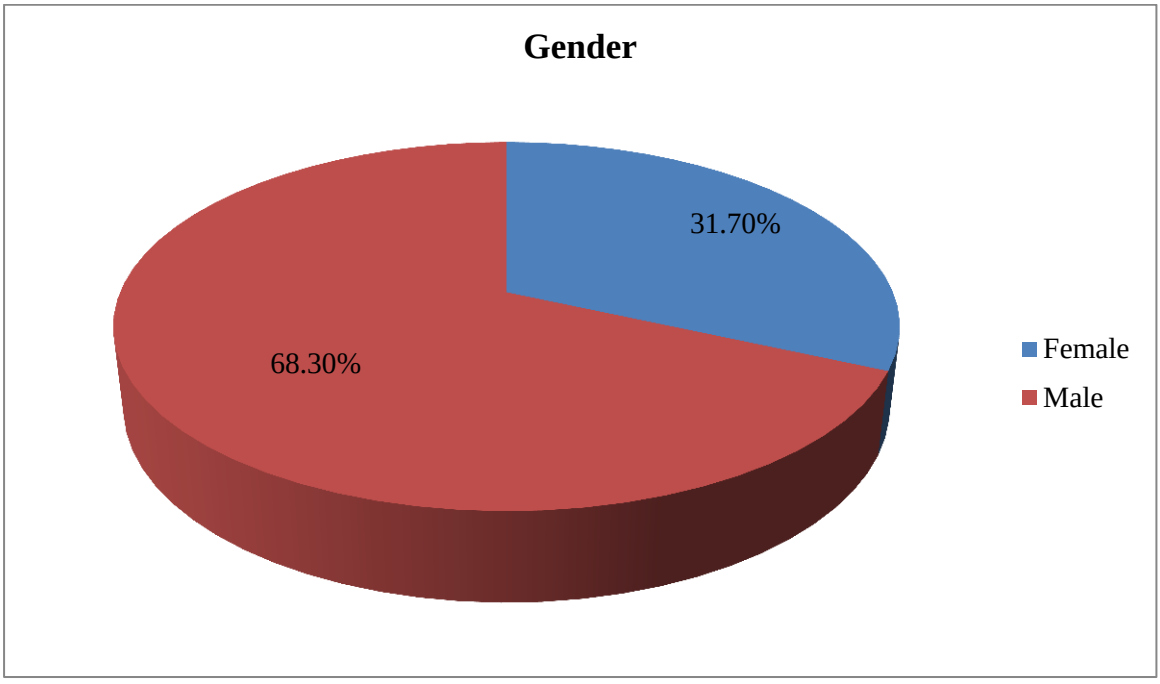


Chart 1 : Pie diagram showing Gender distribution of subjects in the study

Table 5: Age distribution of subjects in the study

		COUNT	%
AGE	<30 years	8	9.8%
	31 to 40 years	16	19.5%
	41 to 50 years	16	19.5%
	51 to 60 years	16	19.5%
	61 to 70 years	24	29.3%
	>70 years	2	2.4%
	Total	82	100.0%

In this study the mean age of subjects was 50.21 ± 14.02 years. Majority of subjects were in the age group 61 to 70 years (29.3%), followed by 19.5% in the age group 31 to 40 years, 41 to 50 years, 51 to 60 years respectively. (Table 5 ; Chart 2)

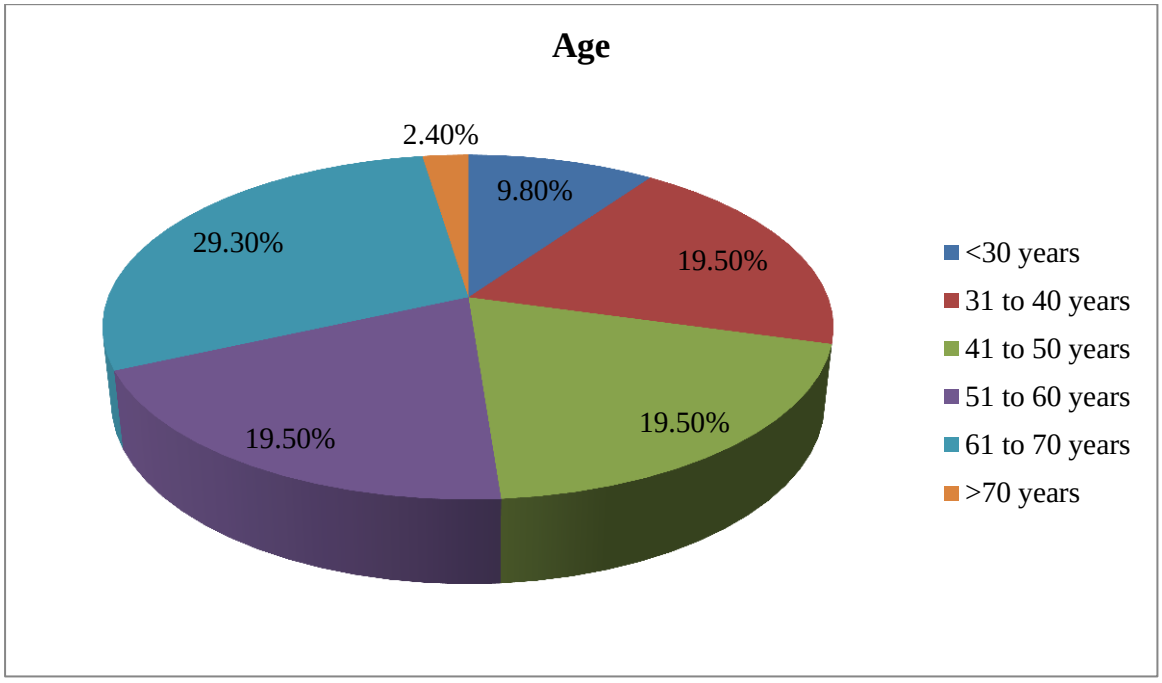


Chart 2: Pie diagram showing Age distribution of subjects in the study

Table 6: Causes of pleural effusion

		COUNT	%
CAUSES	TUBERCULOSIS	31	37.8%
	CCF	16	19.5%
	PNEUMONIA	12	14.6%
	CARCINOMA LUNG	8	9.8%
	CIRRHOSIS OF LIVER	5	6.1%
	CARCINOMA BREAST	2	2.4%
	CKD	2	2.4%
	EMPYEMA	1	1.2%
	MEIGS SYNDROME	1	1.2%
	NEPHROTIC SYNDROME	1	1.2%
	CARCINOMA OVARY	1	1.2%
	PYOTHORAX	1	1.2%
	ACUTE PANCREATITIS	1	1.2%

In the study 37.8% patients with pleural effusion were diagnosed as Tubercular effusion, 19.5% had effusion due to CCF, 14.6% had syn-pneumonic effusion, 9.8% due to Carcinoma Lung, 6.1% due to Cirrhosis of Liver, 2.4% due to Carcinoma Breast and CKD respectively and 1.2% due to Empyema, Meig syndrome, Nephrotic syndrome, Carcinoma ovary, Pyothorax and Acute pancreatitis respectively.

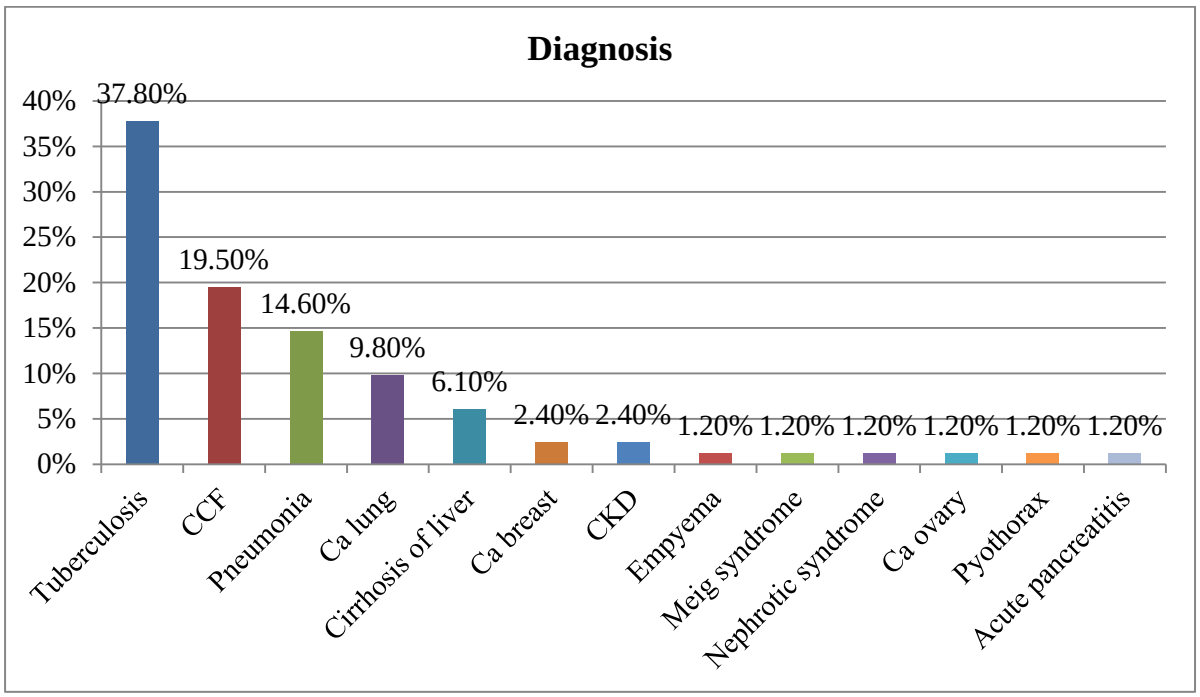


Chart 3: Bar diagram showing Diagnosis among subjects

Table 7: Side of Pleural Effusion among subjects

		COUNT	%
SIDE	RIGHT	48	58.5%
	LEFT	31	37.8%
	BILATERAL	3	3.7%

In the study 58.5% had pleural effusion on right side, 37.8% on left side and 3.7% had bilateral pleural effusion.

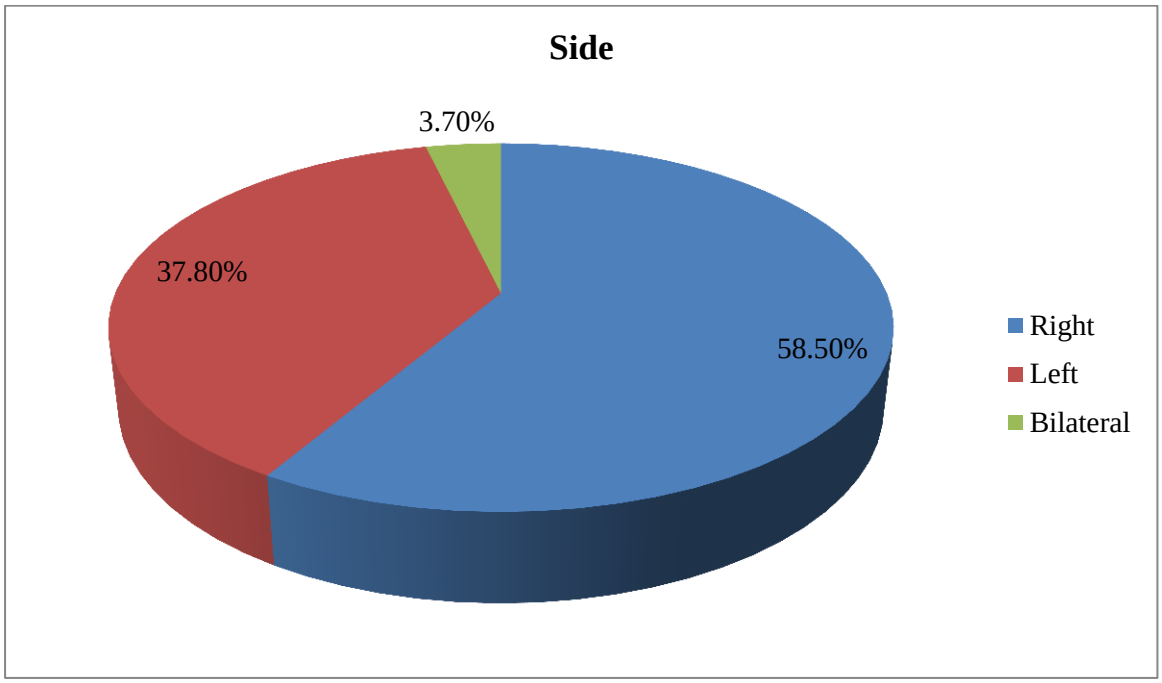


Chart 4 : Pie diagram showing Side of Pleural Effusion among subjects

Table 8: Type of pleural effusion

		COUNT	%
DIAGNOSIS	EXUDATE	57	69.5%
	TRANSUDATE	25	30.5%

In the study 69.5% were diagnosed to have exudative effusion and 30.5% as transudative effusion.

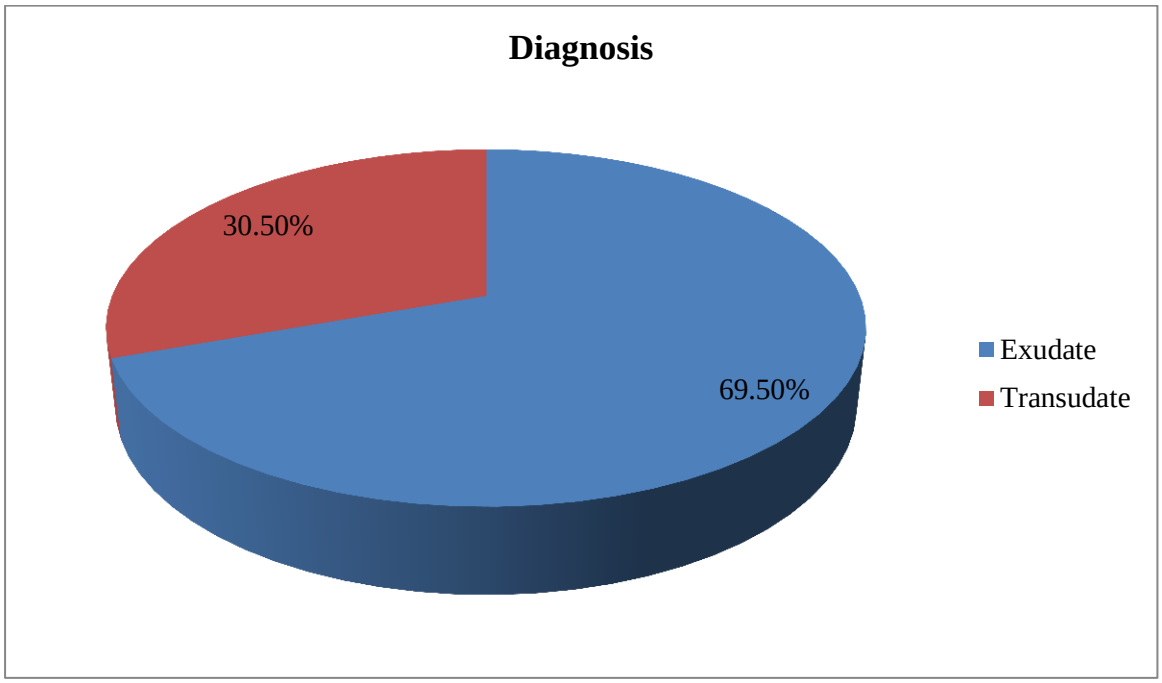


Chart 5: Pie diagram showing Final diagnosis of Pleural Fluid

Table 9: Comparison between etiology of effusion and nature of pleural fluid

			Count	%
DIAGNOSIS	**EXUDATE**	Tuberculosis	31	54.4%
		Pneumonia	12	21.1%
		Ca lung	8	14.0%
		Ca breast	2	3.5%
		Acute pancreatitis	1	1.8%
		Empyema	1	1.8%
		Ca ovary	1	1.8%
		Pyothorax	1	1.8%
	TRANSUDATE	CCF	16	64.0%
		Cirrhosis of liver	5	20.0%
		CKD	2	8.0%
		Meig syndrome	1	4.0%
		Nephrotic syndrome	1	4.0%

Among the exudative pleural effusion majority of patients had tuberculosis(54.4%) and among the transudative effusion majority of the cases were CCF(64.0%).

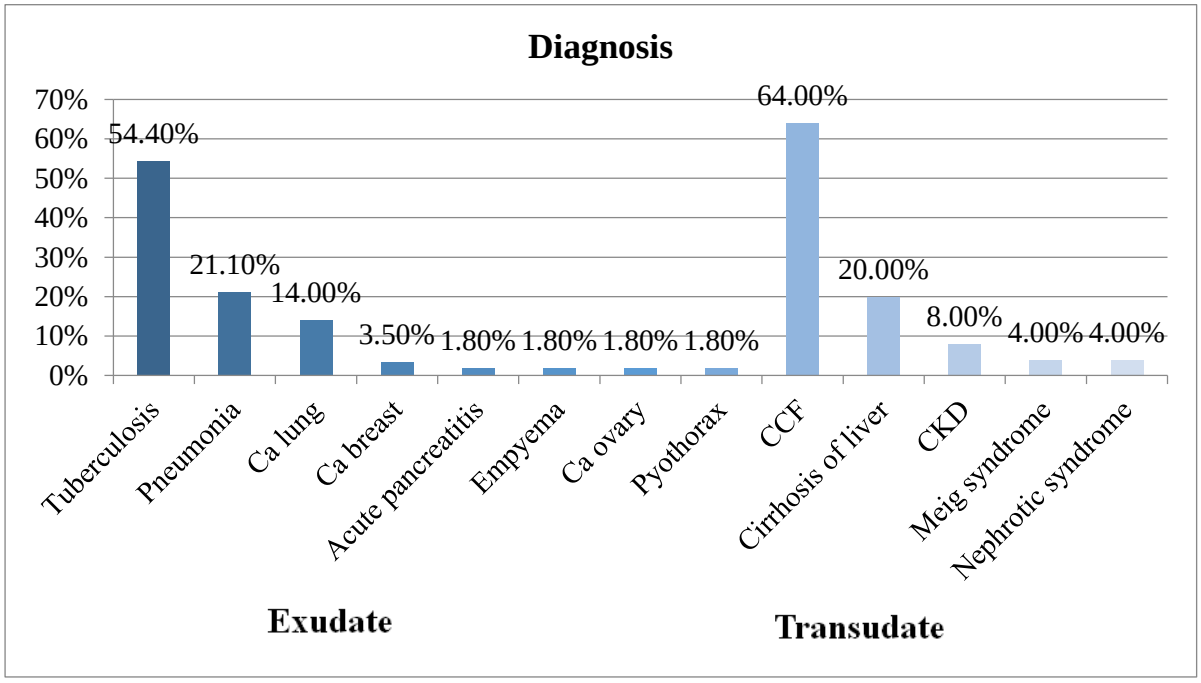


Chart 6: Bar diagram showing Comparison between type of disease and nature of Pleural Fluid

Table 10: Diagnosis of type of Pleural fluid with respect to Light's Criteria

		COUNT	%
LIGHT'S CRITERIA	EXUDATE	54	65.9%
	TRANSUDATE	28	34.1%

Pleural fluid to serum ratio of protein cut of value was taken as 0.5. The average value of pleural fluid to serum protein ratio was 0.8±0.2 in exudates and 0.5±0.1 in transudates.

In case of LDH, two-thirds of the upper limit of normal was used as the cut-off[1,23]. In our hospital laboratory the cut-off value came up to **320U/L**.

The cut-off value for pleural fluid to serum LDH level was **0.6**[1] and the average value in this study was 0.4±0.1 in transudates and 2.1±2.6 in exudates and the difference between the two was statistically significant.(p=<0.001)

According to Light's Criteria 65.9% patients were diagnosed as exudates and 34.1% were diagnosed as transudate.

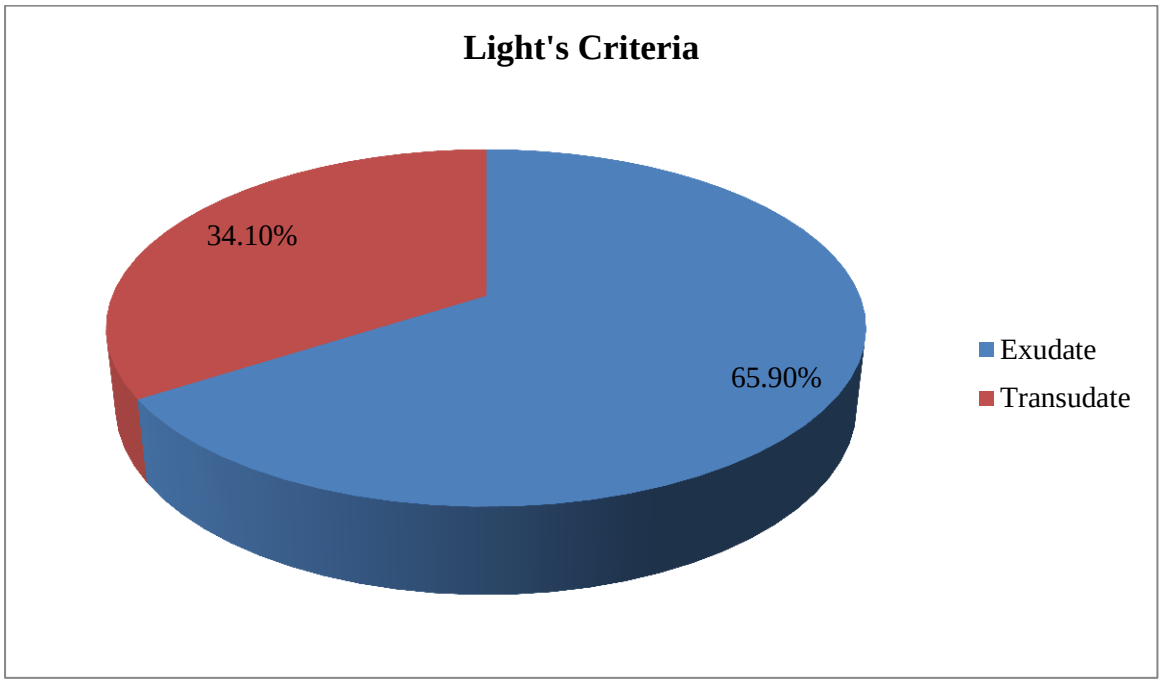


Chart 7: Pie diagram showing Diagnosis of type of Pleural fluid with respect to Light's Criteria

Table 11: Association between type of pleural fluid and Light's criteria

		DIAGNOSIS			
		EXUDATE		TRANSUDATE	
		Count	%	Count	%
LIGHT'S CRITERIA	EXUDATE	53	93.0%	1	4.0%
	TRANSUDATE	4	7.0%	24	96.0%

$\chi 2 = 61.191$, df = 1, p <0.001*

In the study, out of 57 subjects with exudate, 93% were diagnosed to have exudate and 7% were missed and classified as transudate according to Light's criteria. Out of 25 subjects with transudate, 96% were diagnosed to have transudate and 4% were misclassified as Exudate. There was significant association between Light's criteria and diagnosis.

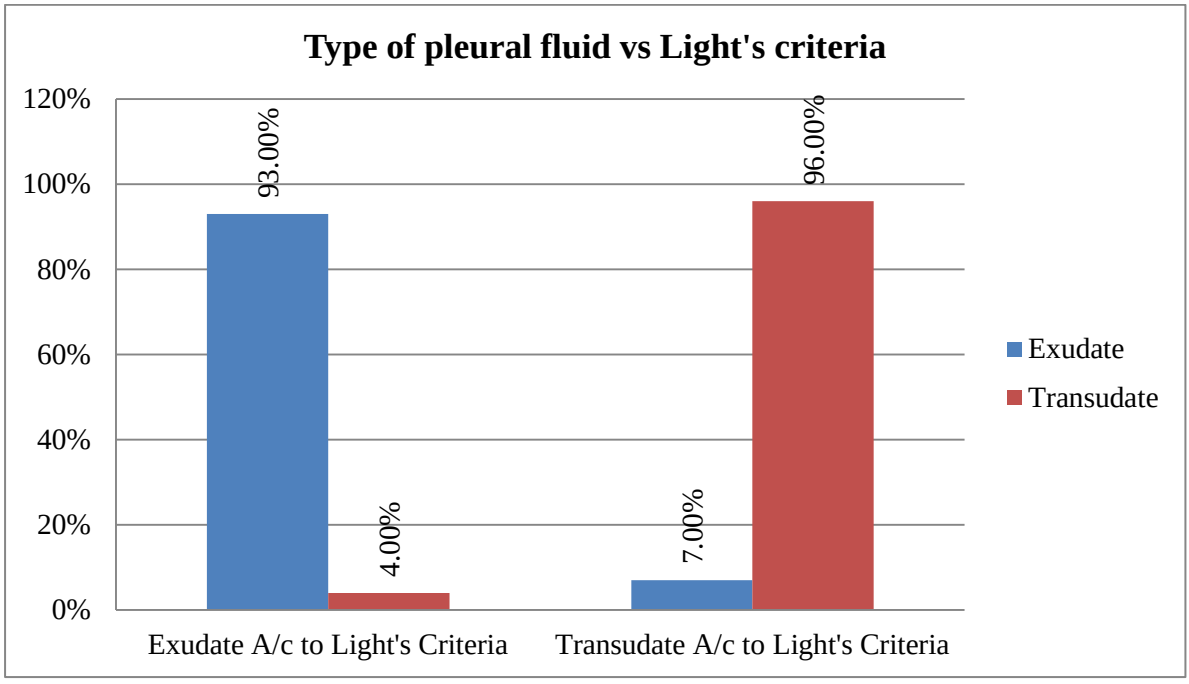


Chart 8: Bar diagram showing association between type of pleural fluid and Light's criteria

Table 12: Association between type of pleural fluid and fluid classification based on pseudo cholinesterase levels.

		DIAGNOSIS			
		EXUDATE		TRANSUDATE	
		Count	%	Count	%
According to pseudo cholinesterase levels	EXUDATE	55	96.5%	1	4.0%
	TRANSUDATE	2	3.5%	24	96.0%

$\chi 2 = 68.65$, df = 1, p <0.001*

The average Pseudocholinesterase (PChE) levels in transudative effusions was 618.9±201.2U/L and in case of exudates it was 2259.1±654.6 U/L. The difference between the two groups was statistically significant (p=<0.001) . The normal levels of ChE varies between laboratories. The cut-off value is $1/10^{th}$ of the upper limit of normal level of PChE in the respective laboratory[12]. In our study the cut-off value was **620U/L.** The cut-off value for pleural fluid to serum ratio of PChE used in this study was 0.24[10]. In this study, the average value was 0.2 for transudates and 0.5±0.1 for exudates. This difference was found to be statistically significant (p=<<0.001) **(Table 12)**.

In the study out of 57 subjects with exudate, 96.5% were diagnosed to have exudative effusion according to pseudocholinesterase levels and 3.5% were misclassified as transudate. Out of 25 subjects with Transudate, 96% were diagnosed to have transudative effusion and 4% were misclassified as Exudate. There was significant association between Pseudo cholinesterase criteria and diagnosis.

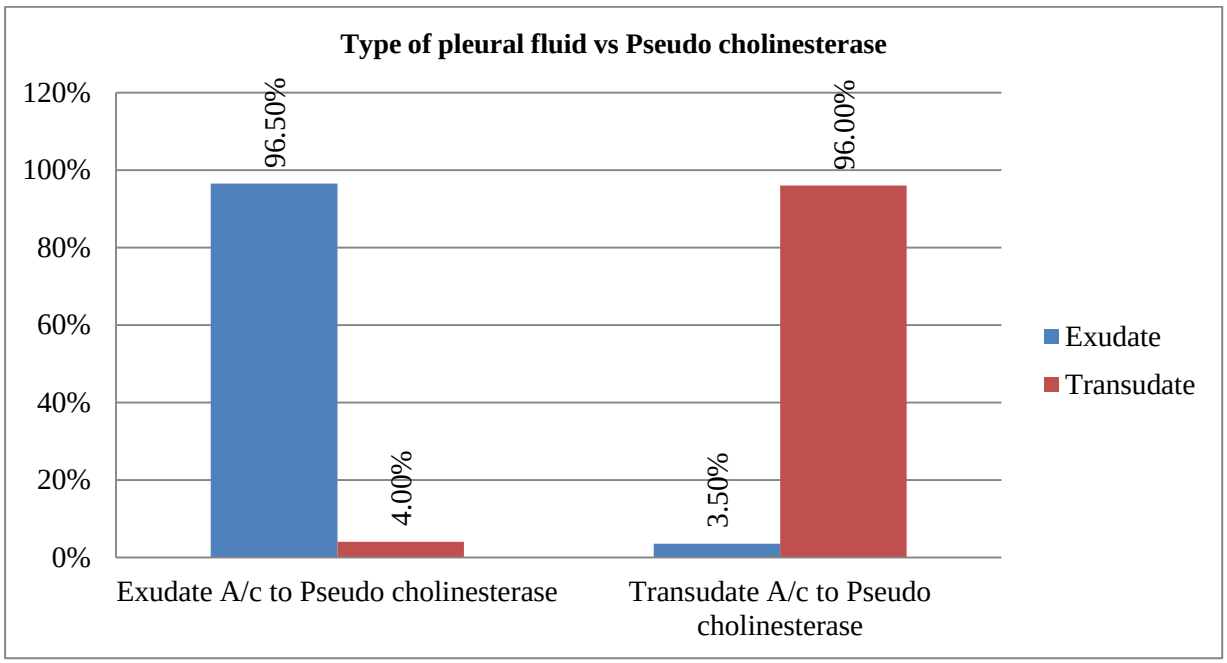


Chart 9: Bar diagram showing association between type of pleural fluid and fluid classification based on pseudo cholinesterase

Table 13: Comparison of Pleural fluid parameters with respect to diagnosis

	DIAGNOSIS				P value
	EXUDATE		TRANSUDATE		
	Mean	SD	Mean	SD	
PL Protein	4.7	1.0	2.7	0.8	<0.001*
PL/Serum protein ratio	0.8	0.2	0.5	0.1	<0.001*
PL LDH	1884.0	1791.3	292.2	183.8	<0.001*
PL/Serum LDH Ratio	2.1	2.6	0.4	0.1	<0.001*
PL Pseudo cholinesterase	2259.1	654.6	618.9	201.2	<0.001*
Serum Pseudo cholinesterase	4458.2	756.1	3543.5	351.6	<0.001*
PL/ Serum Pseudo ratio	0.5	0.1	0.2	0.0	<0.001*

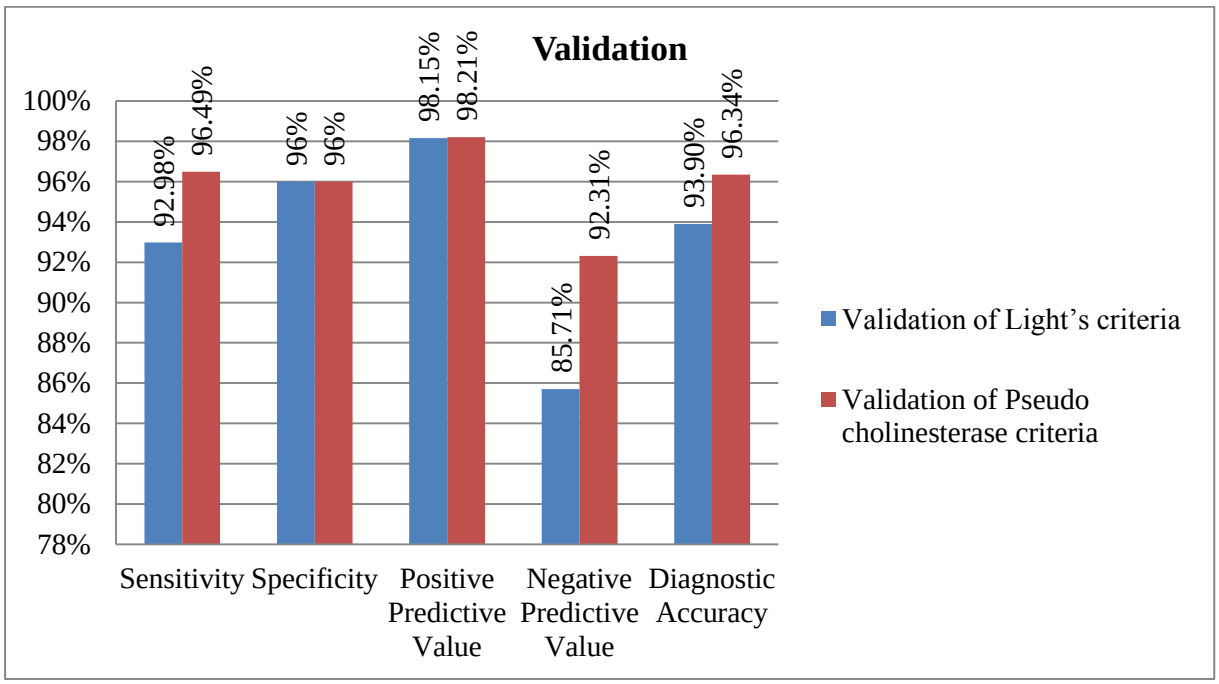


Chart 10: Bar diagram showing comparison between validation of Light's Criteria and Pseudo cholinesterase criteria

Light's criteria had a sensitivity of 92.98%, specificity of 96%, Positive Predictive Value of 98.15%, Negative Predictive Value of 85.71% and Diagnostic Accuracy of 93.9%. Kappa degree of agreement b/w Light's criteria and Final diagnosis was 0.8608.

Pseudo cholinesterase criteria had a sensitivity of 96.49%, specificity of 96%, Positive Predictive Value of 98.21%, Negative Predictive Value of 92.31% and Diagnostic Accuracy of 96.34%. Kappa degree of agreement b/w Light's criteria and Final diagnosis was 0.9146.

Diagnostic accuracy of Light's criteria was 93.9% and based on pseudo cholinesterase was 96.34%.

Table 14: Comparison of Pleural fluid parameters with Type of disease

	Diagnosis										P value
	Tuberculosis		Pneumonia		CCF		Cirrhosis of Liver		Malignancy		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Pleural fluid Protein	5.0	1.0	4.3	1.0	2.8	0.9	2.5	0.7	4.4	1.0	<0.001*
PL/Serum protein ratio	0.8	0.3	0.7	0.2	0.5	0.1	0.4	0.1	0.8	0.3	<0.001*
Pleural fluid LDH	2005.2	1827.6	1616.3	1655.7	297.2	226.7	270.4	94.3	1544.0	1764.6	0.005*
PL/Serum LDH Ratio	1.9	1.8	1.2	0.9	0.4	0.1	0.4	0.1	2.7	4.4	0.028*
PL fluid Pseudocholinesterase	2326.8	620.2	2125.9	555.7	593.3	35.7	568.0	49.1	2266.9	926.4	<0.001*
Serum Pseudo cholinesterase	4453.7	776.1	4518.4	602.6	3510.7	326.8	3587.0	403.9	4366.5	794.6	<0.001*
PL/ Serum Pseudo ratio	0.5	0.2	0.5	0.1	0.2	0.0	0.2	0.0	0.5	0.2	<0.001*

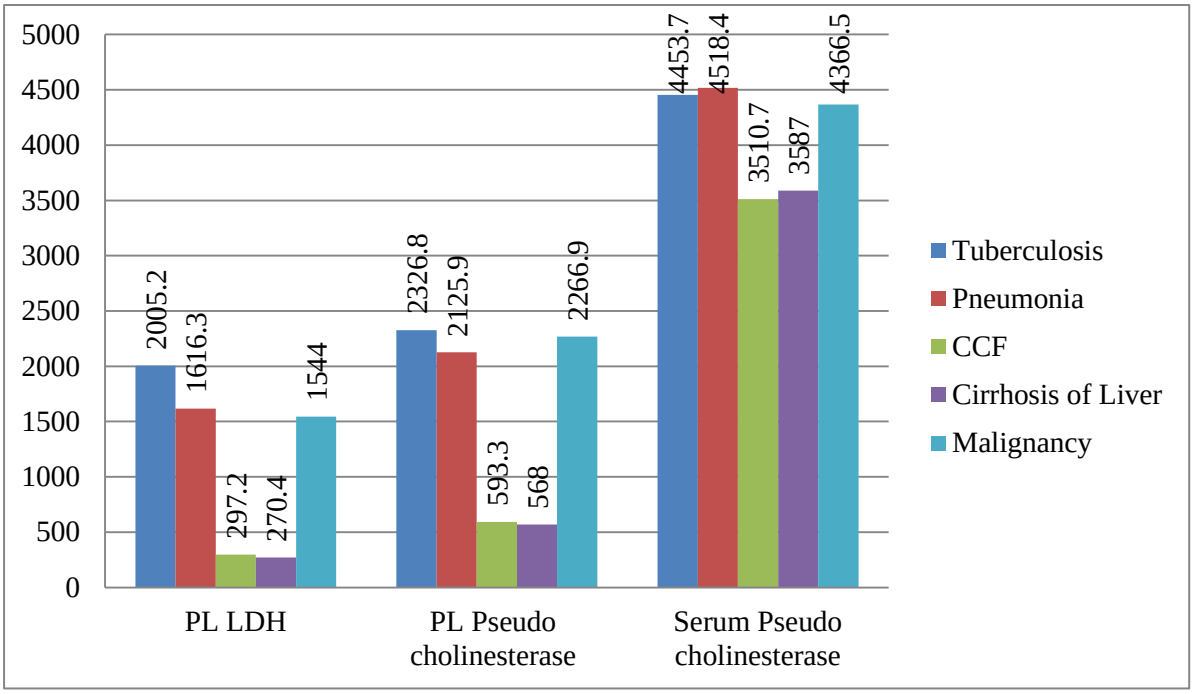


Chart 11: Bar diagram showing Comparison of Pleural fluid parameters with respect to type of disease

In the study the mean pleural fluid LDH values was highest in Tuberculosis (2005.2) and lowest in Cirrhosis of Liver (270.4).

The mean pleural fluid pseudocholinesterase levels were highest in patients with tubercular pleural effusion (2326.8) and lowest in the cirrhosis of liver (568). There was significant difference in mean Pleural fluid parameters with respect to disease.

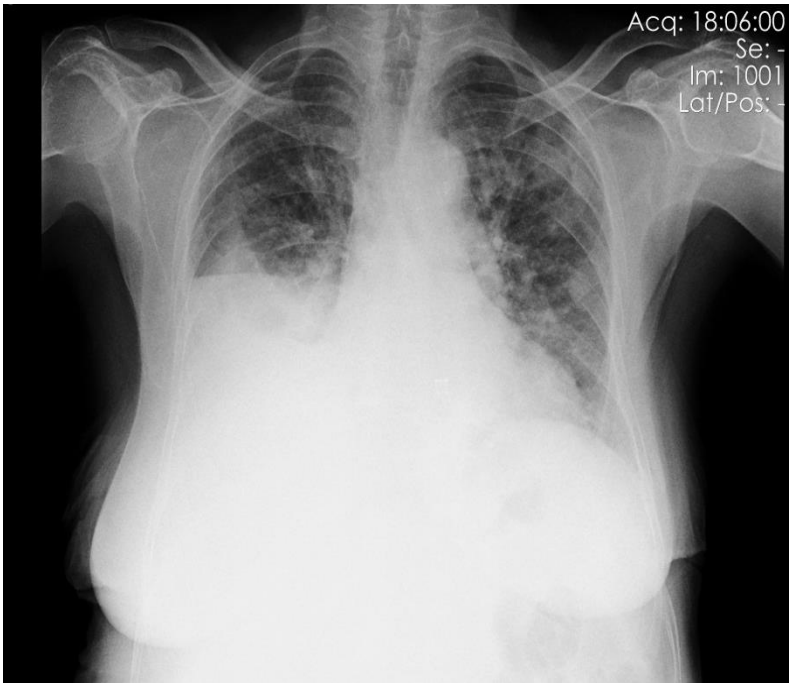


Figure 8: Plain radiograph showing right sided syn-pneumonic pleural effusion.

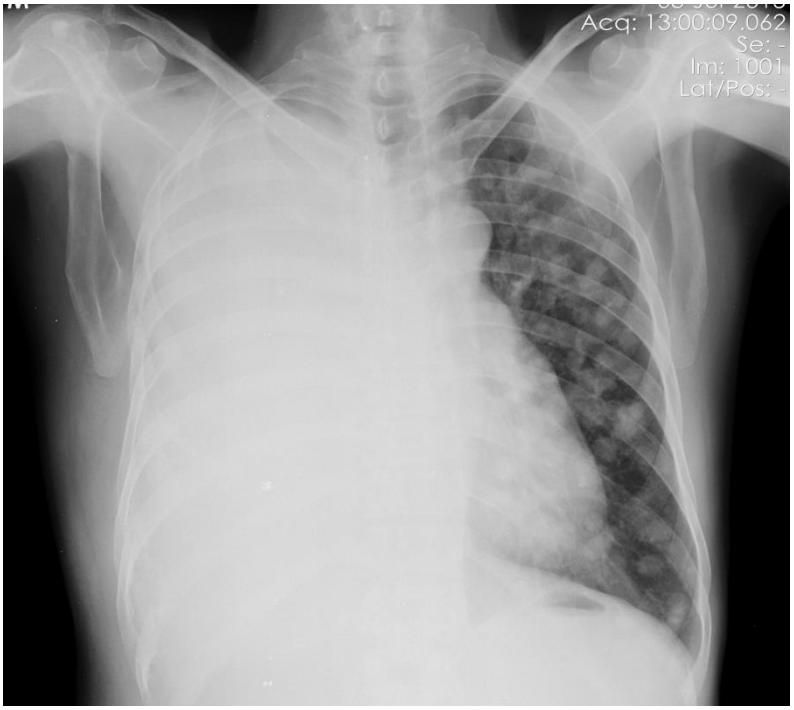


Figure 9: Plain radiograph showing massive right sided pleural effusion with cannon ball opacities.

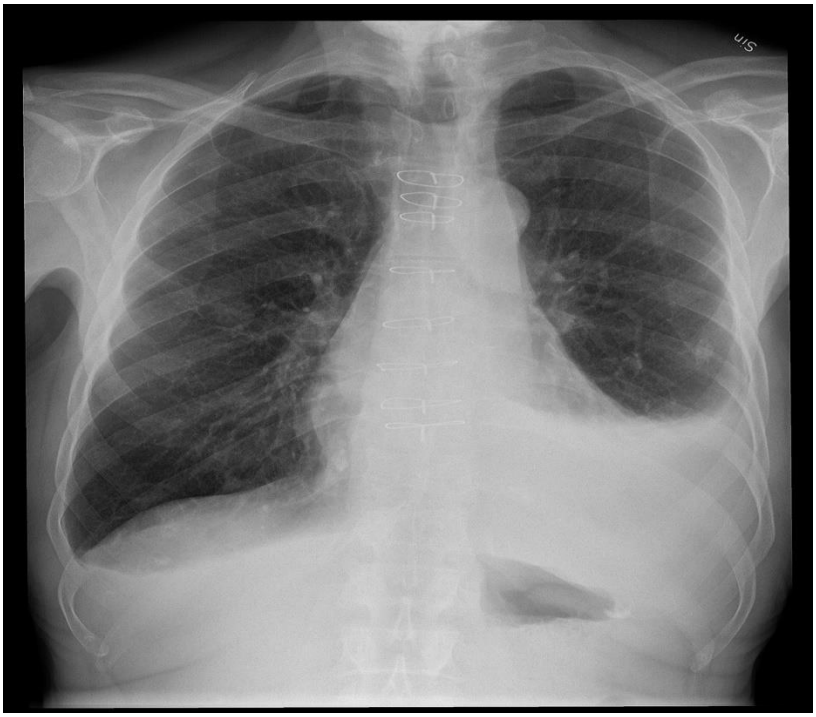


Figure 10: Plain radiograph showing left sided pleural effusion .

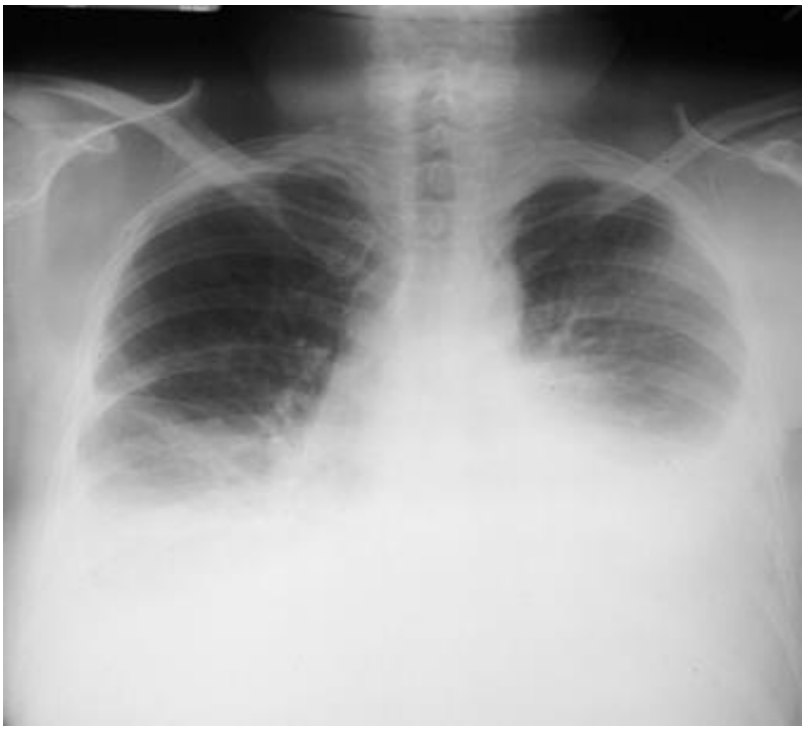


Figure 11: Plain radiograph showing bilateral pleural effusion .

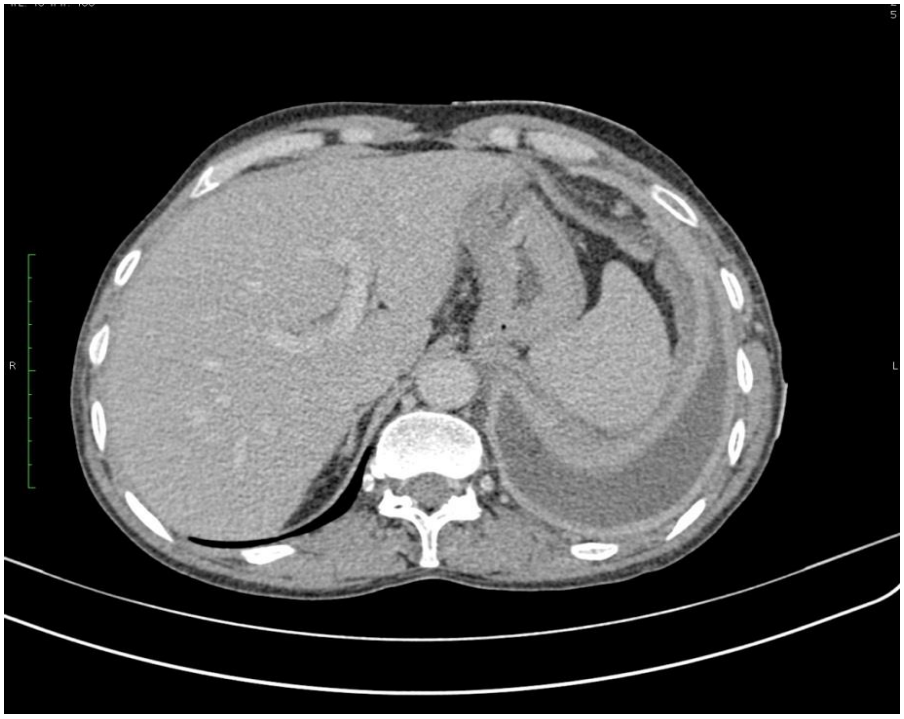


Figure 10: Computed Tomography image showing left sided empyema with split-pleura sign.

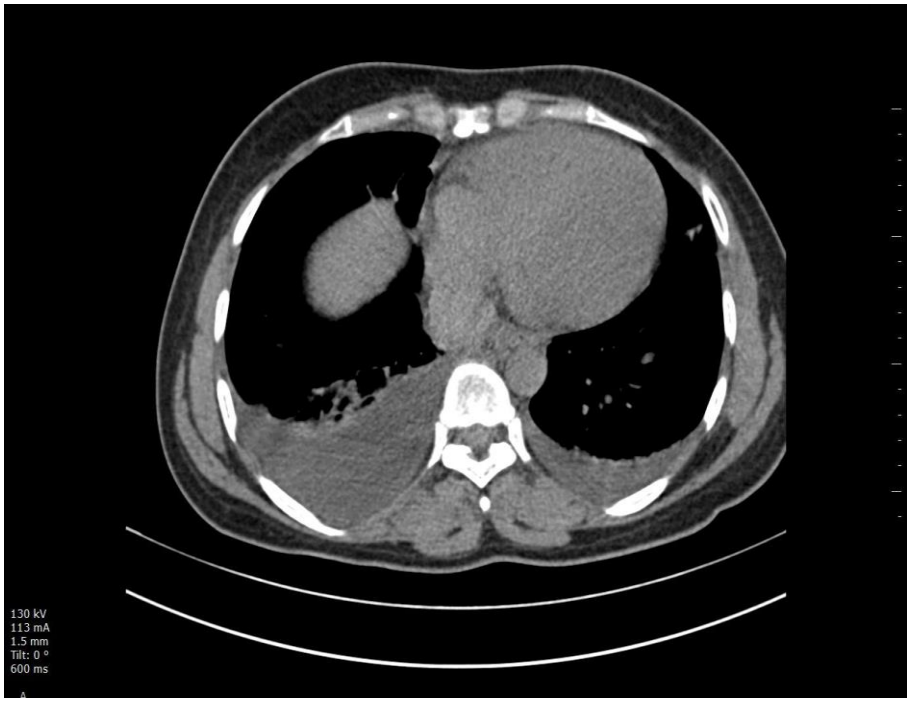


Figure 11: Computed Tomography image showing bilateral pleural effusion due to dengue fever.

DISCUSSION

DISCUSSION:

Pleural effusion is defined as accumulation of excessive pleural fluid (> 10ml) in pleural space. It occurs due to primary manifestation of disease or its complication[45] .Pleural effusion occurs in a large variety of conditions, but the correct diagnosis of underlying diseases is essential for the correct management of pleural effusion. Pleural effusions have more than 60 different causes, and vary in size and risk (and rates) of recurrence. An estimated 3,000 people per million population develop a pleural effusion.[46] Although scientific research in pleural diseases has increased in recent decades, it seems that it has attracted far less attention than other less common respiratory conditions[47]. The first step in the management of pleural effusion is its differentiation into a transudate or exudate. The most popular method used is the Light's criteria. But various studies have concluded that pleural effusions are misclassified by Light's criteria in a substantial number of patients. Hence, better and newer parameters with higher sensitivity and specificity are needed. In this study, a new parameter i.e pleural fluid to serum pseudocholinesterase ratio was compared with the Light's criteria in terms of efficacy.

In the original study by Light et al[1], in a series of 150 patients, the authors correctly classified all but two of the pleural effusions, one transudate and one exudate. In this study, Light's criteria misclassified five cases of pleural effusion with a sensitivity of 92.98% and specificity of 96% . Two of these cases were tubercular effusion, one case was a malignant effusion, one was CCF and one was synpneumonic effusion **(Table 11)**. In the study done by Garcia-Pachon et al[10], Light's criteria misclassified 12 cases (9 transudate and 3 exudate) with a sensitivity of 97.4% and specificity of 74.29% **(Table 15)**.

Table 15: Showing Efficacy of Light's Criteria in Different Studies

Study	Sensitivity	Specificity
Light et al[1]	99%	97.8%
Garcia-Pachon et al[12]	97.4%	74.29%
Sharma et al[10]	91.25%	90%
Present study	92.98%	96%

In this study, the ratio of pleural fluid to serum pseudocholinesterase with a cut-off value of 0.24 misclassified only 3 cases of pleural effusion out of the total 82 cases giving it a sensitivity of 96.49% and specificity of 96% . In studies done by Sharma et al[6] and Garcia-Pachon et al[10], the pleural fluid to serum cholinesterase ratio correctly classified effusions in 98.19% and 98.7% cases respectively. The percentage of misclassification of pleural effusions was lower with P/S ChE in all three studies when compared to Light's criteria. This is a very significant and consistent result making it the most efficient parameter studied.

Table 16: Showing Efficacy of P/S ChE in Various Studies

Study	Sensitivity	Specificity
Garcia-Pachon et al[12]	100%	94.5%
Sharma et al[10]	98.75%	96.67%
Present study	96.49%	96%

Cholinesterase is synthesized in the liver and its levels can be influenced by different disorders like acute hepatitis, cirrhosis, acute infections, pulmonary embolism, chronic renal disease, and after surgical procedures. Hence, the ratio of pleural fluid to serum cholinesterase is a better parameter than the absolute value of cholinesterase in the pleural fluid.

The LDH levels were found to vary widely among exudates and the difference between the mean values of LDH among transudates and exudates was not statistically significant. The pleural fluid to serum ratio of LDH misclassified the maximum number of cases in this study. In the study done by Sharma et al,[6] the ratio of pleural fluid to serum LDH was not found to have a statistically significant difference between transudates and exudates.

The mean pleural fluid pseudocholinesterase levels were highest in patients with tubercular pleural effusion (2326.8 U/L) and lowest in the cirrhosis of liver (568 U/L). This parameter alone can be considered to be used in the diagnosis of tubercular effusion and the pleural fluid to serum pseudocholinesterase ratio can be used for the accurate diagnosis of pleural effusions.

This study had a small sample size of 82. Other studies comparing pleural fluid to serum cholinesterase ratio had sample sizes of 110, 150 and 80 each. Probably a study with a larger sample size would provide better results for analysis.

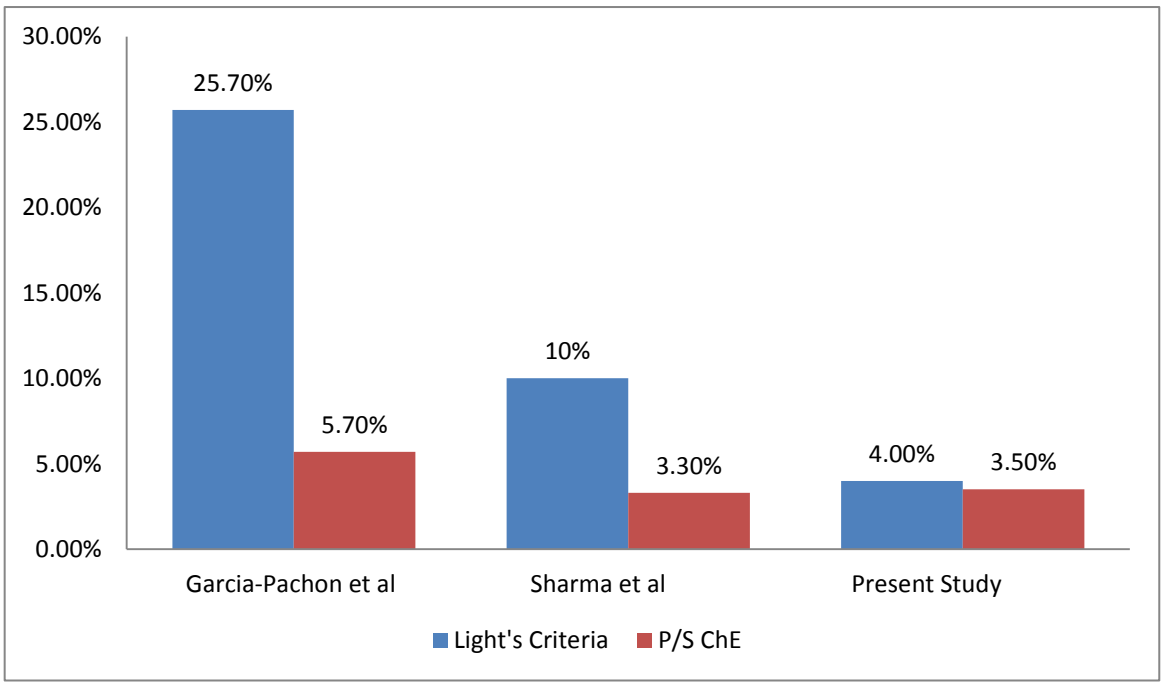


Chart 12: Showing Percentage of Transudates Misclassified in Different Studies

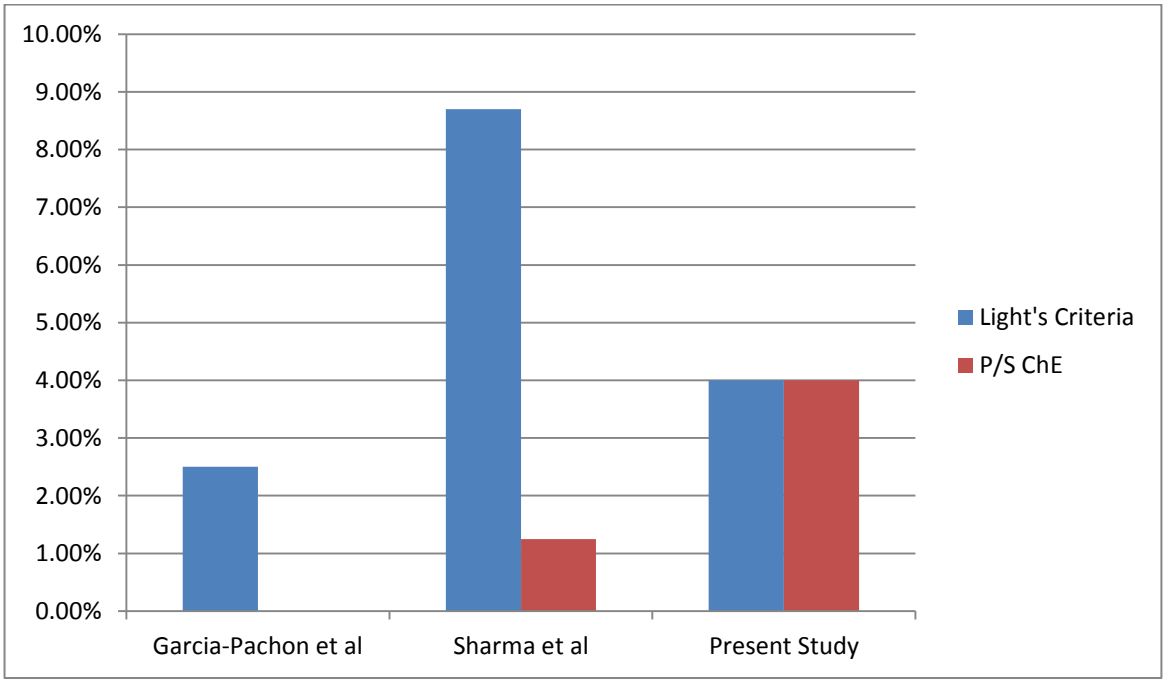


Chart 13: Showing Percentage Misclassification of Exudates in Different Studies

CONCLUSION

CONCLUSION

The levels of pseudocholinesterase in pleural fluid and its fluid to serum ratio are significantly higher in exudative pleural effusions than transudative ones. These two are good parameters that can be used to differentiate between transudates and exudates. The ratio of pleural fluid to serum pseudocholinesterase ratio is probably superior to Light's criteria in differentiating between transudates and exudates.

SUMMARY

SUMMARY

Pleural effusions are a common clinical problem. The first step in the analysis of pleural effusion is the categorization into transudate or exudate. The correct differentiation provides clarity in the direction of patient evaluation.

This study was conducted at RL Jalappa Hospital attached to the Sri Devaraj Urs Academy of Higher Education and Research, Kolar. The study included 82 patients with pleural effusion. Duration of study was 15 months.

Among the 82 patients, 57 had transudative effusions and 25 had exudative effusions. The average values of pleural fluid pseudocholinesterase was significantly higher in exudates than in transudates, highest being in tubercular effusions.

The ratio of pleural fluid to serum pseudocholinesterase was found to be superior to Light's criteria in differentiating between transudates and exudates. This criteria cannot be interpreted in few conditions like acute hepatitis, cirrhosis, pulmonary embolism, chronic renal disease.

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BIBLIOGRAPHY

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ANNEXURE

INFORMED CONSENT FORM

STUDY TITLE: STUDY OF PLEURAL FLUID TO SERUM PSEUDOCHOLINESTERASE RATIO AND ITS CORRELATION WITH CLINICAL PROFILE AND LIGHT'S CRITERIA.

STUDY NUMBER:

SUBJECT'S NAME: **HOSPITAL NUMBER:**

AGE:

It is hoped that the knowledge of relevant prognostic factors might be useful for early identification of patients at high risk requiring intensive care treatment. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. We will collect the treatment and relevant details from your hospital record. This information collected will be used for only dissertation and publication. The institutional ethical committee has reviewed this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

I understand that I remain free to withdraw from the study at any time and this will not change my future care. I have read or have been read to me and understood the purpose of the study, the procedure that will be used, the risk and benefits associated with my involvement in the study and the nature of information that will be collected and disclosed during the study. I have had the opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction. I, the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information for dissertation and publication only.

Signature or thumb impression of the subject: Date:

Name and signature of the witness: Date:

Name and signature of person obtaining consent Date:

PROFORMA

STUDY OF PLEURAL FLUID TO SERUM PSEUDOCHOLINESTERASE RATIO AND ITS CORRELATION WITH CLINICAL PROFLE AND LIGHT'S CRITERIA

1. OP/IP No.: 2.Date:

3. Serial No.:

4. Name: 5.Age: 6. Gender:

7. Occupation:

8. Date of Admission:

9. Date of Discharge:

10. Socioeconomic status:

11. Address with Phone no.:

12. Chief Complaints:

13. Past history:

14. Family history:

15. Personal History:

16. General Physical Examination: (At admission)

PR: BP: Temp: Resp Rate:

Pallor: Icterus: Cyanosis:

Clubbing: Lymphdenopathy: Oedema:

17. Systemic examination:

CVS:

RS:

PA:

CNS:

18. Diagnosis:

19. INVESTIGATIONS

1. Complete Blood Count :
2. Random blood sugar: mg/dl
3. Blood Urea/Serum creatinine: mg/dl
4. Urine albumin/sugar:
5. Serum protein: g/dl
6. Serum LDH: U/L
7. Serum pseudocholinesterase: U/L
8. Pleural fluid pseudocholinesterase: U/L
9. Pleural fluid protein: g/dl
10. Pleural fluid LDH: U/L
11. Pleural Fluid LDH/Serum LDH:
12. Pleural fluid protein/Serum protein:
13. Lights Criteria:
14. Pleural Fluid Pseudocholinesterase/Serum Pseudo ratio:
15. Chest X ray:
16. Other investigations:

SIGNATURE DATE

KEY TO MASTER CHART

IP NO: INPATIENT NUMBER

GENDER: M- MALE, F- FEMALE

DIAGNOSIS:

CA LUNG- CARCINOMA LUNG

CA OVARY- CARCINOMA OVARY

CA BREAST- CARCINOMA BREAST

CCF- CONGESTIVE CARDIAC FAILURE

SIDE:

L- LEFT

R- RIGHT

LIGHTS CRITERIA:

E- EXUDATE

T- TRANSUDATE

PSEUDOCHOLINESTERASE CRITERIA:

E- EXUDATE

T- TRANSUDATE

MASTER CHART

SL N	IP NO	AGE	GENDER	DIAGNOSIS	SIDE	LIGHTS CRITERIA	PL PROTEI	PL/SR prot	PL LDH	PL/SR LDH	PL PSEUDO	SERUM PS	PL/Pseudo	PSEUDO cr
1	247969	66	MALE	CA LUNG	right	EXUDATE	3.3	0.63	506	0.76	1458	4366	0.33	EXUDATE
2	253938	36	FEMALE	PNEUMONIA	right	EXUDATE	3.7	0.71	6410	3.6	1211	4774	0.65	EXUDATE
3	253952	64	MALE	CA LUNG	left	TRANSUDATE	2.9	0.49	302	0.38	1458	4725	0.3	EXUDATE
4	231941	52	MALE	TUBERCULOSIS	left	EXUDATE	4.6	0.8	1263	1.73	2458	4936	0.49	EXUDATE
5	347969	66	MALE	PYOTHORAX	RIGHT	EXUDATE	5.2	0.75	5660	10.6	2084	3139	0.66	EXUDATE
6	440006	43	MALE	TUBERCULOSIS	LEFT	EXUDATE	5.3	0.76	2250	0.76	2250	4136	0.54	EXUDATE
7	411293	71	MALE	CA LUNG	right	EXUDATE	4.4	0.7	1051	1.5	4555	5861	0.77	EXUDATE
8	410511	73	MALE	CA LUNG	left	EXUDATE	5.2	0.81	620	0.97	1112	4956	0.22	TRANSUDA
9	415896	52	FEMALE	PNEUMONIA	right	EXUDATE	4.8	0.64	598	1.17	1567	4556	0.34	EXUDATE
10	409043	60	MALE	CIRRHOSIS OF LIVER	right	TRANSUDATE	3.6	0.47	319	0.28	520	3987	0.13	TRANSUDA
11	442190	48	FEMALE	MEIG SYNDROME	left	TRANSUDATE	2	0.47	310	0.13	425	3995	0.1	TRANSUDA
12	240479	36	MALE	CCF	BILATERAI	TRANSUDATE	4.1	0.46	316	0.29	618	3988	0.15	TRANSUDA
13	441714	28	MALE	CKD	right	TRANSUDATE	3.6	0.47	295	0.15	1556	4002	0.24	EXUDATE
14	248483	45	MALE	CIRRHOSIS OF LIVER	right	TRANSUDATE	2	0.32	102	0.53	601	3556	0.16	TRANSUDA
15	252166	61	FEMALE	CCF	LEFT	TRANSUDATE	3	0.49	105	0.21	559	2967	0.18	TRANSUDA
16	441176	70	FEMALE	TUBERCULOSIS	right	EXUDATE	5.3	0.84	3890	8.72	1557	4051	0.38	EXUDATE
17	283876	42	MALE	TUBERCULOSIS	right	EXUDATE	3.6	0.73	7280	5.6	2598	4552	0.57	EXUDATE
18	284109	28	MALE	TUBERCULOSIS	right	EXUDATE	8	1.29	3920	0.74	2112	5665	0.24	EXUDATE
19	232417	48	FEMALE	PNEUMONIA	LEFT	EXUDATE	4.7	0.9	993	0.63	2550	4999	0.51	EXUDATE
20	451629	33	MALE	TUBERCULOSIS	right	EXUDATE	4.4	1.9	2220	2.83	1998	4006	0.49	EXUDATE
21	247969	55	MALE	TUBERCULOSIS	left	TRANSUDATE	2.7	0.44	299	0.43	1556	5664	0.27	EXUDATE
22	490075	36	MALE	TUBERCULOSIS	right	EXUDATE	5.1	0.76	2253	0.61	3445	4334	0.79	EXUDATE
23	451629	61	MALE	TUBERCULOSIS	right	EXUDATE	5.4	0.95	975	0.77	2556	4339	0.58	EXUDATE
24	307768	65	MALE	CA LUNG	right	EXUDATE	4.7	0.9	6570	15.3	2443	4554	0.53	EXUDATE
25	272243	45	FEMALE	PNEUMONIA	left	EXUDATE	4.6	0.9	920	0.89	1990	4234	0.47	EXUDATE
26	284109	40	FEMALE	PNEUMONIA	right	EXUDATE	3.5	0.8	622	1.14	2770	3998	0.69	EXUDATE
27	234583	32	MALE	TUBERCULOSIS	left	EXUDATE	5.1	0.74	907	2.19	1889	4040	0.46	EXUDATE
28	346147	46	MALE	CIRRHOSIS OF LIVER	left	TRANSUDATE	2	0.44	312	0.31	610	3008	0.2	TRANSUDA
29	326756	58	MALE	CCF	BILATERAI	TRANSUDATE	3.4	0.46	184	0.46	620	3455	0.17	TRANSUDA
30	316570	42	MALE	CKD	right	TRANSUDATE	3.2	0.49	320	0.23	559	3030	0.18	TRANSUDA
31	311420	65	FEMALE	CCF	left	TRANSUDATE	2.1	0.45	318	0.5	610	3998	0.15	TRANSUDA
32	389529	52	FEMALE	CAOVARY	left	EXUDATE	6	0.85	2150	1.94	2778	5099	0.54	EXUDATE
33	372712	65	MALE	TUBERCULOSIS	right	EXUDATE	4.7	0.64	1991	1.19	2099	4088	0.51	EXUDATE
34	307641	70	FEMALE	TUBERCULOSIS	left	TRANSUDATE	2	0.39	289	0.54	2109	3990	0.52	EXUDATE
35	368514	35	FEMALE	TUBERCULOSIS	right	EXUDATE	5.3	0.76	735	1.65	1898	4553	0.41	EXUDATE
36	361623	25	MALE	TUBERCULOSIS	right	EXUDATE	5.2	0.77	1300	1.23	2220	3998	0.55	EXUDATE
37	350535	36	FEMALE	PNEUMONIA	right	EXUDATE	5	0.66	2150	1.94	2001	5050	0.39	EXUDATE
38	347726	32	MALE	TUBERCULOSIS	left	EXUDATE	5.4	0.9	1050	2.45	1995	3443	0.57	EXUDATE
39	342601	35	MALE	TUBERCULOSIS	right	EXUDATE	4.9	0.72	5538	3.51	2101	5001	0.42	EXUDATE
40	410119	69	FEMALE	PNEUMONIA	right	TRANSUDATE	2	0.38	213	0.46	2440	4002	0.6	EXUDATE
41	134918	60	MALE	CA LUNG	right	EXUDATE	5.2	1.67	1666	1.35	2445	3030	0.8	EXUDATE
42	344241	24	MALE	TUBERCULOSIS	left	EXUDATE	5.3	0.74	432	0.86	2201	4122	0.53	EXUDATE
43	343627	57	MALE	TUBERCULOSIS	right	EXUDATE	5.3	0.67	2150	3.88	1997	3099	0.48	EXUDATE
44	338022	56	MALE	PNEUMONIA	left	EXUDATE	4.4	0.69	2002	0.62	2225	4090	0.54	EXUDATE
45	335584	38	FEMALE	CA BREAST	left	EXUDATE	5.4	0.87	1294	0.63	1892	3990	0.47	EXUDATE
46	329068	67	MALE	ACUTE PANCREATITIS	right	EXUDATE	4.5	0.69	824	1.95	2009	4988	0.4	EXUDATE
47	307768	58	FEMALE	CCF	left	TRANSUDATE	2.6	0.48	315	0.45	602	3443	0.17	TRANSUDA
48	367070	22	FEMALE	CCF	right	EXUDATE	5.4	0.87	1090	0.69	599	3445	0.17	TRANSUDA
49	363408	58	FEMALE	CCF	right	TRANSUDATE	2.4	0.38	318	0.48	619	3009	0.2	TRANSUDA
50	113612	65	MALE	NEPHRONIC SYNDRO	right	TRANSUDATE	2.9	0.47	273	0.3	600	3455	0.17	TRANSUDA
51	331492	35	MALE	TUBERCULOSIS	left	EXUDATE	4.4	0.75	4556	3.2	2565	3451	0.74	EXUDATE
52	306567	60	MALE	TUBERCULOSIS	right	EXUDATE	6.5	0.64	777	1.57	1999	4099	0.48	EXUDATE
53	245458	22	MALE	TUBERCULOSIS	right	EXUDATE	4.2	0.6	2500	3.4	1899	4666	0.4	EXUDATE
54	256469	65	FEMALE	PNEUMONIA	left	EXUDATE	4.6	0.9	558	1.01	2099	4887	0.42	EXUDATE
55	244714	45	MALE	CCF	right	TRANSUDATE	2.4	0.43	88	0.44	598	3776	0.15	TRANSUDA
56	347969	55	MALE	PNEUMONIA	left	EXUDATE	5.39	0.76	2250	0.88	2870	5667	0.5	EXUDATE
57	259793	62	MALE	TUBERCULOSIS	right	EXUDATE	5.6	0.67	643	0.63	3099	4826	0.64	EXUDATE
58	270150	65	FEMALE	CCF	left	TRANSUDATE	2.6	0.44	217	0.42	611	3665	0.16	TRANSUDA
59	299647	55	MALE	TUBERCULOSIS	right	EXUDATE	4.5	0.76	445	1.15	566	3554	0.15	TRANSUDA
60	333405	39	MALE	TUBERCULOSIS	right	EXUDATE	5	0.77	1078	1.34	2334	5667	0.41	EXUDATE
61	312151	50	MALE	CCF	left	TRANSUDATE	2.1	0.49	182	0.38	601	3887	0.15	TRANSUDA
62	311420	67	MALE	CCF	right	TRANSUDATE	2	0.28	211	0.45	598	3334	0.17	TRANSUDA
63	405882	48	FEMALE	TUBERCULOSIS	right	EXUDATE	5.4	0.77	736	0.53	3556	4023	0.88	EXUDATE
64	411002	62	MALE	CCF	left	TRANSUDATE	2.9	0.48	317	0.56	475	3007	0.15	TRANSUDA
65	300393	50	MALE	TUBERCULOSIS	right	EXUDATE	4.4	0.47	724	0.67	2665	4087	0.65	EXUDATE
66	410359	62	MALE	CIRRHOSIS OF LIVER	right	TRANSUDATE	2	0.3	306	0.22	600	3951	0.15	TRANSUDA
67	419325	25	FEMALE	TUBERCULOSIS	right	EXUDATE	4.1	0.74	6345	5.2	3443	5661	0.6	EXUDATE
68	420145	69	MALE	CA LUNG	right	EXUDATE	4.6	0.8	849	1.6	2343	3998	0.58	EXUDATE
69	316570	41	MALE	TUBERCULOSIS	left	EXUDATE	5.4	0.65	2150	0.87	2558	6566	0.39	EXUDATE
70	420599	67	MALE	CCF	BILATERAI	TRANSUDATE	2	0.45	314	0.41	612	3651	0.16	TRANSUDA
71	250350	52	MALE	PNEUMONIA	right	EXUDATE	3.7	0.52	1656	0.64	2545	4521	0.56	EXUDATE
72	338022	38	FEMALE	TUBERCULOSIS	right	EXUDATE	4.7	0.65	1232	1.1	3212	4321	0.74	EXUDATE
73	257599	62	FEMALE	TUBERCULOSIS	right	EXUDATE	5.5	0.87	558	1.01	2343	4052	0.58	EXUDATE
74	259316	42	MALE	PNEUMONIA	left	EXUDATE	5.4	0.79	1023	0.87	1243	3443	0.36	EXUDATE
75	268233	48	MALE	CCF	right	TRANSUDATE	2.9	0.43	303	0.43	602	3673	0.16	TRANSUDA
76	268669	67	FEMALE	CA BREAST	right	EXUDATE	3.4	0.56	1543	0.68	2565	3998	0.64	EXUDATE
77	298670	61	FEMALE	CIRRHOSIS OF LIVER	right	TRANSUDATE	2.9	0.45	313	0.52	509	3433	0.14	TRANSUDA
78	266358	38	MALE	TUBERCULOSIS	left	EXUDATE	5.7	0.77	1676	1.72	2852	5075	0.56	EXUDATE
79	262168	58	MALE	CA LUNG	left	EXUDATE	4	0.56	433	1.45	1887	3454	0.54	EXUDATE
80	265195	28	MALE	EMPYEMA	left	EXUDATE	3.4	0.64	2362	2.08	2098	5676	0.36	EXUDATE
81	274136	50	MALE	CCF	right	TRANSUDATE	2.2	0.44	319	0.16	601	3441	0.17	TRANSUDA
82	293322	38	MALE	CCF	left	TRANSUDATE	2.1	0.34	159	0.25	567	3432	0.16	TRANSUDA