# Scholars Journal of Applied Medical Sciences (SJAMS) 

Abbreviated Key Title: Sch. J. App. Med. Sci.

OScholars Academic and Scientific Publisher
A Unit of Scholars Academic and Scientific Society, India
Medicine
www.saspublishers.com

# A Study of Pleural Fluid Cholesterol in Differentiating Transudative and Exudative Pleural Effusion 

Dr. Ayyali Ambresh*<br>Blde (Deemed To Be University) Vijayapura, Karnataka, India

Driginal Research Article<br>*Corresponding author<br>Dr. Ayyali Ambresh

Article History

Received: 02.10.2018
Accepted: 12.10.2018
Published: 30.10.2018

## DOI:

10.36347/sjams.2018.v06i10.029



#### Abstract

Pleural effusion is one of the common condition encountered in day to day practise. Pleural effusions represent a very common diagnostic task to the physician. A correct diagnosis of the underlying disease is essential to rational management. Today there are a number of laboratory tests available to differentiate exudates and transudates which are considered cost effective to the patients. So this study was designed for the measurement of pleural fluid cholesterol to differentiate transudative and exudative pleural effusions (sensitivity-97.8\%, specificity-100\%) with the advantage that a contemporary blood sample is not required, thereby lowering cost of diagnostic procedure. To study the diagnostic value of Pleural fluid Cholesterol in differentiating transudative and exudative pleural effusions. This cross sectional descriptive study was conducted in the Department of Medicine, Shri B M Patil medical college hospital and research centre, Vijayapura on patients of pleural effusion. A study design consists of 60 patients. Age $>18$ years and patients with with definitive clinical diagnosis and evidenced by radiological diagnosis of pleural effusion were taken as inclusion criteria. The results showed majority of the patients were males ( $63.33 \%$ ) and females ( $36.67 \%$ ). According to lights criteria 46 patients were exudates and 14 patients were transudates and according to Pleural fluid Cholesterol criteria 45 patients were exudates and 15 patients were transudates with sensitivity of $97.8 \%$ and specificity of $100 \%$ and accuracy of $98.3 \%$. The pleural fluid cholesterol criteria were found to be the most efficient criteria. Since this parameter involves the measurement of only pleural fluid values of cholesterol, it has following advantages-Economically it reduces number of biochemical tests and Simpler as there is no need to take simultaneous blood sample at the time of thoracocentesis.


Keywords: Pleural Effusion, Transudates, Exudates, Cholesterol.

## INTRODUCTION

Pleural effusions represent a very common diagnostic task to the physician. A correct diagnosis of the underlying disease is essential to the rational management [1].

Normally the pleural space contains only a few millimetres of fluid. Accumulation of excessive amount of fluid is a frequent manifestation of many diseases of both thoracic and extra thoracic. Indeed pleural effusion must be regarded as a trivial event but as a sign of major disorder or disease [2].

The first diagnostic step is the identification of pleural effusions as either a transudate or exudates. This is useful because it indicates the pathophysiological mechanisms involved. Exudates are secondary to alteration of capillary permeability or lymphatic drainage. Transudates are due to either alterations of hydrostatic and / or osmotic pressure in pleural capillaries or to a fluid passing from the peritoneal cavity via diaphragmatic defects.

If an exudate is present further diagnostic procedures and tests are imperative for definitive diagnosis and specific therapy. On the other hand if the fluid is clearly a transudate one need not worry about manoeuvres directed at the pleura and need to treat only the congestive cardiac failure, nephrosis, cirrhosis or hypoproteinemia [3].

Over the years many criteria have been developed by various workers for separation of exudates and transudates.

## OBJECTIVE OF THE STUDY

To study the diagnostic value of Pleural fluid Cholesterol in differentiating transudative and exudative pleural effusions.

## REVIEW OF LITERATURE

## HISTORICAL ASPECTSOF PLEURAL DISEASE

The word 'pleura' means 'rib' in Greek. Galen used the term pleura for both the ribcage and the lining membrane of the chest wall. Later Mandino used the word pleura for the lining membrane exclusively and this has been used ever since.

Pleurisy means inflammation of the Pleura. Hippocrates was the first to use this termin $5^{\text {th }}$ century. The first to establish the site of pleurisy exclusively in the Pleura was Hermann Boerhaave(1668-1730). It was Laennec in 1820 who first to describe the association between phthisis and Pleural effusion. In 1761 AD, Auenbrugger introduced chest percussion which proved to be very useful in clinical detection of Pleural
effusion. GuidoBacelli's description of aphonic pectorilquy of Pleural effusion was another landmark. Grocco (1856-1916) described the Para vertebral dullness known as Grocco's triangle of pleural effusion. Armand trosseau ( $18^{\text {th }}$ century) was the person to aspirate fluid from the Pleural cavity. Later on, Delafouy, his pupil improved the procedure by employing a trocar. But it was Henry Bowditch (180292) who perfected the procedure paracentesis thoracis. In 1925 Jacobaeus first viewed tubercles studded over the pleura through thoracoscopy. In 1954 Sutcliff introduced open pleural biopsy as a diagnostic aid. In 1954 Defrancis used liver biopsy needle for closed biopsy. In 1958 Abram developed pleural biopsy needle which is in general use till today.

Table-1: Shows the historical aspects of the various criteria/ parameters

| Sl. No. | Worker \& year | Criteria/parameters | Comments |
| :--- | :--- | :--- | :--- |
| 1. | Paddok f. k [4] 1940 | Specific Gravity | Unacceptable misclassification rates <br> of both transudates and exudates led <br> to recommendation of abandonment <br> of this criteria in a later review |
| 2. | Leuallen \& carr [5] <br> 1955 | Pleural Fluid Protein Levels <br> $>3.0 / 100 \mathrm{ml}$ | Erroneous classification of both <br> exudates and transudates of up to <br> $10 \%$ noted in a review |
| 3. | Carr \& power [6] <br> 1958 | Pleural Fluid Protein to Serum <br> Protein Ratio >0.5 | Somewhat better results than above <br> but only as for as transudates were <br> concerned. 10\% of exudates still <br> misclassified |
| 4. | Chandras -hekar [7] <br> J. 1958 | Pleura Fluid LDH > 200 IU/L | Was found to be inferior even to <br> Protein criteria |
| 5. | Light R.W [8] 1972 | Combination of Protein and <br> LDH criteria. <br> A) Pleural Fluid to -serum <br> protein ratio >0.5 <br> B) Pleural LDH > 200 IU/L <br> C) Pleural Fluid serum LDH <br> $>0.6$ (LIGHTS CRITERIA) | Used routinely till today. However a <br> large number of studies have not <br> found satisfying results. <br> A large percentage of transudates are <br> misclassified in C.C.F if patient is on <br> diuretics. <br> Both pleural fluid and serum samples <br> required. Hence cumbersome and <br> costly |

It is clear from the above table 1 that many of the criteria have given way to the next successive criteria. It was Lights criteria which had better success since it is based on a combination of both Protein and LDH criteria. Lights [8] criteria is used routinely today as a standard method to separate transudate and exudate.

However Lights criteria has many deficiencies. Firstly, Lights excellent results have not been fully reproduced in several studies with respect to sensitivity and specificity. A large number of prospective studies have reported specificities of only between $70 \%$ and $86 \%$ in contrast to $98 \%$ specificity claimed by Lights
[9], Hirsh [10] 1979, Peterman [11] 1984, Costa, M [12] 1989, Roth [13] 1990, Valdes [14], [15]. The second major disadvantage of Lights criteria is the misclassification of transudative effusions as exudates in patients with congestive cardiac failure on diuretic therapy a phenomenon first noticed by Pillay [16] in 1965 and confirmed by Chaklo [17] in 1989. Thirdly, Lights criteriarequires both Pleural and blood samples and four biochemical measurements Hence, it is both expensive and cumbersome $[18,19]$.

For these reasons in recent years other researchers have proposed several new parameters for separation of transudates and exudates.

Table-2: Shows the newer parameters/criteria proposed as alternative to lights criteria

| Sl. No. | Name of worker | Year | Criteria/ parameters | Comments |
| :--- | :--- | :--- | :--- | :--- |
| 1. | Hamm H [9] | 1987 | Pleural cholesterol >60mg/dl <br> Pleural Cholesterol to Serum <br> Cholesterol ratio >0.3 | First to use cholesterol, found good <br> results |
| 2. | Valdes L [14] | 1991 | Pleural Cholesterol >55 <br> mg/dl and/or P.Cholesterol <br> to Serum Cholesterol ratio <br> $>0.3$ | Confirmed Harum's routine use of <br> this criteria since cheaper and more <br> efficient |
| 3. | Roth.B.J [13] | 1990 | Serum-effusion albumin <br> gradient (1.2g/dl) | Specificity not affected by <br> concomitant diuretic therapy |
| 4. | Meisel. S [20]. | 1990 | Pleural bilirubin to serum <br> bilirubin ratio >0.6 | Good results not obtained in <br> subsequent studies |
| 5. | Tahaoglu. K [21] | 1994 | Alkaline phosphatase levels <br> of Pleural fluid | Further studies needed to confirm <br> claim of authors of high efficacy |
| 6. | Costa. M [12] | 1995 | Pleural. <br> Cholesterol>45mg/dl <br> Pleural LDH>200 IU/L. | No simultaneous serum sample <br> needed. Pleural fluid data alone <br> sufficient. Hence very cost effective. |
| 7. | Eduardo- Garcia <br> p [22] | 1996 | Pleural fluid to serum <br> Cholinesterase ratio | Claimed to be the most accurate of <br> all. Further studies needed since it is <br> the newest in literature |

From table 2, it is evident that the recent literature has seen a plenty of reports on various alternative criteria to Lights criteria. Controversy exists as to which method is more accurate [23].

## General mechanisms of pleural effusion [38]

Increased Pleural Fluid Formation

- Increased interstitial fluid in the lung: e.g. left ventricular failure, pneumonia, pulmonary embolus.
- Increased intravascular pressure in the pleura: e.g. Right or left ventricular failure, SVC obstruction syndrome.
- Increased pleural fluid protein level:
- Protein leak through capillaries
- Protein exudation due to local pleural inflammation
- Defective lymphatic absorption
- Decreased pleural pressure : e.g. Lung atelectasis
- Increased fluid in the peritoneal cavity: e.g. Ascites or peritoneal dialysis.
- Disruption of the thoracic duct: Trauma, tumour, lymphomas, congenital absence of thoracic duct.


## Decreased Pleural Fluid Absorption

- Obstruction of draining lymphatics: Tumourlymphomas, tuberculosis, lymphangiomatosis, yellow nail syndrome, filariasis.
- Elevation of systemic vascular pressure:Right ventricular failure and SVC syndrome.


## DIFFERENTIAL DIAGNOSIS OF PLEURAL EFFUSION <br> Transudative pleural effusion

- Congestive heart failure
- Cirrhosis
- Nephrotic syndrome
- Superior venacaval obstruction
- Fontan procedure
- Urinothorax
- Peritoneal dialysis
- Glomerulonephritis
- Myxoedema.
- Pulmonary emboli
- Sarcoidosis.


## Exudative pleural effusion

## Neoplastic disease

- Metastatic disease eg: Ca Lung, CaBreastand lymphoma.
- Mesothelioma


## Infectious diseases

- Bacterial infections
- Tuberculosis
- Fungal infections
- Parasitic infections
- Viral infections


## Pulmonary embolization

## Gastrointestinal diseases

- Pancreatic diseases
- Subphrenic abscess
- Intrahepatic abscess
- Intrasplenic abscess
- Oesophageal perforation
- After abdominal surgery
- Diaphragmatic hernia
- Endoscopic variceal sclerosis
- After liver transplant


## Collagen vascular diseases

- Rheumatoid pleuritis
- Systemic lupus erythematosis
- Drug induced lupus
- Immunoblastic lymphadenopathy
- Sjogrenssyndrome
- Familial Mediterranean fever
- ChurgStrauss syndrome
- Wegenersgranulomatosis


## Drug induced pleural disease

- Nitrofurantoin
- Dantrolene
- Methysergide
- Bromocryptine
- Amiodarone
- Procarbazine
- Methotrexate


## Miscellaneous diseases and conditions

- Asbestos exposure
- Meig syndrome
- Post myocardial infarction syndrome
- Yellow nail syndrome
- Sarcoidosis
- Pericardial disease
- After coronary artery bypass surgery
- After lung transplant
- Fetal pleural effusions
- Uremia
- Trapped lung


## Haemothorax

## Chylothorax

## CHOLESTEROL IN PLEURAL FLUID

It has long been known that cholesterol is constantly present in all pleural fluids. Until recently the cholesterol content of pleural fluid has been used, together with the concentrations of other lipid fractions to distinguish between Chylothorax and pseudochylothorax. Chylothorax occurs when the thoracic duct is disrupted causing chyle to enter the pleural space. A Pseudochylothorax occurs due to accumulation of large amounts of cholesterol in long standing effusions.

## CHOLESTEROL PLEURAL EFFUSION [84, 85, 86, 87, 83]

(Syn-pseudochylous effusion, cholesterol thorax, chyliform effusion)

## History

Cholesterol pleural effusion is a rare condition. Until 1961 only 99 cases had been reported in literature .The first description was by Nauyn in 1865 and then by Guneau de Moussy in 1874. Churton published the first detailed description in 1882 in his case he found that there was degeneration of cells leading to formation of
cholesterol. Malgatti reviewed 44 cases from literature up to 1929 , in his series the commonest associated condition was tuberculosis. Stein in 1932 reported a male of 45 years with 25 years history of pleural effusion. Pleural fluid cholesterol was $2353 \mathrm{mg} \%$, autopsy revealed gross pleural thickening with calcification enabling the pleural sac to be removed like a cast. Durham and Diamond, Moll and Fowweather 1940, Erwin 1941 have all described cholesterol thorax. In most of their cases the pleural effusion was long standing (mean 7 years).

## Aetiology

The most common causes are tubercular pleuritis and rheumatoid pleuritis.

## Pathogenesis [85, 86, 88]

The precise mechanism of chyliform effusions is not known. Most of the cholesterol is associated with HDL in contrast to the cholesterol in acute exudates where it is mostly bound to LDL [89]. It has been hypothesized that cholesterol that enters the pleural space with acute inflammation becomes trapped and undergoes changein lipoprotein binding characteristics. The diseased pleura results in abnormally slow transfer of cholesterol out of the pleural space resulting in accumulation.

The origin of the cholesterol and other lipids is not definitely known but one possibility is from degenerating red and white blood cells in the pleural fluid. Most patients with cholesterol effusions have no altered cholesterol metabolism because the serum cholesterol levels are normal. Some chyliform effusions contain cholesterol crystals.

## Diagnosis

Is based on pleural fluid appearance, microscopic detection of cholesterol crystals and by elevated pleural fluid cholesterol levels. Lipoprotein analysis may have to be performed if doubt exists whether the fluid is chylous or pseudochylous because only chylous fluid contains chylomicrons. Triglyceride levels may be elevated even in cholesterol effusions and hence are not useful in differentiation from chylous effusion.

## Treatment

Is both by specific therapy (eg Anti Tubercular Therapy) and by therapeutic thoracentesis Decortication may result in markedly improved functional status in many cases.

## MATERIALS AND METHODS

## Source of data

- Data is collected from patients who are attending Medicine OPD and admitted in BLDEU'S Shri B. M. Patil medical college hospital and research centre, VIJAYAPURA.
- Period of study is from November 2016 to July 2018.


## Method of collection of data <br> Inclusion Criteria

- Age >18years
- Patients with definite clinical diagnosis and Pleural effusion evidenced by radiological imaging.


## Exclusion criteria

- Age <18years
- Patients without definitive clinical diagnosis
- Patients previously diagnosed and already on treatment.


## Type of study

Cross sectional descriptive study

## Sample size

Using expected incidence of exudates cases among pleural effusion as $69.4 \%$,expected sensitivity as $88 \%$, expected specificity as $100 \%$ and desired precision as $+/-10 \%$,

The minimum sample is 60 . This sample size will give the precision of $10 \%$ for both sensitivity and specificity.

## Formula used

$$
\mathrm{N}=\mathrm{z}^{2}(1-\mathrm{p}) / \mathrm{d}^{2}
$$

Z-value of $z$ statistic at $5 \%$ level of significance
d-margin of error
p-expected incidence rate

## STATISTICAL ANALYSIS

Data will be analysed using mean+/-SD Chi square test for association, comparison of means using test, ANOVA for comparison between and within groups and diagrammatic presentation.

## RESULTS AND OBSERVATION

The present study was undertaken in 60 cases of Pleural Effusion over a period of 2 and half years from November 2016 to July 2018, the results of which are given below.

Table-1: Age and sex distribution

| AGE (years) | Male |  | Female |  | p value |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | N | $\%$ | N | $\%$ |  |
| $18-20$ | 1 | 2.6 | 0 | 0.0 |  |
| $21-30$ | 5 | 13.2 | 4 | 18.2 |  |
| $31-40$ | 8 | 21.1 | 7 | 31.8 | 0.641 |
| $41-50$ | 12 | 31.6 | 3 | 13.6 |  |
| $51-60$ | 8 | 21.1 | 5 | 22.7 |  |
| $>60$ | 4 | 10.5 | 3 | 13.6 |  |
| Total | 38 | 100.0 | 22 | 100.0 |  |



Fig-1a: Age and sex distribution

The age of the patient in this study ranged from 18 years to 75 years. 1 patient was 18 years, 9 patients were under 21-30years, 15 patients were under 31-40 years, 15 patients were under 41-50years, 13
patients were under 51-60 years, 7 patients were above 60 years. Out of 60 patients there were 38 males and 22 females.

Table-2: Distribution of exudates and transudate according to lights criteria

| BASED ON LIGHTS CRITERIA | N | $\%$ |
| :--- | :---: | :---: |
| EXUDATE | 46 | 76.7 |
| TRANSUDATE | 14 | 23.3 |
| Total | 60 | 100 |



Fig-2a: Distribution of exudates and transudate according to lights criteria

Based on Lights criteria, out of 60 patients 46 were exudates $(76.7 \%)$ and 14 were transudates (23.3\%) (Fig-2a).

Based on pleural cholesterol level criteria, out of 60 patients $45(75 \%)$ were exudates and $15(25 \%)$ were transudates (Fig-3a).

Table-3: Distribution of exudates and transudate according to pleural fluidcholesterol criteria

| BASED ON CHOLESTEROL CRITERIA | N | $\%$ |
| :--- | :---: | :---: |
| EXUDATE | 45 | 75 |
| TRANSUDATE | 15 | 25 |
| Total | 60 | 100 |



Fig-3a: Distribution of exudates and transudate according to pleural fluidcholesterol criteria
Table-4: Distribution of symptoms in pleural effusion at presentation

| PRESENTING SYMPTOMS | NUMBER (N=60) | PERCENTAGE |  |
| :---: | :--- | :---: | :---: |
| $1 . \quad$ COUGH | 50 | 83.3 |  |
| 2. | FEVER | 22 | 36.7 |
| 3. | CHEST PAIN | 34 | 56.7 |
| 4. | DYSPNOEA | 47 | 78.3 |
| 5. SWELLING OF LIMBS | 10 | 16.7 |  |
| 6. | DISTENSION OF ABDOMEN | 10 | 16.7 |
| 7. | FACIAL PUFFINESS | 6 | 10 |
| 8. | LOSS OF APPETITE | 60 | 100 |
| 9. | LOSS OF WEIGHT | 40 | 66.7 |

Cough was present in 50 patients (83.3\%), fever in 22 patients ( $36.7 \%$ ), chest pain in 34 patients (56.7\%), dyspnoea in 47(78.3\%), swelling of limbs and
abdominal distension each in 10 patients (16.7\%) facial puffiness in 6 patients, loss of appetite in 60 patients ( $100 \%$ ), loss of weight in 40 patients ( $66.7 \%$ ).


Fig-4a: Distribution of symptoms in pleural effusion at presentation
Table-5: Distribution of signs in pleural effusion at presentation

| CLINICAL SIGNS |  | NUMBER(N=60) | PERCENTAGE |
| :---: | :--- | :---: | :---: |
| 1. STONY DULLNESS | 60 | 100 |  |
| 2. | ABSENT BREATH SOUND | 50 | 83.3 |
| 3. | DECREASED VF/VR | 52 | 86.7 |
| 4. | MEDIASTINAL SHIFT | 50 | 83.3 |
| 5. PLEURAL RUB | 4 | 6.6 |  |
| 6. | CREPITATIONS | 5 | 8.3 |

Stony dullness in 60 patients (100\%), Decreased/ absent breath sounds in 50 patients ( $83.3 \%$ ) , Mediastinal shift in 33 patients ( $83.3 \%$ ), Decreased $\mathrm{vf} / \mathrm{vr}$ in 52 patients ( $86.7 \%$ ), Pleural rub in 4 patients (6.6\%), Crepitations in 5 patients ( $8.3 \%$ ).

Out of 60 patients, 36 had right sided effusion, 19 had left sided effusion ,5 patients had bilateral pleural effusion (Table-6).


Fig-5a: Distribution of signsin pleural effusion at presentation
Table-6: Pleural effusion right and left side distribution

| SIDE OF EFFUSION | NUMBER( N=60) | PERCENTAGE |
| :--- | :---: | :---: |
| RIGHT | 36 | 60.0 |
| LEFT | 19 | 31.7 |
| BILATERAL | 5 | 8.3 |



Fig-6a: Pleural effusion right and left side distribution
Table-7: Result of sputum AFB

| SPUTUM AFB | TOTAL |  | P VALUE |
| :--- | :---: | :---: | :---: |
|  | N | $\%$ |  |
| NEGATIVE | 28 | 46.7 | 0.232 |
| POSITIVE | 32 | 53.3 |  |
| TOTAL | 60 | 100.0 |  |



Fig-7a: Result of sputum AFB

In the study group of 60 patients, sputum AFB was positive in 32 (53.3\%) patients and 28 (53.3\%) patients had sputum AFB was negative (Fig-7a).

Colour of pleural effusion - 36 patients had amber colour, 18 patients had clear, 4 patients had haemorrhagic and straw colour in 2 patients (Fig-8a).

Table-8: Appearance of pleural effusion

| COLOUR | Total |  | p value |
| :--- | :---: | :---: | :---: |
|  | N | $\%$ |  |
| AMBER | 36 | 60.0 |  |
| CLEAR | 18 | 30.0 |  |
| HAEMORRHAGIC | 4 | 6.7 | 0.864 |
| STRAW | 2 | 3.3 |  |
| Total | 60 | 100.0 |  |



Fig-8a: Appearance of pleural effusion
Table-9: Cytology of pleural effusion

| CYTOLOGY | Total |  | p value |
| :--- | :---: | :---: | :---: |
|  | N | $\%$ |  |
| LYMPHOCYTES + MESOTHELIAL CELLS | 3 | 5.0 |  |
| PREDOMINANTLY LYMPHOCYTES | 42 | 70.0 | 0.476 |
| PREDOMINANTLY NEUTROPHILS | 15 | 25.0 |  |
| Total | 60 | 100.0 |  |



Fig-9a: Cytology of pleural effusion

Out of 60 patients, 3 patients had lymphocytes plus mesothelial cells, 42 patients had predominantly
lymphocytes and 15 patients had predominantly neutrophils.

Table-10: Distribution of pleural protein

| PLEURAL PROTEIN (gram/dl) | Number ( $\mathrm{n}=60$ ) |
| :--- | :--- |
| $1-2$ | 6 |
| $2-4$ | 16 |
| $4-6$ | 34 |
| $>6$ | 4 |
| Total | 60 |

The above table shows the values of pleural protein. 6 patients had pleural protein values ranging from 1-2 gram/dl, 16 patients of pleural protein ranging
from 2-4 gram/dl, 34 patients ranging from 4-6 gram/dl and 4 patients had protein levels above 6 gram $/ \mathrm{dl}$.


Fig-10a: Distribution of pleural protein
Table-11: Distribution of pleural cholesterol

| PLEURAL CHOLESTEROL | NUMBER (N=60) |
| :--- | :--- |
| $\langle 45 \mathrm{mg} / \mathrm{dl}$ | 15 |
| $>45 \mathrm{mg} / \mathrm{dl}$ | 45 |
| Total | 60 |

15 patients had pleural cholesterol levels less than $45 \mathrm{mg} / \mathrm{dl}$ and 45 patients had cholesterol level above $45 \mathrm{mg} / \mathrm{dl}$.


Fig-11a: Distribution of pleural cholesterol
Table-12: Biochemical analysis of pleural effusion

| PARAMETERS | EXUDATES |  | TRANSUDATE |  | P VALUE |
| :--- | :---: | :---: | :---: | :---: | :---: |
|  | MEAN | SD | MEAN | SD |  |
| LIGHTS CRITERIA (TRANSUDATE=14 EXUDATE=46) |  |  |  |  |  |
| SERUM PROTEIN | 5.7 | 1.0 | 6.1 | 1.1 | 0.215 |
| PLEURAL PROTEIN(G/DL) | 4.7 | 1.0 | 2.4 | 0.9 | $<0.001^{*}$ |
| PLEURAL SUGAR | 68.2 | 40.1 | 126.7 | 75.9 | $<0.001^{*}$ |
| PLEURAL FLUID PROTEIN:SERUM PROTEIN | 0.8 | 0.2 | 0.3 | 0.1 | $<0.001^{*}$ |
| PLEURAL CHOLESTEROL CRITERIA(TRANSUDATE=15 EXUDATE=45) |  |  |  |  |  |
| PLEURAL CHOLESTEROL | 78.2 | 23.7 | 21.9 | 9.2 | $<0.001^{*}$ |

Note:* significant at $5 \%$ level of significance ( $\mathrm{p}<0.05$ ). The p value of serum protein is 0.215 , pleural protein is $<0.001$, pleural sugar is $<0.001$, pleural cholesterol is $<0.001$, pleural fluid protein: serum protein is $<0.001$. P value of $<0.001$ is statistically significant.


Fig12a: Biochemical analysis of pleural effusion
Table-13: USG Abdomen examination in pleural effusion

| USG | Total |  | p value |
| :--- | :---: | :---: | :---: |
|  | N | $\%$ |  |
| CIRRHOSIS WITH PORTAL HYPERTENSION | 7 | 11.7 |  |
| MILD HEPATOMEGALY | 1 | 1.7 |  |
| MINIMAL ASCITES | 1 | 1.7 | 0.182 |
| NORMAL | 39 | 65.0 |  |
| NOT DONE | 12 | 20.0 |  |
| Total | 60 | 100.0 |  |



Fig-13a: USG Abdomen examination in pleural effusion

In the study group of 60 patients, cirrhosis was present in 7 patients, hepatomegaly in 1 patient, ascites in 1 patient, and normal in 39 patients.

Based on lights criteria 46 patients were exudate and 14 patients were transudative pleural
effusion, based on cholesterol criteria 45 patients were exudative and 15 were transudative pleural effusion.

The p value is < 0.001 which is statistically significant.

Ayyali Ambresh., Sch. J. App. Med. Sci., Oct, 2018; 6(10): 3814-3829
Table-14: Comparison of exudative and transudative pleural effusion according to pleural fluid cholesterol criteria and lights criteria

|  | ACCORDING TO PLEURAL FLUID CHOLESTEROL CRITERIA ( $\mathrm{N}=60$ ) |  | ACCORDING TO LIGHTS CRITERIA(N=60) |  | P VALUE |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | N | \% | N | \% |  |
| EXUDATE | 45 | 75.0 | 46 | 76.66 |  |
| TRANSUDATE | 15 | 25.0 | 14 | 23.33 | <0.001* |
| TOTAL | 60 | 100.0 | 60 | 100.0 |  |

Note: * significant at 5\% level of significance (p<0.05)
Table-15: Sensitivity analysis of pleural cholesterol criteria

| TP (true positive) | 45 |
| :--- | :--- |
| FN (false negative) | 1 |
| FP (false positive) | 0 |
| TN (true negative) | 14 |
|  |  |
| Sensitivity | $97.8 \%$ |
| Specificity | $100.0 \%$ |
| PPV(positive predictive value) | $100.0 \%$ |
| NPV(negative predictive value) | $93.3 \%$ |
| Accuracy | $98.3 \%$ |

## DISCUSSION

A total of 60 patients were taken up for this study. Out of 60,46 were exudates and 14 were transudates. Among 46 exudates, 40 were tubercular effusions, 5 patients were synpneumonic effusion and 1 patient with malignant effusion.

Among 14 transudative, 7 patients were congestive cardiac failure, 7 patients were cirrhosis.

## AGE AND SEX

The age of the patient in this study ranged from 18 years to 75 years. 1 patient was 18 years, 9 patients were between 21-30 years, 15 patients were between 31-40 years, 15 patients were between 41-50 years, 13 patients were between 51-60 years and 7 patients were above 60 years. Out of 60 patients, males were 38 and females were 22 .

## Biochemical analysis of pleural effusion

Table-16: Biochemical analysis of pleural effusion

| PARAMETERS | EXUDATES |  | TRANSUDATE |  | P VALUE |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | MEAN | SD | MEAN | SD |  |
| LIGHTS CRITERIA (TRANSUDATE=14 EXUDATE=46) |  |  |  |  |  |
| SERUM PROTEIN | 5.7 | 1.0 | 6.1 | 1.1 | 0.215 |
| PLEURAL PROTEIN(G/DL) | 4.7 | 1.0 | 2.4 | 0.9 | $<0.001^{*}$ |
| PLEURAL SUGAR | 68.2 | 40.1 | 126.7 | 75.9 | $<0.001^{*}$ |
| PLEURAL FLUID PROTEIN:SERUM PROTEIN | 0.8 | 0.2 | 0.3 | 0.1 | $<0.001^{*}$ |
| PLEURAL CHOLESTEROL CRITERIA(TRANSUDATE $=15$ | EXUDATE=45) |  |  |  |  |
| PLEURAL CHOLESTEROL | 78.2 | 23.7 | 21.9 | 9.2 | $<0.001^{*}$ |

According to Lights Criteria, the mean serum protein is $5.7 \pm 1.0$ in exudates and $6.1 \pm 1.1$ has $p$ value of 0.215 . The mean pleural protein is $4.7 \pm 1.0$ in exudates and $2.4 \pm 0.9$ has $p$ value of 0.001 . The mean pleural sugar is $68.2 \pm 40.1$ in exudates and $126.7 \pm 75.9$ has $p$ value of 0.001 . The mean pleural protein: serum protein is $0.8 \pm 0.2$ in exudates and $0.3 \pm 0.1$ has p value
of 0.001 . According to pleural cholesterol criteria, the mean pleural cholesterol is $78.2 \pm 23.7$ in exudates and $21.9 \pm 9.2$ and has $p$ value of 0.001 which is statistically significant.

## PLEURAL FLUID CHOLESTEROL

Table-17: Comparison of pleural fluid cholesterol values between the studies

| Sl.no | AUTHORS | SENSITIVITY | SPECIFICITY | PPV | NPV | ACCURACY |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| 1 | Hamm [9] | 93.5 | 100 | 100 | 91 | 96 |
| 2 | Valdes [14] | 92.5 | 87.6 | 95 | 80 | 91.3 |
| 3 | Ram [103] | 96 | 93 | 96 | 92.6 | 95 |
| 4 | B N Mohaptra [27] | 92 | 100 | 100 | 99 | 93 |
| 5 | Burgess [15] | 54 | 92.2 | 87.3 | 50 | 66 |
| 6 | Present study | 97.8 | 100 | 100 | 93.3 | 98.3 |

Hamm [9] first used pleural cholesterol as a parameter. In his study of 150 patients he found excellent results (Sensitivity 93\%, Specificity $100 \%$, Accuracy 96\%). Following Hamm's [9], Valdes [14] aimed to validate this parameter. In his study of 74 patients pleural cholesterol had good results as shown in the above table. Similar results were obtained from studies by Ram [103] in 100 patients and B N Mohaptra [27] in his study of 132 patients. The studies of Burgess [15] and Remero [28] of 124 patients, results were in favour of lights criteria but they had less sensitivity, specificity and accuracy. As a result the present study of 60 patients which contains Pleural Cholesterol criteria has more sensitivity, specificity and accuracy when compared to other studies done by Burgess and Remero which contains Lights criteria.

The study shows that pleural fluid cholesterol criteria (cholesterol $>45 \mathrm{mg} / \mathrm{dl}$ - exudate and cholesterol $<45 \mathrm{mg} / \mathrm{dl}$ - transudate) constitute a useful tool for the separation of pleural effusions.

## CONCLUSION

The pleural fluid cholesterol criteria were found to be the most efficient criteria. Since this parameter involves the measurement of only pleural fluid values of cholesterol, it has following advantages

- Economically, it reduces number of biochemical tests
- Simpler, as there is no need to take simultaneous blood sample at the time of thoracocentesis.

It is concluded that the determination of pleural fluid cholesterol criteria can be included in routine analysis of pleural fluid samples in place of presently used Lights Criteria.

## SUMMARY

This was a cross sectional descriptive study of 60 cases of pleural effusion. The parameter pleural fluid cholesterol levels are used in comparison with Lights criteria to distinguishing transudative and exudative pleural effusion. The following results were obtained in the present study.

- True positive in 45 cases
- False negative 1 case
- False positive 0 case
- True negative 14 case
- Sensitivity $97.8 \%$
- Specificity $100 \%$
- Positive predictive value $100 \%$
- Negative predictive value $93.3 \%$
- Accuracy 98.3\%


## REFERENCES

1. Donald D, Dorey, Ralph A. Defronzo, Eleuterio Ferrannini. Pleural effusion-A Diagnostic dilemma. JAMA 1 976; 236; 2 183-2186.
2. McAleer JJ, Murphy GJ, Quinn RJ. Needle biopsy of the pleura in the diagnosis of pleural effusion The Ulster medical journal. 1987 Apr;56(1):54.
3. Light RW. Approach to Management of Pleural effusion. ANN 1NT MED. 1966; 64: 341-351.
4. Paddock FK. The relationship between the specific gravity and the protein content in human serous effusions. The American Journal of the Medical Sciences. 1941 Apr 1;201(4):569-74.
5. Leuallen CE, KL ZiI. Pleural effusion. A statistical study of 436 patients. NEJM. 1955; 252: 79-83.
6. Carr DT and power HM, Giles WH. Dietz WHClinical value of measurement of protein in pleural fluid. NEJM. 1958; 259: 926-927.
7. Chandrasekhar J and Naval Vikram Pleural effusion LDH activity and protein content its value in diagnosis. Arch nt med. 1969; 128: 48-50.
8. Light RW, Aifredo Candela, Luis Hernandez. Pleural effusions. The diagnostic separation of transudates and exudates. ANN INT MED. 1972; 77: 507-5 13.
9. Hamm H, Jordan D. TObin, Reubin Andres Cholesterol in pleural effusion-A diagnostic aid CHEST. 1987; 92: 296-301.
10. Hirsch, Williams SM, Mann JI, Walker RJ. Pleural effusion. Laboratory tests in 300 cases. THORAX 1979; 34: 106-112.
11. Peterman T, Hosker JP, Ruclenski AS. Evaluating pleural effusion. JAMA. 1984; 252: 1051-1053.
12. Marino Costa, Teresa Quiroga, Edgardo Cruz. Measurement of Pleural Fluid Cholesterol and Lactate Dehydrogenase, A simple and accurate set of indicators for separating Exudates from Transudates. CHEST. 108: 1260-63.
13. Bernard Roth, Carroll MD, Kuczmarski RJ. The serum-effusion albumin gradient in the evaluation of pleural effusion. CHEST. 1990; 98: 546-549.
14. Valdés L, Pose A, Suàrez J, Gonzalez-Juanatey JR, Sarandeses A, San José E, Dobaña JM, Salgueiro M, Suárez JR. Cholesterol: a useful parameter for distinguishing between pleural exudates and transudates. Chest. 1991 May 1;99(5):1097-102.
15. Yilmaz A, Tunaboyu ÏK, Akkaya E, Bayramgürler B. A comparative analysis of the biochemical parameters used to distinguish between pleural exudates and transudates. Respirology. 2000 Dec;5(4):363-7.
16. Pillay VK. Total proteins in serous fluids in cardiac failure. South African Medical Journal. 1965 Feb 1;39(7):142-3.
17. Chakko SC, Caldwell SH, Sforza PP. Treatment of congestive heart failure: its effect on pleural fluid chemistry. Chest. 1989 Apr 1;95(4):798-802.
18. Costa M, Quiroga T, Cruz E. Measurement of pleural fluid cholesterol and lactate dehydrogenase: a simple and accurate set of indicators for separating exudates from transudates. Chest. 1995 Nov 1;108(5):1260-3.
19. Mathew John, AH Zargar, SR Masoodi. Drawbacks of Lightscriteria. CHEST. 1995; 108: 5-11.
20. SimchaMeisel, Bonor E, Kiechl S, Willeit J. Pleural fluid to serum bilirubin ratio for Differentiating transudates and exudates. CHEST. 1990; 98: 141-144.
21. Kemal Tahaoglu, Eriksson JG, Lindstrom J. Alkaline phosphatase for distinguishing between pleural transudates and exudates. CHEST. 1994;107: 1912-1913.
22. Eduardo Garcia-Pachon, Ford ES, Giles WH, Dietz WH. Fluid to serum cholinesterase ratio for separation of transudates and exudates. CHEST. 1996; 110: 97-101.
23. Malloy and Evelyn, DJ. Weatherall, JGGLedingham, DA Warrell. Comparative analysis of the biochemical parameters used to differentiate between pleural exudates and transudates. CHEST. 1992; 111: 1504-1509.
24. Ortego L, Mokdad AH, Ford E. Diagnostic differentiation of exudates and transudates, Value of cholesterol. MED CL1N BASE. 1981; 93: 367370.
25. Gil Suay, Garland PB, Newsholme EA. Value of Pleural cholesterol to differentiate between pleural exudates and transudates. A prospective study of 232 cases. RESPIRATION. 1995; 62: 57-63.
26. K.N. Rao, Shah P, Shrivastava U, Cholesterol Value in pleural fluid. Lung India. 1994; 100:112114.
27. MohapatraB.N, Sastry NG, Mohan V. Significance of Pleural fluid Cholesterol in differentiating transudates and exudates. JAPI. 1995; 116-119.
28. Romero S, Candela A, Martín C, Hernández L, Trigo C, Gil J. Evaluation of different criteria for the separation of pleural transudates from exudates. Chest. 1993 Aug 1;104(2):399-404.
29. Rao S, Gupta PC, Mehta HC. Pleural bilirubin to serum bilirubin ratiG as a diagnostic aid in tuberculous and malignant effusions. Lung India. 1995; 13: 20-21.
30. Vives M, Porcel JM, de Vera MV, Ribelles E, Rubio M. A study of Light's criteria and possible modifications for distinguishing exudative from transudative pleural effusions. Chest. 1996 Jun 1;109(6):1503-7.
31. Antony VB, Holm KA. Testing the waters: differentiating transudates from exudates. Chest. 1995 Nov 1;108(5):1191-2.
32. SyabbaloR A, Eschwege E, Thibult N. Evaluation of pleural fluid. SM J MED. 1980; 43: 745-746.
33. Adam FV, Lillioja S, Kriketos AD. Anatomy of the Pleural Space. JAMA. 1978; 233: 1761-1764.
34. Sahn SA. Joseph J. Basran GS. The pleura. The state of art. AM REV RESP DISEASES 1988; 138: 184-234.
35. Gray SW, M Krssak, K Falk Petersen. Development of pleura in health and disease. Marcel Dekker new York. 1985; 30: 3-19.
36. Bernaudin JF, Fleury J. Anatomy of the blood and lymphatic circulation of the pleural serosa, edited by Chretien, J., Bignon, J. \& Hirsch, A. Lung Biology in Health and Disease.;30:101.
37. Weiner Kronish JP, SM Vogel DL Rothmn. Relatiocadiipofwd effusions to pulmonary hemodynamics in patients with congestive cardiac failure. AM REV RESP DIS. 1985; 132: 12531256.
38. Light RW. Pleural diseases 31(Edn. Williams and Wilkins Baltimore 1995.
39. Massimo Pisolesi, Kahn BB, Flier JS. Pleural liquid and solute exchange. Am rev resp dis. 1989; 140: 825-847.
40. Strange C, 0 ' Rahilly SO, Hattersley A. Value of radiology in Diagnosis of pleural effusion. Radiology. 1988; 137: 959-961.
41. Zimmermann HH, Vaag A. Radiography in pleural effusions. CHEST. 1986; 809: 503-507.
42. VixW A, Gray H. Roentgenographic recognition of pleural effusion. JAMA 1974; 229: 6: 695-698.
43. Collins JD, Haffher SM. Minimal detectable pleural effusions. Radiology. 1972; 105: 5 1-53.
44. Davis S, Hazuda HP. The shape of pleural effusions. BMJ. 1963; 1: 436-437.
45. Rnckin JA, Mitthell BD, Moiales PA, Stem MP. Detection of pleural io. dradiograplis. AiR. 1987; 148: 681-183.
46. Higgins JA. Pollare T, Lithell HOMA, Beme C. Loculated interlobar air filled 1Ihire. ARCH INT MED. 1955;96,:180-197.
47. Jack Robinowitz, Despres JP, Lamarche. Loculated interlobar air filled collection in congestive cardiac failure. CHEST. 1978; 74: 390-393.
48. Gyminski J, Cantin BMI, Dagenais G, Moorjani 5. The diagnosis of pleural effusion by ultrasonagraphic and radiologic techniques. CHEST. 1976; 70: 33-37.
49. Peterman T, Carr MC, Brunze 11 JD. Ultrasound study of Pleural effusion in congestive cardiac failure. JAMA 1984; 252: 1051-1053.
50. Mc Loud T.C, Facchni F, Chen YD. Imaging the pleura, sonography, CT and MRI AJR: 156: 11431153.
51. Grogan DR, Hollenbeck CB, Reaven GRAM. Uses of Ultrasound guided aspiration in pleural effusion. ARCH INT MED. 1990; 150: 873-877.
52. Light RW, Abbasi F, Brown BW. Cells in pleural fluid, and their value in differential diagnosis. ARCH TNT MED. 1973; 132: 854-860
53. Cavina C, Lamendola C, McLaughlin T, Reaven GRAM. Evaluation of cell count in pleural effusions. ANN RADIOLDIAGN. 1958; 31: 163202.
54. Bernard Roth, Lim SC, Tan BY. Evaluating pleural effusion. CHEST. 1996;109: 1419.
55. Berkman N, Chew SK, Tan CE. Diagnostic tests in pleural effusion, an update postgrad med. 3 1993; 69: 8-12.
56. Lung T, Chitturi S, Abeygunaseka S. Diagnostic significance of lymphocytes in pleural effusions. ANN TNT MED. 1976; 66: 972-982.
57. Peterson T, Farrell GC, Walker JH. T and B lymphocytes in pleural effusions. CHEST. 1978; 73: 49-51.
58. BoddingtonM.D, Bergraman RN, Prager R. Absence of mesothelial cells from tubercular effusions. THORAX. 1960; 15: 169.
59. Thaddeus Bartter, Volund A, Olefsky JM. Transudate V/S Exudate. Genug (editorial). CHEST. 1994; 109: 6: 1429-1034.
60. Sood A, Narayan V. Clinical efficacy of measurement of pleural protein. JAPI 1991; 133135.
61. Luetsher JA, Bonora E, Targher 0. Electrophoretic analysis of the proteins of plasma and serous effusions. J CLIN INVEST. 1941; 20: 99-
62. Paddok FK, Alberiche M, Bonadonna RC. The diagnostic significance of serous fluids in diseases. NEJM. 1940; 223: 1010-1015.
63. David Potts, Saggini F, Zenere MB. Glucose and p \{relationship in parapneumonic effusion. ANN TNT MED. 1978; 138: 1378-1380.
64. SherrH P, Katz A, Mather K. Origin of pleural fluid amylase in oesophageal ruptures. ANN TNT MED. 1972; 76: 985-986.
65. LaxmiSarojoni, Sridhar S. LDH and its isoenzymes in biofluids in various diseases. IJMR. 1983; 78: 26 1-265.
66. Good JT, Baron AD, Follmann DA. The diagnostic value of pleural fluid pH CHEST .1980; 78: 55-59.
67. Potts D.E, Legro RS, Finegood D. Pleural fluid p" in parapneumonic effusions CHEST 1976; 70: 328331.
68. Poe RH, Dunaif A. Value of closed pleural biopsy. ARCH TNT MED. 1984; 144: 325-328.
69. Gandhi AK, Nayar M, Bihari N, Chandra M. Diagnostic value of carcinoembryonic antigen
assay of pleural \& peritoneal effusions in malignancy. The Indian Journal of Medical Research. 1989 Feb;90:22-6.
70. Gupta SK, Rajpal Sharma B. Adenosmedeaminase activity in pleural fluid. JAPI1987 ;92: 296-301.
71. Louis Valdes, Anderson RL, Haman RF. Diagnosis of tubercular pleurisy using the biological parameters. ADA, Lysozyme, and irterferon gamma. CHEST. 1993; 103: 458-465.
72. Ocana I, Savage PT, Sand MF. ADA in pleural fluid. Tests for the diagnosis of pleural effusions.CHEST 1983; 84: 51-53.
73. Prasad R, Ramesh Tiwari. ADA in pleural fluid. A diagnostic test of tuberculous pleural effusion. ND J CHEST DIS ALL SCI. 1992; 34: 123-126.
74. Levine H, A, Rodes WW. Tubercular pleurisy-An acute illness. ARCH INT MED W68; 322: 122129.
75. Benjamin PK, M Laakso. Needle biopsy of parietal pleura JAPI. 1970;18: 275.
76. Poe RH, Quon MJ. Value of closed pleural biopsy. ARCH NT MED. 1984; 144: 325-28.
77. Thiruvengadam KV. Mohit Singh. Etiological diagnosis of pleural effusion by punch biopsy of pleura. DIS OF CHEST. 1962; 42 : 529.
78. Udayaprakash BS. Vijay Maihotra. Comparative study of needle biopsy with cytologic analysis for the evaluation of pleural effusion analysis of 414 cases. MAYO CLINIC PROC. 1985; 158-164.
79. Colt HG, Muscelli E, Camastra S. Thorocoscopy, new frontiers. PULM PERSPECTIVES. 1992; 9: 1-4.
80. Menzies R, Gastaldelli A, NataliA,.Thoracoscopy for the diagnosis of pleural diseases. ANN TNT MED. 1991; 114: 27 1-276.
81. Chang S, Masom A, Pecori N. Treatment of congestive cardiac failure, its effect on pleural fluid chemistry. ANN TNT MED. 1989; 149: 855-857.
82. Shi-Chuan-Chang, Susanthii F. The role of fibre optic bronchoscopy in evaluating the causes of pleural effusion. ARCH TNT MED. 1989; 4: 855856.
83. Stein W.W, Moran R, Romero G. cholesterol thorax in tuberculosis (cholesterol pleurisy). ARCH TNT MED. 1932; 49: 42 1-428.
84. Coe J.E, AS Hakim. Cholesterol pleural effusion. ARCH TNT MED. 1961;108: 163-174.
85. Ferguson GC, Haffuer SM, Kennedy E, Cholesterol pleural effusion in rheumatoid lung diseases. THORAX. 196; 21: 577-581.
86. Gunnar Hilledrdal, Gonzalez C, Stem MP. Chyliform (cholesterol) pleual effusion. CHEST. 1985; 88: 426-428.
87. Stein HM, Miettinen H. Cholesterol pleural effusion- report of a case. AM REV TUBERC. 1947; 56: 305-307.
88. Johnston J, McKeigue Pm, Shah BMI. Pleural effusions in hospitalized patients with AIDS. ANN tNT MED. 1993; 118: 856-859.
89. Hickman J, Marmot MG. The analysis of pleural fluid. J of AAPL MED 1976; 2: 661-663.
90. Sassori CS, Chylothwax and pseudochylothorax. CIJN CHEST MED. 19S;6 163-171.
91. Sa NS, CL \&, R Wa*km Oiykimx, diagnosis by lipoprotein of. Ip1 L 11iO4. AX 1977; 32: 98-100.
92. A1-k, J Mauls. Studies for 1 whny drug resistance in the tubercular pleurisy. SCAN J RESP DIS. 1968; 193: 1634.
93. Thiruvengadam KV, Madanagopalan N, SOLOMON V, Anguli VC. Pleuropulmonary Amebiasis: Report of a Case with Pleural Biopsy Findings. Chest. 1962 Jul 1;42(1):111-3.
94. Levine H, Metzger W, Lacera D, Kay L. Diagnosis of tuberculous pleurisy by culture of pleural biopsy specimen. Archives of internal medicine. 1970 Aug 1;126(2):269-71.
95. Berger HW, A Whittles, P Sahota, JA Lockton, G Hogg. Prolonged fever in patients treated for tuberculosis. AM REV RESP DIS. 1968;97: 140143.
96. Epstein, Stubbs RS, Wickremesekera SK. Tubercular pleural effusion. CHEST 1987; 91: 106-109.
97. Poe RH. Ohnishi H Utility of pleural fluid analysis in predicting tube thorocostomy/ decortication in
parapneumonic effusions. CHEST 1991; 100: 963967.
98. Lieberman F, Wahrenberg H, Hertel K, Leijohufvud BM. Pathogenesis and treatment of hydrothorax complicating cirrhosis with ascites. ANN INT MED. 1966; 64: 341-351.
99. Johnston R.F, Stray GJ, Grundy SM. Hepatic hydrothorax, studies to determine the source of fluid and report of 13 cases. ANN NT MED. 1964; 61: 385-401.
100.Cavina C, Radiological aspects of pleural effusions in hypoproteinemia. ANN RADIOLDIAG. 1958; 31: 163-202.
101.Lehrer RI, Ganz TO. Biochemistry and function of monocytes and macrophages. Williams Hematology. 6th ed. New York: Mc Graw Hill. 2001:865-9.
100. Yam LT. Diagnostic significance of lymphocytes in pleural effusions. Annals of internal medicine. 1967 May 1;66(5):972-82.
103.Burgess LJ, Maritz FJ, Taljaard JF. Comparative analysis of the biochemical parameters used to distinguish between pleural transudates and exudates. Chest. 1995 Jun 1;107(6):1604-9.
