Original Research Article

Differentiating transudative and exudative pleural effusion by pleural fluid cholesterol

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ABSTRACT

Pleural effusion is one of the common condition encountered in day to day practise. 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.

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

Materials and Methods: This cross sectional descriptive study was conducted on patients of pleural effusion (n=60) age >18 years patients with definitive clinical diagnosis and evidenced by radiological diagnosis of pleural effusion were taken as inclusion criteria.

Results: The results showed majority of the patients were males (63.3%) and females (36.7%). 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%.

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 and Simpler as there is no need to take simultaneous blood sample at the time of thoracocentesis.

1. 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. 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.

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2. Objective of the study

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

3. Materials and Methods

3.1. Source of data

1. 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.
2. Period of study is from November 2016 to July 2018

4. Method of collection of data

4.1. Inclusion criteria

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

4.2. Exclusion criteria

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

4.3. Type of study

Cross sectional descriptive study

4.4. 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:
$$N = z^2 (1-p)/d^2$$
Z-value of z statistic at 5% level of significance
d-margin of error
p-expected incidence rate

4.5. 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.

5. 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	
41-50	12	31.6	3	13.6	0.641
51-60	8	21.1	5	22.7	
>60	4	10.5	3	13.6	
Total	38	100.0	22	100.0	

The age of the patient in this study ranged from 18 years to 75 years. 1 patient was 18 years, 9 patients were under 21-30 years, 15 patients were under 31-40 years, 15 patients were under 41-50 years, 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 1

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

Based on Lights criteria, out of 60 patients 46 were exudates (76.7%) and 14 were transudates (23.3%).Table 2

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

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

Table 4: Distribution of symptoms in pleural effusion at presentation

Presenting Symptoms	Number (n=60)	Percentage
1. 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%).Table 4

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 VF/VR in 52 patients (86.7%), Pleural rub in 4 patients (6.6%), Crepitations in 5 patients (8.3%).Table 5

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

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

Table 7: Result of sputum AFB

Sputum AFB	Total		P value
	N	%	
Negative	28	46.7	
Positive	32	53.3	0.232
Total	60	100.0	

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.Table 7

Table 8: 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	

Out of 60 patients, 3 patients had lymphocytes plus mesothelial cells, 42 patients had predominantly lymphocytes and 15 patients had predominantly neutrophils.Table 8

Table 9: Distribution of pleural protein

Pleural Protein (gram/dl)	Number (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/dl.Table 9

Table 10: Distribution of pleural cholesterol

Pleural Cholesterol	Number (N=60)
<45 mg/dl	15
>45 mg/dl	45
Total	60

15 patients had pleural cholesterol levels less than 45 mg/dl and 45 patients had cholesterol level above 45 mg/dl.Table 10

Note: * significant at 5% level of significance (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.Table 11

Note: * significant at 5% level of significance (p<0.05)

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.Table 12

The p value is < 0.001 which is statistically significant.

According to Lights Criteria, the mean serum protein is 5.7±1.0 in exudates and 6.1±1.1 has p value of 0.215. The mean pleural protein is 4.7±1.0 in exudates and 2.4±0.9 has p value of 0.001. The mean pleural sugar is 68.2±40.1 in exudates and 126.7±75.9 has p value of 0.001.The mean pleural protein: serum protein is 0.8±0.2 in exudates and 0.3± 0.1 has p value of 0.001. According to pleural cholesterol criteria, the mean pleural cholesterol is 78.2±23.7 in exudates and 21.9±9.2 and has p value of 0.001 which is statistically significant.Table 14

5.1. Pleural fluid cholesterol

6. 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

Table 11: 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*

Table 12: Comparison of exudative and transudative pleural effusion according to pleural fluid cholesterol criteria and lights criteria

	According to pleural fluid cholesterol criteria (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	

Table 13: Sensitivityanalysis 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%

Table 14: 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*

Table 15: Comparison of pleural fluid cholesterol values between the studies

S.No	Authors	Sensitivity	Specificity	PPV	NPV	Accuracy
1	Hamm[4]	93.5	100	100	91	96
2	Valdes	92.5	87.6	95	80	91.3
3	Ram	96	93	96	92.6	95
4	B N Mohaptra	92	100	100	99	93
5	Burgess	54	92.2	87.3	50	66
6	Present study	97.8	100	100	93.3	98.3

were synpneumonic effusion and 1 patient with malignant effusion.

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

6.1. 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.

6.2. Presenting symptoms

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%).

6.3. Signs

Mediastinal shift is seen in 50 patients opposite to the pleural effusion. Over affected side of chest, fullness of chest in 48 patients, decreased chest movements in 50 patients, expansion of chest reduced in 50 patients, decreased vocal fremitus in 52 patients, stony dullness in 60 patients, absent breath sounds in 50 patients, decreased vocal resonance in 52 patients, pleural rub in 4 patients and Crepitations in 5 patients.

6.4. Side of pleural effusion

Out of 60 patients, 36 had right side effusion, 19 had left side effusion, and 5 patients had bilateral pleural effusion.

6.5. Sputum AFB analysis

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.

6.6. Colour of pleural effusion distribution

Colour of pleural effusion 36 patients had amber colour, 18 patients had clear fluid, 4 patients had haemorrhagic and straw colour in 2 patients.

6.7. Cytology of pleural effusion

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

6.8. USG analysis

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.

6.9. Biochemical analysis of pleural effusion

Hammfirst 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,[5] Valdes[6] aimed to validate this parameter. In his study of 74 patients pleural cholesterol had good resultsas shown in the above table. Similar results were obtained from studies by Ram[7] in 100 patients and B N Mohaptra[8] in his study of 132 patients. The studies of Burgess and Remeroof 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[9] and Remero[4] which contains Lights criteria. The study shows that pleural fluid cholesterol criteria (cholesterol >45 mg/dl - exudate and cholesterol <45 mg/dl – transudate) constitute a useful tool for the separation of pleural effusions.

7. 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

1. Economically, it reduces number of biochemical tests
2. 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.

8. 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.

1. True positive in 45 cases
2. False negative 1 case
3. False positive 0 case
4. True negative 14 case
5. Sensitivity 97 8%

6. Specificity 100%
7. Positive predictive value 100%
8. Negative predictive value 93 3%
9. Accuracy 98 3%

9. Source of Funding

No financial support was received for the work within this manuscript.

10. Conflict of Interest

The authors declare that they have no conflict of interest.

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