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Original Research Article

DIAGNOSTIC VALUE OF PLEURAL FLUID CHOLESTEROL IN DIFFERENTIATING BETWEEN EXUDATIVE AND TRANSUDATIVE PLEURAL EFFUSIONS

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ABSTRACT

Background: The present study was undertaken to evaluate the diagnostic utility of cholesterol in pleural fluid to differentiate transudates from exudates and to compare the diagnostic efficacy of pleural fluid cholesterol with that of Light's criteria. Thus, simplifying the diagnostic procedure and lowering the cost.

Materials and Methods: The present study was conducted on 120 patients with clinical and radiological evidence of pleural effusion, in the Department of Respiratory Medicine, Rajarajeswari Medical College, Bangalore & Katuri Medical College and Hospital, Guntur, Andhra Pradesh over a period of one and a half years, from August 2023 to January 2025.

Results: The present study include total of 120 cases were enrolled in the study. All cases underwent thorough clinical and radiological examination. Thoracentesis was performed and pleural fluid analyzed for biochemical, pathological and microbiological parameters. Based on clinical/ aetiological diagnoses, the cases were classified as 100 exudates and 20 transudates. Light's criteria was applied to the same 120 cases and 118 exudates and 2 transudates were found. Pleural fluid Cholesterol ≥ 60 mg/dl was taken as the cut-off to differentiate exudates from transudates. With this criteria 95 exudates and 25 transudates were found. The sensitivity was 86%, specificity 55%, PPV 91%, NPV 44% and The efficacy was 81%, which was similar to Light's criteria.

Conclusion: Thus pleural fluid Cholesterol is a useful parameter in differentiating exudates from transudates. It is simple, cost-effective and does not require a simultaneous blood sample. It has a high diagnostic efficacy and hence can be used as a routine test in pleural fluid analysis.

Keywords: Pleural Fluid, Cholesterol, PPV, NPV, Exudates, Transdutes, Light's criteria.

INTRODUCTION

Pleural effusion can develop in a number of diseases, both thoracic and systemic, often being the only manifestation of the illness.[1] Based on the underlying pathological abnormality effusions are either transudates or exudates.[2]

If the pleural fluid is clinically and radiologically demonstrated, a clinician should consider performing a diagnostic thoracentesis. Analysis of pleural effusions whether it is a transudate or an exudate is an important diagnostic step to guide further investigations and treatment.[2] The diagnostic and therapeutic approach depends on the nature of effusion.

Although many criteria have been established to distinguish a transudate from exudates, none has a 100% sensitivity and specificity.[3] The most commonly accepted, even after >30yrs of practical use is Light's criteria4.However, many workers have found Light's criteria as unsatisfactory. It is foundthat 25% of patients with transudative pleural

effusion are mistakenly identified as having exudative effusion by Light's criteria.

Since the criteria of Light's requires both pleural and blood samples, and four bio-chemical measurements, in the recent years, several researchers have proposed the measurement of pleural fluid cholesterol as a biochemical parameter for separation of transudates from exudates.[2,5, 6,7]

Some of the studies showed that cholesterol in pleural fluid appears to be a reliable parameter for differentiation of transudates and exudates than pleural fluid protein and LDH. They found that protein and LDH levels, as well as their pleural fluid to serum ratios resulted in erroneous classification of 11-15% of the effusions while using pleural cholesterol with a cut off value of 60mg/dl, only 5% were incorrectly classified.[8]

The present study was undertaken to evaluate the diagnostic utility of cholesterol in pleural fluid to differentiate transudates from exudates and to compare the diagnostic efficacy of pleural fluid cholesterol with that of Light's criteria. Thus, simplifying the diagnostic procedure and lowering the cost.

Aims and objectives

1. Estimation of cholesterol in pleural effusion.
2. Analyzing the rationale of using cholesterol as a parameter to differentiate transudates and exudates of diverse etiology.
3. Comparison of diagnostic efficacy of cholesterol with Light's criteria.

MATERIALS AND METHODS

Study Design:

Study Group: 120 patients with pleural effusion, admitted to the department of Respiratory medicine, Rajarajeswari Medical College, Bangalore & Katuri Medical College and Hospital, Guntur were enrolled. Study approved by hospital ethics committee.

Study Period: August 2023 to January 2025.

Inclusion Criteria:

1. Patients above 15 years of age, of both sex.
2. Patients with clinical and radiological evidence of pleural effusion.
3. Patients willing to give informed consent.

Exclusion Criteria:

1. Patients with bleeding diathesis.
2. Patients not willing to participate in the study.

Protocol

Patients were selected as per the inclusion criterion. A detailed clinical history was taken, clinical examination performed and the following investigations were done:

1. Blood investigations (Complete haemogram, platelet count, coagulation profile, LFT, RFT and serum LDH). Blood sugars.
2. Urine examination.
3. Chest radiograph (postero-anterior view).
4. HIV test
5. ECG
6. Sputum smear examination for acid-fact bacilli (AFB).
7. Sputum gram stain and culture sensitivity.
8. Additional investigations like- lateral chest radiograph, USG thorax, USG abdomen and pelvis, CT- chest, 2-D ECHO and pleural biopsy were done as and when indicated.
9. Pleural fluid analysis was done for total protein, glucose, LDH, cholesterol, ADA, total cell count, differential cell count, malignant cells, Ziehl-Neelsen stain for AFB, Gram stain and C/S for bacteria.

The first sample of pleural fluid obtained in each patient was considered for analysis. Protein was measured by Biuret method, LDH by U. V Kinetic method and Cholesterol by enzymatic colorimetric method.

The patients were divided into two groups clinically according to expected nature of the fluid and on the basis of **aetiology** whichwas contributed by clinical, imaging, and pathological evaluations.

Group 1 (Exudates) - Tubercular effusion, malignant effusion and synpneumonic effusion.

Group 2 (Transudates) - Effusions due to CCF, Liver cirrhosis and CRF.

Laboratory classification of pleural effusions was made using **Light's criteria**. According to this criteria, if any one of the following is present then the fluid was classified as an exudate:

1. Pleural fluid to serum total protein ratio greater than 0.5,
2. Pleural fluid to serum LDH ratio greater than 0.6,
3. Pleural fluid LDH greater than 200 IU/L.

Furthermore **Pleural fluid Cholesterol**≥ 60 mg/ dl was taken as the cut-off point to differentiate exudates from transudates.

Thus the pleural effusions were classified as exudativeor transudative on the basis of clinical/ aetiological diagnosis, Light'scriteria, and Pleural fluid Cholesterol.

Statistical Analysis

The significance of statistical differences between the means of different parameters studied was tested by students unpaired t test. The usefulness of each of the biochemical parameters for identifying exudates and transudates were evaluated in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false positives (FP), false negatives (FN) and efficiency. The statistical differences between two proportions were tested, by using the standard error of difference between proportions. P value<0.05 was considered significant.

RESULTS AND DISCUSSION

Pleural effusion occurs in a number of pathological conditions and even exhaustive diagnostic tests fail to reveal the etiology in as many as 15%–20% of the cases. The classification of pleural effusion as transudative or exudative is the primary diagnostic step because, if the effusion is a transudate, no further diagnostic procedures are necessary and therapy is directed towards the underlying disease process. However, if the effusion is exudative a more extensive diagnostic work-up is required to distinguish between the many possible causes of exudative effusions.

In 1972, Light et al. compared various criteria for differentiating between transudative and exudative pleural effusions and found none of them to be specific. They advocated the use of a combination of the following criteria to differentiate between transudative and exudative pleural effusion with nearly 100% sensitivity and specificity. The criteria were: pleural fluid protein to serum protein ratio >0.5; pleural fluid LDH to serum LDH ratio >0.6 and pleural fluid LDH >200 IU/L12. However, several prospective studies,[10,11,12] were unable to reproduce the results obtained by Light et al.

Several studies suggest that pleural cholesterol is increased in pleural exudates, making it a potential biomarker for differentiating exudative and transudative pleural effusions13. Cellular degeneration and vascular leakage due to increased permeability are thought to elevate pleural cholesterol levels.[14]

In our study, we used Pleural fluid cholesterol as a parameter to differentiate between exudative and transudative effusions and its efficacy was compared with that of Light's criteria.

A total of 120 cases who fulfilled the inclusion criteria were enrolled in the study. All these cases had clinical and radiological evidence of pleural effusion. Most of the patients were in the age group of 21 to 30 years, indicating a higher distribution among younger population. Males were more commonly affected than females and they accounted for 87 of the 120 cases. Total 10 patients were <18 yrs of age in the study.

Fever and generalised weakness were the most common presenting symptoms and 70 patients presented within one month of onset of symptoms. It was found that 56 cases had left sided effusion and the pleural fluid was mostly straw coloured, as seen in 51 of the 120 cases.Tuberculosis was the commonest cause of effusion as evidenced in 70 cases.

Of the 120 cases of pleural effusion, 100 were exudates and 20 transudates based on clinical/ aetiological diagnosis. Light's criteria was applied for the same 120 cases and 118 exudates and only 2 transudates were found. Whereas with Cholesterol 95 cases were classified as exudates and 25 as transudates.

Table 1: Sensitivity, Specificity, PPV, NPV, False positive rate, False Negative rate and accuracy of various parameters in the present study

Parameter	Percent (%)							P
	Se	Sp	PPV	NPV	FP	FN	A	Value
Pl PROT	93	10	83.7	22.22	16.2	77.7	79	0.644
P/S PROT	93	15	84.5	47.14	30	15.5	80	0.368
Pl LDH	89	10	83	15.38	16.8	84.6	76	0.628
Pl /S LDH	89	5	82.4	8.3	17.6	91.6	75	0.688
Pl CHOL	86	55	90.5	44	9	56	81	0.001
Light's criteria	98	0	83	0	17	100	81	0.693

In the present study, on comparing various parameters with clinical criteria to differentiate exudates from transudates, it was found that only Cholesterol alone was able to classify the exudates and transudates correctly and the findings were statistically highly significant with a p value < 0.001. But this was not the case with the other parameters (Table 1).

Studies have showed that Light's criteria maximize sensitivity at the expense of specificity: they typically identify 98% of pleural exudates, but theymisclassify approximately 25% of transudates as exudates64. In our study, while using Light's criteria, 17% of the transudates were misclassified as exudates but with Cholesterol only 9% of them were misclassified. These results were similar to that of a meta-analysis conducted by Shen et al1 in 2014. Misclassification of transudates as exudates can lead to inappropriate patient management or potentially unnecessary and invasive diagnostic investigations that increase morbidity and health care costs65. It was found that Pleural cholesterol levels were associated with a significantly lower misclassification rate.

Table 2: Comparison of efficiency of Pleural fluid Cholesterol and Light's criteria in various studies

Studies	Pl Cholesterol Efficiency	Light's criteria Efficiency
Present study	81%	81%
K.B Gupta et al[66], 1999	94%	93%
Ivanka N et al[67], 2004	91%	90%
F. Naghshvar et al[68], 2007	90%	91%

In the present study, the efficiency of pleural fluid cholesterol to differentiate exudates from transudates was same as that of Light's criteria. This finding was also found to be similar to that of various other studies (Table 2).

Table 3: Comparison of sensitivity and specificity of Pleural fluid Cholesterol and Light's criteria in various studies

	Pleural fluid Cholesterol		Light's criteria	
Studies	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Present study	86%	55%	98%	0%
Valdes et al[11], 1991	91%	100%	94.60%	78.40%
Romero S et al[19], 1993	81%*	90%*	98%*	77%*
Gazquez I et al[20], 1998	84%*	84%*	97%*	71%*
Gupta et al[16], 1999	95%*	94%	80%*	92%
Ivanka N et al[17], 2004	92.90%	79.5%*	99.40%	56.8%*
Naghshvar F etal[18] , 2007	85%	100%*	87%	79%*

It was found that pleural fluid cholesterol had a high sensitivity of 86% in our study, which was similar to that found in several other studies (Table 3). The same was true for Light's criteria, which showed a sensitivity of 98%. Pleural fluid cholesterol had a slightly lower sensitivity compared to Light's criteria.

In our study the specificity of pleural fluid cholesterol was 55%, whereas that of Light's criteria was 0%. Meaning, using cholesterol 55% of the transudates were correctly identified, but with Light's none of the transudates could be correctly classified. Both the sensitivity and specificity of pleural fluid Cholesterol to differentiate exudates from transudates was found to be statistically highly significant.

With pleural fluid Cholesterol value of ≥ 60 mg/ dl to differentiate exudates from transudates, the mean value for exudates was 88 mg/ dl and that for transudates was 43 mg/ dl.The difference in mean between exudate and transudate was found to be statistically highly significant (P value < 0.001). This cut off value of 60 mg/ dl has been used in a number of studiesand the findings are similar to that of our study.

Of the 120 cases in our study, using pleural fluid cholesterol ≥ 60 mg/ dl, 95 were found to be exudates. In a study conducted by Hamm et al,[10] of the 62 patients, 28 were classified as exudates. Two Indian studies have been published in this regard. One by Valdes et al,[11] where out of 75 patients 44 were classified as exudates and the other by Patel et al2, who classified 48 of the 60 patients as exudates.

Various studies (Table 2) have used cholesterol levels ranging from 38 to 65 mg/ dl. Hence there is a need to investigate the effective cut-off value so as to optimize the diagnostic accuracy.[13]

All these studies show that there is an association between elevated pleural fluid cholesterol and the presence of pleural exudates, implying that cholesterol contributes to exudate pathogenesis. The same was found to be true in our study as well. Thus concluding that pleural cholesterol level shows substantial promise as a test for distinguishing pleural exudates from transudates.

CONCLUSION

Pleural effusion is a manifestation of several diseases, both pulmonary and extra-pulmonary. Based on the underlying pathological abnormality and mechanism of formation, effusions may be either transudates or exudates73. This differentiation is an important diagnostic step to guide further investigations and treatment. For many years the well-established Light's criteria has been used to distinguish exudates from transudates. But, recent studies have found Light's criteria as being unsatisfactory and also it requires both pleural and blood samples. Hence a number of newer biochemical parameters have become available for this purpose. In the present study we used Pleural fluid Cholesterol ≥ 60 mg/dl as a cut-off to differentiate exudates from transudates and found that it had a high sensitivity and specificity for the same. The efficacy was similar to that of Light's criteria. Pleural fluid cholesterol misclassified lesser number of transudates as exudates, when compared to Light's. Thus pleural fluid Cholesterol is a useful parameter in differentiating exudates from transudates. It is simple, cost-effective and does not require a simultaneous blood sample. It has a high diagnostic efficacy and hence can be used as a routine test in pleural fluid analysis.

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