



“A STUDY OF PLEURAL FLUID CHOLESTEROL IN DIFFERENTIATING EXUDATE AND TRANSUDATE”

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ABSTRACT **Background:** Management of pleural effusion depends on the type of pleural effusion. Pleural fluid cholesterol is considered to be effective in differentiating exudative and transudative type of pleural effusion.
Objective: To study the diagnostic value of pleural fluid cholesterol in differentiating exudative and transudative pleural effusion
Materials and methods: A diagnostic validative study conducted among 162 pleural effusion patients admitted in Medical ward, Department of General Medicine, Govt. Medical College, Kottayam. Definite clinical diagnosis was taken as gold standard and pleural fluid cholesterol values and pleural fluid protein ratio/serum protein ratio was studied for all 162 patients with definite clinical diagnosis.
Results: Pleural fluid cholesterol with a cutoff of ≥ 45 mg/dl have a high sensitivity (97.09 %), specificity (100%), positive predictive value (100%) and negative predictive value (95.16%) in differentiating the type of effusion. Abbreviated Light's criteria have a sensitivity and specificity of 90.29% and 89.83%. Positive predictive value was 93.94% and negative predictive value was 84.13%.
Conclusion: This study showed that the pleural fluid cholesterol has a good diagnostic ability as a single investigation in differentiating exudates from transudates.

KEYWORDS : Pleural effusion, exudates, transudates, cholesterol, abbreviated Light's criteria.

Introduction

Pleural effusion is excess fluids that accumulate between two layers of pleura.¹ Excessive amount of such fluid can impair breathing by limiting the expansion of lung during ventilation. Pleural effusion is divided into two types as transudative and exudative pleural effusion.²

For diagnosis of the cause of pleural effusion relies on comparison of the chemistries in the pleural fluid to those in blood using Light's criteria.³

Light's Criteria³: exudates will have at least one of the following

- Pleural fluid protein to serum protein ratio is greater than 0.5
- Pleural fluid LDH and serum LDH ratio is greater than 0.6
- Pleural fluid LDH is greater than 2/3 times the normal limits of serum.

Abbreviated Light's Criteria⁴: exudates will have at least one of the following

- The ratio of pleural fluid protein to serum protein is greater than 0.5
- Pleural fluid LDH is greater than 2/3 times the normal limits of serum

Abbreviated light's criteria utilize protein ratio and pleural fluid LDH level cut off as 200. So the serum LDH value is not needed.

Since Light's criteria⁴ is questioned by some researchers, measuring of cholesterol in pleural effusion is proposed due to its simplicity in differentiating transudates from exudates when compared with Light's criteria.

So this study evaluates the diagnostic value of pleural fluid cholesterol in differentiating exudates and transudates and it was carried out in Government medical college, Kottayam, a tertiary care center in the center of Kerala.

Objectives of the study are,

Primary objective: To study the diagnostic value of pleural fluid cholesterol in differentiating exudative and transudative pleural effusion.

Secondary objective: To compare the diagnostic accuracy of pleural fluid cholesterol level with abbreviated Light's criteria against etiological classification by clinical diagnosis, pathological

parameters and other investigations as gold standard.

Study design	Diagnostic validative study
Study setting	Medical ward, Department of General Medicine, Govt. Medical College, Kottayam
Study population	Patients admitted in the wards of Department of General Medicine, Govt. Medical College, Kottayam
Sample size	162 pleural effusion patients
Duration of study	10 months(2-1-2014 to 2-11-2014)
Inclusion criteria	1. Age >16 2. Patients giving consent 3. Patients with definite clinical diagnosis* and pleural effusion.
Exclusion criteria	1. Traumatic effusion 2. Patients previously diagnosed and already on treatment 3. Patients with pulmonary embolism and renal insufficiency 4. Incomplete evaluation

*Definite clinical diagnosis means etiological diagnosis of the disease based on clinical diagnosis along with pathological parameters and other investigations excluding the diagnosis based on abbreviated light's criteria.

Thoracocentesis: Diagnostic tapping was done to obtain pleural fluid in all cases, after getting written consent. The procedure was done as mentioned in the Light's text book of pleural disease.^{3,19} USG chest guided aspiration to localize the pleural fluid was done in patients in whom the pleural fluid cannot be obtained from diagnostic tapping and 20ml of fluid was collected. The collected samples were sent to laboratory and were tested for total protein in blood, then in pleural fluid, the following were estimated – total protein, LDH and cholesterol. Both the blood and pleural fluid investigation was done within 24 hours of each other.

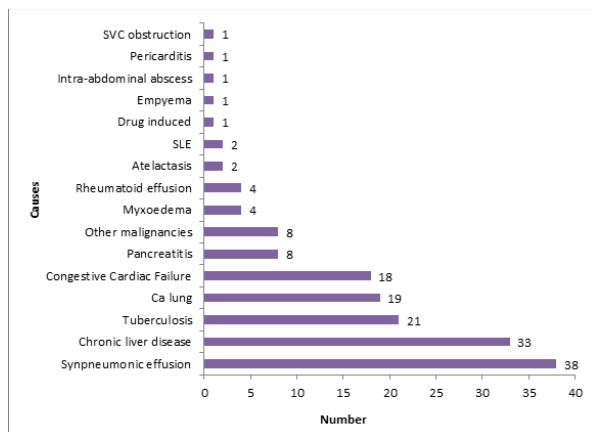
Statistical analysis: Data were entered in Microsoft Office excel sheet 2010, and analysed using SPSS software version 21 and P value < 0.05 was taken as statistically significant. The usefulness of each biochemical parameter was expressed in sensitivity, specificity, positive predictive value and negative predictive value.

Results

A total of 162 eligible patients with definite clinical diagnosis, were included in the study in which 103(63.5%) cases were exudates, and 59(36.5%) cases were transudates. Mean age of study participants was 56 years. Lowest age observed was 16 and highest was 85 among study group. Among 162 people studied, majority (69.1%) were males. Out of 162 patients, 103 were clinically diagnosed as exudative type of pleural effusion and 59 as transudative type of pleural effusion.

Among the 162 patients, half 50% (81) has right sided pleural effusion followed by left sided 38% (62) and bilateral effusion 12% (19). This study says that the side of effusion has statistically significant association with the type of effusion (X² = 16.6 P value = <0.001)

Figure.1: Distribution of causes (definite clinical diagnosis) of pleural effusion

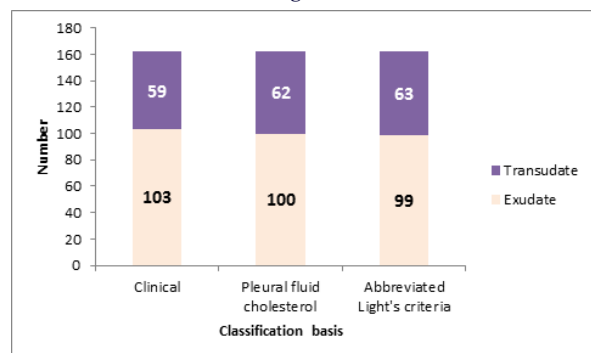


It was observed that synpneumonic effusion was the most common cause of pleural effusion accounting for 38 (23.5%) cases out of 162.

The most common cause of exudates was synpneumonic effusion followed by tuberculosis and carcinoma lung. Among the transudates, most common cause was chronic liver disease followed by congestive cardiac failure.

It was found that mean values (±SD) of pCHOL for exudates was 73.1±15.6 and for transudates it was 34.9±6.7

Figure.2. Cases classified by pCHOL and Abbreviated Light's criteria with definite clinical diagnosis



Among the 162 cases (103 exudates and 59 transudates), of pleural effusion, 100 were diagnosed as exudates and 62 were diagnosed as transudates by pleural fluid cholesterol.

Among the 162 cases (103 exudates and 59 transudates), of pleural effusion, 99 were diagnosed as exudates and 63 were diagnosed as transudates by Abbreviated Light's criteria.

Among the 162 cases (103 exudates and 59 transudates) of pleural effusion, correctly identified 100 exudates and misclassified 3 exudates as transudates. Among the 99 cases identified as exudates by Abbreviated Light's criteria, 93 were actually exudates and 6 were transudates and among the 63 cases diagnosed as transudates, 53 were

actual transudates and 10 were exudates.

Table.1: Diagnostic comparison of Pleural fluid parameters with definite clinical diagnosis

Parameters	Sensitivity	Specificity	PPV*	NPV*
Pleural fluid Cholesterol	97.09%	100%	100%	95.16%
Abbreviated Light's criteria⁵	90.29%	89.83%	93.94%	84.13%

*PPV – Positive Predictive Value NPV - Negative Predictive Value Using a cut-off of pleural fluid cholesterol ≥45 mg/dl a sensitivity of 97.09%, and specificity 100% was obtained for differentiating exudative and transudative pleural effusion. PPV was 100% and NPV was 95.16%.

Abbreviated Light's criteria have a sensitivity of 90.29% and specificity of 89.83% for differentiating exudative and transudative pleural effusion. Positive predictive value was 93.94% and negative predictive value was 84.13%. The differences resulted from a misclassification of ten expected exudates as transudates by Abbreviated Light's criteria.

Discussion

This study is a single centre diagnostic validative study done in General Medicine ward, Medical College Kottayam, with 162 consecutive patients admitted with pleural effusion. The mean age of study patient was 56 years and 69.1% were males. Definite clinical diagnosis was considered as the gold standard and out of 162 patients, 59 were identified as transudates and 103 as exudates as per the clinical diagnosis.

Causes of effusion

Common cause for exudates in the present study was synpneumonic effusion followed by tuberculosis and Carcinoma lung. This is almost similar to results obtained in by Hamal et al⁵ in Nepal where the common cause for exudates found was tuberculosis and carcinoma lung. Most common cause for transudates was chronic liver disease followed by congestive cardiac failure.

In this study the mean cholesterol values obtained for synpneumonic effusion, tuberculous effusion and for malignant effusions were 74.86±12.7 mg/dl, 76.28±17.17 mg/dl and 79.84±9.44 mg/dl. This is similar to mean cholesterol values obtained in study done by Hamal et al⁵, as 70±22, 80.3±22 and 61±25 mg/dl.

Pleural fluid cholesterol and type of effusion: Pleural fluid cholesterol identified 100 exudates correctly and misclassified only 3 exudates as transudates. Among the 3 misclassified exudates, one was due to synpneumonic effusion and one was a case of SLE and remaining was a case of tuberculosis. So using a cut-off of pleural fluid cholesterol > 45 mg/dl a sensitivity of 97.09%, and a specificity 100% was obtained for differentiating exudative and transudative pleural effusion.

Study by Hamal et al⁵ in Nepal found out that pleural fluid cholesterol had a sensitivity of 97.7% and specificity of 100% for differentiating exudative and transudative Pleural effusion and they concluded that pCHOL is of great value in differentiating the type of effusion and should be included in routine analysis of pleural effusion. These results are almost similar to the present study.

Meta-analysis by Shen et al⁶ in china, reported that pleural fluid cholesterol had a sensitivity of 88% and specificity of 96% in differentiating the type of effusion. Present study has identified a higher sensitivity and specificity for pleural fluid cholesterol (97.09% and 100%) when compared with their study.

Abbreviated Light's Criteria and type of effusion:

In this study, Abbreviated Light's criteria⁴ correctly identified 93 exudates among 103 exudates and 10 exudates were mis-classified as transudates. Among the mis-classified exudates, 6 were due to synpneumonic effusion and 4 were due to carcinoma lung. This study identified a high sensitivity and specificity for abbreviated light's criteria as 90.29% and 89.83% with a PPV and NPV of 93.94% and 84.13%. Diagnostic accuracy was 90.12%.

Study by Paramothayan et al⁷ reported a low sensitivity(67%), specificity(80%), PPV (77%) and NPV (84%) for abbreviated light's criteria when compared with present study.

Conclusion

Though this study have reported a high sensitivity, specificity, positive predictive value and negative predictive value for abbreviated light's criteria³, this diagnostic parameter values are low when compared with pleural fluid cholesterol parameters. So even though light's criteria⁴ have mis-classified very few exudates than pleural fluid cholesterol, misclassification can lead to inappropriate patient management or unnecessary and invasive diagnostic investigations that increase morbidity, health care costs, anxiety and suffering of patients. Pleural fluid cholesterol levels were associated with lower misclassification rate when compared with abbreviated Light's criteria. So this can be used in routine diagnosis criteria to reduce misclassifications and to increase diagnostic accuracy.

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