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PLEURAL FLUID CHOLESTEROL IN EXUDATIVE AND TRANSUDATIVE PLEURAL EFFUSION

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ABSTRACT

Background: Light's criteria is the gold standard to differentiate transudative pleural effusion from exudative pleural effusion, but it requires four biochemical estimations which in developing countries such as India, may not be feasible in every patient due to economic constraints. Also it is found that 25% of patients with transudates pleural effusion are mistakenly identified as having exudative effusion by Light's criteria. Pleural fluid cholesterol can be used to classify exudates and transudates as it misclassifies fewer cases than any other Light's parameters. **Materials and methods:** In this prospective study, 60 patients with pleural effusion were included. Pleural fluid total protein, LDH and cholesterol, serum total protein and LDH levels along with other investigations were studied. Clinical classification of transudate or exudate was done based on aetiology. **Results:** Based on clinical signs and symptoms, chest radiograph and other investigations, 52 of these effusions were classified as exudates and 8 as transudates. Using the pleural fluid cholesterol cut-off point >45 mg/dL to differentiate exudates and transudates, the sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) were found to be 100%. Using Light's criteria to differentiate exudates and transudates, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were found to be 98%, 87.5%, 98% and 87.5% respectively. The differences resulted from misclassification of 1 expected exudate as transudate out of 52 and 1 expected transudate as exudate out of 8 by Light's criteria. **Conclusion:** Pleural fluid cholesterol is a simple, cost effective and useful parameter in differentiating pleural exudates from transudates, with the advantage of requiring only one laboratory determination and no simultaneous blood sample, as compared to the use of Light's criteria.

KEYWORDS: Pleural Fluid Cholesterol, Exudates and Transudates.

1. INTRODUCTION

Light's criteria has sensitivity and specificity of 99% and 98%, respectively, for differentiating transudative and exudative PEs (ratio of protein in pleural fluid and serum >0.5; ratio of LDH in pleural fluid and serum >0.6; pleural fluid LDH >2/3rd of upper limit of serum LDH).[1] Some investigators could only reproduce specificities of 70–86% using Light's criteria. 25% of patients with transudates pleural effusion are mistakenly identified as having exudative effusion by Light's criteria. In cases of heart failure on diuretic therapy, the transudative PE has high protein.[2]

Pleural fluid cholesterol can be used to classify exudates and transudates as it misclassifies fewer cases than any other Light's parameters.[3] From meta-analysis, Heffner et al. 2002 have identified pleural effusion of exudative type with at least one of the following conditions.[4]

1. Pleural fluid protein >2.9 gm/dl.
2. Pleural fluid cholesterol >45 mg/dl (1.16 mmol/l).
3. Pleural fluid LDH >2/3rd of upper limit of serum.

Pleural cholesterol is thought to be derived from degenerating cells and vascular leakage from increased permeability. Though the cause of the rise in cholesterol levels in pleural exudates is unknown, two possible explanations have been put forward. First, the cholesterol is synthesized by pleural cells themselves for their own needs[5] and the concentration of cholesterol in pleural cavity is increased by the degeneration of leukocytes and erythrocytes, which contain large quantities.

The second possible explanation is that pleural cholesterol derives from plasma and the increased permeability of pleural capillaries in pleural exudate patients would allow plasma cholesterol to enter the pleural cavity.

The reason to select the cutoff value of pleural fluid cholesterol as 45 (1.16 mmol/L) is that this cutoff value

eliminates the possibility of being equivocal to transudates and exudates and measurement of pleural cholesterol >45 mg/dL (1.16 mmol/L) has been used to improve the accuracy of differentiating transudative and exudative effusions.[6]

MATERIALS AND METHODS

This prospective study was conducted in Department of Pathology, Shyam Shah Medical College and Sanjay Gandhi Memorial Hospital, Rewa (M. P.), a tertiary care hospital, from duration April 2015 to March 2016. The study comprised of 60 patients who were admitted to SGMH with signs or symptoms of pleural effusion by adhering strictly to certain inclusion and exclusion criteria.

Inclusion Criteria

(1) Age of patient >15 years.
(2) Clinically and radiologically demonstrable moderate to large pleural effusion.
(3) Willingness of patient to participate in the study.
(4) Patients of pleural effusion who have not received any therapy for his/her present disease.
(5) Indoor patients.

Exclusion Criteria

(1) Age of patient <15 years.
(2) Patients with contraindications to perform thoracocentesis like bleeding diathesis, local infection, thrombocytopenia, renal insufficiency, etc.
(3) Patient's refusal.
(4) Outdoor patients.
(5) Patients with history of pleural effusion due to trauma.

All the patients underwent a detailed history of fever, productive or dry cough, night sweats, haemoptysis, chest pain, weight loss, lower extremity oedema, orthopnoea, paroxysmal nocturnal dyspnoea, decreased urine output and other relevant symptoms. Clinical assessment including general survey and systemic examination were done. Blood investigations (complete haemogram, total protein, cholesterol and LDH), urine examination, chest radiograph (Postero-anterior view), electrocardiography, echocardio-graphy, renal function test, liver function test, sputum examination for acid-fast bacilli, ultrasonography, were done in all the patients. Further investigations, such as computed tomography scan of chest, bronchoscopy and fine needle aspiration cytology (FNAC), were also done to determine etiology of pleural effusion when needed. Pleural fluid and blood sample collected at same time.

All pleural fluid samples were tested for cell count, protein, glucose, LDH, pCHOL, Gram stain, bacterial culture, acid fast stain and cytology. Protein was measured by the biuret method, LDH by UV spectrophotometry at 37°C and 340 nm[7] and cholesterol with the Boehringer-Mannheim enzymatic method CHOD PAP (cholesterol oxidase peroxidise).[8]

Pleural effusions associated with congestive cardiac failure, hypoalbuminemia and liver cirrhosis were classified as transudates and all others as exudates.

Thus, pleural fluid was categorized as transudative and exudative pleural effusion on the basis of etiology which was contributed by clinical, imaging and pathological evaluations. The pleural effusions were classified as exudative and transudative on the basis of etiological diagnosis, Light's criteria and pCHOL (taken a cutoff value of 1.16 mmol/L or 45 mg/dL, given by Heffner et al. 2002).[4]

Quiroga et al.[9], using 45 mg/dL of cholesterol as the cutoff in 80 patients, also reported a sensitivity of 83% and a specificity of 100%. The statistical significance of the parameters for etiological diagnosis was measured to find their usefulness.

RESULTS

This study comprised of 60 patients. All of them were inpatients both male and female with signs or symptoms of pleural effusion admitted to wards of S.G.M.H., Rewa. Patients were divided into 2 groups: patients with clinically suspected exudative effusion and patients with clinically suspected transudative effusion. A total of 60 patients were taken for study which included 52 patients with exudative effusion and 8 patients with transudative effusion.

In this study exudative effusion was seen in a majority of study population i.e. 86.7% (n=52) and transudative effusion was seen in 13.3% (n=8) of study population.

It was observed that both exudative and transudative effusions were more prominent in male patients i.e. 75% (n=39) were male and 25% (n=13) were female out of 52 exudative effusion. Similarly, 75% (n=6) were male and 25% (n=2) were female out of 8 transudative effusions.

In patients with exudative effusion, the majority (n=24 and 46.2%) of study population were in >65 years age group, followed by the 41-65 years (n=18 and 34.6%) and 15-40 years (n=10 and 19.2%) age groups. Similarly, in patients with transudative effusion, the majority i.e. 62.5% (n=5) of study population were in >65 years age group, followed by the 41-65 years (25% and n=2) and 15-45 years (12.5% and n=1) age groups.

Figure 1 Shows the distribution of study population by effusion type and clinical diagnosis. As can be seen from data, among the patients with exudative effusion, tuberculosis was the most common cause, diagnosed in 23 patients (44.2%) followed by pneumonia (12 and 23%), malignancy (7 and 13.3%), empyema (5 and 9.6%), pericardial disease (3 and 5.7%) and pulmonary embolism (2 and 3.8%). However, among the patients with transudative effusion, congestive heart failure (6 and 75%) was the most prevalent condition, followed by hepatic cirrhosis (2 and 25%).

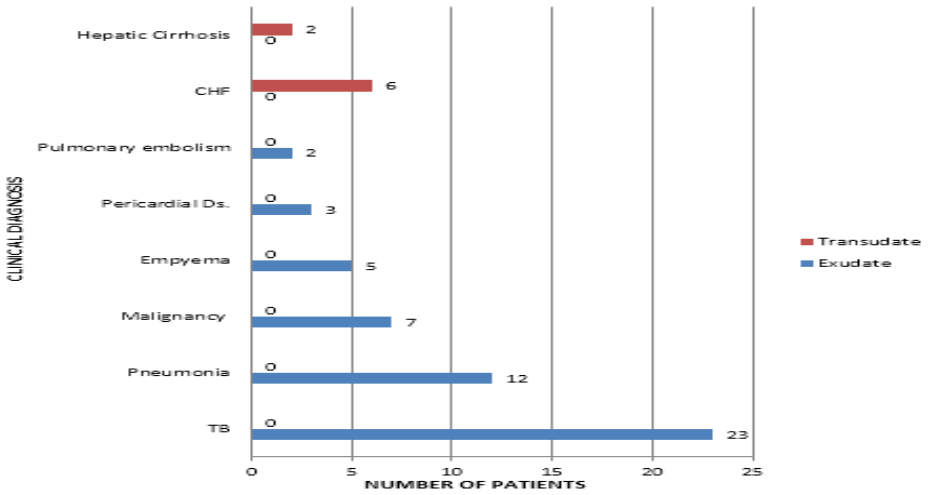

Figure 1. Distribution of Study Population by Effusion Type and Clinical Diagnosis.

Figure 2 Shows sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for differentiation of exudate and transudate while using pleural fluid cholesterol cut-off point >45 mg/dL. As from data it can be seen that sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 100%, 100%, 100% and 100% respectively, when using pleural fluid cholesterol cut off point >45 mg/dL to differentiate exudate and transudate.

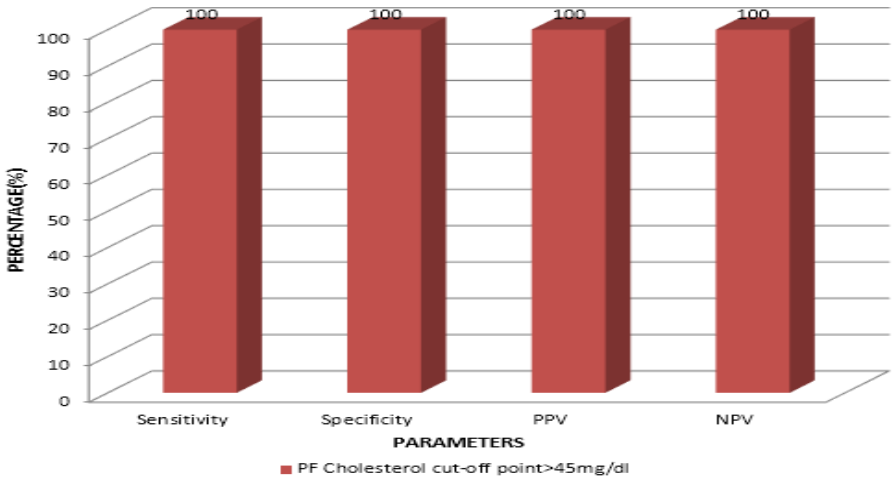

Figure 2: Sensitivity, Specificity, PPV and NPV for Differentiation of Exudate and Transudate by using Pleural Fluid Cholesterol Cut-off Point >45 mg.

DISCUSSION

This study was carried out on 60 patients divided into 2 groups; exudate and transudate. Exudate consists of 52 patients including patients with clinical diagnosis of tuberculosis, pneumonia, malignancy, empyema, pericardial disease, pulmonary embolism. Transudate consists of 8 patients with clinical diagnosis of congestive heart failure and hepatic cirrhosis. Out of 52 patients, 39 were male and 13 were female, with maximum number of patients falling in age group >65 years with mean age 57.11 years. Out of 8 patients, 6 were male and 2 were female with maximum number of patients falling in >65 years age group with mean age 58.62 years.

Present study demonstrates that the sensitivity, specificity, positive predictive value and negative predictive value were 98%, 87.5%, 98% and 87.5% respectively when using Light's Criteria to differentiate exudate and transudate while the sensitivity, specificity, positive predictive value and negative predictive value were 100%, 100%, 100% and 100% respectively when using pleural fluid cholesterol cut-off point >45 mg/dL to differentiate exudate and transudate. Present study shows that using pleural fluid cholesterol to differentiate exudate and transudate was more sensitive and specific than using Light's criteria because in our study 1 exudate out of 52 exudates was misclassified as transudate (Sensitivity 98%) and 1 out of 8 transudates was erroneously labelled as exudate (Specificity 87.5%) when using Light's criteria to differentiate exudate and transudate. When using the pleural fluid cholesterol cut-off point >45 mg/dL, all the 52 exudates were correctly

classified (sensitivity 100%) and all the 8 transudates were correctly labelled (specificity 100%).

Table 1: Shows comparison of sensitivity, specificity, positive predictive value and negative predictive value when using Light's criteria to differentiate exudate and transudate and when using pleural fluid cholesterol to differentiate exudate and transudate among various studies.

		Marina Costa MD et al[10]	Rohit Rungta et al[11]	Anand K. Patel et al[12]	Present Study
Light's criteria	Sensitivity	98%	98%	98%	98%
	Specificity	82%	82%	100%	87.5%
	PPV	-	90%	100%	98%
	NPV	-	82.9%	92%	87.5%
Pleural fluid Cholesterol		**Cut-off point >45 mg/dL**	**Cut-off point >45 mg/dL**	**Cut-off point >60 mg/dL**	**Cut-off point >45 mg/dL**
	Sensitivity	90%	90%	98%	100%
	Specificity	100%	99%	100%	100%
	PPV	-	93%	100%	100%
	NPV	-	95%	92%	100%

Table 1. Comparison of Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value when using Light's Criteria to Differentiate Exudate and Transudate and when using Pleural Fluid Cholesterol to Differentiate Exudate and Transudate among Various Studies

CONCLUSION

The present study has been an attempt to determine the role of pleural fluid cholesterol and to suggest that the pleural fluid cholesterol is a better criterion than Light's criteria to differentiate exudative and transudative effusion. The sensitivity, specificity, positive predictive value and negative predictive value when using pleural fluid cholesterol to differentiate exudate and transudate is higher than the sensitivity, specificity, positive predictive value and negative predictive value when using Light's criteria to differentiate exudate and transudate. Thus, it is suggested that the measurement of pleural fluid cholesterol to differentiate exudate and transudate is better than the Light's criteria, with the advantage of no simultaneous collection of blood sample, especially in country like India where financial and technical constraints are immense.

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