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Research Article

EVALUATION OF PLEURAL FLUID TO SERUM CHOLINESTERASE RATIO FOR DIFFERENTIATING PLEURAL TRANSUDATES FROM EXUDATES

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ABSTRACT
Pleural effusion (PF) is a common clinical entity where differentiation between transudate and exudate is necessary to assist in differential diagnosis. It has been reported in various studies that Light's criteria have lower specificity, and new recommendations have emerged. Several studies have revealed that the widely used Light et al criteria misclassify an unacceptably high proportion of pleural effusions as being exudates or transudates. Several parameters such as pleural fluid cholesterol level, PF to serum cholesterol ratio, PF to serum bilirubin concentration ratio, alkaline phosphatase value, pleural cholinesterase, PF to serum cholinesterase ratio and serum-pleural effusion albumin gradient have been proposed in segregating the transudates from exudates more reliably than those of Light's criteria. The pleural fluid/serum cholinesterase ratio has been considered to be more promising differentiator. A study was conducted to judge the efficacy of this criterion, in comparison with the Light et al criteria.

Keywords: *Pleural Effusion, Light's Criteria, Pleural Cholinesterase, Exudates*

INTRODUCTION
Pleural effusion occurs in a large variety of pathological conditions, but determination of the cause of pleural effusion is not always easy. Transudative pleural effusion is caused by a limited number of diseases, whereas the exudate effusion requires more extensive diagnostic investigations. Therefore, the first step is to classify them as transudate or exudate effusion, even if this differentiation does not contribute to the etiological diagnosis. Presently, Light's criteria2 are used to distinguish between transudates and exudates (pleural fluid/serum protein ratio >0.5, pleural fluid/serum LDH ratio >0.6 and absolute pleural fluid LDH >200U denote an exudate). But many pleural effusions, misclassified as transudates or as exudates have been reported using these criteria (Hamm *et al.*, 1987; Gupta *et al.*, 1999). Cholinesterase (ChE) activity is significantly inhibited in the presence of untreated pulmonary tuberculosis and its activity remains stable in anyone individual. Therefore, measurement of its activity may serve as a useful diagnostic too. Cabrer *et al.*, (1978) estimated ChE activity in pleural effusions of diverse etiologies and concluded that there exists differences in the activity of ChE and it was possible to differentiate transudate and exudate.

MATERIALS AND METHODS
The study was conducted in Department of Medicine, Basaveshwara Teaching and general hospital, attached to Mahadevappa Rampure Medical College, Gulbarga.
50 patients with pleural effusion were selected for study between December 2006 to April 2008.

Inclusion Criteria:

- Tubercular effusion was diagnosed by X-ray, pleural fluid and sputum AFB.
- Malignant effusion – malignant cells in the pleural fluid with or without histological evidence.
- CHF effusion as diagnosed by cardiomegaly on roentgenogram and echocardiography, presence of pulmonary congestion and absence of other lesions in the chest X-ray.

- Nephrotic syndrome as diagnosed by establishing protenuria of > 3 gm/ 24 hours, oedema, hypoalbuminemia and hypercholesterolemia.
- Pancreatitis as diagnosed by history, serum amylase > 1000 u/ml and ultrasound abdomen.
- Pleural effusion due to other well determined cause.

Exclusion Criteria:

- Effusions of undetermined origin
- Effusions with more than one possible cause
- Empyemas
- Hemothorax
- Persons with history of exposure to organophosphorus compounds.

All the patients selected for the study were evaluated in detail, comprising of detailed history, clinical examination and relevant investigations.

Patients with clinical evidence of pleural effusion were first send for chest X-ray PA and lateral view and ultrasound thorax if required.

Following investigations were done on all the patients in the study group.

1. Partial haemogram including ESR
2. Urine albumin, sugar
3. RBS
4. Blood urea/ creatinine
5. Liver function tests
6. Serum lactic dehydrogenase
7. Serum cholinesterase

Then the diagnostic thoracentesis was performed taking great care not to let the fluid mix with blood.

1. Pleural fluid was immediately sent for following investigations.

1. Pleural fluid cytology including malignant cells
2. Proteins, sugar
3. Lactic dehydrogenase
4. Cholinesterase

Effusions were individually classified as transudates or exudates after careful evaluation of all clinical data and investigation results. The criterias analyzed for separation of transudative and exudative pleural effusions are as follows:

1. The criteria of Light et al, is in based on three parameters

a. Pleural fluid to serum proteins >0.5
b. Pleural fluid to serum LDH > 0.6
c. Pleural fluid LDH > 200 IU

Exudative pleural effusions meet at least one of the following criteria, whereas transudative pleural effusion meets none.

2. Pleural fluid cholinesterase values > 2000 U/L are taken as exudates and those< 2000 U/L are taken as transudate.

1. Pleural fluid to serum cholinesterase ratio: Ratio > 0.5 is taken as exudates and those < 0.5 are taken as transudate.

RESULTS

Following observation were made after studying 50 cases of pleural effusion admitted to Basaveshwara Teaching and General Hospital, Gulbarga between Dec. 2006 to April 2008.

The misclassification of transudates and exudates were less pleural fluid to serum cholinesterase ratio, compared to all other parameters and Light's criteria. But even pleural fluid to serum cholinesterase ratio misclassified one each case of transudate and exudate.

Table 1: Showing Number and Percentage of Misclassifications as Transudates and Exudates by using different Parameters

Investigations	Transudates No. of Cases (n = 20)	Percentage	Exudate No. of Cases (n = 30)	Percentage
Light's criteria	03	06	02	04
Pleural fluid cholinesterase	02	04	02	00
PF/S cholinesterase ratio	01	02	01	02

Table 2: Number and Percentage of Misclassified Transudates

Criteria's	CCF (n = 18)	Nephrotic syndrome (n=1)	Cirrhosis (n = 1)	Total (n = 20)	Percentage
Light's criteria	03	00	00	03	06
Pleural fluid cholinesterase	02	00	00	02	04
PF/S cholinesterase ratio	01	00	00	01	02

Light's criteria misclassified 3 transudates, while PF/S cholinesterase 1 transudate.

Table 3: Number and Percentage of Misclassified Exudates

Criteria's	PTB	Pneu.	CRF	Post CABG	Malig.	Others	Total	Percentage
Light's criteria	2	0	0	0	0	0	2	4
Pleural fluid cholinesterase	0	0	0	0	0	0	0	0
PF/S cholinesterase ratio	0	1	0	0	0	0	1	2

Light's criteria misclassified 2 exudates, PF/S cholinesterase ratio misclassified only 1 exudate and pleural fluid cholinesterase misclassified none.

Table 4: Showing Diagnostic Validity of Various Parameters

Investigation	Sensitivity	Specificity	PPV %	NPV %	Efficiency %
Light's criteria	93	85	90	89	90
PF Cholinesterase	100	90	94	100	97
PF/S Cholinesterase	97	95	97	95	96

DISCUSSION

Pleural effusion is a common clinical entity: approximately 4% of all attendances at chest clinics.

The initial step in diagnosis is to distinguish between transudates and exudates (Sahn, 1988; Light *et al.*, 1972; Light, 1977; Romero *et al.*, 1993; Bartter *et al.*, 1994; Valdes *et al.*, 1994; Vives *et al.*, 1996; Lakhotia *et al.*, 1996; Padilla, 1996; Garquez *et al.*, 1998). The criteria used for the purpose were proposed by Light *et al.*, with misclassifications varying from 2% to 40.

Table Showing Comparison of Misclassification of Pleural Effusion by Eduardo et al study and Present Study using Various Parameters

Criteria Used	Study of Eduardo et al % of Misclassification	Present Study % of Misclassification
Light's criteria	7.8	10
PF Cholinesterase	8.5	4
PF/S Cholinesterase	1.38	4

In the present study, the misclassifications using PF to serum cholinesterase ratio is higher than the study by Eduardo *et al.*, (1996). But both the studies shows that compared to Light et al criteria, pleural fluid to serum cholinesterase ratio is a better parameter to separate transudate from exudates.

Janmeja *et al.,* in 2000, studied 50 cases of pleural effusion with different etiology using PF/S cholinesterase as criteria.

They made two groups in study population:

Group A: Compromise 10 case each of PTB, malignancy and para pneumonic plural effusion total of 30 cases.

Group B: Compromised 10 pleural effusions due to CHF and 10 cases due to nephrotic syndrome total of 20 cases.

By using 0.5 as the cutoff value for PF/S cholinesterase ratio they were able to classify 98% of effusion accurately, by taking 1600 IU of pleural fluid cholinesterase as cutoff value they misclassified 3 cases of effusion, by using Light's criteria 5 cases were misclassified.

Table Showing Comparison of Misclassification of Pleural Effusion by Janmeja et al and Present Study using Various Parameters

Criteria Used	Study of Eduardo et al % of Misclassification	Present Study % of Misclassification
Light's criteria	10	10
PF Cholinesterase	06	04
PF/S Cholinesterase	02	04

In the present study the misclassifications using PF to serum cholinesterase is higher than the study of Janmeja *et al.,* (2000). Misclassifications using Light's criteria is also high with the present study. But both studies shows that PF to serum cholinesterase is a better parameter to separate transudates from exudates.

The present study and the study by Eduardo et al shows that number of misclassification is higher using only pleural fluid cholinesterase, compared to pleural fluid to serum cholinesterase ratio. While present study, using PF cholinesterase misclassified 6% of pleural effusions, Eduardo *et al.,* (1996) and Janmeja *et al.,* (2000) misclassified 8.5% and 6% cases each respectively. This could be attributed to the fact that, since the cholinesterase is synthesized in the liver, the levels can be influenced by different disorders. This hepatitis, cirrhosis, acute infections, pulmonary embolism chronic renal failure and after surgical procedures.

In the present study the cut of value of pleural fluid cholinesterase and pleural fluid to serum cholinesterase ratio is 2000IUand 0.5 respectively. Pleural fluid cholinesterase > 2000 and pleural fluid to cholinesterase ratio > 0.5 is taken as exudates and the value < 2000 a ratio < 0.5 is taken as transudates. This cut of value is based on mean and standard deviation (Mean – 2 SD) with clinical features and positively of that test. For transudate the value is 1111 ± 362 and for exudates the value is 5433 ± 1587. The difference between transudates and exudates are statistically highly significant ($p < 0.001$).

The present study and various other studies, brings to the light the fact that Light's et al criteria. Misclassify transudate more than the exudates. In the present study using Light's criteria the misclassification ratio were 6% for transudates 4% for exudates.

Conclusion

Misclassifications are present with all parameters used. Number of misclassifications using PF/S cholinesterase ratio and pleural fluid cholinesterase level are less compared to other parameter used. Sensitivity and specificity of PF/S cholinesterase ratio and pleural fluid cholinesterase level as diagnostic parameter to differentiate transudates and exudates are higher than all other parameters used in the study. The number of misclassifications are more with the Light's criteria than the PF/S cholinesterase ratio. Hence, the pleural fluid to serum cholinesterase ratio and pleural fluid cholinesterase level are the reliable method in separating pleural transudates from exudates. If further studies with larger study group confirm our results, cholinesterase ratio and pleural fluid cholinesterase level could be used as the first step in diagnostic study of pleural effusion.

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