

Pleural Fluid Pseudocholinesterase and Its Ratio to Serum Pseudocholinesterase: For Differentiating Pleural Transudates from Exudates

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Abstract

Context: The lights criteria is the system that has stood the test of time in classifying pleural effusions into transudates and exudates. But studies have shown that there is significant number of misclassification with the lights criteria. Several newer parameters are being postulated as an alternative to lights criteria for classifying effusions. Pleural fluid pseudocholinesterase and its ratio to serum pseudocholinesterase is one such parameter

Aim Of The Study: To evaluate the usefulness of pleural fluid pseudocholinesterase (PChE) level and its ratio with serum pseudocholinesterase in order to differentiate between transudates and exudates. To compare the diagnostic efficacy of: (1) pleural fluid PChE value and (2) pleural fluid PChE to serum PChE ratio; with the efficacy of Light's criteria

Settings And Design: Cross sectional analytical study

Materials And Methods: 60 patients with pleural effusion with known etiology were selected and divided into transudates and exudates based on the etiology. lights criteria was applied to all patients. Pleural fluid PChE level and its ratio to serum PChE were estimated in all patients. ROC analysis and unpaired t test was done

Statistical analysis: ROC analysis was done for pleural fluid PChE and pleural fluid to serum PChE ratio. Youden index was calculated. Unpaired t test was applied for pleural fluid PChE and pleural fluid to serum PChE ratio of transudates and exudates

Results: There was significant difference between the values of both Pleural fluid PChE level and pleural fluid to serum PChE ratio between exudates and transudates. Misclassification was less with the new parameters compared to lights criteria. Sensitivity, specificity, PPV, NPV of Pleural fluid PChE level (96.2%, 85.36%, 89.36%, 97.6% respectively) and pleural fluid to serum PChE ratio (97.14%, 91.6%, 94.2%, 98.3%) were better than that of lights criteria (93.3%, 77.7%, 83.3%, 95.6%).

Conclusions: Both pleural fluid PChE and P/S PChE ratio are reliable parameters in differentiating transudates and exudates. PChE and P/S PChE ratio are more efficient than lights criteria in differentiating transudates and exudates. P/S PChE ratio is the most sensitive and specific parameter among the parameters studied.

Keywords: pseudocholinesterase (PChE), negative predictive value (NPV), positive predictive value (PPV)

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I. Introduction

Collection of abnormal quantity of fluid within the pleural space is called pleural effusion. It is a common clinical condition known since the time of Hippocrates (641 – 539 B.C) and still commonly encountered in everyday practice. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. Due to the various etiologies that can cause a pleural effusion, it may often cause a diagnostic dilemma. The initial step in the evaluation of pleural effusion is to differentiate it as either an exudate or a transudate; as this gives an indication of pathophysiological mechanisms, differential diagnosis and the need for further investigation. Many criteria have been used to distinguish pleural exudates from transudates, but none of them have been found to be satisfactory.

Light's criteria is the most commonly used method According to Light's criteria, one or more of the following are required to diagnose Exudates.

1. Pleural fluid protein / Serum protein > 0.5
2. Pleural fluid LDH / Serum LDH > 0.6
3. Pleural fluid LDH more than 2/3rd of the upper limit of serum LDH

It was found that even Light's criteria misclassified a large number of effusions - 25% of transudates as exudates and 2-3% exudates as transudates (total ~7.8% misclassification rate) Several alternative parameters have been proposed in segregating the transudates from exudates more reliably than those of Light's criteria [such as pleural fluid(PF)cholesterol level, PF to serum cholesterol ratio, PF to serum bilirubin concentration ratio, alkaline phosphatase value, and serum-pleural effusion albumin gradient]. The pleural fluid pseudocholinesterase level and pleural fluid/serum pseudocholinesterase ratio are newer alternative parameters postulated to be better differentiator of transudates from exudates Hence, this study is done to evaluate the usefulness of pleural fluid pseudocholinesterase(PChE) level and its ratio with serum pseudocholines in order to differentiate between transudates and exudates..

II. Materials And Methods

STUDY POPULATION :

• Patients with pleural effusion (evaluated cases with a proven etiology) from the dept. of general medicine, dept of thoracic medicine, dept of medical oncology, dept of nephrology and dept of cardiology in GRH. • 60 patients with pleural effusion resulting from a single disease (CCF, nephrotic syndrome, malignancy, tuberculosis, pneumonia)were selected for the study

Inclusion criteria:

- Patients with malignant effusion
- Patients with Tubercular effusion
- Patients with parapneumonic effusion
- Patients with pleural effusion due to cardiac failure
- Patients with pleural effusion due to nephrotic syndrome

Exclusion criteria

- Effusions of undetermined origin)
- pleural effusion with > 1 possible etiology
- liver disease 57
- OCPs, anti-cancer drugs, MAO inhibitors, neostigmine, chlorpromazine)
- Pregnany
- Pts with h/o exposure to OPC
- Pts with uremia
- Malignant effusions who are already started on chemotherapy and those with superior vena caval obstruction.

Ethical Committee Approval: Obtained.

Study Protocol :

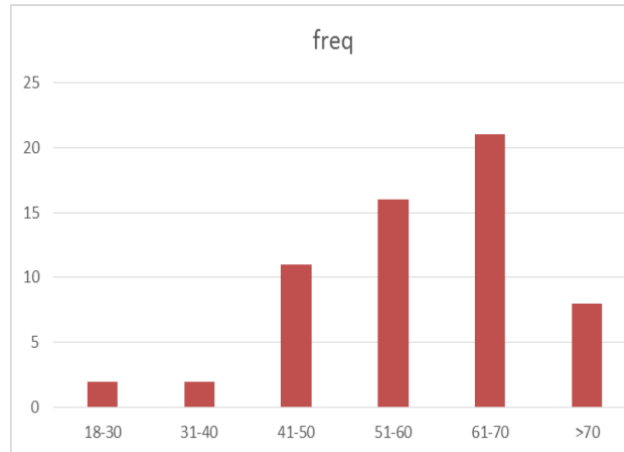
Patients with pleural effusion with a proven etiology were selected for the study. Then a detailed clinical examination with brief history and a battery of investigations were done on these patients so that they meet the inclusion and exclusion criteria specified for the study . Thus the study population was selected and they were further classified as exudates and transudates , based on the etiology of pleural effusion . In all patients Pleural fluid pseudocholinesterase & Serum pseudocholinesterase , Pleural fluid total protein, Serum total protein , Pleural & Serum LDH were estimated. Then the patients are classified in to exudates and transudates on the basis of Light's criteria” . Now the classification of exudates and transudates done on the basis of Pleural fluid pseudocholinesterase & Serum pseudocholinesterase is compared with results of the classification of exudates and transudates done on the basis of Light's criteria.” Sensitivity, specificity , Positive predictive value , negative predictive value of each tests are calculated.

STATISTICAL ANALYSIS:

ROC analysis was done for pleural fluid PChE and pleural fluid to serum PChE ratio. Youden index was calculated for each of the plotted values and the value with the maximum youden index was taken as the cut off point with optimum sensitivity and specificity . Unpaired t test was applied for for pleural fluid PChE and pleural fluid to serum PChE ratio of transudates and exudates

III. Results

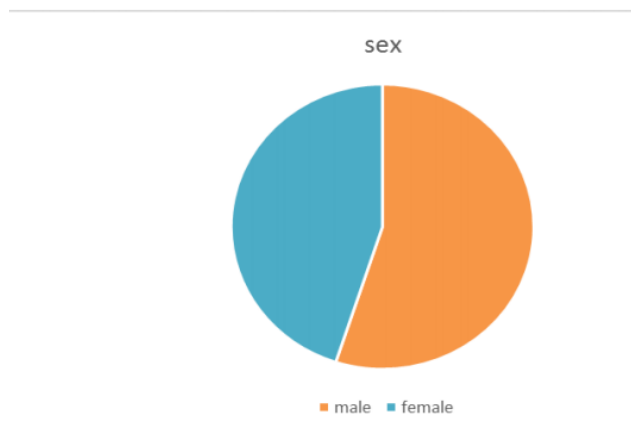
AGE DISTRIBUTION



| age | freq | % |
|-------|------|-------|
| 18-30 | 2 | 3.33 |
| 31-40 | 2 | 3.33 |
| 41-50 | 11 | 18.33 |
| 51-60 | 16 | 26.67 |
| 61-70 | 21 | 35 |
| >70 | 8 | 13.33 |

35% of the study subjects were in the age group of 56-70yrs, 26.67% were in the age group of 51-60yrs, 18.33% were in the age group of 41-50 yrs. 13.33% patients were more than 70 yrs. 3.33% were 21- 30 yrs. 3.33% were 18-20 yrs

SEX DISTRIBUTION

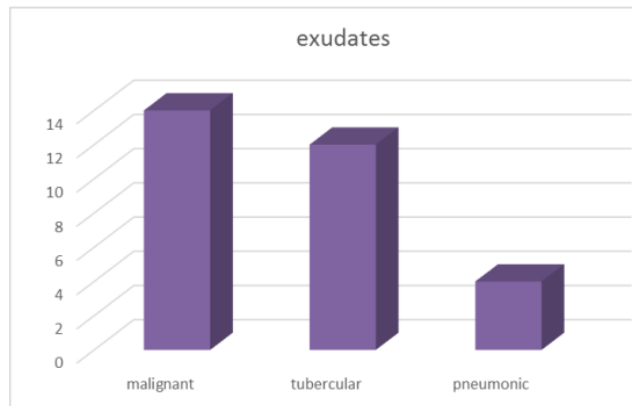


| Sex | freq | percent |
|--------|------|---------|
| Male | 33 | 55% |
| female | 27 | 45% |

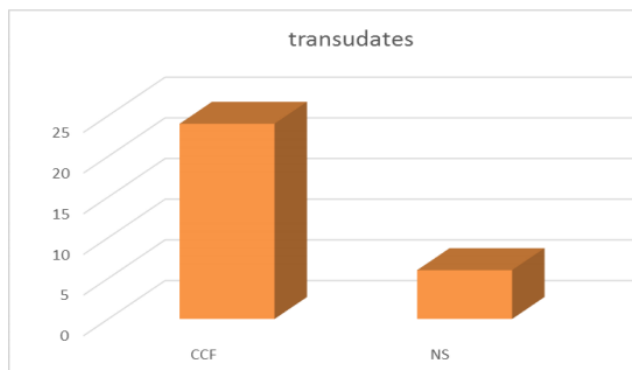
Majority of the study subjects were males 55% while remaining 45% were females

ETIOLOGICAL CLASSIFICATION:

Exudates and transudates distribution in our study is as follows:



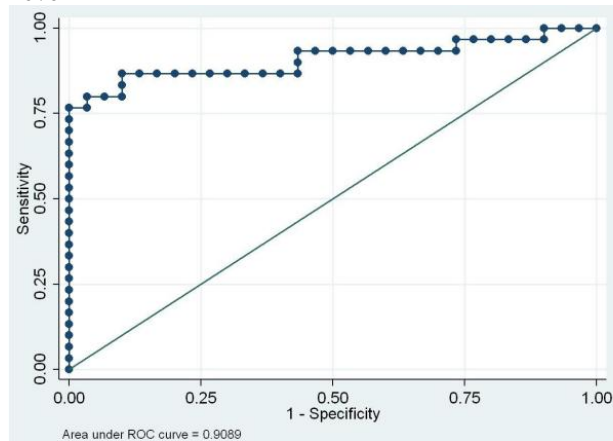
| etiology | freq (total-30) | percent |
|------------|-----------------|---------|
| malignant | 14 | 46.67% |
| tubercular | 12 | 40% |
| pneumonic | 4 | 13.33% |



| etiology | frequency (total-30) | percent |
|----------|----------------------|---------|
| CCF | 24 | 80% |
| NS | 6 | 20% |

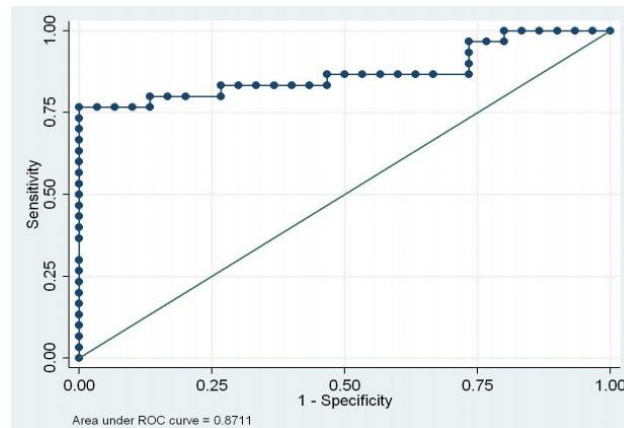
In our study about 55% of the study subjects were exudates while 45% were transudates. Among the exudates, about 40 % of study groups have tuberculosis, 46.67% have malignancy and 13.33 % have parapneumonic effusions. Among the transudates, 80% were due to congestive cardiac failure and 20% due to nephrotic syndrome.

ROC Pleural fluid PChE level



After ROC analysis, the cutoff point of pleural fluid PChE level with optimum sensitivity and specificity was calculated as 589 U/L

ROC Pleural fluid to Serum PChE ratio



After ROC analysis, the cutoff point of pleural fluid to serum PChE ratio with optimum sensitivity and specificity was calculated as 0.26.

| | transudates misclassified as exudates (total-30) | exudates misclassified as transudates(n-30) |
|--------------------|-------------------------------------------------------------|--------------------------------------------------------|
| lights criteria | 8(26%) | 2(6%) |
| PF PChE | 2(6%) | 2(6%) |
| P/S PChE | 2(6%) | 0 |

Lights criteria misclassified 8 transudative effusions and 2 exudates. Pleural fluid PChE misclassified 2 transudates and 2 exudates. Pleural fluid to serum PChE ratio misclassified 2 transudates whereas no exudates were misclassified in the study population.

Mean values

| | exudates | transudates |
|----------------------------|-----------------|--------------------|
| PF PChE(mean+/-2SD) | 1071+/- 448 | 447+/-121 |
| P/S PChE ratio(mean+/-2SD) | 0.508+/-0.257 | 0.176+/-0.069 |

The mean pleural fluid PChE was 1071U/L in exudates and 447U/L in tansudates. The mean value of P/S PChE ratio was 0.508 in exudates and 0.176 in transudates. Unpaired T test done on pleural fluid PChE and pleural fluid to serum PChE ratio showed statistically significant difference between exudates and transudates with p value <0.001 in both groups

| parameter | sensitivity(%) | specificity(%) | PPV(%) | NPV(%) |
|-----------------|-----------------------|-----------------------|---------------|---------------|
| lights criteria | 93.3 | 77.7 | 83.3 | 95.6 |
| PF PChE | 96.2 | 85.36 | 89.6 | 97.6 |
| P/S PChE | 97.14 | 91.6 | 94.2 | 98.3 |

IV. Discussion

Earlier, exudates were separated from transudates by means of specific gravity, cell count and presence or absence of clotting of fluid. Later in 1972, ,lights criteria was developed to differentiate between exudates and transudates. But lights criteria misclassified a significant number of effusions. Thus dawned the need for newer parameters. Our study focused on pleural fluid pseudocholinesterase and its ratio with serum pseudocholinesterase for differentiating transudates and exudates.

In a study done by Manju Sharma et al found that, using a cutoff of 0.24 for P/S PChE ratio they classified 98.1% of effusions correctly with PPV 98.75% and NPV 96.67%. In another study done by Prakash Kikkeri Gowdaiah et al, the sensitivity and specificity were 100% and 96.7%, PPV was 96.7% and NPV was 100%. In our study, sensitivity and specificity are 97.14 and 91.6%, PPV is 94.2% and NPV is 98.3% which is comparable to the other studies.

Similarly, the sensitivity and specificity of Light’s criteria according to Prakash et al was 93% and 96% respectively while in the present study, it is 93.3% &77.7% respectively. These results are also comparable.

Comparison of Light’s Criteria in various studies

| | Present study | Prakash et al | Manju Sharma et al |
|-----------------|---------------|---------------|--------------------|
| Sensitivity (%) | 93.3 | 93 | 91.25 |
| Specificity (%) | 77.7 | 96 | 90 |
| PPV (%) | 83.3 | 96 | 96.05 |
| NPV (%) | 95.6 | 93 | 79.42 |

Comparison of pleural fluid PChE in various studies

| | Present study | Manju Sharma et al |
|-----------------|---------------|--------------------|
| Sensitivity (%) | 96.2 | 97.5 |
| Specificity (%) | 85.36 | 90.0 |
| PPV (%) | 89.6 | 96.29 |
| NPV (%) | 97.6 | 93.11 |

Comparison of P/S PChE in various studies

| | Present study | Prakash et al | Manju Sharma et al |
|-----------------|---------------|---------------|--------------------|
| Sensitivity (%) | 97.14 | 100 | 98.7 |
| Specificity (%) | 91.6 | 96.7 | 96.67 |
| PPV (%) | 94.2 | 96.7 | 98.7 |
| NPV (%) | 98.3 | 100 | 96.6 |

In our study, the mean pleural fluid PChE was 1071 U/L in exudates and 447 U/L in transudates. The mean value of P/S PChE ratio was 0.508 in exudates and 0.176 in transudates. Students t test was applied to these values and it was found that this difference was statistically significant (p value < 0.001)

MEAN VALUES

| | EXUDATES | TRANSUDATES |
|--------------------|----------|-------------|
| Pleural fluid PChE | 1071 | 447 |
| P/S PChE ratio | 0.508 | 0.176 |

In a study by Prakash et al, the mean PChE levels in exudates was 2074 +/- 660 U/L and in case of transudates, it was 385 +/- 142 U/L. and was found to be statistically significant. In the study by Manju Sharma et al, the mean PChE and P/S PChE were significantly higher in the exudates compared to transudates (P < 0.0001).

After ROC analysis, the cutoff point of pleural fluid to serum PChE ratio with optimum sensitivity and specificity was calculated as 0.26 and the cutoff value for pleural fluid PChE was 589.

In our study, it was found that the sensitivity and specificity of pleural fluid PChE and P/S PChE was found to be higher than Light's criteria. Both pleural fluid PChE and its ratio misclassified lesser number of cases than Light's criteria and had a better discriminatory capacity. These results were also comparable to the previous studies.

V. Conclusion

It is concluded from the above study that Both pleural fluid PChE and P/S PChE ratio are reliable parameters in differentiating transudates and exudates. PChE and P/S PChE ratio are more efficient than Light's criteria in differentiating transudates and exudates. P/S PChE ratio is the most sensitive and specific parameter among the parameters studied.

LIMITATIONS OF THE STUDY :

The study was conducted in a relatively small group. So more studies with larger study population are needed for establishing the usefulness of the studied parameters and also for defining the cutoff levels of the parameters in differentiating exudates and transudates in the general population.

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Bibliography

- [1]. Manju Sharma*, KB Gupta**, Kirori M Goyal**, Nitya Nand Evaluation of Cholinesterase to Differentiate Pleural Exudates and Transudates © JAPI • VOL. 52 • MAY 2004
- [2]. Naveen M1, Vanitha S2, Chowdareddy Comparison of Diagnostic Efficacy of Cholinesterase Levels to Differentiate Pleural Exudates and Transudates that of Lights Criteria © Sch. J. App. Med. Sci., 2014 2(3C):1037-1040
- [3]. Transüda-Eksüda Ayriminda Plevral Sivi Psödokolinesteraz Düzeyinin Tanısal DeğeriDiagnostic Efficiency of Pseudocholinesterase Level in Discrimination of Transudates-Exudates Tüberküloz ve Toraks Dergisi 2003; 51(4): 398-404
- [4]. Prakash Kikkeri Gowdaiah1, Amrutha Avati2, Priya Prakash Bhate3, Akkamahadevi V. Nippanal4 pleural fluid to serum psuedocholinesterase ratio and its validation with light's criteria -Journal of Evolution of Medical and Dental Sciences/Volume 3/Issue 01/ January 06, 2014
- [5]. Nag D and De SC. Cholinesterase activity in pulmonary tuberculosis. Ind J Chest Dis All Sci 1988;30:93-7. 80
- [6]. Eduardo GP, Isabel PN, Jose FS, Jimenez B, Custardoy J. Pleural fluid to serum cholinesterase ratio for the separation of transudates and exudates. Chest 1996;110:97-110.
- [7]. Garcia PE and Padilla NI. The diagnostic usefulness of cholinesterase in pleural exudates. Rev Clin Esp (Spain) 1997;197:402-5
- [8]. Light RW, MacGregor MI, Luchsinger PC. Pleural effusions The diagnostic separation of transudates and exudates. Ann Intern Med 1972;77:507-13
- [9]. Ellman GE, Courtney KD, Andees V, Featherstone RM. A new and rapid colorimetric determination of acetyl cholinesterase activity. Biochem Pharmacol 1961;7:88-95.
- [10]. Lakhotia M, Shah PKD, Yadav A, Gupta A, Modi PK, Sinha HY. Comparison of biochemical parameters in pleural effusion. J Assoc Phys Ind 1996;44:612-4.
- [11]. A. Lone Mushtaq, Abdul Wahid, S.M. Saleem, Alkaline phosphatase in pleural effusions, Indian J. Chest Dis. Allied Sci. 45 (2003) 161–163.
- [12]. Isabel Gazquez, Jose Manuel Porcel, Manuel Vives, et al, Pleural alkaline phosphatase in separation of transudative and exudative pleural effusions, Chest 112 (1997) 569–570. 81
- [13]. K. Tahaoglu, O. Kizkin, R. El, Alkaline phosphatase: distinguishing between pleural exudates and transudates, Chest 105 (1994) 1912–1913.
- [14]. N.C. Syabbalo, Use of pleural alkaline phosphatase content to diagnose tuberculous effusions, Chest 99 (1991) 522–523.
- [15]. A.A. Jadhav, J.S. Bardapurkar, A. Jain, Alkaline phosphatase: distinguishing between tuberculous and nontuberculous pleural effusion, Lung India 26 (3) (2009) 77–80 transudative from exudative pleural effusions. Indian J Tub 2002 ; 49 : 97

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