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ORIGINAL ARTICLE

Evaluation Of Biochemical Parameters To Differentiate Transudates From Exudates In Certain Diseases

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ABSTRACT

Background: Pleural effusion is a common occurrence in medicine wards/OPD. To determine the cause of the pleural effusion is not always easy. The distinction between an exudate and a transudate is the first and the most important step in the differential diagnosis of a pleural effusion. Several biochemical markers are used to classify the type of pleural effusion. The oldest and the most conventional way of classifying the pleural effusion is by the Light's criteria. There are multiple other biochemical markers which are available, the diagnostic accuracy of which is not well established and is a subject of debate.

Aim: To evaluate the diagnostic performance of the pleural fluid protein, LDH, cholesterol, bilirubin and their ratio with serum values, as well as the albumin gradient in differentiating the pleural fluid into transudate and exudate .

Materials And Methods: A total of 50 cases of pleural effusion due to different diseases were analysed using certain biochemical parameters like pleural fluid cholesterol, protein and LDH. Their ratio with serum values and the albumin gradient were also analysed.

Statistical Analysis: ROC curves were drawn for individual markers and the areas under the curve were computed and compared using the SPSS version 17. The optimal cut off with a combination of highest sensitivity and specificity was defined.

Result: The pleural fluid protein, its ratio to serum protein and pleural fluid LDH had excellent diagnostic accuracy in differentiating exudative pleural effusions from transudative effusions. Pleural fluid LDH levels were not influenced by serum LDH levels. The optimal threshold for pleural fluid LDH was 175 IU/L.

Conclusion: The pleural fluid to serum protein ratio and pleural fluid LDH had excellent diagnostic accuracy in classifying the pleural fluid type. A single test pleural fluid LDH had diagnostic performance higher than or comparable to most of the other biochemical parameters.

Key Words : Transudate, Exudate, Lactate dehydrogenase, Cholesterol, Albumin gradient.

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Introduction

Clinical evaluation of a patient with pleural effusion relies heavily upon the examination of the fluid which is obtained by thoracentesis. Defining the exact aetiology is difficult and is not always possible. The pleural effusion is most conveniently separated into trasudate (ultra filtrates of plasma resulting from increased hydrostatic pressure or profoundly decreased serum oncotic pressure) and exudate (protein-rich effusions resulting from increased capillary permeability depending upon their characteristics)[1],[2]. Such discrimination directs towards the nature of the underlying disorder and is helpful in narrowing down the possible aetiologies. A transudative effusion might not warrant further diagnostic procedures, whereas in exudative effusion, further detailed investigations might need to be carried out to establish the cause. Multiple biochemical markers are used to differentiate the exudates from the transudates. The conventional method for classifying the pleural fluid is based on Light's criteria. As per Light's criteria, an effusion is termed as exudative if the pleural fluid to serum ratio of the total protein (TPR) is >/= 0.5, if the pleural fluid absolute lactate dehydrogenase (LDH) level is >/= 200 IU/L, or if the pleural fluid to serum ratio of LDH (LDHR) is >0.6 and as transudative if the TPR is <0.5, if the fLDH level is <200 IU/L and the LDHR is <0.6. The aim of the present study was to evaluate the diagnostic accuracies of the pleural fluid protein, pleural fluid lactate dehydrogenase, pleural fluid total cholesterol and pleural fluid bilirubin, their ratios to serum values and pleural fluid albumin as well as the albumin gradient (serum-fluid albumin) in differentiating pleural fluids into transudates and exudates [3].

Materials And Methods

The present study was carried out at the Government Medical College and Hospital, Aurangabad and was approved by the institutional ethical committee. A total of 50 patients having pleural effusions and suffering from various diseases were included in this study. Pleural fluids and blood samples were taken simultaneously in the fasting state. The blood and pleural fluids were collected in plain sterile bulbs. Serum and pleural fluid LDH was estimated by a modified IFCC method [4].

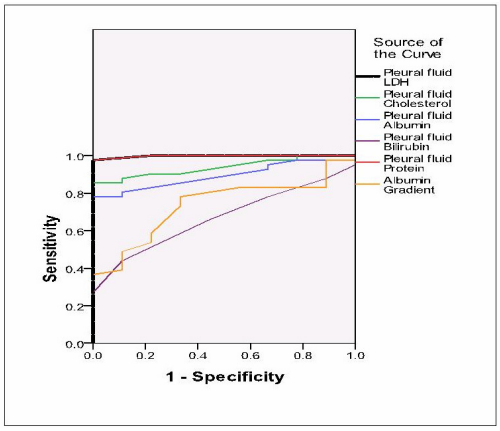
Serum and pleural fluid total protein was estimated by the Biuret method [5],[6],[7]. Serum and pleural fluid albumin was estimated by the BCG dye binding method [7],[8],[9]. Serum and pleural fluid cholesterol was estimated by the CHOD-PAP method [10]. The pleural fluid to serum ratio of the above mentioned markers were calculated. The albumin gradient was calculated by computing the difference between the serum and pleural albumin levels. The enrolled subjects were grouped into exudates and transudates based on Light's criteria [11],[12],[13],[14],[15],[16],[17].

Statistical Analysis

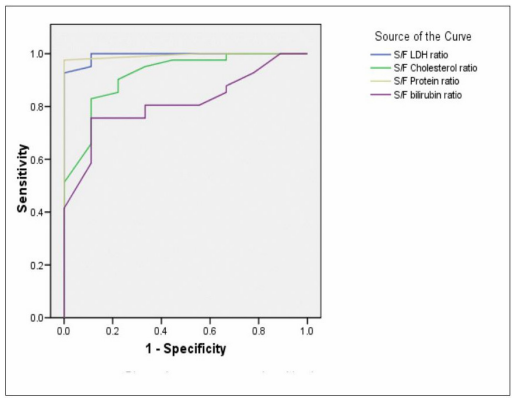
ROC curves were drawn for individual markers and the areas under the curve were computed and compared using SPSS version 17. The optimal cut off with a combination of highest sensitivity and specificity was defined from the table of coordinates of the parameters (based upon the value with the highest sum of sensitivity and specificity).

Results

A total of 50 patients with pleural effusions were analysed. In nine, the pleural effusions were transudative and the remaining 41 of the 50 were exudative, as per Light's criteria. The socioeconomic and the nutritional aspects of the groups were comparable. The ROC curves of individual biochemical parameters (pleural fluid value) and their ratio/difference with serum values are depicted in [Table/Fig 1] and [Table/Fig 2]. The numerical values of optimal threshold with their sensitivity/specificity are shown in [Table/Fig 3]. Values of area under curve for each parameters is shown in [Table/Fig 4]. The pleural fluid levels of LDH and total protein and their ratios with serum levels had the highest value of AUC and fluid bilirubin had the lowest value.



(Table/Fig 1)



(Table/Fig 2)

(Table/Fig 3)The optimal discriminatory cut off values for each parameter in differentiating exudates from transudates.

Test variable	Discriminatory cut off value	Sensitivity %	Specificity %
Pleural fluid LDH	175	100	78
Pleural fluid Cholesterol	18.5	100	22
Pleural fluid Protein	2.2	100	78
Pleural fluid Bilirubin	0.75	44	89
Pleural fluid Albumin	0.8	95	33
F/S LDH ratio	0.54	100	88
F/S Cholesterol ratio	0.39	83	89
F/S Protein ratio	0.42	97	100
F/S bilirubin ratio	0.72	76	89
Albumin gradient	1.25	80	67

F = Pleural fluid and S = Serum

(Table/Fig 4) area under ROC curve for individual biochemical parameter/ratios

Test Result Variable(s)	Area under curve
Pleural fluid LDH	0.99
Pleural fluid Protein	0.99
Pleural fluid Cholesterol	0.94
Pleural fluid Albumin	0.89
Pleural fluid Bilirubin	0.67
F/S LDH ratio	0.99
F/S Cholesterol ratio	0.92
F/S Protein ratio	0.99
F/S bilirubin ratio	0.81
Albumin gradient	0.74

F = Pleural fluid and S = Serum

Correlation between serum levels and pleural fluid levels of different parameters is shown in [Table/Fig 5]. All parameters other than LDH showed a significant correlation between serum and pleural fluid values.

(Table/Fig 5) Correlation between serum levels and pleural fluid levels of biochemical parameters

Parameter	Correlation coefficient (r)	P value
Protein	0.36	0.01
Albumin	0.64	0.00
LDH	0.12	0.38
Cholesterol	0.31	0.03
Bilirubin	0.60	0.00

Discussion

Differentiating the pleural fluid in a transudate or an exudate is an important step in the evaluation of pleural effusions. The conventional method which is used to classify pleural fluid is the Light's criteria, which is based upon the pleural fluid to serum protein ratio, pleural fluid LDH levels and the pleural fluid to serum LDH ratio. The accuracy of these tests has been reported to be 100% [18]. However, classifying pleural effusion on the basis of the above mentioned criteria needs the measurement of 4 biochemical parameters, the pleural fluid total protein, serum total protein, pleural fluid LDH and serum LDH levels. As an individual parameter, each of the above parameters has different sensitivities and specificities and pleural fluid LDH has been reported to be the more sensitive and specific than the total protein ratio or the LDH ratio [19], [20]. In our study, we observed an excellent discriminatory accuracy of pleural fluid protein and LDH levels (and their ratios with serum), AUC 0.99. Pleural fluid cholesterol and its ratio with serum also had good discriminatory ability with AUC >0.9. Pleural fluid bilirubin and the albumin gradient had the

least discriminatory accuracy. These observations reaffirm the utility of Pleural fluid to serum protein and the LDH ratio , as well as pleural fluid LDH levels in differentiating exudative pleural effusions.

The basis for using the pleural fluid to serum ratio of protein and LDH (rather than using absolute pleural fluid levels) is that their pleural fluid levels might be influenced by the changes in serum levels and so, absolute pleural fluid levels might give erroneous results in the face of varying serum levels. In our study, the pleural fluid levels of all biochemical parameters other than LDH showed a statistically significant correlation with serum values (though the correlation coefficient was poor for most parameters). The pleural fluid LDH levels were not influenced by the serum levels and hence, pleural fluid LDH can independently (rather than its ratio to the serum level) be used in classifying pleural effusion. Our observation is similar to the report by Joseph et al and it is suggested that in classifying pleural fluid, the absolute fluid value rather than its ratio with serum levels, should be used as it will save the cost of serum testing. Further, there is a possibility of the misclassification of the pleural fluid into exudates in the face of low serum LDH levels, as low serum LDH levels can result in high LDHR, thus causing the false classification of a transudate as an exudates [20].

The optimal cut off of pleural fluid LDH levels to define exudates as per Light's criteria is >200 IU/L. The optimal threshold for pleural fluid LDH in our study was much lower (175 IU/L) than those suggested by Light. Similarly, a lower cut off point (163 IU/L) has been reported by Joseph et al [20]. We suggest that the optimal threshold for pleural fluid LDH levels should be redefined and validated in a larger study with a higher number of subjects.

Conclusion

To summarize that pleural fluid to serum protein ratio and pleural fluid LDH have excellent diagnostic accuracy in classifying the pleural fluid type. A single test, the pleural fluid LDH has a performance which is comparable to the other parameters. The optimal cut off point of pleural fluid LDH still needs to be addressed.

References

[1] Wilson et al. Harrison's principles of internal medicine. 12th ed. 1991. P. 1111-6,

[2] Cotran RS, Kumar V, Robbins SL. Robbins pathologic basis of disease. 4th ed. Philadelphia: W.B. Saunders International Edition; 1989. P. 39-41.

[3] Light RW, Macgregor MI, Luchsinger PC, Ball WC. Pleural effusions: The diagnostic separation of transudates and exudates. Ann Int Med 1972;77:507-13.

[4] Recommendations for the measurement of LDH in human serum at 30 c. Ann Biol Chem 1982;40:87.

[5] Tietz NW. Text book of Clinical Chemistry. Philadelphia: W.B. Saunders Co; 1986. P. 579-82.

[6] Reinholdnjg. In standard methods of clinical chemistry. New York and London Academic Press;1953; 1: 88.

[7] Alan H Gowenlock. Varley's practical clinical biochemistry. 6th ed. Delhi: CBS Publishers; 1988. P. 407-8.

[8] Douman et al. Standard methods of clinical chemistry. Chicago: Academic press; 1972. P. 175-89.

[9] Doumas BT, Watson WA, Biggs HG. Clin Chim Acta 1971;31:87.

[10] Allain CC et al. Enzymatic determination of total serum cholesterol. Clin Chem 1974;20:470-5.

[11] Jain AP, Gupta OP, Khan N. Comparative diagnostic efficiency of criteria used for differentiating transudate and exudates pleural effusions. J A P I 1982; 30 (11):823-6.

[12] Ortega L, Heredia JL, Armengol R, Mir I Romanillas T, Armengol J. The differential diagnosis between exudates and transudates: the value of cholesterol. Med Clin (Barc) Spanish 1991; 96(10):367-70.

[13] Lakhotia M, Shah PKD, Yadav A, Gupta A, Modi RK, Sinha HV. Comparison of biochemical parameters in pleural effusion. J A P I 1996;44: 612-4.

[14] Heffner JE, Brown LK, Barbieri CA. Diagnostic value of tests that discriminate between exudative and

[15] transudative pleural fluids - primary study investigators. Chest 1997;111(4):970-80.

[16] Gazquez I, Porcel M, Vives M, Vicente de, Vera MC, Rubio M et al. Comparative analysis of Light's criteria and other biochemical parameters for distinguishing transudates from exudates. Respir Med 1998;92:762-5.

[17] Light RW. Diagnostic principles in pleural disease. Eur Respir J 1997;10(2): 476-81.

[18] Jay SJ. Diagnostic procedures for for pleural disease. Cli Chest Med 1985; 6: 33-48

[19] Chandrasekhar AJ, Palatao A, Dubin A et al. Pleural fluid lactic acid dehydrogenase activity and protein content. Value in diagnosis. Arch Intern Med 1969; 123: 48-50

[20] Joseph J, Badrinath P, Basran GS, Sahn SA. Is the pleural fluid transudate or exudates? A revisit of the diagnostic criteria. Thorax 2001; 56: 867-70