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ORIGINAL ARTICLE

Cut-off value of pleural fluid C-reactive protein in etiologic diagnosis of pleural fluid



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KEYWORDS

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Abstract *Background:* Classification of effusion into transudates or exudates is considered as the corner stone in the etiological diagnosis of pleural effusion.

Objectives: To determine the validity of pleural fluid (high sensitivity-CRP) concentration in etiologic diagnosis of pleural effusion and to obtain a cut-off value of pleural fluid CRP at which we can discriminate between exudative and transudative pleural effusions.

Patients and methods: A study was conducted upon a hundred patients with pleural effusion. All patients were subjected to: history, clinical examination, chest radiography and thoracic ultrasound, tuberculin test and aspiration of pleural fluid. The fluid was sent for biochemical examination including: Protein, L.D.H, A.D.A and CRP levels, cytological examination and bacteriologic examination. Classification of pleural fluid into transudative or exudative is based upon Light's criteria. Data were compared by independent sample *t*-test for 2 groups or by a one-way analysis of variance (ANOVA) for more than 2 groups of variables. Simple correlations between variables were examined by calculating Pearson's product correlation coefficient, Receiver operating characteristic (ROC) curve used to calculate cut off points, area under the curve (AUC), sensitivity and specificity, and 2 tailed $P < 0.05$ was considered significant.

Results: There were significant differences between both groups as regards serum, fluid levels and fluid/serum ratio for LDH, total protein and CRP except for CRP fluid/serum ratio. There was a significant correlation between CRP and LDH and total protein fluid levels. Receiver operating characteristic (ROC) curve was used to calculate the sensitivity and specificity of CRP fluid level and also the cut off value of CRP fluid level. Out of the 44 patients with exudative pleural effusion, two cases were diagnosed as cardiac effusion and one case as liver cirrhosis. The three cases were receiving diuretics and the pleural fluid analysis was repeated after withdrawal of the diuretics which turned to be transudative according to Light's criteria.

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Conclusion: CRP could be a useful diagnostic marker for differentiation between exudative and transudative pleural effusions and also it is more accurate than protein in distinguishing those transudative effusions receiving diuretic therapy which are falsely diagnosed by Light's criteria to be exudates.

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Introduction

Pleural effusion is defined as an accumulation of fluid in the pleural space that exceeds the physiological amount of 10–20 ml, pleural effusion develops either when the formation of pleural fluid is excessive and or when the fluid resorption is disturbed. Pleural effusions may represent as a primary manifestation of many diseases but most often they are observed as 2ry manifestations or complications of other diseases [1].

The following tests are used in etiologic diagnosis of pleural effusion: (Protein in pleural fluid, pleural fluid protein/serum protein ratio, bilirubin ratio, lactate dehydrogenase in pleural fluid, lactate dehydrogenase ratio, cholesterol in pleural fluid, cholesterol ratio, and albumin gradient). All eight tests had similar diagnostic accuracies except for the bilirubin ratio which was less diagnostically accurate [2].

C-reactive protein is an acute phase protein synthesized mainly in hepatocytes in response to tissue inflammation in individuals. Pleural Fluid CRP level was significantly higher in exudates than that in transudative effusion [3].

In a previous study; pleural fluid-C-reactive protein was considered a useful diagnostic tool to differentiate pleural effusion of bacterial origin from others [4].

The aim of this current study is to determine the validity of pleural fluid high sensitivity-CRP concentration in etiologic diagnosis of pleural effusion and to obtain a cut-off value of pleural fluid CRP at which we can discriminate between exudative and transudative pleural effusions.

Patients and methods

This prospective study was conducted upon a hundred patients with pleural effusion who were admitted to the Abbasia Chest Hospital in the period between March 3, 2012 and March 3, 2013.

All patients were subjected to: history, clinical examination, chest radiography and thoracic ultrasound, Tuberculin test: using 5 units P.P.D in 0.1 ml intradermal injection, laboratory investigation including:

- a. Serum Protein, L.D.H and hs C.R.P.
- b. Liver and kidney functions.
- Collection and preservation: Blood samples were fresh or stored for a maximum of one week at 2 °C.
- Serum C.R.P. was analyzed by the quantitative immunometric assay method in machine (Nycocard: CRP Single Test).
- Standardization: Nycocard CRP single test is calibrated against ERM-DA470 (CRM 470), IFCC/BCR/CAP reference preparation.
- Measuring range: serum or plasma samples 5–120 mg/L.

Aspiration of pleural fluid was done and was sent immediately for the following:

- a. Biochemical examination including: Protein, L.D.H, A.D.A and CRP levels.
- b. Cytological examination.
- c. Bacteriologic examination: Gram-staining, Ziehl–Neelsen stain and culture.

Tissue biopsy

One of the following was done according to case:

- Ct guided biopsy.
- Abram's needle pleural biopsy.
- Classification of pleural fluid into transudative or exudative is based upon Light's criteria which are:
 - Total fluid protein is less than half of that of the total serum protein level in case of transudative pleural effusion.
 - Fluid Lactate Dehydrogenase (LDH) is less than 0.6 of that of the serum LDH in case of transudative pleural effusion.
 - Pleural fluid LDH is less than two thirds the upper limit of the normal of that of the serum level in the case of transudative pleural effusion [2,16].
- Effusions were considered malignant if malignant cells were found on the cytology examination of pleural fluid or in the pleural biopsy specimens,
- The diagnosis of tuberculous pleurisy was based upon high tuberculin positivity, lymphocytic pleural fluid, few mesothelial cells, elevated ADA level in pleural fluid or pleural biopsy showing caseating granuloma.
- Criteria for parapneumonic effusion were; clinical, biochemical and radiological signs of suspected acute inflammation, positive Gram staining, positive culture for bacteria or neutrophil predominance in pleural effusion [1,5].

Data analysis

Data are presented as mean \pm SD for continuous variables or frequency (percentage %) for categorical variables. Data were compared by independent sample *t*-test for 2 groups or by a one-way analysis of variance (ANOVA) for more than 2 groups of variables. Simple correlations between variables were examined by calculating Pearson's product correlation coefficient, Receiver operating characteristic (ROC) curve used to calculate cut off points, area under the curve (AUC), sensitivity and specificity, and 2 tailed $P < 0.05$ was considered significant.

Analysis of data was performed using Statistical package for Social Science (SPSS 15.0.1 for windows; SPSS Inc., Chicago, IL, 2001).

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