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SIGNIFICANCE OF C REACTIVE PROTEIN IN DIAGNOSTIC APPROACH OF PLEURAL EFFUSION

Community Medicine

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ABSTRACT

Present study included 115 Pleural Effusion patients. Pleural fluid were collected and separated as Transudate and Exudate. Further analysis determined the provisional diagnosis of exudates. Pleural Fluid C-Reactive Protein(CRP) concentrations indicated towards diagnosis and severity of exudates. CRP in pleural fluid is a helpful tool in diagnosis and monitoring of pleural effusion patients.

KEYWORDS

Pleural effusion,Exudate, CRP

INTRODUCTION:

Pleural effusion is described as abnormal accumulation of fluid in pleural space (more than 10-20 ml). It develops when production of pleural fluid is excessive or when pleural fluid resorption is less. Usually pleural effusion develops as a secondary manifestation or as a complication resulting from other diseases [1]. Diagnosis and management of pleural effusion becomes a challenge because of its causative role in a number of diseases. It may be transdudate, exudate, benign or malignant. The dilemma still exists, since management differs in different outcomes [2]. Furthermore, many false negative cases have been reported regarding cytological examination of pleural fluid [3]. C Reactive Protein (CRP) is considered as a sensitive and non-specific marker of systemic inflammation. CRP synthesis is stimulated by a number of cytokines like interleukin-6 which are released at inflammatory region [4]. Raised (S) CRP levels has been found in many pulmonary diseases like pneumonia,malignancies and thromboembolisms[5]. However, a very few studies have been reported regarding value of CRP in differential diagnosis of pleural fluid in pleural effusion. So the present study has been undertaken to evaluate the CRP levels in differential diagnosis of pleural effusion at our region, so that the CRP analysis can indicate towards the diagnosis in pleural effusion.

MATERIALS AND METHODS:

Study design- This hospital based, cross sectional study was conducted in the Department of Biochemistry, Calcutta National Medical College, Kolkata, West Bengal from January 2018 to June 2018.

Selection of case group- The study group includes 115 adult(age group between 25 – 55 years) patients (79 male and 36 female) admitted with provisional diagnosis of pleural effusion.

All patients were subjected to

(a) Medical history and clinical examinations.
(b) (S) Lactate Dehydrogenase(LDH) and CRP.
(c) Liver and renal function tests.
(d) Plain chest radiography (Anteroposterior and lateral view).
(e) Tuberculin skin testing, in case of suspected tubercular pleuricy.
(f) Diagnostic thoracocentesis- Collection and processing of pleural fluid(appx 300-500 ml) which is subjected to following examinations.

i) Physical examinations.
ii) Biochemical examinations include protein levels, TC,DC, Adenisine Deaminase(ADA) for suspected tubercular effusions.
Iii) Bacteriological examinations.
iv) Cytological examinations for malignant cells.
v) Quantitative measurement of pleural fluid CRP.
(vi) CT guided biopsy.

EXCLUSION CRITERIA:

a) Patient being under radiotherapy or chemotherapy.
b) Empyma
c) Immunocompromised patients.
d) Patient with poor general conditions.
e) Quantity of pleural fluid is insufficient.
f) Congestive heart failure

Classification of pleural fluid into transudate or exudates is based upon Light's criteria by one or more of the following:

a) Ratio of LDH in pleural fluid to that of serum is more than 0.6 (exudates).
b) Ratio of total protein in pleural fluid to that of serum is more than 0.5 (exudates).
c) Pleural effusion LDH level is more than two third of upper limit of lab reference of (S) LDH (exudate).

Different exudate groups included in the present study are Tuberculosis, Malignancy, Parapneumonic and chronic non-specific

- Diagnosis of tuberculous pleurisy was based upon high tubercular positivity in tuberculin test, lymphocytic predominance, and elevated ADA level in pleural fluid.
- Effusions were considered malignant if malignant cells were found in cytological examination or by pleural biopsy.
- For parapneumonic effusion, clinical, biochemical and radiological signs of suspected acute inflammation, positive bacterial culture and neutrophil predominance.

Measurement of CRP: CRP analysis was performed by Autoanalyzer Konelab Prime 600 i using an immunoturbidimetric method. The diagnostic reagent used for analysis was GmBH (Hamburg Germany). Normal value < 5 (according to the kit literature)[6].

Statistical methods used: Statistical analysis was done by Independent t test and ANOVA. P value <0.05 was considered as significant.

Data collection and processing for statistical analysis:
Statistical analysis was aimed

- To asses the significance of difference between the mean values of CRP between transudate and exudates.
- To asses the significance of difference between the mean values of CRP within the different groups of exudates.

RESULTS:

One hundred and fifteen patients suffering from pleural effusion were participated in the study. Pleural fluid of twenty three patients were diagnosed as transudate, the same of ninety two patients were diagnosed as exudates according to Light's criteria.

TABLE 1- Serum mean CRP levels and significance between transudative and exudative pleural fluid.

Biochemical parameters	Transudative pleural fluid(n=23) Mean±SD	Exudative pleural fluid(n=92) Mean±SD	Standard error of mean	95% CI	Significance
(S)CRP (mg/L)	19.50±3.99	46.54±28.41	5.95	15.23-38.84	P<0.0001

Table 2- Mean values of different subgroups of exudative pleural effusion.

Biochemical parameter	Malignant pleural effusion (n=19) Mean±SD	Tubercular pleural effusion(n=31) Mean±SD	Parapneumonic pleural effusion(n=29) Mean±SD	Chronic nonspecific pleural effusion(n=13) Mean±SD
(S) CRP (mg/L)	26.73±4.36	34.40±3.48	86.71±5.27	14.84±3.04

	Sum of squares	df	Mean square	F	P
Between	71883.86	3	23961.28	1322.81	0.0000
Within	1594.02	88	18.114		
Total	73477.88	91			

TABLE 3- ANOVA showing significance between and within the subgroups of exudative fluid.

DISCUSSION:

The cornerstone of etiological diagnosis of pleural effusion is that whether it is transudate or exudate (7). The excess of 15-20 ml of fluid in pleural space is considered as pleural effusion. It develops from changes in hydrostatic or colloidal osmotic pressure between pleural and pulmonary capillaries, changes in vascular permeability of pleura and impaired lymphocytic drainage (8). CRP is an acute phase protein primarily synthesized and secreted by hepatocytes [9].

The present study was designed to measure the level of CRP in pleural fluid in pleural effusion. Furthermore the measurement of CRP was done in transudate and exudates. The present study selected four types of exudates, like tubercular,malignant, parapneumonic and chronic non-specific.

The results of the present study have clearly shown that there is a significant difference ($p<0.0001$) between the mean values of CRP between transdudate and exudates. Furthermore, significant difference of mean values of CRP also exists between the four groups of exudative fluid within the groups.

In the present study, 20% of total patients were found to have transudate, 16.5% have malignancy, 26.9% were tuberculosis, 25.2% were parapneumonic and 11.3% were non-specific.

In comparision , one study with exudative pleural effusion, the tuberculosis accounts for 67.5%, malignant effusion 25%, chronic non-specific 11%, and parapneumonic 7.5% [10]. Few authors focussed majority as exudative effusion as tuberculosis (58.3%), followed by malignancy (16.7%)[11]. Another study indicated the commonest of pleural effusion was tuberculosis (55.8%), followed by malignancy (44.2%)([12].

From the different studies, accommodated evidence suggested that the most common cause of transudative pleural effusion was heart failure or a low blood protein count whereas CRP is increased in inflammartory conditions [13,15,18]. Classification of transudate and exudates in pleural effusion mainly based on Light's criteria [19].However, as the exudative group includes many subtypes, in order to achieve a particular diagnosis, some more tests have entered like ADA in blood, cytological examination or bacterial culture.

Antibiotic therapy in parapneumonic effusion and diuretic therapy misdiagnose the conditions.CRP can be measured in pleural fluid after withdrawal of diuretics [20].

Recently many studies have focused on CRP in pleural effusion [21,22,23] .

The present study tried to evaluate the CRP levels in different subtypes of exudative pleural effusion.

Vidriales et al documented that, the CRP levels were highly elevated in inflammatory conditions than others [21]. They also indicated that pleural to serum CRP ratio was significantly elevated in

exudative effusions. Furthermore, they observed the high ratio in parapneumonic and tubercular effusions than malignant effusions.

Turay et al [17] observed that the serum CRP levels are generally elevated in infective conditions, but usually they do not consistent in all bacteriaemic process.

In tubercular pleural effusion, the CRP levels were lower than parapneumonic effusions but as an indicator of inflammation, they are higher than those found in transudates. Vidriales et al [21] observed the CRP levels were twice as high in tuberculosis than in malignancy.

In conclusion, pleural fluid CRP levels may be an useful marker of exudative pleural effusion, it reflects the extent of inflammation, therefore indicating towords diagnosis.

In agreement with our results (Significant difference of CRP between transudate and exudates), Alexandrasis et al found the similar trend [13]. Present study was also supported by Ahmed et al [14]. Furthermore, Rezaeetala B et al and Yousuf et al had reported the similar type of results [15,16]. The later study also demonstrated the higher level of CRP in exudative effusion ,than that of transudative effusion [16].

The results of the present study have shown the significant difference of mean CRP levels ($P<0.0001$) between subtypes of exudative fluid.

Yilmaz et al [17] suggested that the pleural fluid CRP can be used as differential diagnosis of exudative pleural fluid. They had the subgroup of parapneumonic,tuberculosis and malignant effusion.

From the different studies, accommodated evidence suggested that the most common cause of transudative pleural effusion was heart failure or a low blood protein count whereas CRP is increased in inflammartory conditions [13,15,18]. Classification of transudate and exudates in pleural effusion mainly based on Light's criteria[19]. However, as the exudative group includes many subtypes, in order to achieve a particular diagnosis, some more tests have entered like ADA in blood, cytological examination or bacterial culture.

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