



Evaluation of Pleural Fluid C-reactive Protein Level in Differentiation of Transudative and Exudative Pleural Effusion

Vyankatesh T. Anchinmane^{1*}, Shilpa Vijay Sankhe²

1. Professor, Department of Pathology, Zydus Medical College and Hospital, Dahod, Gujarat, India.
2. Tutor, Department of Pathology, Zydus Medical College and Hospital, Dahod, Gujarat, India.

*Corresponding author's E-mail: vyankatesha78@gmail.com

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ABSTRACT

The therapeutic strategy of any pleural effusion case depends upon diagnostic approaches which determine the nature of pleural effusion. Timely diagnosis of etiology of pleural effusion is very crucial to reduce morbidity and mortality associated with the same. The pleural effusions are broadly categorized into two groups- transude and exudate. The misclassification of transude as exudate and vice versa, may leads to wrong diagnosis and loss of initial crucial time of management. The present study was undertaken to analyze diagnostic role of pleural fluid C - reactive protein (CRP) level for the differentiation of transudative and exudative pleural effusion. Based on etiology, all 100 cases were divided into two groups of exudates and transudates. The 56 cases were exudates, due to malignancy, tuberculosis and pneumonia diseases. The remaining 44 cases were transudates due to anaemia-hypoproteinemia, liver cirrhosis, chronic heart disease and chronic renal disease. All 100 cases pleural fluids were analyzed for CRP level marker with autoanalyser. The statistical analysis was done with SPSS software. The 10 mg/dl cut-off for the pleural effusion CRP level had the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of 96.4 %, 93.1 %, 95.0 %, 94.7 % and 95.3 %, respectively for differentiating transudative and exudative pleural effusion. The results obtained in our study concluded that the CRP level in the pleural effusion fluid is useful parameter in diagnosing transudative and exudative nature of pleural effusions.

Keywords: Pleural effusion, CRP, transude and exudate.

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INTRODUCTION

In the daily clinical practice, accurate diagnosis and establishment of the etiology of pleural effusion is an ongoing challenge. The global incidence of pleural effusion is estimated to be approximately 3 million cases per year. The transudative effusions are generally due to medical diseases chronic renal disease, chronic heart disease, anemia-hypoproteinemia, liver cirrhosis etc. and are treated by medical treatment. The exudative effusions are generally due to tuberculosis, malignancy like reasons, which need biopsy like invasive investigative modalities, for further confirmation of diagnosis and surgical / medical treatment of the cause.¹

Various pleural fluid markers like fluid total protein, fluid albumin, fluid ADA, Serum albumin effusion gradient (SAEG), fluid cholesterol, fluid pH, fluid glucose, lights criteria etc. have been utilized in past for pleural fluid differentiation into transudate and exudate.^{2,3} Recently, markers like pre-albumin, C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-a)

were analyzed for their accuracy for pleural fluid differentiation.⁴

The exudative pleural effusion is developed due to inflammatory responses. The C-reactive protein (CRP) is synthesized in the hepatocytes and is an inflammatory marker.⁵ Hence, many studies have been conducted to analyse the accuracy of pleural fluid CRP, for exudative and transudative pleural effusions differentiation. The results showed the possibility of CRP to utilize it as a pleural fluid study marker.^{6,7,8} There were some studies which also showed that pleural fluid CRP works well to distinguish amongst the exudative effusions.⁹ The present study was conducted to analyse the accuracy of pleural fluid CRP level for pleural fluid differentiation into transude and exudate.

MATERIALS AND METHODS

The study was done in tertiary care hospital central laboratory in the period from January 2022 to June 2022. The 100 pleural fluids received in the laboratory were analyzed for CRP level. The blood samples received were processed sugar, LFT, RFT and lipid profile. In malignancy cases, cytology investigation was done for fluid malignant cells. Tuberculosis cases were confirmed by sputum or fluid specimen, after processing with Ziehl-Neelsen stain and culture. Malignancy cases were confirmed with histopathology and radiological investigations.

The cases were labeled as anemia-hypoproteinemia, chronic heart failure (CHF), chronic renal failure (CRF), liver cirrhosis, pneumonia, tuberculosis, malignancy, as per the



clinical history and laboratory and radiological investigations.

All pleural fluids were categorized as transudate and exudate as per etiology. Pleural fluids CRP level were obtained on autoanalyser, using an immuno-turbidometric method. Pleural fluid CRP level with cut off of more than 10 mg/dl was utilized to label the case as exudates.

The SPSS software was used to evaluate pleural fluid CRP for accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), for

differentiating pleural effusions into transudate and exudate.

RESULTS AND DISCUSSION

Out of 100 cases, 71 were male and 29 were female patients and their age ranges from 26 to 79 years. As per etiology, total 56 were exudates and 44 were transudative pleural effusions. The causes of exudative effusions were tuberculosis, pneumonia, malignancy. The transudative effusions diagnosis was anemia-hypoproteinemia, chronic heart failure (CHF), chronic renal failure (CRF), Cirrhosis. (Table 1)

Table 1: Etiological distribution of pleural effusion

Disease	Exudate	Transudate	Total number of cases
Tuberculosis	25	-	25
Pneumonia	19	-	19
Malignancy	12	-	12
Cirrhosis	-	18	18
Anemia-hypoproteinemia	-	12	12
CRF	-	09	09
CHF	-	05	05
Total	56	44	100

Table 2: CRP test evaluation for differentiation of transudative and exudative pleural effusion

	Exudate	Transudate	Total	Predictive value (PV)
CRP > 10 mg/dl	54	03	57	PPV (94.7 %)
CRP < 10 mg/dl	02	41	43	NPV (95.3 %)
Total	56	44	100	
	Sensitivity (96.4 %)	Specificity (93.1 %)	Accuracy (95 %)	

The CRP level analysis was done for 100 pleural fluid samples with CRP cut off level of 10 mg/dl. Pleural fluid was considered as exudate for CRP level 10 mg/dl and above and CRP level less than 10 mg/dl were labeled as transudate. (Table 2)

As per etiology, the 56 pleural effusions were categorized as exudate, of which, 54 pleural fluid samples showed the pleural fluid CRP level more than 10 mg/dl and confirmed the exudative nature of pleural fluids. The 44 pleural fluid cases shows transudative etiology like CRF, CHF, cirrhosis etc., of which 41 pleural fluid samples confirmed transudative nature of fluid, with their fluid CRP level less than 10 mg/dl. Hence, the pleural fluid CRP level showed Sensitivity, Specificity, Accuracy, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of 95.4 %, 93.1 %, 95 %, 94.7 % and 95.3 % respectively, for differentiation of pleural fluids into transudates and exudates. (Table 2)

The pleural fluids were classified into transudate and exudate as per Light's criteria in 1972. Later in 2013, Light et al himself submitted that 25% cases of transudates were categorized as exudates due to Light's criteria.¹⁰ The similar

finding was also observed by Romero-Candeira S et al.¹¹ Several studies were done with various markers including CRP for analysis of pleural fluids.^{2,3}

CRP, an acute phase reactant protein, is utilized as marker of inflammation and tissue injury. As response to various stimuli, CRP is produced in liver and its production accentuated by TNF- alpha and IL-6. Serum CRP levels increases in including bacterial infections, malignancies and a number of pulmonary disorders. The serum CRP level has co-relation with pleural fluid CRP level as inflamed capillary leakage leads to increased diffusion of CRP from blood to pleural fluid.⁵

CRP was studied worldwide to differentiate transudates and exudates. It was also studied to differentiate exudates into its etiological reasons like tuberculosis, malignancy, pneumonia etc. However, there is no validation for CRP cut off level. Majority study done ROC analysis to find suitable CRP cut off for their institute/ regional level.^{2,7,9}

Alexandrakis MG et al in his study showed that CRP with cut off of 1 mg/dL had a good accuracy for differentiating

transudates and exudates.¹² Mansour et al submitted in his study that mean pleural fluid CRP level was 5.7 ± 0.9 mg/dl in transudates and 16.1 ± 7.2 mg/dL in exudates and was statistically significant with $P=0.0001$.¹³ In the study done by Gabhale SD et al, the pleural fluid CRP level cut off of 30 mg/L showed better sensitivity for excluding the malignancy.¹⁴ Rismantab O et al in his study showed that the CRP cut off level of 3.31 mg/dl had sensitivity, specificity, PPV and NPV of 96.3%, 72.1%, 86% and 91.7% respectively for differentiating exudative from transudative pleural effusions.⁶ Watanabe et al. showed that with pleural fluid CRP cut-off 4.91 mg/dL the sensitivity 63.6% and specificity 89.3% for discrimination of exudative and transudative pleural effusion.⁷ In the study done by Babu AS et al the CRP cut off value 10 mg/L and 20 mg/L showed sensitivity of 92.86% and 100% respectively and specificity of 40% and 50% respectively, for distinguishing transudative and malignant pleural effusion.⁸ In the present study, with accuracy of 95%, the pleural fluid CRP level maker findings were consistent with previous studies for differentiation of transudates and exudates in pleural fluid.

The small sample size of 100 pleural fluid samples study is the limitation of this study. Hence, further etiological classification amongst exudative samples was not done in this study.

CONCLUSION

Pleural fluid CRP is a statistically significant, inexpensive, simple and rapid method, for differentiation between transudative and exudative pleural effusions. Pleural fluid CRP can be used as an additional marker along with conventional fluid protein, Light's criteria like markers, for better accuracy, in confirmation of transudative and exudative nature of pleural effusion sample. More studies needed to be conducted worldwide with larger sample size, for the validation of CRP cut off level, in all routine clinical circumstances.

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For any questions related to this article, please reach us at: globalresearchonline@rediffmail.com

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