ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 8, Issue – 3, June – 2023 , Page No. : 83 – 88

Prospective study of pleural fluid c-reactive protein for differentiation between tubercular and malignant pleural effusion at IRD, SMS medical college Jaipur.

[1]Dr. Pramraj Meena, Junior Resident, Institute of Respiratory Diseases, S.M.S Medical College, Jaipur.
[2]Dr. Mohmmad Javed Qureshi, Associate Professor, Institute of Respiratory Diseases, S.M.S Medical College, Jaipur.
[3]Dr. Chand Bhandari, Senior Professor, Institute of Respiratory Diseases, S.M.S Medical College, Jaipur.
[4]Dr. Batoee Ram Meena, Senior Resident, Institute of Respiratory Diseases, S.M.S Medical College, Jaipur.
[5]Dr. Manoj Saini, Assistant Professor, Institute of Respiratory Diseases, S.M.S Medical College, Jaipur.

Corresponding Author: Dr. Pramraj Meena, Junior Resident, Institute of Respiratory Diseases, S.M.S Medical College, Jaipur.

Citation this Article: Dr. Pramraj Meena, Dr. Mohmmad Javed Qureshi, Dr. Chand Bhandari, Dr. Batoee Ram Meena, Dr. Manoj Saini, "Prospective study of pleural fluid c-reactive protein for differentiation between tubercular and malignant pleural effusion at IRD, SMS medical college Jaipur", IJMSIR- June - 2023, Vol – 8, Issue - 3, P. No. 83 – 88.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: CRP has been used along with other markers to identify causes of pleural effusion. However, there are few studies conducted specifically to determine the cutoff of CRP for differentiating tubercular pleural effusion from malignant pleural effusion.

Methods And Material: The hospital-based cross-sectional observational study was done on 40 patients of pleural effusion with etiology of either malignant or tubercular, who attended outdoor patient department (OPD) and admitted at Institute of Respiratory Diseases, S.M.S. Medical College, Jaipur. The information about demographic characteristics (such as age, gender, area of residence); addiction; and symptoms was collected. All of them underwent baseline investigations of pleural fluid, CRP and ADA levels.

Results: Mean ± SD of age(years) in MPE was 55.56 ± 8.61 which was significantly higher as compared to TBPE (38 ± 17.24). Median (25th-75th percentile) of pleural fluid CRP (mg/dL) in TBPE was 38.55(36.15-41.55) which was significantly higher as compared to MPE (18.2(16.2-20.225)) (p value <0.0001). Significant positive correlation was seen between pleural fluid ADA (U/L) with pleural fluid CRP (mg/dL) with correlation coefficient of 0.692.

Conclusion: Our study indicate that ADA and CRP are useful markers for differentiating the different types of pleural effusion and differentiate tuberculous and MPE. Pleural fluid CRP can be a reliable novel, noninvasive in nature can be used in routine test for predictive TBPE in resources limited settings.

Introduction

Pleural effusion is "an abnormal collection of fluid in the pleural space resulting from excess fluid production or decreased absorption." In India, tubercular effusion is the most frequent cause of exudative effusions, followed by malignant effusion.[1]

The distinction of TB and malignant effusion demands various investigations which include pleural fluid cytology analysis, histological examination of surgical tissue biopsy and image-guided biopsy. [2]

The use of various markers such as pleural fluid lymphocytes, neutro phils, eosinophils, lactate dehyd ro genase (LDH), adenosine deaminase (ADA), C-reactive protein (CRP), Among them CRP seems to be an upcoming cheap marker used for this distinction.[3,4] This study evaluates the diagnostic capacity of pleural fluid CRP in the differentiation of tubercular pleural effusion (TBPE) and malignant pleural effusion (MPE), also determine the cut-off which may be the guiding point of distinction between TB and MPE.

Material & methods

This study (Hospital-based cross-sectional observational study) was conducted at the Institute of Respiratory Diseases, S.M.S. Medical College, Jaipur, after approval from the institutional ethics committee and review board.

Total 40 patients were enrolled in which 16 patients had malignant pleural effusion and 24 had tubercular pleural effusion, after applying Inclusion criteria (All confirmed cases of tuberculosis and lung malignancy with pleural effusion.) and Exclusion criteria (Pregnancy and lactation at preliminary presentation, all transudative pleural effusion, exudative effusion other than tuberculosis and lung malignancy, other causes of elevation of pleural fluid CRP level.)

The presentation of the "Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means ± SD and as median with 25th and 75th percentiles (inter quartile range).

The comparison of the "variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used".

The data normality was checked by using Kolmogorov-Smirnov test. The cases in which the data was not normal, we used non parametric tests."

"Spearman rank correlation coefficient was used for correlation of pleural fluid ADA (U/L) with pleural fluid CRP (mg/dL)."

The data entry was done in the "Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) soft ware, IBM manufacturer, Chicago, USA, Ver 25.0. For statistical significance, p value of less than 0.05 was considered statistically significant."

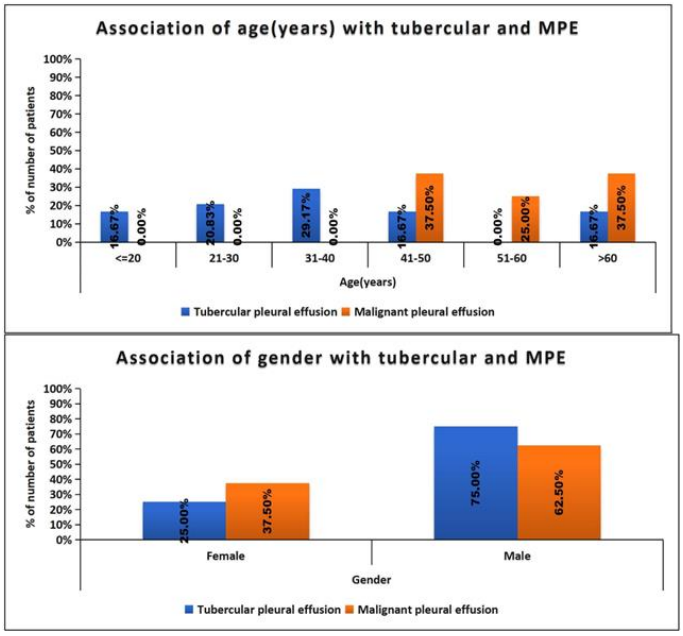
Observations & results

Table 1: Association of demographic characteristics with tubercular and MPE.

Demographic Chara cteristics	TBPE(n=24)	MPE(n=16)	Total	P value
Age(years)				
<=20	4 (16.67%)	0 (0%)	4 (10%)	0.0004*
21-30	5 (20.83%)	0 (0%)	5 (12.50%)	
31-40	7 (29.17%)	0 (0%)	7 (17.50%)	
41-50	4 (16.67%)	6 (37.50%)	10 (25%)	
51-60	0 (0%)	4 (25%)	4 (10%)	

>60	4 (16.67%)	6 (37.50%)	10 (25%)	
Mean ± SD	38 ± 17.24	55.56 ± 8.61	45.02 ± 16.73	0.0001‡
Median (25th-75th percentile)	34(24.75- 43.75)	54.5(49.75- 62)	44.5(32- 60.25)	
Range	17-80	42-69	17-80	
Gender				
Female	6 (25%)	6 (37.50%)	12 (30%)	0.398†
Male	18 (75%)	10 (62.50%)	28 (70%)	

‡ Independent t test, * Fisher's exact test, † Chi square test.



Proportion of patients of ager group: - <=20, 21-30, 31-40 years was significantly higher in TBPE as compared to MPE. (<=20 years: 16.67% vs 0% respectively, 21-30 years: - 20.83% vs 0% respectively, 31-40 years: - 29.17% vs 0% respectively). Proportion of patients of age group: - 41-50, 51-60, >60 years was significantly lower in TBPE as compared to MPE. (41-50 years: - 16.67% vs 37.50% respectively, 51-60 years: - 0% vs 25% respectively, >60 years: - 16.67% vs 37.50% respectively). (p value=0.0004)

Mean ± SD of age(years) in MPE was 55.56 ± 8.61 which was significantly higher as compared to TBPE (38 ± 17.24). (p value=0.0001)

Distribution of gender was comparable between tuber cular and MPE. (Female: - 25% vs 37.50% respecti vely, Male: - 75% vs 62.50% respectively) (p value = 0.398). It is shown in table 1

Table 2: Association of pleural fluid CRP (mg/dL) with tubercular and MPE.

Pleural fluid CRP (mg/dL)	**TBPE(n=24)**	**MPE(n=16)**	**Total**	**P value**
Mean ± SD	38.65 ± 3.3	19.4 ± 4.74	30.95 ± 10.31	<.0001§
Median (25th-75th percentile)	38.55 (36.15-41.55)	18.2 (16.2-20.225)	35.4 (19.025-40.05)	
Range	32-43.8	13.7-32.2	13.7-43.8	

§ Mann Whitney test

Median (25th-75th percentile) of pleural fluid CRP (mg/dL) in TBPE was 38.55(36.15-41.55) which was significantly higher as compared to MPE (18.2(16.2-20.225)) (p value <.0001). It is shown in table 2

Table 3: Correlation of pleural fluid ADA(U/L) with pleural fluid CRP (mg/dL).

Variables	Pleural fluid CRP (mg/dL)
Pleural fluid ADA(U/L)	
Correlation coefficient	0.692
P value	<0.0001

Spearman rank correlation coefficient

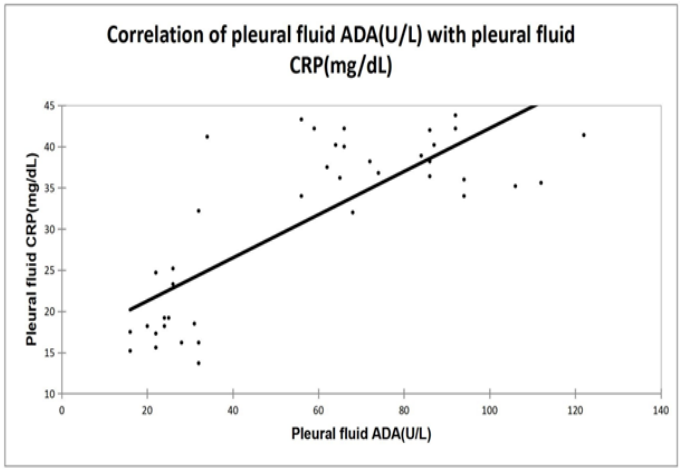


Figure 3: Correlation of pleural fluid ADA(U/L) with pleural fluid CRP (mg/dL).

Significant positive correlation was seen between pleural fluid ADA(U/L) with pleural fluid CRP (mg/dL) with correlation coefficient of 0.692. It is shown in table 3 and figure 3.

Table 4: Receiver operating characteristic curve of Pleural fluid CR P(mg/dL) for predicting TBPE.

Variables	Values
Area under the ROC curve (AUC)	0.997
Standard Error	0.00368
95% Confidence interval	0.907 to 1.000
P value	<0.0001
Cut off	>32.2
Sensitivity (95% CI)	95.83% (78.9 - 99.9%)
Specificity (95% CI)	100% (79.4 - 100.0%)
PPV (95% CI)	100% (85.8 - 100.0%)
NPV (95% CI)	94.1% (71.3 - 99.9%)
Diagnostic accuracy	97.5%

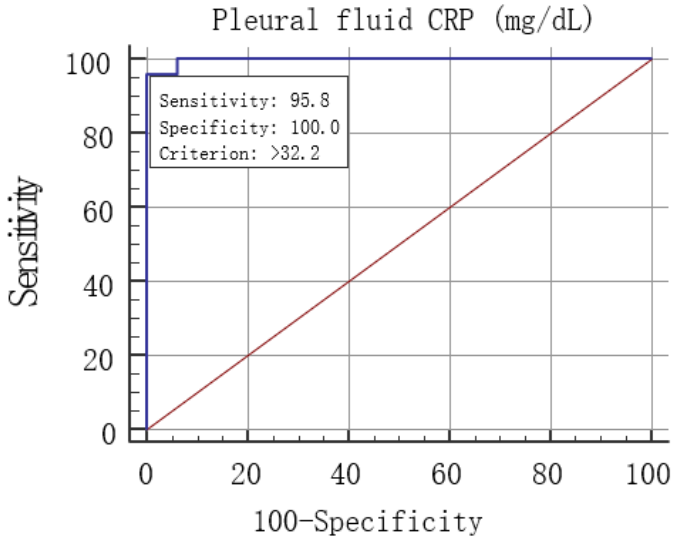


Figure 4: Receiver operating characteristic curve of Pleural fluid CRP (mg/dL) for predicting TBPE.

Interpretation of the area under the ROC curve showed that the performance of pleural fluid CRP (mg/dL) (AUC .997; 95% CI: 0.907 to 1.000) was outstanding. Pleural fluid CRP (mg/dL) was the significant predictor of TBPE at cut off point of >32.2 with area under curve of 0.997 for correctly predicting TBPE.

The above table shows that the patients who had TBPE, 95.83% of patients had pleural fluid CRP (mg/dL) >32.2. If pleural fluid CRP (mg/dL) >32.2, then there was 100.00% probability of TBPE and if Pleural fluid CRP (mg/dL) <=32.2, then 94.1% chances of MPE.

Among patients who had MPE, 100.00% of patients had Pleural fluid CRP (mg/dL) <=32.2.

It is shown in table 4 and figure 4.

Discussion

This study analysed various demographic and clinical characteristics with respect to malignant and TB pleural aetiology. The mean age of the patients in our study was 45.02 ± 16.7 years. We observed that compared to TBPE, patients with MPE had significantly higher mean age (55.56 ± 8.61 vs. 38 ± 17.24, P=0.0001).

Similarly, our study, Makwana Set al.[5] reported that compared to TBPE, patients with MPE had significantly higher mean age (70 vs. 45.55, P= 0.00132).

Qu SY et al.[6] reported that the mean age of the patients with TBPE and MPE was 56 and 65 years, respectively (P=0.07), Compared to TBPE, patients with MPE had comparable number of males (62.50% vs. 75%) and females (37.50% vs. 25%) (P=0.398).

Our study showed the correlation of pleural fluid ADA and CRP, we found a significant positive correlation between pleural fluid ADA and pleural fluid CRP (r=0.692, P<0.0001) indicating that pleural fluid CRP shows a direct increase in relation to pleural fluid ADA in tubercular aetiology.

Similarly, our study, Radhakrishnan P et al.[7] found that the mean pleural fluid ADA value and CRP value was 92.6 mg/dL and 37.5 mg/dL for tuberculosis PE, which was significantly higher than that of malignant PE (ADA-28.6 mg/dL and CRP 28.2 mg/dL, p<0.001). Hakani L et al.[8] found that compared to TBPE, MPE, had ADA levels (108.65 vs. 54.11, IU/L) and CRP levels (33.60 vs. 12.21, mg/L) (P<0.05).

We observed that cut-off of >32.2 mg/dl pleural fluid CRP carried 97.5% diagnostic accuracy for predicting TBPE; the sensitivity, specificity, NPV, and PPV were 95.83%, 100%, 100%, and 94.1%, respectively. Mak wana S et al.[5] reported that the optimal cut-off value of CRP ≥34.5 mg/dl yielded poor diagnostic efficacy in distinguishing malignant effusion from tuberculous effusion, with sensitivity and specificity being 42.9% and 56.2%, respectively.

Gabhale et al.[9] reported that the optimal cut-off value of CRP ≥51.6 mg/dl yielded poor diagnostic efficacy in distinguishing malignant effusion from tuberculous effusion, with sensitivity, specificity, and AUC being 97.06%, 71.76%, and 0.282, respectively.

Limitations

1. The study was done on a small sample size and thus the statistical association needs further validation with larger sample size.
2. The present study was conducted at a single center; thus its results may need further validation with multi centric studies.
3. Markers other than CRP and ADA were not correlated.

Conclusion

Our study indicate that ADA and CRP are useful markers for differentiating the different types of pleural effusion and differentiate tuberculous and MPE. Pleural fluid CRP can be a reliable novel, noninvasive in nature can be used in routine test for predictive TBPE in resources limited settings

References

1. 1.Maikap MK, Dhua A, Maitra MK. Etiology and clinical profile of pleural effusion -. Int J Med Sci Pub Health 2018;7(4):316–21.
2. Na MJ. Diagnostic tools of pleural effusion. Tuberc Respir Dis (Seoul) 2014;76(5):199-210.
3. Zhang X, Duan H, Yu Y, Ma C, Ren Z, Lei Y, et al. Differential diagnosis between benign and MPE with dual -energy spectral CT. PLoS One 2018;13(4): e01 93 714.
4. 4.Li M, Wang H, Wang X, Huang J, Wang J, Xi X. Diagnostic accuracy of tumor necrosis factor-alpha, interferon - gamma, interleukin -10 and adenosine deami nase 2 in differential diagnosis between tuber culous pleural effusion and MPE. J Cardiothorac Surg 2014; 9:118.
5. Makwana S, Gohil P, Gab hawala Y. The role of pleural fluid Creactive protein in the diagnosis of exudative pleural effusions.
Cureus 2022;14(7): e27000.

6. Qu SY, Zhang Y, Wu S, Wang MM, Liu LL, Yang XM, et al.
Combined analysis of C-reactive protein in pleural fluid and serum is effective in the differential diagnosis of exudative pleural effusions. Ann Transl Med 2021; 9 (14):1183.
7. Radhakrishnan P, Mathanraj S. Role of pleural fluid C-reactive protein in the aetiological diagnosis of exudative pleural effusion. J Clin Diagn Res 2020;14(8): OC04-OC07.
8. Hakani L, Mitre A. The diagnostic value of C-reactive protein and adenosine deaminase biomarkers for differentiation of exudative pleural effusion. Int J Res Med Sci 2016;4(4):975–9.
9. Gabhale SD, Taparia P, Yadav D, Agnihotri SP. Usefulness of pleural fluid CRP level in differential diagnosis of exudative pleural effusion – a pilot study. Int J Clin Biochem Res 2015;2(2):97–109.