Research Article

Diagnostic accuracy of combined Pleural fluid Adenosine Deaminase and Lymphocyte/Neutrophil ratio in Tubercular pleural effusion

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Introduction: Increased pleural fluid adenosine deaminase (ADA) activity is classically associated with tuberculous pleural effusion. However, increased activity can also occur in a number of other diseases and this may negatively affect the diagnostic utility of ADA measurements and decrease its specificity for the diagnosis of tuberculosis (TB). The presence of ADA in pleural fluids reflects the cellular immune response in the pleural cavity and in particularly, the activation of T lymphocytes. Different disease entities are typically associated with the presence of particular types of leukocytes. Objective of present study is to evaluate efficacy of combined use of ADA activity and lymphocyte/neutrophil ratio for diagnosing tuberculous pleural effusion. **Methods:** Biochemistry, cytology, and microbiology studies were performed on 164 consecutive pleural fluids. ADA and differential cell counts were determined on all exudative effusions. **Results:** Pleural fluid ADA activity at a level of ≥40 U/L have sensitivity=95.5%, specificity=93.4%, positive prediction value=94.4%, negative prediction value=94.7% and efficacy= 94.5 %. It was statistically significant (p value<0.001). When the additional requirement of a lymphocyte/neutrophil ratio of ≥0.75 was included they have sensitivity=95.45, specificity=100%, positive prediction value=100%, negative prediction value=97.45 and efficacy=97.5 respectively. **Conclusion:** ADA is a highly sensitive diagnostic marker of tubercular pleural effusion. Combined pleural fluid ADA and Lymphocyte /neutrophil ratio increases diagnostic accuracy in tubercular pleural effusion patients compared to pleural fluid ADA alone.

Key words: Adenosine deaminase, Pleural effusion, Tuberculosis, lymphocyte/neutrophil ratio

Introduction

Pleural effusion refers to an excessive fluid accumulation in the pleural cavity. Normally, the pleural cavity contains about 10 ml of fluid on each side [1]. Pleural effusion occurs due to an imbalance between the production of the fluid and its resorption. It can be an initial manifestation of any cardiac disorder or any pulmonary disorder.

Pleural effusion is indicative of an underlying disorder and it is not by itself an individual disease entity. In the case of diagnosis of pleural effusion, there should be an effort to diagnose the causative disorder.

According to the criteria laid out by Light [1] pleural effusion is broadly divided into transudative and exudative. Transudative effusion is usually caused by congestive heart failure or a hypoalbuminemic state. Exudative effusion occurs due to pleuro-pulmonary infection, local or metastatic malignancy, pulmonary thromboembolism or local trauma etc.

Tuberculosis is the most common infectious cause of death around the globe [2]. Pleural tuberculosis is the second most common extra pulmonary manifestations of tuberculosis, next only to tubercular lymphadenitis [3].

In India and many other countries, the most common cause of pleural effusion is tuberculosis, in the absence of any demonstrable pulmonary disease. IF left untreated, the tubercular pleural effusion develops into active tuberculosis [4] and thus it is very crucial to diagnose it early and institute an appropriate treatment. The definitive diagnosis is at times difficult because the

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sole site of the infection is pleura, in more than half of the patients [4].

The definitive diagnosis of tubercular pleural effusion is done by the demonstration of tubercle bacilli either in pleural fluid or in a pleural biopsy specimen/sputum, or by the demonstration of pleural granulomas. Because there is a paucity of the tubercle bacilli in the pleural fluid, whenever a tubercular pleural effusion is a possibility, the pleural biopsy is believed to be crucial for an accurate diagnosis. But because the pleural biopsy is a difficult process, and moreover, sampling of pleural fluid is an easier alternative, there has been ample effort being done in study of pleural fluid markers of tubercular pleural effusion.

Pleural fluid adenosine deaminase level is a chemical biomarker which is cost effective and therefore it is an attractive screening tool particularly, in areas endemic to tuberculosis. Raised levels of ADA can also be encountered in malignancies, immunological disorders, pyogenic empyemas etc.

In pleural effusion there is a significant influx of the inflammatory cells in the pleural space [5]. Different type of leucocytic predominance is seen in different types of diseases and also in different stages of the same disease [6]. In parapneumonic and empyematous effusions, neutrophils are significantly raised [7]. Lymphocytic predominance is seen in malignant and tubercular pleural effusions [7]. The enzyme ADA is involved in purine catabolism. It deaminates adenosine to inosine and deoxyadenosine to deoxyinosine. It also regulates the proliferation and differentiation of lymphocytes, more importantly the T-lymphocytes. Compared to the erythrocytes, its concentration is ten times higher in the lymphocytes. When T cells get activated due to the entry of the tubercle bacilli, they secrete ADA in the medium. ADA thus serves as a marker of the T cell mediated immunity

In view of the controversy surrounding the diagnostic utility of ADA in pleural fluids, we endeavoured to determine whether the combined use of ADA activity and differential cell counts would provide a more efficient means for diagnosing tubercular pleural effusion than the use of ADA levels alone.

Materials and Methods

This study was a hospital based prospective study carried out in the department of Pulmonary Medicine, JIPMER, Puducherry, during the period between June 2012 & June 2014. This study was approved by Institute ethics sub-committee (human studies).

Patient selection

Inclusion criteria:

1. All exudative pleural effusion cases

Exclusion criteria:

1. Patients with transudative pleural effusion.
2. Patients with malignant pleural effusion.
3. Patients with immunodeficient states like HIV & those on chemotherapy.
4. Patients with empyema and hemothorax.

Brief procedure: According to a predetermined pro forma, demographic data collected, a thorough clinical history was taken and clinical examination done. The patients underwent the following investigations for the evaluation of the pleural effusion –sputum for AFB smear and mycobacterium culture, hemogram, random blood sugar, ESR, liver function test, renal function test, tuberculin skin testing, pleural biopsy, pleural fluid-glucose, protein, albumin, gram staining, auraminerhodamine staining, LDH, ADA, cytology and cell count.

A total of 244 patients who were clinically/radiologically examined and diagnosed to have pleural effusion were taken up for the study after written consent and further evaluated.

As per Light's criteria (pleural fluid protein/serum protein >0.5; fluid LDH/serum LDH > 0.6), 238 patients diagnosed as exudative effusion and 6 patients were diagnosed as transudative pleural effusion.

Among these238 exudative pleural effusion patients on further evaluation, 44(18.5%) patients had malignant pleural effusion and 22(9.2%) had empyema thoracic and 8(3.3%) had pleural effusion with HIV infection. These patients were excluded from the study. So only 164 patients included in our study.

Among the 164 exudative pleural effusion patients, 76 patients had non tubercular pleural effusion [includes 72 patients with par pneumonic, 3 with pancreatic pleural effusion and 1 with chylothorax] and 88 patients were tubercular pleural effusion as per criteria mentioned below

Patients were diagnosed as a case of tubercular pleural effusion based on presence of first or more than one of the following criteria.[8]

1. Bacteriological confirmation of presence of Mycobacterium tuberculosis in pleural fluid or in sputum (direct smear or culture or histological finding),
2. Histopathologically proven cases of tuberculosis,
3. Radiological findings consistent with TB,
4. Clinical presentation consistent with TB with exclusion of other clinical considerations,
5. Definite clinical and radiological improvement in 6 – 8 weeks of administration of anti- tubercular treatment,
6. Positive reaction (> 10 mm induration) to the 1 tuberculin unit (TU) purified protein derivative (PPD),
7. Pleural fluid adenosine deaminase levels of > 40U/L.

Chest X ray-PA view was taken for all 88 patients with tubercular pleural effusion. Quantity of fluid, side of involvement, hilar/mediastinaladenopathy, parenchymal involvement, cavitation and other radiological abnormalities were noted. Effusions occupying more than two thirds of the hemithorax were considered massive, one-third to two thirds of the hemithorax as moderate and less than one third of the hemithorax as minimal.

Tuberculin skin testing was done by administering 0.1 mL volume containing 1 TU (tuberculin units) PPD in a tuberculin syringe intradermal [into the top layers of skin of the forearm]. Reading was done after 72 hours. The basis of the reading of the skin test was the presence or absence and the amount of induration (localized swelling) measured across the arm. Any measurement of induration >10mm was considered positive and <10mm negative.

All patients' with pleural effusion underwent diagnostic thoracocentesis. After site for thoracentesis was identified, the skin surrounding the site was cleansed thoroughly with an antiseptic solution over an area of 4 inches in all directions from the proposed thoracentesis site. The sterile drape with the center hole was then placed to the patient's back, and another sterile drape is placed on the bed. The skin was anaesthetized using a 25-gauge needle by injecting 2 % lidocaine, then a 22-gauge needle attached to a 50- to 60-mL syringe containing 1 mL of heparin is inserted. Heparin is added into the syringe to prevent clotting of the pleural fluid.

Sputum specimens was examined for acid-fast bacilli .Smears were stained with Auramine-Rhodamine

staining according to standard confirmed procedures done in *designated Microscopy Centre in* pulmonary medicine department under RNTCP programme. LED fluorescent microscope was used for reporting. The results of staining were reported after viewing 100 fields.

Pleural fluid was examined for acid-fast bacilli with Auramine-Rhodamine staining according to standard confirmed procedures. LED fluorescent microscopy was used for reporting. The results of staining were reported after viewing 100 fields

Pleural fluid culture and sputum culture for Mycobacterium were done by inoculating processed sputum/ pleural fluid specimens on to Lowenstein-Jensen media.Samples (0.25 ml) of each specimen were inoculated onto each of two slants of glycerol-free LJ medium supplemented with sodium pyruvate and one slant of LJ medium containing nalidixic acid (35 mg/liter), vancomycin (20 mg/liter), polymyxin B (1,600 U/ml).

All cultures were examined 48-72 hours after inoculation to detect gross contaminants. Thereafter cultures were examined weekly, up to 8 weeks on a specified day of the week. The colony with doubtful morphology, the acid-fastness was confirmed by Ziehl-Neelsen (ZN) staining.

Effusion was called as malignant when pleural fluid cytology or pleural biopsy showed evidence of malignancy or if the patient had proved metastatic malignancy with no other detectable cause of effusion.

The method described by Giusti was used for the determination of the pleural fluid ADA levels. Berthelot reaction forms the basis of this calorimetric method in which the ammonia produced due to the reaction of ADA with adenosine is estimated. One unit of ADA is defined as the amount of enzyme required to release 1 µmol ammonia per minute from adenosine under standard assay conditions. The enzyme is stable for at least 24 h at 25°C, for 7 days at 4°C, and for 3 months at −20°C.

Portions of each pleural fluid sample were placed in EDTA tube and refrigerated at 4°C until the WBC

counts and differential counts were obtained. Total WBC cell count was done manually using a hemacytometer. Remaining specimen was centrifuged for five minutes at 3000 rpm. Decant the supernatant into a sterile tube, leaving approximately 0.5 ml fluid in which to vortex the sediment, which is used for preparation of a Wright-stained smear for differential count. Wet film was prepared by placing one drop of sediment and a drop of toluidine blue on a slide, mixing them and putting a cover slip. Wet film was observed under the microscope for identification of cell morphology. 100 cells were counted manual for differential count.

18 patients diagnosed as tubercular pleural effusion started on anti-tubercular treatment as in patients, subsequently they were registered under RNTCP DOTS and referred to concerned designated DOTS centre for further treatment and advice to continue treatment under DOTS.

Remaining 70 patients diagnosed to have tubercular pleural effusion were also registered under RNTCP DOTS and referred to concerned designated DOTS centre for treatment and advice to continue treatment under DOTS.

32 patients reported to our department for follow-up while on treatment. It was observed that 3patients of tubercular pleural effusion having associated parenchymal lesion developed hydro pnemothorax in less than 1 month of their course of treatment. They were managed conservatively with intercostals tube drainage with under water seal, oxygen therapy and analgesics and continued anti tubercular drugs.

Methods of Analysis

Patients demographic, clinical and laboratory parameters was collected in a proforma and data was entered in excel spread sheet. All categorical data was presented as frequencies/percentage. Continuous variables are expressed as mean (SD) while categorical variables are expressed as number and group percentages. Differences in ADA levels between groups were analyzed using unpaired Student t test and one way Anova. Correlation between ADA and specified variables was quantified using Pearson correlation coefficient. This was performed for the whole study population (n = 164) as well as individually for the TPE and non TPE groups. All statistical analyses were performed using IBM SPSS Statistics version 20. A 2 tailed p value of < 0.05 was taken to be statistically significant.

In all 164 cases included in the study, the sensitivity, specificity, positive predictive value and negative predictive value using pleural fluid ADA alone and in combination with lymphocyte neutrophil ratio for diagnosing tubercular pleural effusion were calculated. Analysis was done using a cut off value of $\geq$40 for ADA and lymphocyte neutrophil ratio $\geq$75 for diagnosing tubercular effusion.

We made an attempt to evaluate and identify any correlation between pleural fluid ADA, pleural fluid lymphocyte /neutrophil ratio with sputum status, chest X-ray finding and pleural biopsy reports in tubercular pleural effusion patients.

Results

Among 88 tubercular pleural effusion patients 66(75%) were males and 22 (25%) were female. Among 88 tubercular pleural effusion patients, mean age was 40.7 years with standard deviation of ±15.8 years (range 14 to 76 years)

Among 88 patients with tubercular pleural effusion, 49(55.7%) were positive [>10mm] for tuberculin skin test. On sputum smear examination for acid fast bacilli was found to be positive in 28(31.8%) & sputum culture for mycobacteria was positive in 31(35.2%).

Among 88 patients with tubercular pleural effusions chest x-ray showed,19(21.6%) had massive pleural effusion, 62[70.5%] had moderate pleural effusion effusions and 7[8%] had minimal pleural effusions.

All 88 patients with tubercular pleural effusion had unilateral effusion. Right sided in 50 patients (56.82%), and left sided in 38 patients (43.18%).

Among 88 patients with tubercular pleural effusion, 16 underwent closed needle biopsy of the parietal pleura. Among these 16 patients, histopathological examination of the biopsy revealed caseation granuloma in11 (68.7%) and remaining 5 were inconclusive.

Table 1: Sensitivity and specificity of pleural fluid ADA≥40

ADA level	Tubercular pleural effusion	Non-tubercular pleural effusion	Total
ADA≥40 IU	84	05	89
ADA<40 IU	04	71	75
Total	**88**	**76**	**164**

Among 88 of tubercular pleural effusion patients, pleural fluid ADA ≥40 for diagnosis of tubercular pleural effusion had Sensitivity = 95.5%, Specificity = 93.4%, Positive Predictive Value = 94.4%, Negative Predictive Value = 94.7% Efficacy = 94.5 %

Table 2: Sensitivity and specificity of pleural fluidlymphocyte neutrophil ratio≥75

Lymphocyte neutrophil ratio	Tubercular pleural effusion	Non-tubercular pleural effusion	Total
L/N≥75	86	0	86
L/N<75	2	76	78
Total	**88**	**76**	**164**

Among 88 of tubercular pleural effusion patients, , pleural fluid lymphocyte /neutrophil ratio ≥0.75 for diagnosis of tubercular pleural effusion had pleural fluid lymphocyte /neutrophil ratio ≥0.75 for diagnosis of tubercular pleural effusion had Sensitivity = 97.72%, Specificity = 100%, Positive Predictive Value = 100%, Negative Predictive Value = 97.44%

Table 3: Sensitivity and specificity of pleural fluid combinedADA≥40 and lymphocyte neutrophil ratio≥75

Combined ADA and L/N	Tubercular pleural effusion	Non-tubercular pleural effusion	Total
ADA≥40 and lymphocyte neutrophil ratio≥75	84	0	84
ADA<40 and/or lymphocyte neutrophil ratio<75	04	76	80
Total	**88**	**76**	**164**

Among 88 of tubercular pleural effusion patients, combined ADA levels of ≥40U/L and pleural fluid lymphocyte /neutrophil ratio ≥0.75 for diagnosis of tubercular pleural effusion had
Sensitivity = 95.45%, Specificity = 100%, Positive Predictive Value = 100%, Negative Predictive Value = 97.45%, Efficacy = 97.5

Table 4: Comparison of pleural fluid ADA value with sputum results in study subjects.

Mycobacterium tuberculosis in sputum (direct smear and/or culture)	Number of patients	Pleural fluid ADA mean ±Standard deviation	p- value
Positive	31	77.41±31.13	0.628
Negative	57	74.44±25.27	

In our study, among 34 patients with both parenchymal lesion and pleural effusion in chest x-ray, pleural fluid ADA mean±Standard deviation was 72.55±24.52 and among 54 patients with pleural effusion only in chest x ray, pleural fluid

ADA mean±Standard deviation was 77.34±29.04. Pleural fluid ADA value of both groups was comparable (p>0.05) (Table 4).

Table 5: Comparison pleural fluid Lymphocyte /neutrophil ratiowith sputum results in study subjects.

Mycobacterium tuberculosis in sputum (direct smear and/or culture)	Number of patients	Pleural fluid Lymphocyte /neutrophil ratio mean ±Standard deviation	p- value
Positive	31	86.71±8.66	0.45
Negative	57	85.43±7.27	

In our study, among 34 patients with both parenchymal lesion and pleural effusion in chest x-ray,pleural fluid Lymphocyte /neutrophil ratio mean±Standard deviation was86.41±8.486 and among 54 patients with pleural effusion only in chest x ray, pleural fluid Lymphocyte /neutrophil ratio mean±Standard deviation was 85.57±7.337. Pleural fluid ADA value of both groups was comparable (p>0.05) (Table 5).

Table 6: Comparison of pleural fluid ADA value with chest X ray finding in study subjects.

Chest x ray finding	Number of patients	Pleural fluid ADA mean ±Standard deviation	p-value
Suggestive of parenchymal lesion and pleural effusion	34	72.55±24.52	0.42
Suggestive of pleural effusion only	54	77.34±29.04	

In our study, among 31 patients positive for mycobacteria sputum culture and/or smear, Pleural fluid ADA mean±Standard deviation was 77.41±31.13 and among 57 patients negative for mycobacterium sputum culture and smear, pleuralfluid ADA mean ±Standard deviationwas 74.44±25.27. Pleural fluid ADA value of both group were comparable (p>0.05) (Table 6).

Table 7: Comparison pleural fluid Lymphocyte /neutrophil ratio with chest X ray finding in study subjects

Chest x ray finding	Number of patients	Pleural fluid Lymphocyte /neutrophil ratio mean ±Standard deviation	p-value
Suggestive of parenchymal lesion and pleural effusion	34	86.41±8.486	0.62
Suggestive of pleural effusion only	54	85.57±7.337	

In our study, among 31 patients positive for mycobacteria sputum culture and/or smear, pleural fluid Lymphocyte /neutrophil ratio mean±Standard deviation was 86.71±8.66and among 57 patient negative for mycobacterium sputum culture and smear, pleural fluid Lymphocyte /neutrophil ratio mean±Standard deviation was 85.43±7.27. Pleural fluid ADA value of both group were comparable (p>0.05) (Table 7).

Discussion

Pleural effusions can pose a diagnostic challenge because of the various differential diagnostic possibilities. Most common causes include congestive heart failure (CHF), malignancy, and pneumonia related effusion. In our study, diagnostic methods were evaluated individually and in combination. We have explored combinations of methods the complementary strengths of which offer diagnostic options that can be utilized advantageously in countries with high TB prevalence and lower technology.

Pleural fluid evaluation:

In our study, among 164 of exudative pleural effusion, 76 patients had non tubercular pleural effusion and 88 patients were tubercular pleural effusion.

In our study, among 88 patients of tubercular pleural effusion (34 patients with parenchymal lesion and pleural effusion, 54 patients with pleural effusion only by chest x ray), 84 had pleural fluid ADA ≥40 and 4

patients had ADA<40. Among 76 patients of non-tubercular pleural effusion, 5 had pleural fluid ADA ≥40 and 71 patients had ADA <40. Hence in exudative pleural effusion cases, pleural fluid ADA ≥40 for diagnosis of tubercular pleural effusion had Sensitivity=95.5%, Specificity=93.4%, Positive prediction value=94.4%, Negative prediction value=94.7% and Efficacy= 94.5 %. It was statistically significant (p value<0.001) [Table 1]. Similar observation was made in the study done by Bharat et al, Susmitha et al, by Mehta AA et al, Bergess LJ et al [10,11,12,13].

Bharat et al[10], consecutively selected 96 lymphocytic pleural fluid samples and divided them into two groups: tuberculous (n = 56) and non-tuberculous (n = 40). They found that the ADA with cut-off value of 40 for diagnosis of tubercular pleural effusion had a Sensitivity of 92%, Specificity of 90%, Positive prediction value of 92.8%, and Negative prediction value of 90%. In a study by Susmitha et al[11], ADA with cut-off value of ≥40 for diagnosis of tubercular pleural effusion had sensitivity of 97%,specificity of 93%,positive prediction value of 94% and negative prediction value of 97%. In a study by Mehta AA et al[12], in evaluation of 121 cases of exudative pleural effusion including 49 tubercular pleural effusion. They have found that ADA with cut-off value of ≥40 for diagnosis of tubercular pleural effusion had sensitivity of 85.7%, specificity of 80.8%,positive prediction value of 75% and negative prediction value of 89.5%. Bergess LJ et al[13], in retrospective study has evaluated 246 cases of exudative pleural effusion including 143 tubercular pleural effusion. They have found that, ADA with cut-off value of ≥50 for diagnosis of tubercular pleural effusion had a sensitivity of 91%, specificity of 81%, positive prediction value of 84% and negative prediction value of 89%.

The results of our study had sensitivity similar to above mentioned studies. This is partly because of the high prevalence of tubercular pleural effusion in this region, which increases the positive predictive value and efficiency of ADA concentration as a diagnostic marker.

In our study, among 88 of tubercular pleural effusion patients, 86 had pleural fluid Lymphocyte /neutrophil ratio ≥0.75 and 2 patients had lymphocyte /neutrophil ratio <0.75. Similar observation was made in the study done Mohan K et al[14], they evaluated 70 cases of exudative pleural effusion including 62 tubercular pleural effusion. They have found that, pleural fluid Lymphocyte /neutrophil ratio ≥0.75 for diagnosis of tubercular pleural effusion had sensitivity of 100%, specificity of 88.6%, positive prediction value of 100% and negative prediction value of 91.1%.

Among 88 tubercular pleural effusion patients, 84 patients had the combination of Pleural fluid ADA levels ≥40U/L with pleural fluid lymphocyte /neutrophil ratio ≥0.75 and remaining 4 patients had Pleural fluid ADA levels <40U/L. The following observation shows that combination of pleural fluid Lymphocyte /neutrophil ratio ≥0.75 and ADA≥40 increases the specificity and efficacy for diagnosis of tubercular pleural effusion. Similar observations were made in the study done by Burgess LJ et al[13] and where it was seen that combining pleural fluid Lymphocyte /neutrophil ratio ≥0.75 and ADA ≥50 increased the specificity and efficacy for diagnosis of tubercular pleural effusion.

We made an attempt to evaluate and identify any correlation between pleural fluid ADA, pleural fluid lymphocyte /neutrophil ratio with sputum status, chest X-ray finding and pleural biopsy finding in tubercular pleural effusion patients.

In our study, pleural biopsy was done for 16 patients of tubercular pleural effusion. , on histopathological examination 11 were reported as tuberculosis and remaining 5 were inconclusive.

Limitations

1. Pleural fluid cell count in present study was done manually instead of machine and if counting by machine was done it would have been more reliable and accurate.
2. Number of patients studied is small. Small sample size may impede for detecting significant effects because of lack of power.

Conclusions

1. 1 ADA is a highly sensitive diagnostic marker of tubercular pleural effusion.
2. Combined pleural fluid ADA and Lymphocyte /neutrophil ratio increases diagnostic accuracy in tubercular pleural effusion patients compared to pleural fluid ADA alone.

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References

1. Light RW, Macgregor MI, Luchsinger PC, Ball WC. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med. 1972 Oct;77(4):507–13.

2. Raviglione MC, Luelmo F. Update on the global epidemiology of tuberculosis. Curr Issues Public Health. 1996 Aug;2(4):192–7.

3. Mehta JB, Dutt A, Harvill L, Mathews KM. Epidemiology of extrapulmonary tuberculosis. A comparative analysis with pre-AIDS era. Chest. 1991 May;99(5):1134–8.

4. Porcel JM. Tuberculous pleural effusion. Lung. 2009 Oct;187(5):263–70.

5. Antony VB, Godbey SW, Kunkel SL, Hott JW, Hartman DL, Burdick MD, et al. Recruitment of inflammatory cells to the pleural space. Chemotactic cytokines, IL-8, and monocyte chemotactic peptide-1 in human pleural fluids. J Immunol Baltim Md 1950. 1993 Dec 15;151(12):7216–23.

6. Sahn SA. State of the art. The pleura. Am Rev Respir Dis. 1988 Jul;138(1):184–234.

7. Light RW, Erozan YS, Ball WC. Cells in pleural fluid. Their value in differential diagnosis. Arch Intern Med. 1973 Dec;132(6):854–60.

8. Gupta BK, Bharat V, Bandyopadhyay D. Sensitivity, specificity, negative and positive predictive values of adenosine deaminase in patients of tubercular and non-tubercular serosal effusion in India. J Clin Med Res. 2010 May 19;2(3):121–6.

9. Berger HW, Mejia E. Tuberculous pleurisy. Chest. 1973 Jan;63(1):88–92.

10. Gupta BK, Bharat V, Bandyopadhyay D. Role of Adenosine Deaminase Estimation in Differentiation of Tuberculous and Non-tuberculous Exudative Pleural Effusions. J Clin Med Res. 2010 Apr;2(2):79–84.

11. Chaudhary S PA. Role of pleural fluid adenosine deaminase (ADA) for the diagnosis of tuberculous pleural effusion. Calicut Med J. 2010;8:e4; 2010.

12. Mehta AA, Gupta AS, Ahmed S, Rajesh V. Diagnostic utility of adenosine deaminase in exudative pleural effusions. Lung India Off Organ Indian Chest Soc. 2014;31(2):142–4.

13. Burgess LJ, Maritz FJ, Le Roux I, Taljaard JJ. Combined use of pleural adenosine deaminase with lymphocyte/neutrophil ratio. Increased specificity for the diagnosis of tuberculous pleuritis. Chest. 1996 Feb;109(2):414–9.

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