



SIGNIFICANCE OF ADENOSINE DEAMINASE (ADA) IN EXUDATIVE PLEURAL EFFUSION

Respiratory Medicine

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KEYWORDS

INTRODUCTION

Presence of fluid in the pleural cavity, it is referred to as pleural effusion. This fluid can either be exudative or transudative. There is a wide range of illnesses that can result in exudative pleural effusion. These conditions include tuberculosis, neoplasms, infections, sarcoidosis, graft rejection in transplant patients, pulmonary embolism, and pulmonary edema for example. "This is especially true when considering the fact that the diagnosis of tuberculous pleural effusion is difficult to make".^{1,2}

Exudative fluid in the pleural space is most commonly caused by pleural TB, which stands out as a primary causal factor. The paucibacillary structure of the fluid frequently renders pleural fluid smear and culture unimpressive, despite the fact that pleural fluid aspiration is a regular operation that is used in diagnostic tests.^{3,4} The etiology of tuberculosis can be determined through the use of techniques such as acid-fast bacilli (AFB) smear, mycobacterial culture, and histology". However, mycobacterial culture is considered to be the gold standard when it comes to determining the efficacy of medication therapy for tuberculosis.^{5,6}

Histological analysis of tuberculosis specimens reveals distinctive features such as lymphocytic infiltration, granular necrosis with caseous necrosis, distributed multinucleated cells, and Langhans' giant cells.⁷ ADA, or adenosine deaminase, is an enzyme that is released by lymphocytes that are engaged in purine metabolism. ADA testing is a method that is generally applied because of its simplicity, cost-effectiveness, quickness, and low invasiveness. However, there are certain limitations associated with this procedure. Tubercular pleural effusion is indicated by elevated ADA levels in pleural fluid; however, other illnesses such as empyema, cancer, or rheumatoid pleurisy can also result in increased ADA levels. An elevated ADA level in pleural fluid is symptomatic of tubercular pleural effusion.⁸

Due to the much greater quantities that are detected in patients who have lymphocytic-rich exudative pleural effusion, ADA becomes a useful diagnostic tool for tubercular pleural effusion. This is because these patients show significantly higher levels of the substance. On the other hand, a low pleural fluid ADA can be helpful in excluding the potential of treating pleural effusion particularly in people who are at a low risk for the disorder.^{9,10}

The current study focuses on the role of ADA in exudative pleural effusion.

The purpose of this study is to contribute to the understanding of rapid and less painful diagnostic procedures for this problematic condition.

AIM AND OBJECTIVES

AIM

To assess Adenosine Deaminase (ADA) in Exudative Pleural Effusion

OBJECTIVES

- To diagnose EXUDATIVE PLEURAL EFFUSION by Light's

criteria.

- To evaluate significance of Adenosine Deaminase (ADA) in the diagnosis of TUBERCULAR PLEURAL EFFUSION

MATERIALS AND METHODS

Setting -

This study was conducted in department of respiratory medicine , Rajshree Medical Research Institute, Bareilly.

Study Design -

The prospective study was carried out on patients coming with chief complaint and signs suggestive of pleural effusion along with Chest Xray findings suggestive of pleural effusion in Department of Respiratory Medicine . The study was conducted after approval from institutional scientific and ethical committee review board.

Inclusion Criteria:

Patients who had been identified as having pleural effusion by clinical examination, chest x-ray, and diagnostic thoracentesis for fluid analysis demonstrating exudative nature were eligible for inclusion.

Exclusion Criteria:

- Refusal of patients to consent to thoracentesis
- Transudative pleural effusions.
- Hemothorax , Chylothorax and malignant pleural effusion.

SAMPLE SIZE -

Patients presenting to department of Respiratory Medicine, Rajshree Medical and Research Institute Bareilly fulfilling inclusion and exclusion criteria were included in this study.

A total of 100 cases of exudative pleural effusion were taken up for the study.

Study Tool-

- Pre-designed proforma for data collection.
- Informed consent
- Chest XRAY/USG Thorax
- Pleural fluid LDH, protein , AFB smear, ADA and CBNAAT
- Serum LDH, S. Protein

METHODOLOGY

After obtaining informed written consent, medical history taking, full clinical examination, Chest xray or USG Thorax followed by diagnostic thoracentesis under aseptic conditions was done in all cases of pleural effusion. Thoracentesis is a diagnostic and therapeutic procedure for pleural effusion. It involves placing a needle into the pleural space to remove some of the fluid. Aspirated pleural fluid to be sent for sugar, protein, LDH , routine microscopy. Serum protein and serum LDH will be evaluated.

Patients with exudative effusion underwent pleural fluid ADA.

Pleural fluid cytology: Tuberculosis and malignancy have cell counts

<5000/mm³ with a predominance of lymphocytes. A cell count of 90-95% lymphocytes is usually associated with tuberculous effusion, but is a nonspecific finding and may be seen in malignancy, collagen vascular diseases, sarcoidosis etc.

If any of the following conditions are true, the fluid was regarded as exudates: Light's standards (1972)

1. A higher than 0.5 pleural fluid to serum protein ratio
2. A larger than 0.6 ratio of pleural fluid to serum lactate dehydrogenase (LDH).
3. Pleural fluid LDH over the top limits of normal serum levels by more than two thirds

ADA: ADA was evaluated with Digital Photo Calorimeter using Adazyme-LS enzyme. In general, a Cut off level of between 40 and 45 IU/L was used with levels above this being indicative of tuberculosis. The following was considered sufficient in the study to classify a case as tuberculous:

Exudative lymphocytic pleural effusion with ADA > 40 IU/L (according to Light's criteria).

All cases of cancer determined by pleural fluid cytology and demonstrating the presence of malignant cells were disregarded.

RESULTS

Table 1: Table Showing Distribution Of Age Among The Study Participants (N=100)

Age	Frequency	Percentage
10-20	7	7
21-40	41	41
41-60	31	31
61-80	19	19
>80	2	2

Among 7% were in between 10-20 years, 41% 21-40 years, 31% 41-60 years, 19% 61-80 years and 2% >80 years.

Table 2: Table Showing Distribution Of Gender Among The Study Participants (N=100)

Gender	Frequency	Percentage
Female	27	27
Male	73	73

Males were about 73% and females 27%.

Table 3: Table Showing Distribution Of History Of Smoking Among The Study Participants (N=100)

History of smoking	Frequency	Percentage
Present	58	58
Absent	42	42

There were about 58% with history of smoking.

Table 4: Table Showing Distribution Of History Of Cough Among The Study Participants (N=100)

History of Cough	Frequency	Percentage
Present	94	94
Absent	6	6

Around 94% had history of cough.

Table 5: Table Showing Distribution Of History Of Fever Among The Study Participants (N=100)

History of fever	Frequency	Percentage
Present	66	66
Absent	34	34

Around 66% had history of fever.

Table 6: Table Showing Distribution Of Shortness Of Breath Among The Study Participants (N=100)

Shortness of breath	Frequency	Percentage
Present	50	50
Absent	50	50

Around 50% had shortness of breath.

Table 7: Table Showing Distribution Of Chest Pain Among The

Study Participants (N=100)

Chest pain	Frequency	Percentage
Present	78	78
Absent	22	22

Around 78% had chest pain.

Table 8: Table Showing Distribution Of Night Sweats Among The Study Participants (N=100)

Night sweats	Frequency	Percentage
Present	50	50
Absent	50	50

Around 50% had night sweats.

Table 9: Table Showing Distribution Of Loss Of Weight Among The Study Participants (N=100)

S.no	Loss of weight	Frequency	Percentage
1	Present	55	55
2	Absent	45	45

Around 55% had loss of weight.

Table 10: Table Showing Distribution Of Loss Of Appetite Among The Study Participants (N=100)

Loss of appetite	Frequency	Percentage
Present	55	55
Absent	45	45

Around 55% had loss of appetite.

Table 11: Table Showing Distribution Of Presence Of HIV Co-infection Among The Study Participants (N=100)

S.no	HIV co-infection	Frequency	Percentage
1	Present	0	0
2	Absent	100	100

Around 0% had HIV co-infection.

Remark: The prevalence of HIV in the study area is low . Hence, any correlation between HIV and tuberculosis cannot be attained in our study.

Table 12: Table Showing Distribution Of Presence Of Diabetes Among The Study Participants (N=100)

Diabetes	Frequency	Percentage
Present	11	11
Absent	89	89

Around 11% had diabetes.

Table 13: Table Showing Distribution Of Past History Of TB Among The Study Participants (N=100)

Past history of TB	Frequency	Percentage
Present	13	13
Absent	87	87

Around 13% had past history of TB.

Table 14: Table Showing Distribution Of History Of TB Contact Among The Study Participants (N=100)

History of TB contact	Frequency	Percentage
Present	2	2
Absent	98	98

Around 2% had history of TB contact.

Table 15: Table Showing Distribution Of Site Of Effusion Of Chest X-ray Among The Study Participants (N=100)]

Chest x-ray	Frequency	Percentage
Left	65	65
Right	25	25
Bilateral	10	10

Around 65% had left sided on chest x-ray, 25% had right sided effusion on chest x-ray and 10% had bilateral effusion on chest x-ray.

Table 16: Table Showing Distribution Of Presence Of Pulmonary

Lesion Among The Study Participants (N=100)

Pulmonary lesion	Frequency	Percentage
Yes	43	43
No	57	57

Around 43% had presence of pulmonary lesions.

Table 17: Table Showing Distribution Of Pleural Fluid Examination For The Diagnosis Of Pleural Tuberculosis (N=100)

Pleural fluid examination	Frequency	Percentage
Exudate with protein >3g/dL	100	100
Pleural fluid glucose >60 mg/dL	80	80
>50% lymphocytes	93	93
Pleural fluid ADA>40 IU/L	94	94

Around 100% had exudate with protein >3g/dL, 80% had pleural fluid glucose >60 mg/dL, 93% >50% lymphocytes and 94% had pleural fluid ADA>40 IU/L

Table 18: Table Showing Distribution Of Pleural Fluid ADA Levels Among The Study Participants (N=100)

ADA	Frequency	Percentage
<40 IU/L	6	6
40-70 IU/L	34	34
>70 IU/L	60	60

Around 6% had <40 IU/L, 34% 40-70 IU/L and 60% >70 IU/L.

DISCUSSION

We can learn a lot about the research population's demographics and clinical aspects from these results, and we can see how useful different metrics are for diagnosing pleural effusions and pulmonary lesions.

According to the demographic breakdown, most of the research participants were in the age bracket of 21–60, with the largest number being in the 21–40 age bracket. This study's male preponderance is in line with previous epidemiological data on pulmonary tuberculosis (TB), which has shown that men are more likely to be affected than females in many settings. Smoking may serve as a risk factor for pulmonary tuberculosis, and the fact that it was very common among the study's participants is significant because of this.

Respiratory symptoms, which are hallmarks of pulmonary tuberculosis, characterized the clinical presentation of the study population. Coughing, fever, difficulty breathing, chest pain, and night sweats were some of the symptoms. In addition, systemic symptoms including loss of appetite and weight loss were also frequently reported, highlighting the disease's systemic nature even further.

When performing clinical evaluations and managing cases of pulmonary TB, it is crucial to consider the study's participants' high prevalence of comorbidities, such as diabetes and a history of tuberculosis. Furthermore, as the majority of the participants in the study were HIV-negative, the lack of HIV coinfection in the studied population is also indicative of this. The generalizability of the results to populations living with HIV may be affected by this.

Pulmonary lesions were found in a considerable portion of the study group, according to diagnostic criteria. In order to diagnose pulmonary tuberculosis, radiographic evaluation is crucial. Characteristic results consistent with tuberculous pleural effusion were discovered by the analysis of pleural fluid. The results showed a preponderance of lymphocytes and elevated levels of adenosine deaminase (ADA).

Approximately 60% of patients had ADA levels over 70 IU/L, suggesting a possible link between elevated ADA levels and tuberculosis (TB), according to the distribution of Adenosine Deaminase (ADA) values among the study participants. Around 6% had <40 IU/L, 34% 40-70 IU/L and 60% >70 IU/L.

All the patients were treated with anti tubercular drugs and all the patients showed significant improvement symptomatically and radiologically.

Hence, ADA can be considered as a reliable test for the diagnosis of tubercular pleural effusion.

CONCLUSION

After obtaining informed consent for 100 patients with exudative

pleural effusion patient underwent diagnostic tapping and was completely evaluated.

The results of the study were as follows:

1. Majority of the population belonged under the age group of 21-40 yrs followed by 41-60 yrs
2. Males were more affected than females
3. Predominant symptom was cough followed by chest pain, fever, shortness of breath, loss of weight and appetite
4. Around 100% had exudate with protein >3g/dL, 80% had pleural fluid glucose >60 mg/dL, 93% >50% lymphocytes and 94% had pleural fluid ADA>40 IU/L

REFERENCES

1. Aggarwal AN, Gupta D, Jindal SK. Diagnosis of tuberculous pleural effusion. Indian J Chest Dis Allied Sci. 1999; 41(2):89–100. PMID: 10437321
2. Light RW. Update on tuberculous pleural effusion. Respirology. 2010; 15(3):451–8.
3. Pai M, Nathavitharana R. Extrapulmonary tuberculosis: new diagnostics and new policies. Indian J Chest Dis Allied Sci. 2014;56:71-3.
4. Light RW. Update on tuberculous pleural effusion. Respirol. 2010;15:451-8.
5. Oommen S, Banaji N. Laboratory diagnosis of tuberculosis: Advances in technology and drug susceptibility testing. Indian J Med Microbiol. 2017 Jul-Sep;35(3):323–331.
6. Jain AK, Jena SK, Singh MP, Dhammi IK, Ramachandran VG, Dev G. Evaluation of clinicoradiological, bacteriological, serological, molecular and histological diagnosis of osteoarticular tuberculosis. Indian J Orthop. 2008;42(2):173–177.
7. Garg RK, Somvanshi DS. Spinal tuberculosis: a review. J Spinal Cord Med. 2011;34(5):440–54.
8. Hooper C, Lee YC, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010; 65 Suppl 2:i14–17.
9. Vorster MJ, Allwood BW, Diacon AH, Koegelenberg CF. Tuberculous pleural effusions: advances and controversies. J Thorac Dis. 2015; 7(6):981–91.
10. Sehgal IS, Dhooria S, Aggarwal AN, et al. Diagnostic performance of xpert MTB/RIF in tuberculous pleural effusion: systematic review and meta-analysis. J Clin Microbiol. 2016;54(4):1133–6.
11. Chakraborty A, Ramaswamy S, Shivananjiah AJ, Puttaswamy RB, Chikkavenkatappa N. The role of genexpert in the diagnosis of EXUDATIVE PLEURAL EFFUSION in India. Adv Respir Med. 2019;87(5):276–280.
12. Nishimura SL, Broadus VC. Asbestos-induced pleural disease. Clin Chest Med. 1998;19:311–329.
13. Ordenez NG. What are the current best immunohistochemical markers for the diagnosis of epithelioid mesothelioma. A review and update. Hum Pathol. 2007;38(1):1–16.
14. Albertine KH, Wiener-Kronish JP, Roos PJ, Staub NC. Structure, blood supply, and lymphatic vessels of the sheep's visceral pleura. Am J Anat. 1982;165:277–294.
15. Oldmixon EH, Hoppin FGJ. Comparison of amounts of collagen and elastin in pleura and parenchyma of dog lung. J Appl Physiol. 1956;56:1383–1388.
16. Hoganson DM, Owens GE, O'Doherty EM, et al. Preserved extracellular matrix components and retained biological activity in decellularized porcine mesothelium. Biomaterials. 2010;31(27):6934–6940.
17. Foley-Comer AJ, Herrick SE, Al-Mishlab T, Prele CM, Laurent GJ, Mutsaers SE. Evidence for incorporation of free-floating mesothelial cells as a mechanism of serosal healing. J Cell Sci. 2002;115(Pt. 7):1383–1389.
18. Albertine KH, Wiener-Kronish JP, Staub NC. The structure of the parietal pleura and its relationship to pleural liquid dynamics in sheep. Anat Rec. 1984;208:401–409.
19. Wang N-S. The preformed stomas connecting the pleural cavity and the lymphatics in the parietal pleura. Am Rev Resp Dis. 1975;111:12–20.
20. Li J. Ultrastructural study on the pleural stomata in human. Funct Develop Morphol. 1993;3(4):277–280.
21. Li YY, Li JC. Ultrastructure and three-dimensional study of the lymphatic stomata in the costal pleura of the rabbit. Microsc Res Techn. 2003;62:240–246.
22. Courtice FC, Simmonds WJ. Physiological significance of lymph drainage of the serous cavities and lungs. Physiol Rev. 1954;34:419–448.
23. Miura T, Shimada T, Tanaka K, Chujo M, Uchida Y. Lymphatic drainage of carbon particles injected into the pleural cavity of the monkey, as studied by video-assisted thoracoscopy and electron microscopy. J Thoracic Cardiovasc Surg. 2000;120(3):437–447.
24. Oshiro H, Miura M, Iobe H, et al. Lymphatic stomata in the adult human pulmonary ligament. Lymphatic Res Biol. 2015;13(2):137–145.
25. Burke HE. The lymphatics which drain the potential space between the visceral and the parietal pleura. Am Rev Tuberc Pulm Dis. 1957;79:52–65. 26. Liu J, Wong HL, Moselhy J, Bowen B, Wu XY, Johnston MR. Targeting colloidal particulates to thoracic lymph nodes. Lung Canc. 2006;51(3):377–386.