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Comparison of Adenosine Deaminase (ADA) level in Different Exudative Causes of Pleural Effusion in a Tertiary Care Hospital of Sirajganj, Bangladesh

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ABSTRACT

Introduction: *Pleural effusion is abnormal collection of fluid in the pleural space. Tuberculosis is one of the oldest and commonest infectious diseases which are responsible for pleural effusion. Adenosine deaminase (ADA) has been proposed to be a useful marker for the diagnosis of tubercular pleural effusion. The study had been carried out for comparison of ADA level in different etiology of pleural effusion.* ***Methods:*** *This observational study enrolled a total 161 cases of pleural effusion. We divided cases into three groups: group 1(tuberculosis): 87 cases, Group 2 (malignancy):31 cases and Group3 (non-tuberculous and non-malignant): 43 cases. ADA estimation was done by spectrophotometer.* ***Results:*** *Tuberculosis was the primary etiology of 87 cases (54.04%) whereas malignancy was the next most prevalent cause accounting to 31 cases (19.25%). These two were followed by other non-tubercular and nonmalignant 43 cases (26.71%). Mean ADA level was highest in TB (68.67 IU/L) in comparison with malignancy and other causes.* ***Conclusion:*** *It can be concluded that, most common cause of pleural effusion was tuberculosis, followed by malignancy and ADA level was highest in TB than any other causes.*

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INTRODUCTION

Accumulation of excess fluid between the two pleural layers is called pleural effusion.[1] Tuberculosis (TB) is the leading cause of pleural effusion in some countries and a global burning problem, which is now the world's seventh leading cause of death.[2,3]

Pleural effusion is a common problem clinical problem which can result from a number of diseases. The available test and procedures for the confirmation of its etiology are ineffective in majority of cases. Thus, there is need for a sensitive and specific test that is reliable and rapid.[4] The sensitivity of acid-fast staining and

culture for *M. Tuberculosis* in pleural fluid is inadequate.[5] Elevated levels of adenosine deaminase (ADA) in the pleural fluid exhibit sensitivity and specificity values exceeding 90% for diagnosis of pleural tuberculosis.[6,7] Analysis of pleural fluid can have an important contribution for diagnosis of patients with pleural effusion.[8] Cytological examination not only helps for diagnosing tuberculous pleural effusion but also for staging and prognosis of malignant causes of pleural effusion.[9] Levels of ADA are particularly useful in areas where the prevalence of tuberculosis is high.[10] This study was carried out to compare the ADA level in various exudative causes of pleural effusion.

METHODS

This observational study was carried out in the Department of Pathology of Khawaja Yunus Ali Medical College Hospital (KYAMCH), Enayetpur, Sirajganj, Bangladesh over a period of eight months from 10th September, 2020 to 10th May, 2021. According to selection criteria a total of 161 patients presenting with pleural effusion were included in this study after taking informed written consent and ethical clearance. Study cases were divided into three groups: Group 1: Tuberculosis, Group 2: Malignancy and Group 3: Others (Non tubercular and non-malignant). Inclusion criteria were: 1.Patient over 10 years of age from both sexes and 2.Patients with exudative causes of pleural effusion. Exclusion criteria were: 1. Patients with hem thorax and chylothorax, 2. Hemodynamically unstable patient, 3. Patients whom ADA level was not measured and 4. Patients of pleural effusion with transudative cause. Detailed history was taken from all study subjects. Relevant investigations such as haemoglobin concen-tration, total and differential leucocyte count (TDLC), erythrocyte sedimentation rate (ESR), random blood sugar, serum proteins, urine and sputum examination, tuberculin test and plain X-ray chest P/A view were done. Physical and cytological examinations were carries out. ADA level, glucose and protein estimation of pleural fluid were also done by spectrophotometric method using AU-400-Olympus instrument. Clinicocytological and ADA correlation was done in all the cases for the diagnosis of tubercular pleural effusion. Pleural fluid was collected in two separate containers; one for biochemical analysis: protein, glucose and ADA estimation, and another for TDLC and cytological examination. About 20ml fluid was collected for this study. The pleural fluid was examined for above-mentioned tests within 3 to 4 hours of collection. Gram's stain, Ziehl-Neelsen (ZN) stain, culture and sensitivity was done. Frequency and percentage calculation was done by scientific calculator.

RESULTS

A total of 161 cases of diagnosed pleural effusion were taken in this study maintaining the selection criteria. All the cases were exudative type of pleural effusion.

Table I: Age and sex distribution of patients

Age group in years	Male	Female	Total (%)
11-20	2	6	8(4.97)
21-30	11	16	27 (16.77)
31-40	10	16	26 (16.15)
41-50	24	6	30 (18.63)
51-60	24	7	31 (19.25)
>60	30	9	39 (24.20)
Total	**101 (62.73%)**	**60 (37.27%)**	**161 (100%)**

Out of 161 patients majority were male (101, 62.73%) and maximum patients belonged to >60 years (Table I).

Table II: Distribution of exudative pleural effusion according to causes

Causes of pleural effusion	Frequency	Percentage (%)
TB	87	54.04
Malignancy	31	19.25
Others	43	26.71
Total	**161**	**100**

Tuberculosis was the primary etiology of the total 87 cases (54.04%) whereas malignancy was the next most prevalent cause of exudative pleural effusion accounting for 31 cases (19.25%). Other causes were 43(26.71%) (Table II).

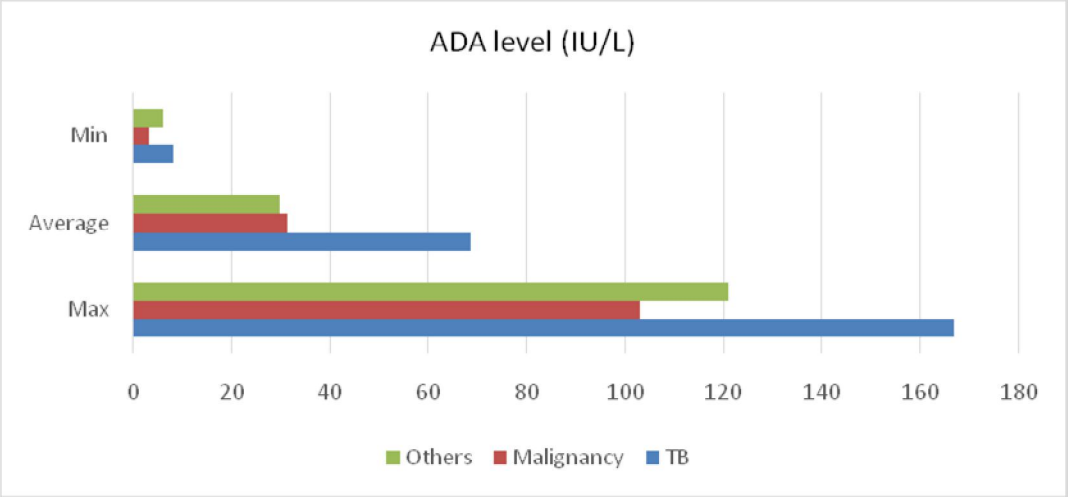

Figure 1: Comparison of ADA (IU/L) level among TB, malignancy and others

Table III: ADA level in different groups of patient

Name of diseases	Level of ADA (Mean ± SD)IU/L	Range (IU/L)
TB	68.67±38.17	8-167
Malignancy	31.29±21.69	3-103
Others(Non-malignant and non-TB.)	29.79±26.13	6-121

ADA level in TB (68.67±38.17 IU/L) was higher than malignancy (31.29±21.69 IU/L). (Figure 1 and Table III).

Table IV: Cut value of ADA in different diseases

Name of diseases	ADA>40IU/L	ADA ≤40IU/L	Total
TB	57	30	87
Malignant	4	27	31
Others	9	34	43

Cut value of ADA for TB is 40 IU/L above 40 ADA level was in 57 cases for TB and ≤40IU/L in 30 cases. In case of malignancy >40 IU/L only in 4 cases and ≤40IU/L in 27 cases, similarly other causes (non malignant and non-tuberculous) ADA level>40 only in 9 cases but ≤40IU/L was in 34 cases. Therefore, In case of non-TB (malignant and others), ADA >40 in only 13 (4+9) cases and ADA≤40 in 61 (27+34) cases (Table IV).

Table V: Comparison of sensitivity and specificity between tubercular and non-tubercular pleural effusion

Diagnostic test (ADA >40 IU/L)	Tubercular effusion	Non-tubercular effusion	Total
Positive	57 (TP)	13 (FP)	70
Negative	30 (FN)	61(TN)	91
Total	**87 (TP+ FN)**	**74 (FP+TN)**	**161**

Considering ADA=40IU/L as cut value for tuberculosis, we found 57 cases as true positive (TP) and 13 case as false positive (FP).On the other hand, 30 cases are false negative (FN) and 61 cases are true negative (TN) Table (V).

Sensitivity = TP/ (TP+FN) = 57/ 87 = 65.51%

Specificity = TN/ (FP+TN) = 61/ 74 = 82.43 %

Positive predictive value (PPV) = TP/ (TP+FP) = 57/ 70 = 81.43%

Negative predictive value (NPV) = TN/ (FN+TN) = 61/91=67.03%

Positive likelihood ratio = Sensitivity/ (100-specificity) = 65.51/ (100- 82.43) = 3.72

Negative likelihood ratio = (100- sensitivity)/ specificity = (100 - 65.51)/ 82.43 = 0.418

As PPV is 81.43%, it means that test positive individual(s) (ADA>40 IU/L) there is 81.43% chance for tuberculosis and NPV is 67.03%, it means when ADA ≤40 IU/L there is no chance of tuberculosis in 67.03% of cases. As well as here positive likelihood ratio is more than one (1) indicating that the test (high ADA) has diagnostic value; tubercular patients are 3.72 times more likely to have high ADA. Similarly, as negative likelihood ratio is less than one (1) its indicating patient with tubercular effusion less likely to have negative test (low ADA); but test is not too unfailing to exclude the disease as negative likelihood ratio is not ≤0.1.

DISCUSSION

In this study, out of 161 patients maximum belonged >60 (39, 24.2%) years of age and majority were male (101, 62.73%). Most common cause of exudative pleural effusion was tuberculosis (54.04%), followed by malignancy (19.25%). This result supports the findings of Valdes et al.[11]

Table VI: Comparison of causes of pleural effusion with other studies

Type of pleural effusion	This study (%)	Dambal et al.[12] (%)	Bhabshar et al.[13] (%)	Vinay et al.[14] (%)	Khan et al.[15] (%)
Tuberculous pleural effusion	54.04	65.5	66	58	33
Malignant pleural effusion	19.25	18.2	18	17	16
Others (non tuberculous and non-malignant effusion)	26.71	16.3	16	25	51
Total	**100**	**100**	**100**	**100**	**100**

In this study, incidence of tuberculous pleural effusion was 54.04% which is consistent with the studies of Dambal et al.[12], Bhabshar et al.[13] and Vinay et al.[14] but Khan et al.[15] observed other causes are more common for pleural effusion (Table VI).

Table VII: Comparison of mean ADA level in various group of pleural effusion

Type of effusion	Mean ADA level (IU/L)		
	This study	Vinay et al.[14]	Lamsal et al.[16]
Tuberculous Pleural effusion	68.67	67.78	34.53
Malignant pleural effusion	31.29	22.90	18.20
Non-tubercular and non malignant effusion	29.79	22.17	16.71

In this study mean ADA value of tubercular pleural effusion was higher as compared with non-tubercular and malignant pleural effusion, which was consistent with the study findings of Vinay et al.[14] and Lamsal et al.[16]

Tuberculosis was also the leading cause of pleural effusion in another study conducted by Maikap et al.[17] Similar study conducted in a respiratory intensive care set up by Chinchkar et al.[18] found malignancy to be the most frequent cause of pleural effusion.

Majority of the cases of pleural effusion were males as compared to females in this study (62.73% vs 37.27%) having male: female ratio 1.68:1. Maikap et al.[17]and Sharma et al.[19] also found similar male majority in their studies.

Current study revealed, the patients with pleural effusion were found in all age groups ranging from 11 to 84 years. Patients aged more than 60 years represent the largest group (24.22%). In between 31 and 40 age group (29.34%) was the largest group in the study of Parikh et al.[20]

Many authors[15,21] reported that values of ADA were significantly higher in tubercular pleural effusions. Similar result was observed in this study. Malignant pleural effusion was found in 19.25% of cases which was quite similar to different researches done previously by Khan et al.[15] (15.55%), Maikap et al.[17] (14%) and Chinchkar et al.[18] (24%). This study limitations were small sample size and short duration of study period.

CONCLUSION

It can be concluded that, most common cause of pleural effusion in a tertiary hospital was tuberculosis, followed by malignancy. In biochemical study, ADA level is the highest in tuberculosis than any other causes of pleural effusion.

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