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Diagnostic Significance of Pleural Fluid ADA and Hematological Parameters in Pediatric Tubercular Versus Non-Tubercular Pleural Effusion

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Abstract

Background:
Pediatric pleural effusions arise from diverse etiologies, with tuberculous pleural effusion (TPE) and non-tuberculous causes being the most common. Early differentiation is essential for timely management.

Objective:
This study aimed to evaluate the diagnostic significance of pleural fluid ADA and hematological parameters in distinguishing pediatric tubercular versus non-tubercular pleural effusions.

Methods:
A cross-sectional study was conducted at Bangladesh Shishu Hospital and Institute from July 2019 to January 2022, including 47 children aged 1-18 years with pleural effusion. The diagnostic performance of pleural fluid ADA and key hematological parameters was analyzed using SPSS 26.

Results:
Pleural ADA was markedly higher in TPE than in non-TPE cases (90.6±52.0 vs. 36.0±11.5 U/L). TPE patients showed significantly lower total WBC counts and polymorph percentages, but higher lymphocyte percentages and ESR ($P<0.05$). Hemoglobin, platelet count, and CRP showed no significant group differences.

Conclusion:
Pleural fluid ADA, combined with selected haematological parameters, provides meaningful discrimination between tubercular and non-tubercular pediatric pleural effusions and supports clinical decision-making.

Keywords: Pleural fluid, ADA, Pediatric tuberculosis, Pleural effusion

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Introduction:

Pleural disease contributes substantially to illness and death in both adults and children[1] and represents about 4% of all cases seen in chest hospitals.[2,3] Pleural effusion occurs when excess fluid accumulates in the pleural space due to a disruption of the balance between vascular hydrostatic and oncotic pressures.[4] Pleural effusion in children poses significant diagnostic challenges, especially in distinguishing a tuberculous pleural effusion (TPE) from non-tuberculous causes, such as parapneumonic effusion (PPE), empyema, or other infections. Microbiological confirmation for TB in pleural fluid or tissue is hampered by low bacillary load in most pediatric TPE cases. Hence, much attention has focused on pleural fluid cytology and biochemical markers to improve diagnostic accuracy.[5] Adenosine deaminase (ADA) remains a widely used biomarker. For example, in a study of children with PPE and tuberculosis, pleural fluid ADA >40 IU showed sensitivity ≈ 87.5% and specificity ≈ 82.4% for diagnosing TPE in pediatric settings. Also, higher ADA levels have been demonstrated in TPE compared to PPE and other non-TB causes.[6] However, ADA alone is imperfect: false positive results can occur in parapneumonic infections, empyema, lymphomas, and other inflammatory conditions.[7] To enhance diagnostic

discrimination, several studies have evaluated ratio indices. In recent work from China, the 10Ч ADA/LDH ratio showed excellent performance in distinguishing TBPE from non-TBPE; at ADA >20 U/L, this index had a sensitivity ≈ 95% and specificity ≈ 94%.[8] Similarly, a 2024 study showed that the pfLDH/pfADA ratio has greater diagnostic value than ADA alone, with an area under the ROC curve (AUC) of 0.946, sensitivity of ~93.9% and specificity of 87.0% for differentiating TPE vs non-TPE.[9] Other laboratory parameters are also helpful. Differential cell count (lymphocytic vs neutrophilic predominance) is a classic discriminator. TPE is often lymphocyte-predominant, while non-tubercular effusions show neutrophils or mixed cells.[10] Pleural fluid glucose is often lower, and LDH markedly higher in PPE/empyema compared to TPE.[11] Further, factors associated with negative ADA in childhood TPE have been identified: lower pleural protein levels, lower LDH levels, and the absence of chest pain are associated with ADA ≤40 U/L, even in confirmed TB effusion.[12] Given variability in cut-off values, patient age, and the aetiology mix across settings, there is a need for locally validated marker combinations (ADA, LDH, cell counts, glucose, protein) to distinguish TPE from non-TPE efficiently.[13] This study aims to evaluate the diagnostic significance of pleural fluid ADA and hematological parameters in distinguishing pediatric tubercular versus non-tubercular pleural effusions.

Methods:

This cross-sectional study was conducted at the Department of Pediatric Respiratory Medicine at Bangladesh Shishu Hospital and Institute, Dhaka, from July 2019 to January 2022. Children aged 1 to 18 years who were admitted with pleural effusion during the study period were considered for inclusion. A total of 47 patients who met the defined inclusion and exclusion criteria were enrolled through convenience sampling. The study population comprised children and adolescents diagnosed with either tuberculous pleural effusion or parapneumonic effusion. Patients with transudative pleural effusion, malignancy, previously treated pleural effusion, empyema, loculated effusion, connective tissue disorders such as systemic lupus erythematosus, or those testing positive for COVID-19 were excluded. Following approval from the Ethical Review Committee (ERC) of the Bangladesh Institute of Child Health, children with clinically and radiologically confirmed pleural effusion underwent thoracocentesis for both diagnostic and therapeutic purposes. Effusions were categorized as exudative or transudative according to Light's criteria. The diagnosis of Tubercular pleural effusion based on detection of Mycobacterium tuberculosis was performed using Xpert MTB/RIF or Xpert MTB/RIF Ultra. Effusions were classified as exudate or transudate using Light's criteria. All collected data were entered into a personal computer, thoroughly checked for accuracy, and analyzed using SPSS version 26.0. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean±standard deviation (SD). The unpaired t-test was used for comparisons of continuous variables, and the chi-square (χ^2) test was applied for categorical data. Statistical results were presented in tables and charts, and p-values <0.05 were considered statistically significant.

Results:

Table-I showed the demographic characteristics of the study population. It was observed that most patients (48.9%) were in the 1-5year age group with mean age 5.57±2.89 years. Regarding admitted patients, the proportion was higher among male children (31 [61.9%]), with a male: female ratio of 1.9:1. The Majority of patients (53.2%) were from the low socioeconomic group.

Table-I: Demographic characteristics of the study patients (N=47)

Demographic characteristics	no. (%)
Age group (years)	
1-5	23(48.9)
6-10	21(44.7)
>10	3(6.4)
Mean±SD	5.57±2.89
Gender	
Male	31(66.0)
Female	16(34.0)
Male: female	1.9:1
Socio-economic status	
Low group	25(53.2)
Middle group	16(34.0)
High group	6(12.8)

Table-II summarized the vaccination and exposure status of the study children (N=47). Among the

participants, three children (17.7%) showed a tuberculin skin test (TST) induration of ≥10 mm, and all of them had previously received the BCG vaccine. Additionally, three children (17.6%) had a documented history of contact with known tuberculosis cases.

Table-II: Active or passive vaccination status (N=47)

Characteristics	no. (%)	Notes
Tuberculin skin test induration ≥10 mm	3(17.7)	All BCG vaccinated
History of contact with tuberculous cases	3(17.6)	

Among 58 patients, 36.2% pleural effusion was due to tuberculosis (Figure-1)

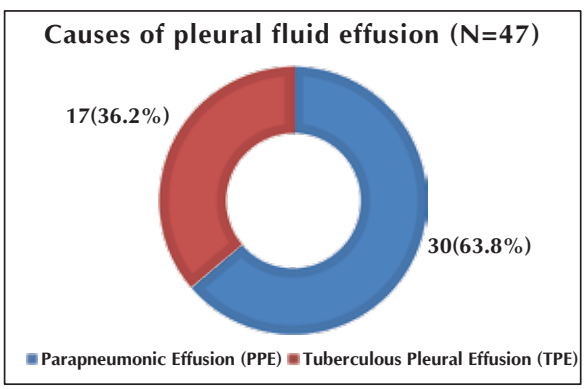

Figure-1: Causes of pleural fluid effusion (N=47)

Table-III: Comparison of pleural fluid ADA between two groups (N=47)

Variables	TPE (n=17)	non-TPE (n=30)	p-value
Pleural fluid ADA (U/L)	90.6±52.0	36.0±11.5	<0.001

Pleural fluid ADA significantly increased in TPE (Table-III). The mean polymorph (%) of WBC in TPE was 49.8±14.0, and in non-TPE, 68.26±5.3. The mean difference was statistically significant (P<0.001). Mean Lymphocyte (%) of WBC in TB was 45.3±13.8, and non-TPE was 29.0±5.3. The mean difference was statistically significant (P<0.001). Mean total count of WBC was 11708.3±2936.7 and 16110.7±3722 in TPE and non-TPE cases, which was found statistically significant (P=0.001). ESR was statistically significant. Other parameters, Hb, platelet count, and CRP, were not statistically significant (Table-IV).

Table-V showed the pleural fluid parameters of the studied children. It was observed that the mean polymorph of pleural fluid in TPE was 22.9±19.4 % and in non-TPE was 72.7±12.2%. The mean difference in polymorphs was statistically significant (P<0.001). Mean Lymphocyte count of pleural fluid in TPE was 77.1±19.4 % and in non-TPE was 27.4±12.3%. The mean difference was statistically significant (p<0.001). The mean difference of the total count and sugar level was statistically significant.

Table-IV: Laboratory parameters of the study patients (N=47)

Variables	TPE (n=17)	non-TPE (n=30)	p-value
Hb (gm/dl)	9.9±1.1	10.21±0.8	0.272
Total count WBC (/cumm)	11708.3±2936.7	16110.7±3722.0	0.001
Polymorph (%)	49.8±14.0	68.3±5.3	<0.001
Lymphocyte (%)	45.3±13.8	29.0±5.3	<0.001
Platelate count (/cumm)	410916±150251	369000±203733	0.523
ESR	50.2±13.3	37.3±12.1	0.002
CRP	23.0±13.9	25.5±14.0	0.605

Table-V: Pleural fluid parameters of the study patients (N=47)

Variables	TPE (n=17)	non-TPE (n=30)	p-value
Total count (/cumm)	2152.9±816.5	4490.0±2564.5	0.001
Polymorph (%)	22.9±19.4	72.7±12.2	<0.001
Lymphocyte (%)	77.1±19.4	27.4±12.3	<0.001
Protein (mg/dl)	4.34±1.1	4.2±0.8	0.145
Sugar (mg/dl)	27.0±15.2	62.7±37.4	<0.001
Pleural fluid LDH (U/L)	480.3±126.9	411.3±90.9	0.055

Discussion:

In this study, the majority (48.9%) of children were in the 1-5 years age group, followed by the 6-10 years age group (44.7%). The mean age was 5.57±2.89 years. Almost two-thirds (66.0%) of patients were male with a male: female ratio 1.9:1. This finding was consistent with the results shown in previous studies where the maximum number of children were in the age group 1-4 years (32%)[2,14] where as Saliya and Joshi[6] found 32% of children were in 6 -10 years. In this study, male children were more. This may be because male children are genetically more susceptible to disease than females. We observed significantly higher pleural fluid ADA levels in TPE patients (90.6±52.0 U/L) than in non-TPE patients (36.0±11.5 U/L; p<0.001). These findings align with previous studies, such as those by Hou et al,[15] who reported elevated pleural fluid ADA levels in TPE patients. Regarding haematological parameters, our study found that total white blood cell (WBC) counts were significantly higher in non-TPE patients (16,110.7±3,722.0 cells/μL) than in TPE patients (11,708.3±2,936.7 cells/μL; p=0.001). This contrasts with the findings of Zhao et al,[9] who reported higher WBC counts in TPE patients, suggesting variability in immune responses across populations. The percentage of polymorphonuclear cells (PMNs) was significantly higher in non-TPE patients (68.3±5.3%) compared to TPE patients (49.8±14.0%), with a p-value of <0.001. Conversely, the percentage of lymphocytes was significantly higher in TPE patients (45.3±13.8%) than in non-TPE patients (29.0±5.3%), with a p-value of <0.001. These findings are consistent with previous studies, such as those by Mercer et al,[16] who reported a higher lymphocyte percentage in TPE cases, and by Zhao et al,[9] who observed a higher PMN percentage in non-TPE cases. Our study also found that the erythrocyte sedimentation rate (ESR) was significantly higher in TPE patients (50.2±13.3 mm/h) than in non-TPE patients (37.3±12.1 mm/h; p=0.002). This is consistent with the findings of Lee et al,[17] who reported elevated ESR levels in TPE patients. However, parameters such as hemoglobin (Hb), platelet count, and C-reactive protein (CRP) levels did not show significant differences between TPE and non-TPE groups in our study. These results are consistent with those of Zhao et al,[9] who also found no significant differences in these parameters between the two groups.

Limitations:

This single-centre study had a small sample size, which may limit generalizability. Not all cases had microbiological confirmation of tuberculosis, and some classification depended on clinical judgment. Essential factors, such as nutritional status and prior treatment, were not fully controlled, which may have influenced the laboratory findings.

Conclusion:

Elevated pleural fluid ADA levels, along with hematological markers such as WBC count, lymphocyte and polymorph percentages, and ESR, are valuable in distinguishing tuberculous pleural effusion from non-tuberculous cases. These parameters can serve as useful adjuncts in the diagnostic evaluation of pediatric pleural effusions, though further research is warranted to identify additional biomarkers and improve diagnostic accuracy.

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