

ORIGINAL ARTICLE

Pleural Fluid Cytology and Biochemical Profiles in Pediatric Pleural Effusion

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**ABSTRACT**

Introduction: Pleural effusion, the accumulation of excess fluid in the pleural cavity, is a common cause of respiratory morbidity in children and can result from a variety of infectious and non-infectious conditions. In the pediatric population, parapneumonic effusion and tuberculous pleural effusion are among the most frequently encountered causes, each with distinct cytological and biochemical profiles. This study aims to evaluate the pleural fluid cytology and biochemical parameters in children with pleural effusion. **Methods & Materials:** This cross-sectional study was conducted at the Department of Pediatric Respiratory Medicine, Bangladesh Shishu Hospital and Institute, Dhaka, from July 2019 to January 2022. A total of 58 children from 1 to 18 years of age admitted with pleural effusion were selected as study subjects. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0. **Result:** Among the 47 study patients, parapneumonic effusion (63.8%) was the most common cause of pleural effusion, followed by tuberculous pleural effusion (36.2%). Pleural fluid analysis showed that TPE cases had significantly lower total cell counts and polymorph percentages, but higher lymphocyte percentages compared to non-TPE cases ($P < 0.001$). Glucose levels were also significantly lower in TPE ($P < 0.001$), while protein and LDH levels did not differ significantly between the groups. **Conclusion:** Analysis of pleural fluid cytology and biochemical profiles in pediatric pleural effusion revealed that tuberculous pleural effusion is characterized by significantly higher lymphocyte percentages and lower polymorphonuclear cell counts, along with reduced glucose levels and lower total cell counts, compared to non-tuberculous effusions.

Keywords: Pleural Effusion, Pleural Fluid Cytology, Biochemical Profiles, Tuberculosis

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INTRODUCTION

Pleural disease is a significant cause of morbidity and mortality in adults and children, accounting for approximately 4% of all chest hospital attendances [1,2,3]. Pleural effusion is the collection of excess fluid in the pleural cavity, resulting from an imbalance between vascular hydrostatic and oncotic pressure [4]. It is classified as exudative or transudative; pneumonia and tuberculosis are the most common causes of exudative effusion in children worldwide. Tuberculosis (TB) remains a major health problem in developing countries, with an increasing proportion of extrapulmonary TB [5]. National guidelines classify pleural TB as extrapulmonary TB (EPTB). According to the WHO Global TB Report 2020, an estimated 10 million people developed TB worldwide, including 1.1

million children [6]. Thirty high-burden countries accounted for 86% of new cases, with India leading, followed by China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa. TB is caused by *Mycobacterium tuberculosis*. A study at Bangladesh Shishu Hospital and Institute identified 61 cases of extrapulmonary TB versus 30 pulmonary TB cases [7]. Pleural effusion is the second most common EPTB manifestation, with a global incidence of about 4.9%, ranging from 4% in the US to 23% in Spain [8]. Around 50% of untreated pleural TB cases progress to pulmonary TB within five years, emphasizing the need for early diagnosis and treatment [9]. Diagnosis of TB in children is difficult, and adult diagnostic strategies may miss many pediatric cases. Definitive diagnosis is made by detecting *M. tuberculosis* in

sputum, pleural fluid, or biopsy specimens, supported by the Mantoux test and chest X-ray [10]. Smear microscopy, although highly specific (>95%), has low sensitivity (25–65%) because childhood pleural TB usually has paucibacillary disease. Conventional culture remains the gold standard but is time-consuming, taking 6–8 weeks. Chest X-ray is neither sensitive nor specific, and TST/IGRA has limited ability to differentiate latent from active TB and may be negative in malnourished or immunosuppressed children [11]. Cartridge-based nucleic acid amplification test (CBNAAT) shows limited sensitivity (43.7%) in pleural fluid (WHO X-pert MTB/RIF Manual). Although pleural biopsy offers better sensitivity, it is invasive and not always feasible. Therefore, diagnosis is often based on clinical suspicion, contact history, TST positivity, and pleural fluid showing unilateral exudative lymphocytic effusion with high protein content [10]. Pleural fluid cytology and biochemical analysis play a crucial role in differentiating the etiology of pediatric pleural effusion. Cytological evaluation helps distinguish between neutrophilic effusion, commonly seen in parapneumonic effusion, and lymphocytic effusion, which is characteristic of tuberculous pleural effusion [12]. Biochemical profiles, including protein, lactate dehydrogenase (LDH), glucose, and adenosine deaminase (ADA) levels, are essential to classify effusions as exudates or transudates based on Light's criteria [13]. Combined cytological and biochemical assessment, therefore, provides a cost-effective, minimally invasive, and reliable approach for early diagnosis and management of pediatric pleural effusion. This study aims to evaluate the cytological and biochemical profiles of pleural fluid in pediatric patients with pleural effusion.

METHODS & MATERIALS

This cross-sectional study was conducted at the Department of Pediatric Respiratory Medicine, Bangladesh Shishu Hospital and Institute, Dhaka, from July 2019 to January 2022. All children from 1 to 18 years of age admitted with pleural effusion in Bangladesh Shishu Hospital and Institute, Dhaka, during the study period were enrolled in the study. A total of 58 patients were selected as study subjects as per the inclusion and exclusion criteria. Subjects were selected by a convenience sampling technique. The study included children and adolescents aged 1 to 18 years who were diagnosed with either tuberculous pleural effusion or parapneumonic effusion. Patients with transudative pleural effusion, malignancy, previously treated pleural effusion, empyema, loculated effusion, connective tissue diseases such as systemic lupus erythematosus, or those who tested positive for COVID-19 were excluded from the study. After approval from the ethical review committee (ERC) of the Bangladesh Institute of Child Health, children diagnosed with pleural effusion both clinically and radiologically were enrolled and subsequently underwent thoracentesis for diagnostic and therapeutic

purposes. The diagnosis of Tubercular pleural effusion based on Mycobacterium tuberculosis detection was done by Xpert MTB/ RIF or Xpert MTB/ RIF Ultra before statistical procedure. Effusions were classified as exudate or transudate using Light's criteria. All the data were entered into a personal computer, carefully checked for errors, and then processed and analyzed using the Statistical Package for Social Science (SPSS) version 26.0. Categorical variables were expressed as numbers and percentages, while quantitative variables were presented as mean $\pm$ standard deviation (SD). The unpaired t-test was used to compare continuous variables, and the chi-square (χ^2) test was applied for categorical variables. The results of the statistical analysis were presented in tables and charts, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Table I shows the demographic characteristics of the study population. It was observed that the majority of patients (48.9%) belonged to the age group 1-5 years. The mean age was 5.57 ± 2.89 years. Regarding admitted patients, the proportion was found to be higher in male children; 31(61.9%) with a male: female ratio, i.e., 1.9:1. The Maximum patients (53.2%) were in the low socioeconomic group. [Table I]

Table – I: Demographic characteristics of the study patients (n=47)

Variables	Frequency (n)	Percentage (%)
Age group (years)		
1-5	23	48.9
6 - 10	21	44.7
> 10	3	6.4
Mean $\pm$ 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

Results are expressed as frequency, percentage, and mean $\pm$ SD Socio-economic status based on the modified Kuppuswami scale [14].

Table II summarizes the vaccination and exposure status of the study children (n=47). Among the participants, 3 children (17.7%) showed a tuberculin skin test (TST) induration of ≥ 10 mm, and all of them had previously received the BCG vaccine. Additionally, 3 children (17.6%) had a documented history of contact with known tuberculosis cases. [Table II]

Table – II: Active or Passive vaccination status (n=47)

Characteristics	Number of Children	Percentage (%)	Notes
Tuberculin skin test induration ≥ 10 mm	3	17.7	All BCG vaccinated
History of contact with tuberculous cases	3	17.6	—

Among the 47 study patients, parapneumonic effusion (PPE) was the most common cause, accounting for 63.8% of cases,

followed by tuberculous pleural effusion (TPE) in 36.2% of patients. [Table III]

Table – III: Causes of pleural fluid effusion (n=47)

Cause of Pleural Effusion	Number of Patients (n = 47)	Percentage (%)
Parapneumonic Effusion (PPE)	30	63.8%
Tuberculous Pleural Effusion (TPE)	17	36.2%
Total	47	100%

Table IV shows 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 of polymorph 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].

Table – IV: 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

Results were expressed as mean $\pm$ SD, P -value<0.05=significant. An unpaired t -test was done to measure the level of significance.

DISCUSSION

In this study, the majority (48.9%) of children belonged to the age group 1-5 years, followed by 6-10 years (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 was in the age group 1-4 years (32%) where as Saliya and Joshi found 32% of children were in 6 -10 years [2,15]. On comparing different types of exudative pleural effusion in this study, parapneumonic effusion (63.8%) was more common than tubercular pleural effusion (36.2%). This finding was consistent with the results shown in previous studies, where parapneumonic effusion was more common 38.23% than tubercular pleural effusion (23.50%) but Akand et al. found empyema (40%) was more common than tubercular pleural effusion (30%) and parapneumonic effusion (26.7%) which was not consistent with this study [2,15]. It may be because, before the COVID-19 pandemic, children were more exposed to environmental hazards, bacterial exposure, and the development of pneumonia. A positive tuberculin skin test result is helpful evidence in diagnosing TB pleural effusions in areas of low prevalence (or no vaccination). However, a negative tuberculin skin test result may occur in roughly one-third of patients [8]. In our series, three children (17.7%) showed an induration of ≥ 10 mm in the tuberculin skin test, and all of them were BCG vaccinated. A history of contact with tuberculous cases was present in 3 children (17.6%). In Akand et al. study, positive history was identified in 9 (15%) patients, and 9 (15.5%) had MT positive, which is not similar to our finding [2]. We observed a significantly lower total white blood cell (WBC) count in TPE cases (2152.9 ± 816.5 cells/ μ L)

compared to non-TPE cases (4490.0 ± 2564.5 cells/ μ L), with a p -value of 0.001. This aligns with findings from a study by Mukhida et al., which reported a mean WBC count of 3657 ± 1245 cells/ μ L in TPE patients, suggesting a less inflammatory response in TPE [16]. The percentage of polymorphonuclear cells (PMNs) was significantly lower in TPE cases (22.9 ± 19.4 %) compared to non-TPE cases (72.7 ± 12.2 %), with a p -value of <0.001. This finding is in agreement with a study by Choe et al. (2024), which observed a lower PMN count in TPE cases, indicating a predominantly lymphocytic response.

Conversely, the percentage of lymphocytes was significantly higher in TPE cases (77.1 ± 19.4 %) compared to non-TPE cases (27.4 ± 12.3 %), with a p -value of <0.001. This lymphocytic predominance is characteristic of TPE and supports the findings of a study by Antonangelo et al., which reported a mean lymphocyte percentage of 76.2 ± 20.1 % in TPE patients [17]. Regarding pleural fluid glucose levels, we found a mean of 27.0 ± 15.2 mg/dL in TPE cases, which is lower than the 62.7 ± 37.4 mg/dL observed in non-TPE cases, with a p -value of <0.001. This is consistent with findings from a study by Antonangelo et al., which reported reduced pleural fluid glucose levels in TPE cases [17]. The pleural fluid lactate dehydrogenase (LDH) levels in our study were 480.3 ± 126.9 U/L for TPE cases and 411.3 ± 90.9 U/L for non-TPE cases, with a p -value of 0.055, indicating no significant difference. This is in line with a study by Zhao et al., which found that pleural fluid LDH levels are elevated in TPE but not significantly different from those in non-TPE cases [18].

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

In conclusion, analysis of pleural fluid cytology and biochemical profiles in pediatric pleural effusion revealed that tuberculous pleural effusion is characterized by significantly higher lymphocyte percentages and lower polymorphonuclear cell counts, along with reduced glucose levels and lower total cell counts, compared to non-tuberculous effusions.

RECOMMENDATION

It is recommended to routinely assess pleural fluid cytology and biochemical parameters, including lymphocyte and polymorphonuclear cell percentages, total cell count, and glucose levels, to aid in the early and accurate differentiation of tuberculous and non-tuberculous pleural effusions in pediatric patients.

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