Etiological Spectrum and Outcome of Pleural Effusion in Children: A Hospital-Based Study from Bangladesh

S Tahura[1], A B Anowar[2], M Kamruzzaman[3], M J Alam[4], P K Sarkar[5]

Abstract

Background: Pleural effusion is a frequent cause of respiratory morbidity in children, with variable etiology and outcomes depending on geography, vaccination status, and underlying diseases and timely management.

Methods: This prospective observational study was conducted in the department of Respiratory Medicine of Bangladesh Shishu Hospital and Institute, enrolling 511 consecutive children diagnosed radiologically as pleural effusion between January 2022 and June 2024. Clinical features, imaging findings and pleural fluid analyses including cytology, biochemistry, microbiology, Gene Xpert, adenosine deaminase (ADA), lactate dehydrogenase (LDH) and immunochromatographic test (ICT) for Streptococcus pneumoniae were performed for all patients. Data was analyzed descriptively using SPSS v24.

Results: Among the children enrolled total 218 (42.7%) were aged 5–<10 years. All children below 10 years (n=343) were fully immunized with PCV-10 as per EPI schedule of Bangladesh. Empyema was found in 112 (21.9%) and tubercular pleural effusion in 103 (20.2%) cases. Among bacterial infectious etiologies were found *Streptococcus pneumoniae* the leading isolate (49 cases/42.1%) followed by *Pseudomonas aeruginosa* (17) and *Klebsiella pneumoniae* (10). Multi Drug Resistant *S. pneumoniae* was detected in 13 (26.5%) cases. Two (0.4%) children had co-infection of *Mycobacterium tuberculosis* and *S. pneumoniae*. The remaining cases included nonspecific exudative effusions. A total of 472 (92.3%) children improved with appropriate management including antibiotics, chest tube drainage, and antitubercular therapy. Thirty-nine (7.7%) had persistent or loculated effusions requiring surgical intervention and prolonged hospitalization.

Conclusion: Despite widespread coverage of PCV-10 vaccination, S. pneumoniae remained the main pathogen and emergence of MDR Pneumococcus is alarming. It might be highlights the possible serotype replacement and vaccine escape.

Keywords: Pleural effusion, Empyema, Tuberculosis, Children, Bangladesh, PCV-10 Vaccine.

DOI: https://doi.org/10.3329/nimcj.v16i1.86516

Northern International Medical College Journal Vol. 16 No. 1-2 July 2024-January 2025, Page 712-715

[1]Dr. Sarabon Tahura
Associate Professor
Dept. of Pediatric Respiratory Medicine
Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh

[2]Dr. Asma Bint Anowar
FCPS (Pediatric Pulmonology) part-II student,
Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh

[3]Dr. Md Kamruzzaman
Associate Professor

[4]Dr. Md Jahangir Alam
Professor

[5]Dr. Prabir Kumar Sarkar
Professor

1,3,4,5
Dept. of Pediatric Respiratory Medicine
Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh

Correspondence
Dr. Sarabon Tahura
Associate Professor
Dept. of Pediatric Respiratory Medicine, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh
email: drsarabon@yahoo.com

Introduction

Pleural effusion is defined as abnormal fluid accumulation within the pleural cavity. It remains as a significant cause of respiratory morbidity and hospitalization in children especially in low- and middle-income countries (LMICs) where infections predominate and diagnostic or treatment resources may be constrained.[1] The etiology of pediatric pleural effusion varies widely depending on local epidemiology, immunization status (particularly for pneumococcal disease), underlying illnesses and the timeliness of management. Historically, bacterial pneumonia complicated by parapneumonic effusion or empyema has been dominated by Streptococcus pneumoniae globally.[2] The introduction of pneumococcal conjugate vaccines (PCVs) into national immunization program has been a major public health intervention. Many studies demonstrate the reduction in invasive pneumococcal disease (IPD) caused by vaccine serotypes. But concurrently evolving evidence of many studies showed serotype replacement, persistence of non-vaccine serotypes and emergence of multidrug resistant (MDR) pneumococci.[3–5] For instance, in European countries by using PCV-10 or PCV-3, incidence of IPD declined but non-vaccine serotype disease increased by >100% in children <5 years in some settings.[3]

In Bangladesh, the 10-valent pneumococcal conjugate vaccine (PCV-10) was introduced into the national Expanded Program on Immunization (EPI) in 2015 with subsequent high coverage reported.[6] Despite this achievement, hospital-based surveillance and case-series data suggest

that pneumococcal disease including complicated pneumonia and pleural effusion continues to be reported in children.[7,8] The persistence of pneumococcal pleural disease in a vaccinated population raises important questions about vaccine serotype coverage, immune response in the local population, the role of non-vaccine serotypes and antibiotic resistance. Given that pleural effusion and empyema represent complications associated with higher morbidity, longer hospital stay and cost, up-to-date local data on their etiology, microbiology (including resistance) and outcome are essential to guide the prevention and management strategies.

This prospective observational study was undertaken at a major tertiary pediatric respiratory center in Bangladesh. Our objectives were to determine the etiological spectrum (including bacterial, tubercular and nonspecific causes) of pleural effusion in children, to evaluate the microbiological profile of pleural fluid with a focus on S. pneumoniae, to assess antimicrobial resistance (particularly MDR pneumococcus) and to evaluate clinical outcomes. Importantly, we sought to examine the paradox of persistent pneumococcal pleural disease despite PCV-10 immunization and to discuss implications for vaccine policy and antimicrobial stewardship in the Bangladeshi pediatric setting.

Materials and Methods

This prospective hospital-based observational study was conducted in the Department of Pediatric Respiratory Medicine, Bangladesh Shishu Hospital & Institute (BSH&I), Dhaka, between January 2022 and June 2024. A total of 511 consecutive children aged ≤16 years who presented with radiologically confirmed pleural effusion (via chest X-ray and/or ultrasonography) were enrolled after obtaining written informed consent from parents or guardians. Children with pleural effusion secondary to cardiac, renal, rheumatological causes, post-surgical or traumatic origin or malignancy were excluded. The immunization status of children was verified through immunization card and parental interview.

Detailed demographic and clinical data (age, sex, symptoms, immunization status) were recorded on a structured proforma. All children underwent chest imaging (X-ray and ultrasound) to determine effusion characteristics (free vs loculated or empyema). Pleural fluid was aspirated (as clinically indicated) for cytology (cell count, differential), biochemical tests (protein, glucose, lactate dehydrogenase [LDH], adenosine deaminase [ADA]), Gram stain, aerobic culture and sensitivity, immunochromatographic test (ICT) for S. pneumoniae antigen, and Gene Xpert MTB/RIF for Mycobacterium tuberculosis. Blood investigations included complete blood count and C-reactive protein (CRP) were performed in every enrolled children.

Empyema was defined as pleural fluid that was grossly purulent or had evidence of loculation or septations on imaging or positive bacterial culture. Tubercular pleural effusion was defined as Gene Xpert positive for M. tuberculosis in fluid and/or ADA > 40 IU/L in a compatible clinical-radiological context with response to anti-tubercular therapy (ATT). Multi-drug resistant (MDR) S. pneumoniae was defined as pneumococcal isolate resistant to two or more major antibiotic classes (e.g., penicillin, macrolides, cephalosporins).

Children were managed according to institutional protocols: empirical broad-spectrum antibiotics changed after culture results if required, chest-tube drainage, Anti TB drugs for tubercular cases, and symptomatic and supportive care.

Outcome was classified as "improved" (clinical and radiological resolution) or persistent/loculated effusion requiring surgical intervention. Data were entered into SPSS version 24 and analyzed descriptively with frequencies and percentages.

Results

A total of 511 children were enrolled, with 125 (24.5%) aged <5 years, 218 (42.7%) aged 5–<10 years, and 168 (32.8%) aged 10–16 years (fig.1). Among them, 57% were male (fig.2). All 343 children below 10 years were fully immunized with PCV-10 under the EPI schedule. Fever (93%), cough (87%), and dyspnea (65%) were the most frequent presenting symptoms and chest pain was reported in 42% of patients (Table I).

Table I. Demographic and Clinical Characteristics of Children with Pleural Effusion (n = 511)

Parameter	n (%)
Age (years)	
< 5	125 (24.5)
5 – < 10	218 (42.7)
10 – 16	168 (32.8)
Sex	
Male	292 (57.1)
Female	219 (42.9)
Symptoms	
Fever	476 (93.2)
Cough	445 (87.1)
Dyspnea	332 (65.0)
Chest pain	215 (42.1)
Radiological finding	
Free fluid	399 (78.1)
Loculated/empyema	112 (21.9)
Outcome	
Improved	472 (92.3)
Persistent/loculated → Surgical intervention	39 (7.7)
Mortality	0 (0.0)

Radiological evaluation revealed free fluid in 399 (78.1%) and loculated or empyemic collections in 112 (21.9%) (Table I). Bacterial infectious etiology was found in 42.1% of cases, tubercular in 20.2%, and nonspecific exudative effusion in 37.7%. Streptococcus pneumoniae was the predominant

organism, isolated or antigen-positive in 49 (9.6%) children, followed by Pseudomonas aeruginosa (17; 3.3%), Klebsiella pneumoniae (10; 2.0%) and Staphylococcus aureus (8; 1.6%). Gene Xpert detected Mycobacterium tuberculosis in 93 (18.2%) cases, including two (0.4%) with dual infection of S. pneumoniae and M. tuberculosis (Table II).

Table II. Etiology and Microbiological Spectrum of Pleural Effusion

Etiology / Pathogen	n (%)	MDR (%)
Bacterial infectious cases	215 (42.1)	–
S. pneumoniae	49 (9.6)	13 (26.5)
P. aeruginosa	17 (3.3)	3 (17.6)
K. pneumoniae	10 (2.0)	2 (20.0)
S. aureus	8 (1.6)	1 (12.5)
Mixed bacterial infection	6 (1.2)	–
Tubercular effusion	103 (20.2)	–
Gene Xpert positive M. tuberculosis	93 (18.2)	–
Co-infection (MTB + S. pneumoniae)	2 (0.4)	–
Nonspecific exudative effusion	193 (37.7)	–

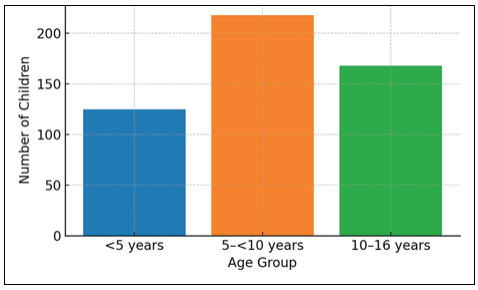

Fig.1: Age distribution of children with pleural effusion

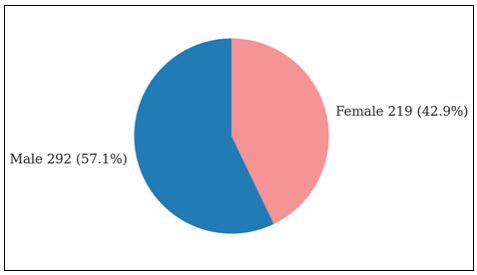

Fig.2: Sex distribution of children with pleural effusion

Among 49 pneumococcal isolates, 13 (26.5%) were multidrug resistant (MDR). MDR pneumococci were notably more frequent among vaccinated children <10 years (Table II). With standard management e.g. antibiotics, chest tube drainage and anti-tubercular therapy as indicated, 472 (92.3%) children improved, whereas 39 (7.7%) had persistent or loculated effusion necessitating surgical intervention or extended hospital stay. No deaths occurred during hospitalization (Table I).

Discussion

In this large prospective pediatric cohort from Bangladesh, Streptococcus pneumoniae remains the predominant bacterial pathogen in pleural effusion cases despite widespread PCV-10 immunization among children <10 years of age. The persistence of pneumococcal pleural disease in a vaccinated population highlights several important phenomena. First, the concept of serotype replacement is well documented: following PCV introduction many countries have noted reductions in vaccine-type disease but simultaneous increases in non-vaccine serotype invasive disease, including in empyema and pleural effusions.[3,9] For example, in a European multi-country study of PCV-10 / PCV-13 use, non-vaccine type IPD increased by 111% in children <5 years, offsetting some of the gains from vaccination.[3] Similarly, carriage studies show increases in serotype 19A carriage among vaccinated children.[6] Our finding of 26.5% MDR among pneumococcal isolates further reinforces that non-vaccine serotypes may have higher resistance profiles and are increasingly implicated in complicated disease.[2,4] This is of concern because resistant pneumococcal strains are associated with worse clinical outcomes, longer hospital stays and more frequent need for invasive intervention.

Secondly, although PCV-10 has achieved high coverage in Bangladesh, its valency is lower than that of PCV-13, PCV-15 or PCV-20 and omits several serotypes that have been implicated in complicated pneumonia/empyema globally (e.g., 19A, 22F, 33F).[10] Our data thus suggest that vaccine escape by non-vaccine serotypes may already be contributing to the burden of pleural effusion and empyema in this pediatric population. The detection of MDR pneumococci in fully vaccinated children supports this conjecture.

Thirdly, the continued substantial proportion of tubercular pleural effusion (20.2%) underlines that in high-TB burden settings like Bangladesh, Mycobacterium tuberculosis remains an important differential. The rare occurrence of dual infection (S. pneumoniae + M. tuberculosis) in our cohort (0.4%) highlights diagnostic complexity, clinicians must maintain vigilance for mixed etiologies in pleural disease.

From a public health and clinical perspective, the implications of this result are multifold. The persistence of pneumococcal pleural disease in vaccinated children argues strongly for consideration of higher-valency pneumococcal conjugate vaccines (PCV-13/15/20) in the national immunization program to widen serotype coverage. Concurrently, systematic surveillance for circulating pneumococcal serotypes and antimicrobial resistance patterns is imperative to guide vaccine policy and empirical treatment guidelines. At the clinical management level, our finding of 7.7% of children with persistent or loculated effusions requiring surgical intervention underscores the need for early recognition, timely drainage (including chest-tube plus fibrinolysis where available) and appropriate antibiotic therapy guided by local susceptibility data. Antibiotic stewardship is needed to minimize emergence of MDR pathogens. Finally, the dual etiology possibilities demand that children with pleural effusion in TB endemic settings undergo

both bacterial and MTB evaluation.

Strengths of our study include a large consecutive cohort, comprehensive pleural fluid analysis including antigen testing and Gene Xpert, documented immunization status and real-world outcome data in a LMIC tertiary center. Limitations include single-center design (possible referral bias), absence of pneumococcal serotyping (which precludes direct attribution of breakthrough to specific serotypes), and possible under-detection of bacterial pathogens due to prior antibiotic exposure.

Conclusion

Our study demonstrates that S. pneumoniae remains the major cause of pediatric pleural effusion in Bangladesh despite PCV-10 immunization, and the emergence of MDR strains is an urgent concern. Tubercular pleural disease remains a significant part of the spectrum.

Recommendation:

To further reduce the burden of pleural infections and their complications in children, Bangladesh should pursue surveillance of pneumococcal serotypes and resistance, consider adoption of higher-valency PCVs, and strengthen antibiotic stewardship and pleural drainage protocols.

References

1. Shetty AK. Current trends in Streptococcus pneumoniae infections. Curr Pediatr Rev. 2013;9(2):166-74.
2. Sapkota P, Lamichhane S, Bhattarai R, Shrestha A. Prevalence of para-pneumonic effusion and the associated factors among children: a three-year experience in a single tertiary hospital. Int J Child Health Nutr. 2024;13(1):27-34.
3. Hanquet G, Krizova P, Dalby T, Ladhani SN, Nuorti JP, Danis K, Mereckiene J, Knol MJ, Winje BA, Ciruela P, De Miguel S, Portillo ME, MacDonald L, Morfeldt E, Kozakova J, Valentiner-Branth, P, Fry NK, Rinta-Kokko H, Varon E, Savulescu C. Serotype Replacement after Introduction of 10-Valent and 13-Valent Pneumococcal Conjugate Vaccines in 10 Countries, Europe. Emerging Infectious Diseases,2022; 28(1): 127-138.
4. Lin TY, Chiu CH, Woo PC, Razak Muttalif A, Dhar R, Choon Kit L, Morales G, Ozbilgili E. Pneumococcal serotype prevalence and antibiotic resistance in children in South and Southeast Asia, 2012-2024. Hum Vaccin Immunother. 2024 Dec 31;20(1):2417554.
5. Ekinci E, Van Heirstraeten L, Willen L, Desmet S, Wouters I, Vermeulen H, Lammens C, Goossens H, Van Damme P, Verhaegen J, Beutels P, Theeten H, Malhotra-Kumar S; NP Carriage Study Group. Serotype 19A and 6C Account for One-Third of Pneumococcal Carriage Among Belgian Day-Care Children Four Years After a Shift to a Lower-Valent PCV. J Pediatric Infect Dis Soc. 2023 Feb 9;12(1):36-42.
6. Fardows, J., Siddique, A. B., Farhana, N., & Islam, T. B. (2017). Review Update on Pneumococcal Conjugate Vaccine: A New Hope for Reduction of Pneumococcal Disease in Bangladesh. Bangladesh Journal of Infectious Diseases. 2017; 2(1): 19–22.
7. Anglemyer A, McNeill A, DuBray K, 5. 5. Sonder GJB, Walls T. Invasive Pneumococcal Disease: Concerning Trends in Serotype 19A Notifications in New Zealand. Clin Infect Dis. 2022 May 30;74(10):1859-1861
8. van Gils EJ, Veenhoven RH, Hak E, Rodenburg GD, Keijzers WC, Bogaert D, Trzcinski K, Bruin JP, van Alphen L, van der Ende A, Sanders EA. Pneumococcal conjugate vaccination and nasopharyngeal acquisition of pneumococcal serotype 19A strains. JAMA. 2010 Sep 8;304(10):1099-106.
9. Vestjens SMT, van Mens SP, Meek B, Lalmahomed TA, de Jong B, Goswami D, Vlaminckx BJM, Ahmed D, de Jongh BM, Endtz HP, Brooks WA, Rijkers GT. Streptococcus pneumoniae serotype distribution in Bangladeshi under-fives with community-acquired pneumonia pre-10-valent pneumococcal conjugate vaccination. Pneumonia (Nathan). 2024 Nov 5;16(1):29
10. WHO. Pneumococcal conjugate vaccines in infants and children under 5 years of age – WHO position paper, February 2019. Geneva: World Health Organization; 2019.