Trends in Pediatrics 2026;7(1):71-76
DOI: 10.59213/TP.2026.400

Original Article

Determinants of disease severity in pediatric protracted bacterial bronchitis

Evrim Hepkaya[1], Pelin Güler[2]

[1]Department of Pediatric Pulmonology, Ümraniye Training and Research Hospital, İstanbul, Türkiye
[2]Department of Pediatrics, Kartal Dr. Lütfi Kırdar Training and Research Hospital, İstanbul, Türkiye

Cite this article as: Hepkaya E, Güler P. Determinants of disease severity in pediatric protracted bacterial bronchitis. Trends in Pediatrics 2026;7(1):71-76.

ABSTRACT

Background: Protracted bacterial bronchitis (PBB) is an increasingly recognized cause of chronic wet cough in children and may lead to bronchiectasis if not adequately treated. However, data regarding its clinical presentation and associated risk factors remain limited.

Objective: To evaluate the clinical, radiological, and microbiological characteristics of children diagnosed with PBB and to identify factors associated with disease severity and recurrence.

Methods: This cross-sectional study included 49 children followed in a pediatric pulmonology clinic with a diagnosis of PBB. Demographic features, comorbidities, sputum microbiology, pulmonary function tests, thoracic computed tomography (CT) findings, and serum vitamin D levels were analyzed. The association between clinical parameters and annual bronchitis frequency was evaluated using correlation analyses.

Results: Forty-nine children were analyzed (69.3% female), with a median age of 7 years. Asthma and atopy were present in 65.3% and 30.6% of patients, respectively. A pathogen was isolated in 63.3% of sputum samples, with Haemophilus influenzae being the most common agent (41.9%). A moderate inverse correlation was detected between serum vitamin D levels and the annual number of bronchitis episodes ($\rho = -0.56$; $p = 0.0016$). Spirometry values were mostly within normal limits; however, weak inverse correlations were observed between pulmonary function parameters and exacerbation frequency. Thoracic CT abnormalities were identified in 81.9% of patients, most commonly bronchial wall thickening.

Conclusion: PBB is frequently accompanied by asthma and recurrent infections. H. influenzae appears to be associated with increased disease burden. Low vitamin D levels may contribute to higher susceptibility to recurrent bronchitis. Early diagnosis and targeted microbiological evaluation are essential to prevent long-term pulmonary complications.

Keywords: bronchitis, bronchiectasis, Hemophilus influenzae, Vitamin D

INTRODUCTION

Protracted bacterial bronchitis (PBB) is now recognized as one of the most frequent causes of persistent wet cough in early childhood, yet it remains underdiagnosed in routine clinical practice. The condition is characterized by a chronic productive cough lasting longer than four weeks that cannot be explained by alternative diagnoses, including asthma, structural airway abnormalities, or immunodeficiency disorders. A key hallmark of PBB is complete symptom resolution following appropriate antibiotic therapy, supporting its bacterial origin.[1,2] The disease primarily affects the lower airways, where bacterial colonization—most commonly involving Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pneumoniae—induces sustained neutrophilic inflammation.[3] Mechanisms

✉ Evrim Hepkaya ▪ dr_ekarakaya@yahoo.com

Received: 24.12.2025 **Accepted:** 06.03.2026

such as biofilm formation and impaired mucociliary clearance contribute to epithelial injury and excessive mucus production.[4] When inadequately treated, this ongoing inflammatory process may result in structural airway damage and progression toward bronchiectasis.[5]

Recurrent PBB, often defined as three or more episodes annually, has been associated with a greater likelihood of chronic suppurative lung disease, particularly among children infected with H. influenzae.[6,7] These observations emphasize the importance of early diagnosis, improved clinical awareness, and implementation of appropriate treatment strategies.

The aim of this study was to evaluate the clinical, microbiological, and radiological characteristics of children diagnosed with PBB and to identify factors associated with disease severity and recurrence.

MATERIALS AND METHODS

Study design and population

The study was designed as a cross-sectional study, evaluating data collected from patients diagnosed with PBB. A total of 49 patients who were systemically followed by the pediatric pulmonology department enrolled in the study. Patients with persistent productive cough were screened for underlying conditions such as cystic fibrosis, immunodeficiency, tuberculosis, primary ciliary dyskinesia, congenital cardiac and neuromuscular diseases, and foreign body aspiration. Those diagnosed with any of these conditions were excluded. PBB was defined when all three of the following criteria are fulfilled; 1) Presence of continuous chronic (>4 weeks' duration) wet or productive cough; 2) absence of symptoms or signs (i.e. dyspnea, exertional dyspnea, haemoptysis, respiratory distress, digital clubbing, chest wall deformity, failure to thrive) suggestive of other causes of wet or productive cough and 3) cough resolved following a 2–4-week course of an appropriate oral antibiotic.[8]

Variables and data collection

Demographic variables, including age, gender, age at diagnosis, annual number of bronchitis attacks, and serum vitamin D levels, were recorded. During outpatient visits, patients were systematically assessed for comorbidities, including prematurity, breastfeeding history, and prior diagnoses of pneumonia, asthma, or atopy.

Spirometry was performed in children aged over 6 years who were able to cooperate, using the same technician for all tests. The key parameters measured included forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, and forced expiratory flow between 25% and 75% of the pulmonary volume (FEF25–75). Normal values were defined as >80% of the predicted value for FVC, FEV_1, and FEV_1/FVC, and >70% of the predicted value for FEF25–75.[9] A positive bronchodilator response (BDR) was defined as a relative increase of >10% in FEV_1 or FVC following bronchodilator administration.[10] Spontaneous or induced sputum samples were obtained and cultured from patients presenting with a productive cough. Bronchoscopy was performed in patients with radiological or clinical signs of infection who were unable to expectorate sputum, and in those with persistent radiological findings despite appropriate medical treatment. All patients with chronic cough were screened for pulmonary tuberculosis, cystic fibrosis, and immunodeficiency. Immunological evaluation included measurement of total serum immunoglobulins (IgA, IgG, IgM, and IgE), IgG subclasses, lymphocyte subpopulations, and antibody responses to vaccine antigens. A sweat test was performed using direct chloride measurement and interpreted according to established guidelines.[11] Screening for tuberculosis included the purified protein derivative (PPD) skin test; in cases with anergic PPD results, interferon-gamma release assays (IGRAs) were also used.[12] Patients with early-onset disease or severe bronchitis episodes who had negative results for these screening tests underwent further genetic analysis to investigate underlying conditions. Thoracic computed tomography (CT) was performed in children who showed abnormal findings on chest X-ray—such as bronchial wall thickening, atelectasis, or air trapping—or in those with persistent respiratory symptoms and recurrent bronchitis. Disease severity was assessed using data on the annual number of bronchitis attacks, accompanying comorbidities, microbiological findings, spirometry results, and radiological characteristics.

Data analysis

Statistical analyses were performed using SPSS version 29. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or as median with interquartile range (25th–75th percentiles) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. Normality was assessed using histograms, probability plots, and the Shapiro–Wilk test. Spearman's rank correlation coefficient (ρ) was utilized to assess the associations between ordinal

categorical variables, and for nominal categorical variables, the Chi-square test and Fisher's exact test were used. A two-tailed p-value <0.05 was considered statistically significant. A multivariable Poisson regression analysis was performed to evaluate the independent associations between serum vitamin D levels and annual bronchitis exacerbation frequency, adjusting for asthma status, sputum culture results, and pulmonary function parameters.

Ethical statement

Ethical approval for the study was obtained from the Umraniye Training and Research Hospital Ethics Committee (date: 18.12.2025, number: 2025-446), and the research was conducted in full accordance with the principles of the Declaration of Helsinki. Informed consent was thoroughly obtained, reflecting our adherence to the highest ethical standards in research. All participants' rights were strictly protected throughout the study, and no procedures or inquiries were conducted that could compromise the children's physical or psychological well-being. Written informed consent for participation was obtained from the parents during clinic visits, and official consent forms were duly signed.

RESULTS

A total of 49 patients were evaluated, of whom 71.4% (35/49) were female. The median age was 7 (3-15) years, while the median age at first symptom was 4.5 (0.5-15) years. Prematurity was observed in 10 (20.4%) patients, and breastfeeding for over 6 months was observed in 40 (81.6%) patients. Asthma was associated with PBB in 32 (65.3%) patients, and atopy was reported in 15 (30.6%) patients. Pneumonia history was reported in 20 (40.8%). The median vitamin D level was 16.9 ng/ml (6.7-112) among patients. Serum vitamin D levels were inversely correlated with the number of annual bronchitis attacks (Spearman rho = –0.56, p = 0.0016) (Table 1). In multivariable analysis, serum vitamin D levels were not independently associated with annual bronchitis exacerbation frequency (IRR 1.02, 95% CI 0.96–1.08; p = 0.521) (Table 2).

The median annual number of bronchitis attacks was 3 (1-15). A positive culture was obtained from 31 patients (63.3%). Haemophilus influenzae was the most common pathogen 13 (41.9%), while the others were 8 (25.8%) Streptococcus pneumoniae, 3 (9.6%) were methicillin-resistant Staphylococcus aureus, 3(9.6%) were coinfection with H. influenzae and S. pneumoniae, 2 (6.4%) were Klebsiella pneumonia, 1 (3.2%) Haemophilus parainfluenzae, and 1 (3.2%) patient Streptococcus pyogenes (Table 3). Bronchoscopy was performed in 3 (6.1%) patients with normal anatomical appearance and negative microbiological cultures.

Table 1. Characteristics of the study population

Sex (female), n (%)	35 (71.4%)
Age (yr), median (25th-75th)	7 (3-15)
Age at first symptom (yr), mean (±SD)	4.5 (0.5-15)
Annual bronchitis attacks, median (25th-75th)	3 (1-15)
Prematurity, n (%)	10 (20.4%)
Breastfeeding (> 6 m), n (%)	40 (81.6%)
Atopy, n (%)	15 (30.6%)
Asthma, n (%)	32 (65.3%)
History of pneumonia, n (%)	20 (40.8%)
25-OH Vit. D levels, ng/ml, median (25th-75th)	16.9 (6.7-112)

yr: year, m: month, SD: standard deviation, Vit: vitamin.

Out of the total, 23 patients were able to perform spirometry. The mean FEV1 was 84.94±11.68, FVC was 86.70±9.12, and the FEV1/FVC was 96.52±8.81 (Table 3). The associations between FEV1, FVC, and FEV1/FVC and the annual exacerbation frequency were examined using Pearson correlation analysis. The analysis demonstrated weak inverse correlations across all spirometry parameters (FEV1: r = –0.21; FVC: r = –0.15; FEV1/FVC: r = –0.13), indicating that higher exacerbation rates were associated with lower pulmonary function values.

Thirty-three patients were screened with Thorax CT scans. Bronchial wall thickness was the most common finding observed in 8 (24.2%) patients. Other findings were, consolidation in 7 (21.2%), atelectasis in 5 (15.1%), mosaic perfusion in 3 (9%), ground-glass opacities in 2 (6%), bronchial dilatation in 1 (3%) and interlobular septal thickness in 1 (3%) patient respectively, 6 (18.1%) of CT scans were normal (Table 4). Thorax CT scan findings were not associated with spirometry values (p>0.05). The majority (40/49) of the patients had a history of 3 bronchitis attacks in the previous year. Of them, 6 (15%) had≥ 10 bronchitis attacks. Patients with positive sputum cultures had more bronchiolitis attacks without a significant difference (4.74 vs 4.11, p>0.05). Regarding the association between sputum cultures, patients with methicillin-resistant Staphylococcus aureus (MRSA) had an annual mean of 10 bronchitis attacks, while patients with H. influenza had a mean of 5.08 attacks, and those with coinfection with H. influenza and S. pneumoniae had a mean of 4.66 attacks.

Table 2. Multivariable Poisson regression analysis for annual bronchitis exacerbations					
Variable	**β (Estimate)**	**SE**	**p value**	**IRR**	**95% CI for IRR**
Intercept	4.062	1.344	0.003	–	-
FEV_1 (% predicted)	−0.029	0.016	0.062	0.97	0.94 – 1.00
Serum Vitamin D (ng/mL)	0.019	0.030	0.521	1.02	0.96 – 1.08
Asthma (Yes vs No)	−1.398	0.779	0.073	0.25	0.05 – 1.16
Sputum Culture (Negative vs Positive)	−0.378	0.306	0.216	0.69	0.38 – 1.26

FEV1: forced expiratory volume in one second.

Table 3. Microbiological and spirometry findings of the patients	
Sputum samplings	**n (%)**
Hemophilus influenza	13 (41.9%)
Streptococcus pneumoniae	8 (25.8%)
MRSA	3 (9.6%)
Coinfection (H. influenza and S. pneumoniae)	3 (9.6%)
Klebsiella pneumoniae	2 (6.4%)
Hemophilus parainfluenza	1 (3.2%)
Streptococcus pyogenes	1 (3.2%)
Spirometry values	**mean±SD**
FEV1	84.9±11.68
FVC	86.70±9.12
FEV1/FVC	96.52±8.81

MRSA: methicillin resistant staphylococcus aureus, FEV1: forced expiratory volume in one second, FVC: forced vital capacity.

Table 4. Radiological findings of the patients	
	n (%)
Bronchial wall thickness	8 (24.2%)
Consolidation	7 (21.2%)
Atelectasis	5 (15.1%)
Mosaic perfusion	3 (9.1%)
Ground glass opacities	2 (6.1%)
Bronchial dilatation	1 (3.1%)
Interlobular septal thickness	1 (3.1%)
Normal	6 (18.1%)

DISCUSSION

This study provides an overview of the clinical, radiological, and microbiological characteristics of children diagnosed with protracted bacterial bronchitis (PBB). Although PBB has been increasingly recognized over the past decade, it remains an underdiagnosed cause of chronic wet cough in childhood. The demographic structure of our cohort, in which symptoms began in early childhood, and the median age at evaluation was 7 years, is consistent with the epidemiological profile reported in previous studies.[13,14] While some authors have noted a slight male predominance among affected children, our sample showed a higher proportion of females; this discrepancy may reflect regional differences or variations in referral patterns rather than a true sex-related predisposition.[5]

A key finding of our study was the high rate of positive sputum cultures, identified in nearly two-thirds of patients, supporting the central role of bacterial pathogens in PBB pathogenesis. Consistent with previous reports, H. influenzae was the most frequently isolated organism, followed by S. pneumoniae and MRSA.[15,16] The predominance of H. influenzae is attributed to its ability to induce neutrophilic inflammation, form biofilms, and persist in the lower airways. Recurrent PBB episodes (>3/year) and H. influenzae infection have been associated with bronchiectasis.[17] In our cohort, H. influenzae–positive patients had higher annual exacerbation rates, suggesting a more severe phenotype.[18] Although the difference between culture-positive and culture-negative groups was not statistically significant, the numerical trend toward higher exacerbation rates in culture-positive patients remains clinically relevant. Notably, patients with MRSA had the highest exacerbation burden. Given the association between PBB and chronic suppurative lung disease or early bronchiectasis, these findings underscore the importance of close follow-up and early microbiological evaluation.[19]

Spirometry results showed that pulmonary function was largely preserved in most patients, consistent with previous reports indicating normal lung mechanics in early or moderately severe PBB.[17,20] However, a weak inverse correlation was observed between spirometric parameters and the annual number of bronchitis exacerbations, suggesting that recurrent infections may gradually impair lung function despite initially normal measurements. Supporting this, one study reported that 24% of patients demonstrated at least one abnormal spirometric

parameter.[21] These findings highlight the importance of close follow-up, particularly in persistent cases.

Radiological evaluation revealed bronchial wall thickening as the most common CT abnormality, followed by consolidation and atelectasis. These imaging patterns align with structural changes typically attributed to chronic bacterial inflammation and impaired mucociliary clearance.[5,16] CT findings did not correlate with lung function measures in our study, which may be explained by the fact that structural changes often precede measurable declines in spirometric values. Previous studies also describe a similar dissociation between imaging abnormalities and pulmonary function in children with chronic wet cough.[16]

An additional noteworthy finding was the inverse association between vitamin D levels and annual bronchitis episodes. Vitamin D deficiency is well known to impair innate immune responses, particularly epithelial integrity and antimicrobial signaling pathways.[22] Ferri et al. demonstrated that serum vitamin D levels in children with bronchiectasis were significantly associated with disease severity.[23] Moreover, the use of vitamin D as an anti-inflammatory agent in cystic fibrosis has been hypothesized based on its beneficial effects on lung function.[24] In line with the literature, the moderate negative correlation observed in our study suggests that low vitamin D status may contribute to increased susceptibility to respiratory infections in this patient population and may represent a potentially contributing risk factor. Although a significant inverse correlation was observed, this association did not persist in the adjusted model, suggesting potential confounding effects. FEV_1 demonstrated a borderline inverse relationship with exacerbation frequency, indicating a possible trend toward lower attack rates with better lung function. These findings imply that while vitamin D deficiency may be associated with disease burden, it may not act as an independent determinant of exacerbation frequency in children with PBB.

Comorbid conditions such as asthma and atopy were common, observed in nearly two-thirds and one-third of patients, respectively. In a 5-year longitudinal study, asthma was present in 27.1% of children with PBB.[17] Similarly, another study reported that asthma and episodic wheezing were identified in 36% of patients presenting with prolonged cough.[25] The coexistence of asthma and PBB complicates clinical decision-making, as chronic cough in these patients may be erroneously attributed to asthma alone, potentially delaying appropriate antibiotic therapy. These findings reinforce the importance of distinguishing PBB from asthma-related cough and highlight the need for a systematic diagnostic approach.[2,26]

This study has several limitations. First, its cross-sectional design precludes causal inferences regarding the identified associations, particularly between vitamin D levels and disease severity, and the relatively small sample size from a single center limits generalizability.

Taken together, our results emphasize several key clinical implications. First, early recognition of PBB and timely initiation of appropriate antibiotic therapy remain fundamental to preventing disease progression. Second, identifying underlying pathogens—particularly in recurrent or severe cases—may provide valuable prognostic information. Finally, evaluation of potentially correctable contributing factors to disease severity, such as vitamin D deficiency, may offer additional opportunities to reduce exacerbation frequency. Long-term prospective studies are warranted to clarify the natural course of PBB, identify markers of recurrence, and determine which children are at the highest risk for developing bronchiectasis or other chronic airway diseases.

Ethical approval

This study has been approved by the Umraniye Training and Research Hospital Ethics Committee (approval date 18.12.2025, number 2025-446). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: EH; data collection: EH, PG; analysis and interpretation of results: EH, PG; draft manuscript preparation: EH, PG. All authors reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Wurzel DF, Marchant JM, Yerkovich ST, et al. Prospective characterization of protracted bacterial bronchitis in children. Chest. 2014;145:1271-8. [Crossref]
2. Chang AB, Oppenheimer JJ, Weinberger M, Weir K, Rubin BK, Irwin RS. Use of management pathways or algorithms in children with chronic cough: systematic reviews. Chest. 2016;149:106-19. [Crossref]
3. Gallucci M, Pedretti M, Giannetti A, et al. When the cough does not improve: a review on protracted bacterial bronchitis in children. Front Pediatr. 2020;8:433. [Crossref]
4. Craven V, Everard ML. Protracted bacterial bronchitis: reinventing an old disease. Arch Dis Child. 2013;98:72-6. [Crossref]
5. Wurzel DF, Marchant JM, Yerkovich ST, et al. Protracted bacterial bronchitis in children: natural history and risk factors for bronchiectasis. Chest. 2016;150:1101-8. [Crossref]
6. Ruffles TJC, Goyal V, Marchant JM, et al. Duration of amoxicillin-clavulanate for protracted bacterial bronchitis in children (DACS): a multi-centre, double blind, randomised controlled trial. Lancet Respir Med. 2021;9:1121-9. [Crossref]
7. Wiltingh H, Marchant JM, Goyal V. Cough in protracted bacterial bronchitis and bronchiectasis. J Clin Med. 2024;13:3305. [Crossref]
8. Chang AB, Upham JW, Masters IB, et al. Protracted bacterial bronchitis: the last decade and the road ahead. Pediatr Pulmonol. 2016;51:225-42. [Crossref]
9. Castile RG, Davis SD. Pulmonary function testing in children. In: Wilmott RW, Bush A, eds. Kendig and Chernick's disorders of the respiratory tract in children. 8th ed. Philadelphia: Elsevier Saunders; 2012: 211-33. [Crossref]
10. Martins B, Marinho A, Amorim P. Impact of the 2022 ATS/ERS update criteria on the bronchodilator responsiveness test result. Pulmonology. 2024;30:673-4. [Crossref]
11. LeGrys VA, Rosenstein BJ, Doumas BT, et al. Sweat testing: sample collection and quantitative analysis; approved guideline-second edition. Wayne (PA): NCCLS; 2000. (NCCLS document C34-A2).
12. Menentoğlu B, Şimşek C, Hatipoğlu N. PPD testi uygulaması ve yorumu. J Pediatr Inf. 2021;15:57-62. [Crossref]
13. Chang AB, Redding GJ, Everard ML. Chronic wet cough: protracted bronchitis, chronic suppurative lung disease and bronchiectasis. Pediatr Pulmonol. 2008;43:519-31. [Crossref]
14. Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. Chest. 2006;129:1132-41. [Crossref]
15. King PT, Sharma R. The lung immune response to nontypeable haemophilus influenzae (Lung Immunity to NTHi). J Immunol Res. 2015;2015:706376. [Crossref]
16. Gaillard EA, Carty H, Heaf D, Smyth RL. Reversible bronchial dilatation in children: comparison of serial high-resolution computer tomography scans of the lungs. Eur J Radiol. 2003;47:215-20. [Crossref]
17. Ruffles TJC, Marchant JM, Masters IB, et al. Outcomes of protracted bacterial bronchitis in children: a 5-year prospective cohort study. Respirology. 2021;26:241-8. [Crossref]
18. Cadenas-Jiménez I, Camps-Massa P, Gonçalves-Carvalho F, et al. Epidemiological insights into Haemophilus influenzae and Pseudomonas aeruginosa persistent colonization in non-cystic fibrosis bronchiectasis patients: a longitudinal and multicenter study. Respir Res. 2026;27:87. [Crossref]
19. Rosenfeld M, Gibson RL, McNamara S, et al. Early pulmonary infection, inflammation, and clinical outcomes in infants with cystic fibrosis. Pediatr Pulmonol. 2001;32:356-66. [Crossref]
20. Kantar A, Chang AB, Shields MD, et al. ERS statement on protracted bacterial bronchitis in children. Eur Respir J. 2017;50:1602139. [Crossref]
21. Hermann J, Brückner K, Koerner-Rettberg C, et al. Long-term pulmonary sequelae 5-14 years after protracted bacterial bronchitis in early childhood. Pediatr Pulmonol. 2025;60:e71111. [Crossref]
22. Greiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. Nutrients. 2015;7:4240-70. [Crossref]
23. Ferri S, Crimi C, Heffler E, Campisi R, Noto A, Crimi N. Vitamin D and disease severity in bronchiectasis. Respir Med. 2019;148:1-5. [Crossref]
24. Herscovitch K, Dauletbaev N, Lands LC. Vitamin D as an anti-microbial and anti-inflammatory therapy for Cystic Fibrosis. Paediatr Respir Rev. 2014;15:154-62. [Crossref]
25. Mallet MC, Elmiger A, Glick S, et al. Diagnosis in children with prolonged or recurrent cough: findings from the swiss paediatric airway cohort. Pediatr Pulmonol. 2025;60:e27499. [Crossref]
26. Ullmann N, Mirra V, Di Marco A, et al. Asthma: differential diagnosis and comorbidities. Front Pediatr. 2018;6:276. [Crossref]