



ORIGINAL ARTICLE

Clinical, radiological, and spirometric outcomes of pediatric bronchiolitis obliterans: A ten-year single-center experience

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Abstract

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Bronchiolitis obliterans (BO) is a chronic and irreversible obstructive lung disease in children. Due to nonspecific clinical manifestations and limited disease-modifying treatment options, BO remains a diagnostic and therapeutic challenge, and data describing long-term clinical, radiological, and functional outcomes are limited. This study aimed to retrospectively evaluate the pediatric patients with bronchiolitis obliterans at a tertiary pediatric pulmonology center. This retrospective descriptive study included children diagnosed with bronchiolitis obliterans and followed at the Pediatric Pulmonology Clinic of in a tertiary care center between January 2015 and January 2025. All data records were reviewed retrospectively. Demographic and clinical features, chest computed tomography (CT) findings, laboratory parameters, treatment modalities, and spirometric indices at baseline and follow-up were analyzed. Also, baseline and follow-up spirometry and CT findings were compared. The median age at diagnosis was 48 months (IQR, 39–66), and



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57.6% of patients were male. At diagnosis, 38% of patients required supplemental oxygen. Chest CT revealed diffuse air trapping and mosaic attenuation in most of patients, with no statistically significant changes observed on follow-up imaging ($p > .05$). Baseline spirometry demonstrated an obstructive pattern, with a median FEV₁ of 66.0% predicted (IQR, 57.5–71.5). Follow-up spirometry showed persistently reduced lung function, with no statistically significant differences between baseline and follow-up values for FEV₁, FVC. BO in children is a chronic disease characterized by persistent respiratory symptoms, fixed airflow obstruction, and stable radiologic abnormalities. Current therapies may improve symptoms and reduce oxygen dependence in some patients but do not reverse established structural lung damage. Early diagnosis, regular pulmonary function monitoring, and a multidisciplinary approach are essential to optimize long-term outcomes.

Introduction

Bronchiolitis obliterans (BO) is an irreversible chronic lung disease characterized by subepithelial inflammation and fibrotic narrowing of the small airways, resulting from various etiologic and triggering factors [1]. To date, three main categories of BO have been identified: (i) postinfectious BO (PIBO), (ii) BO following hematopoietic stem cell transplantation (HSCT), and (iii) BO after lung transplantation (LT) [2]. Less common etiologic factors include connective tissue diseases, exposure to toxic fumes, and gastroesophageal reflux in children. In the pediatric population, BO most commonly develops after a severe lower respiratory tract infection and is therefore referred to as PIBO. Adenovirus is the most frequently reported causative agent; however, other viral and atypical pathogens—such as respiratory syncytial virus, influenza virus, parainfluenza virus, measles virus, and *Mycoplasma pneumoniae*—have also been implicated [1,2].

The diagnosis of BO in children is challenging due to its nonspecific clinical presentation and the limited feasibility of histopathological confirmation. Consequently, diagnosis relies primarily on clinical history, characteristic radiologic findings, pulmonary function test abnormalities, and the exclusion of other chronic lung diseases [3].

The aim of this study was to retrospectively evaluate the demographic characteristics, clinical features, radiologic findings, pulmonary function test results, and treatment approaches of pediatric patients diagnosed with bronchiolitis obliterans at a tertiary pediatric pulmonology center. Additionally, we aimed to assess disease course and treatment outcomes by comparing baseline and follow-up radiologic and spirometric findings.

Materials and Methods

Study design and population

Ethical approval for this study was obtained from the Necmettin Erbakan University Faculty of Medicine Ethics Committee. (Decision No: 2026/6307). All data were anonymized to ensure patient confidentiality. This retrospective, descriptive study included pediatric patients diagnosed with BO, who were treated and followed at the Pediatric Pulmonology clinic in a tertiary care center, between January 2015 and January 2025. Medical records of all eligible patients were reviewed retrospectively. Patients with incomplete medical records or alternative diagnoses with co-existing cystic fibrosis, congenital heart disease, primary ciliary dyskinesia or bronchopulmonary dysplasia were excluded from the study.



Demographic data, including age at diagnosis, sex, and current age, were recorded. Clinical data included presenting symptoms, duration of symptoms prior to diagnosis, history of hospitalization, intensive care unit admission, mechanical ventilation, oxygen requirement at diagnosis and during follow-up, and presence of comorbid conditions.

Laboratory parameters obtained at presentation included complete blood count, inflammatory markers, and immunoglobulin levels. Identified infectious agents during the initial lower respiratory tract infection were recorded when available.

Diagnostic criteria

BO diagnosis is usually based on a few factors, including a good medical history, positive clinical findings, lung function test, imaging results, although biopsy and histopathology remain as the optimum diagnostic approach pathologically. BO is characterised by luminal obstruction with inflammation, granulation tissue, and/or fibrosis and obliteration of the small airways and bronchiectasis. Histopathological confirmation was not routinely performed due to the invasive nature of lung biopsy and the patchy distribution of the disease [2,3].

Clinical picture

Patients were included if they had a clinical diagnosis of BO based on persistent respiratory symptoms lasting longer than six weeks; for PIBO, symptoms most commonly followed a severe lower respiratory tract infection. Respiratory symptoms included persistent cough, wheezing, tachypnea, exercise intolerance, or hypoxemia persisting for more than six weeks after an acute episode of bronchiolitis or pneumonia, poor response to bronchodilator therapy [4,5].

Radiological evaluation

All patients underwent chest computed tomography (CT) as part of the diagnostic evaluation. Computed tomography images were reviewed for characteristic features of BO, including mosaic attenuation, air trapping, bronchial wall thickening, bronchiectasis, ground-glass opacities, and unilateral or regional hyperlucency [6,7]. Radiological findings were recorded at baseline and during follow-up when repeat imaging was available. Changes in radiological findings over time were assessed descriptively.

Pulmonary function tests

Pulmonary function tests (PFTs) were performed using standard spirometric techniques. Recorded parameters included forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and forced expiratory flow between 25% and 75% (FEF_{25-75}). Spirometric values were expressed as percentages of predicted values adjusted for age, sex, and height in accordance with ATS/ERS guidelines [8-10].

Baseline spirometry at diagnosis and follow-up spirometry obtained during routine outpatient visits were analyzed. Changes in spirometric parameters over time were calculated for patients with available paired measurements.

Treatment and follow-up

Treatment strategies were individualized and determined by the treating pediatric pulmonologists. Therapeutic modalities included inhaled and/or systemic corticosteroids, macrolide antibiotics (primarily azithromycin), leukotriene receptor antagonists, intravenous immunoglobulin therapy, and supportive treatments such as long-term oxygen therapy when indicated [11,12]. Duration and combinations of treatments were recorded.



Patients were followed regularly in the outpatient clinic, and clinical status, oxygen requirement, spirometric findings, and radiological evaluations were monitored during follow-up.

Statistical analysis

Statistical analyses were performed using appropriate statistical software. Given the descriptive nature of the study, analyses were primarily focused on summarizing patient characteristics and clinical findings.

Continuous variables were assessed for distribution and are presented as mean \pm standard deviation or median with minimum–maximum values, as appropriate. Categorical variables are presented as numbers and percentages.

Comparative analyses were limited to selected parameters of clinical relevance. For comparisons between baseline and follow-up measurements in patients with available paired data, paired statistical tests were applied. The paired *t* test was used for normally distributed variables, while the Wilcoxon signed-rank test was used for non-normally distributed variables. For comparisons between independent groups, the independent samples *t* test or Mann–Whitney U test was used, depending on data distribution [13].

All statistical tests were two-sided, and a *p* value < 0.05 was considered statistically significant.

Results

Demographic characteristics

A total of 6.5% of patients ($n=6$) were diagnosed with bronchiolitis obliterans (BO) following lung transplantation (LT) or hematopoietic stem cell transplantation (HSCT), while 3 patients (3.2%) had BO related to gastroesophageal disease, and 83 patients (90.2%) were diagnosed with post-infectious bronchiolitis obliterans (PIBO). The median age at diagnosis was 48 months (interquartile range [IQR]: 39–66), and the median current age at the time of evaluation was 108 months (IQR: 72–144). The median height and weight z-scores were -0.19 (IQR: -0.74 to -0.04) and -0.10 (IQR: -0.91 to 0.72), respectively. Of the patients, 57.6% ($n=53$) were male and 42.4% ($n=39$) were female. Demographic characteristics are summarized in Table 1.

Table 1. Demographic characteristics of the study.

Demographic findings	Value
Total patients (BO) n (%)	$n=92$ (100)
Post-transplant	$n=6$ (6.5)
GERD	$n=3$ (3.2)
PIBO	$n=83$ (90.2)
Age at diagnosis, months	48 [IQR]: (39–66)
Current age, months	108 IQR: (72–144)
Male sex, n (%)	53 (57.6)
Female sex, n (%)	39 (42.4)
Height z score*	-0.19 (-0.74 to -0.04)
Weight z score*	-0.10 (-0.91 to 0.72)
Comorbidity, n (%)	10 (10.9)
-Immunodeficiency, n (%)	7 (7.6)
-Congenital heart disease, n (%)	2 (2.1)
-Achondroplasia, n (%)	1 (0.92)

Demographic findings	Value
Total patients (BO) n (%)	n=92 (100)
Post-transplant	n=6 (6.5)
GERD	n=3 (3.2)
PIBO	n=83 (90.2)
Swyer–James–Macleod syndrome, n (%)	4 (4.3)
Identified respiratory pathogens n (%)	
-RSV	8 (8.6)
-Adenovirus	6 (6.5)
-Influenza	5 (5.4)
-Parainfluenza	4 (4.3)
-Rhinovirus	3 (3.2)
-Human metapneumovirus	3 (3.2)
-Bocavirus	2 (2.1)

BO, bronchiolitis obliterans; PIBO, postinfectious bronchiolitis obliterans; GERD: gastroesophageal reflux disease, RSV, respiratory syncytial virus. IQR, interquartile range.

Clinical characteristics

All patients presented with respiratory symptoms, most commonly wheezing, chronic cough, dyspnea, and recurrent respiratory infections. The mean duration of symptoms at presentation was month (Median)= 12 (Min: 2-Max:46). Follow up duration (month) (Median)= 42 (Min:3- Max: 118). Chronic cough was present in all patients.

Ten patients (10.8%) required admission to the intensive care unit, and the same proportion had a history of mechanical ventilation. At the time of diagnosis, 38% of patients (n = 35) required supplemental oxygen therapy, with a mean duration of oxygen dependence of 15.2 months (range: 0–72 months).

Comorbid systemic diseases were present in 15% of patients (n = 10), including immunodeficiency (n = 7), congenital heart disease (n = 2), and achondroplasia (n = 1). One patient had undergone lung transplantation due to cystic fibrosis, and five patients had a history of hematopoietic stem cell transplantation. Macleod syndrome was identified in four patients.

Respiratory pathogens identified during the initial infectious episode included respiratory syncytial virus (n = 8), adenovirus (n = 6), influenza virus (n = 5), parainfluenza virus (n = 4), rhinovirus (n = 3), human metapneumovirus (n = 3), and bocavirus (n = 2). Clinical characteristics are presented in Table 2.

Table 2. Clinical characteristics and severity indicators.

Clinical variable	Value
Symptom duration at presentation, months	70.6 (22–128) *
Chronic cough at presentation, n (%)	92 (100)
History of ICU admission and/or mechanical ventilation, n (%)	10 (10.8)
Oxygen requirement at diagnosis, n (%)	35 (38.0)
Duration of oxygen therapy, months	15.2 (0–72) *
Oxygen requirement at follow up, n (%)	6 (6.5)
Treatment n (%)	6 (6.5)
-FAM protocol (fluticasone, azithromycin, and montelukast)	34 (36.9)
-Inhaled and/or systemic corticosteroids	39 (42.3)
-Azithromycin prophylaxis combined with inhaled and/or systemic corticosteroids	
-Inhaled and/or systemic corticosteroids combined with IVIG and azithromycin prophylaxis	13 (14)

*Presented as mean (min–max), as reported in the study dataset/summary. ICU: intensive care unit, IVIG: Intravenous immunoglobulin



Laboratory evaluation at presentation revealed a median hemoglobin level of 12.35 g/dL (IQR: 10.58–12.85), median hematocrit of 37.0% (IQR: 35.0–39.5), and median mean corpuscular volume of 80.0 fL (IQR: 74.0–83.0). Leukocyte and platelet counts were generally within normal reference ranges.

The most commonly administered treatments included inhaled and/or systemic corticosteroids, azithromycin, intravenous immunoglobulin, and montelukast. Treatment regimens varied among patients, reflecting individualized management strategies. The mean duration of treatment was 23.3 months (range: 3–72 months). The most commonly prescribed treatment was corticosteroids combined with azithromycin prophylaxis, administered to 42.3% of patients (n = 39). The distribution of treatment modalities is presented in Table 2.

Radiological findings

Chest computed tomography revealed characteristic findings consistent with bronchiolitis obliterans. The most frequently observed radiological features included mosaic attenuation %43,4(n=40). Other radiological findings are diffuse patchy air trapping with increased lung lucency, widespread patchy ground-glass opacities, peribronchial wall thickening, and fibrotic parenchymal bands.

During follow-up, repeat chest computed tomography was available for a subset of patients. No significant changes in radiological findings were observed over time ($p < 0.05$). The distribution of radiological findings is summarized in Table 3.

Table 3. Comparison of chest CT findings at baseline and follow-up.

CT finding n(%)	Baseline CT	Follow-up CT	<i>p</i> value
Mosaic attenuation	40 (43.3)	43 (46.7)	>0.05
Patchy ground-glass opacities+ increased lung lucency	31 (33.6)	28 (30.4)	>0.05
Peribronchial wall thickening+ Mosaic attenuation	8 (8.2)	7 (7.6)	>0.05
Bronchiectasis + increased lung lucency	7 (7.6)	8 (8.2)	>0.05
Unilateral hyperlucent lung (Swyer–James–Macleod syndrome)	4 (4.3)	4 (4.3)	1.00

Baseline and follow-up chest CT findings were compared using the McNemar test for paired categorical variables. CT, computed tomography.

Pulmonary function test results

Baseline spirometric evaluation demonstrated an obstructive ventilatory pattern. The median baseline FEV₁ was 66.0% of the predicted value (IQR: 57.5–71.5), median FVC was 73.0% predicted (IQR: 63.0–75.5), and median FEV₁/FVC ratio was 92.0% (IQR: 90.5–95.0). The median baseline FEF_{25–75} was 44.0% predicted (IQR: 41.0–54.0).

Follow-up spirometry showed persistently reduced FEV₁ and FVC values. The median change in FEV₁ was –9.0 percentage points (IQR: –13.0 to –5.0). A similar decline was observed in FVC values. No significant change was observed in the FEV₁/FVC ratio over time. Spirometric findings are presented in Table 4.

Table 4. Comparison of baseline and follow-up spirometry parameters.

Parameter	Baseline, median (IQR)	Follow-up, median (IQR)	p value
FEV ₁ , % predicted	66.0 (57.5–71.5)	60.0 (45.0–62.5)	0.21
FVC, % predicted	73.0 (63.0–75.5)	69.0 (61.0–70.0)	0.70
FEV ₁ /FVC, %	92.0 (90.5–95.0)	81.0 (68.0–91.5)	0.90
FEF _{25–75} , % predicted	44.0 (41.0–54.0)	39.0 (24.5–54.5)	0.88

Baseline and follow-up spirometry values were compared using the Wilcoxon signed-rank test, FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; FEF_{25–75}, forced expiratory flow between 25% and 75% of FVC; IQR, interquartile range.

Discussion

In this retrospective descriptive study, we evaluated the demographic, clinical, radiological, and spirometric outcomes of pediatric patients diagnosed with bronchiolitis obliterans, predominantly postinfectious bronchiolitis obliterans, over a ten-year period at a tertiary referral center. Our findings highlight the chronic and irreversible nature of BO, characterized by persistent respiratory symptoms, progressively declining spirometric parameters over time, and stable radiologic abnormalities despite long-term follow-up and multimodal treatment approaches.

The demographic profile of our cohort is consistent with previous reports. The predominance of male patients and the relatively young age at diagnosis support earlier observations that PIBO, which accounted for more than 90% of our cohort, most commonly develops in early childhood and demonstrates a male preponderance. Although the inciting lower respiratory tract infection typically occurs during infancy, the median age at diagnosis in our cohort indicates a substantial delay between the initial insult and definitive diagnosis [14]. This diagnostic delay has been widely reported in the literature and likely reflects the clinical overlap between PIBO and recurrent wheezing disorders, such as asthma, as well as the nonspecific nature of early symptoms. Our findings underscore the importance of maintaining a high index of suspicion for PIBO in children with persistent respiratory symptoms following a severe lower respiratory tract infection [15].

Clinically, all patients in our study presented with chronic respiratory symptoms, most notably persistent cough, wheezing, dyspnea, and exercise intolerance. A considerable proportion of patients required supplemental oxygen at the time of diagnosis, indicating chronic hypoxemia and advanced small airway involvement. Although oxygen dependency decreased during follow-up in some patients, a subset remained oxygen-dependent, underscoring the long-term morbidity associated with PIBO. Similar rates of chronic oxygen requirement have been reported in previous pediatric series and are considered markers of disease severity [15-17].

Radiological evaluation revealed typical chest CT findings associated with bronchiolitis obliterans, including diffuse air trapping, mosaic attenuation, ground-glass opacities, bronchial wall thickening, and bronchiectasis. Importantly, no statistically significant differences were observed between baseline and follow-up CT findings. The persistence of radiological abnormalities over time is consistent with the irreversible fibrotic remodeling of the small airways that characterizes BO. Previous studies have demonstrated that radiological improvement is uncommon once the disease is established, and our findings further support the concept that therapeutic interventions primarily aim to stabilize disease progression rather than reverse structural lung damage [18,19].

Pulmonary function testing revealed a ventilatory defect in the majority of patients, with reduced FEV₁ and markedly decreased mid-expiratory flow rates, reflecting predominant small airway involvement.



Although median values of FEV₁ and FVC declined during follow-up, these changes did not reach statistical significance. The absence of significant differences between baseline and follow-up spirometric parameters may be attributed to the relatively small sample size of patients with paired spirometry, heterogeneity in follow-up duration, and the variable natural course of PIBO. Nonetheless, the observed trend toward declining lung function in some patients is clinically relevant and aligns with previous longitudinal studies reporting gradual deterioration or stabilization rather than recovery of pulmonary function in PIBO [20,21].

Notably, the FEV₁/FVC ratio remained relatively stable over time, further supporting the presence of fixed airflow limitation. The heterogeneity observed in changes in FEF_{25–75} values highlights inter-individual variability in disease progression, which has been described in prior studies and may reflect differences in disease severity, extent of airway involvement, and response to therapy. These findings emphasize the importance of regular longitudinal pulmonary function monitoring to detect early functional decline and guide clinical management [9,10].

Treatment strategies in our cohort were heterogeneous and largely empirical, reflecting the absence of standardized treatment guidelines for PIBO [11,12]. Most patients received combinations of inhaled and/or systemic corticosteroids, macrolide antibiotics, leukotriene receptor antagonists, and supportive therapies. While subjective clinical improvement and reduced oxygen dependency were observed in some patients, objective improvements in spirometric or radiological parameters were limited. This observation is consistent with existing literature suggesting that treatment efficacy is greatest when anti-inflammatory therapy is initiated early in the disease course, before irreversible fibrosis develops. In patients with established disease, treatment is more likely to stabilize lung function rather than induce significant improvement [22].

The lack of significant radiological and functional improvement despite treatment underscores the chronic and irreversible nature of PIBO and highlights the need for early recognition and intervention. Emerging evidence suggests that combination therapy, including inhaled corticosteroids, macrolides, may provide symptomatic benefit and stabilize lung function in selected patients. However, robust prospective studies are lacking, and treatment decisions continue to rely on clinical judgment and extrapolation from other forms of bronchiolitis obliterans [23].

This study has several limitations. Its retrospective design and reliance on medical record review may have resulted in incomplete data, particularly regarding the initial infectious etiology and long-term outcomes. The relatively small number of patients with available paired pulmonary function tests limited the statistical power to detect significant longitudinal changes. Additionally, the absence of a control group precludes definitive conclusions regarding treatment efficacy. Nevertheless, the strengths of this study include a well-characterized cohort, long-term follow-up, and comprehensive evaluation of clinical, radiological, and functional parameters in a real-world setting.

Conclusion

BO in children is a chronic condition associated with persistent respiratory symptoms, fixed airflow obstruction, and stable radiological abnormalities over time. Our findings emphasize that while current therapeutic approaches may alleviate symptoms and reduce oxygen dependency in some patients, they do not reverse established structural lung damage. Early diagnosis, regular follow-up with pulmonary function testing, and a multidisciplinary approach remain essential for optimizing long-term outcomes in children with PIBO. Future research should focus on identifying novel therapeutic strategies aimed at preventing airway inflammation and fibrosis.



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Conflict of interest

The authors declared that they have no conflict of interest.

Data availability statement

Available upon request to the corresponding author.

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