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Clinical characteristics and outcome of non-cystic fibrosis bronchiectasis in children: A tertiary care perspective

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Abstract

Introduction: Bronchiectasis is a chronic respiratory disease caused by various respiratory and systemic conditions. It is now considered a potentially reversible disease, particularly when diagnosed early and managed with appropriate respiratory care strategies. Although rare in children, it typically develops in patients with recurrent lower respiratory tract infections. The etiology of bronchiectasis in children differs from that in adults. This study aims to identify the clinical features, causes, and outcomes of non-cystic fibrosis bronchiectasis in children at a tertiary center.

Methods: A retrospective review was conducted among children with non-cystic fibrosis bronchiectasis who attended a university-affiliated hospital between January 2007 and December 2021. Clinical outcomes were assessed based on pulmonary function tests, exacerbation, and mortality.

Results: The study included 35 children with non-cystic fibrosis bronchiectasis. The median age at diagnosis was 36 months (IQR: 24–170 months). Bronchiectasis was linked to underlying conditions in 22 cases (62.9%), such as primary immunodeficiency, chronic aspiration, and primary ciliary dyskinesia. Thirteen children had infectious-associated bronchiectasis (37.1%), with four cases related to pulmonary tuberculosis. At diagnosis, cystic bronchiectasis was most common ($n = 17$, 48.6%), followed by varicose ($n = 13$, 37.1%) and cylindrical bronchiectasis ($n = 5$, 14.3%). Pulmonary exacerbation occurred in 28 (80%) children, with a higher rate in noninfectious bronchiectasis than postinfectious bronchiectasis (90.9% vs 61.5%, $p = 0.036$). Hospitalization was required for 26 (77.1%) children, with a higher rate of noninfectious bronchiectasis than postinfectious bronchiectasis (86.3% vs 53.8%, $p = 0.033$).

Conclusions: Primary immune deficiency and chronic aspiration are the most common non-infective causes of non-cystic fibrosis bronchiectasis. Noninfectious bronchiectasis leads to higher exacerbation and hospitalization rates.

Keywords

Non-cystic fibrosis bronchiectasis, children, pulmonary exacerbations

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Background and introduction

Bronchiectasis is a condition characterized by the permanent widening of the bronchial tubes, which can lead to the blockage of airways due to frequent bacterial infections and inflammation.[1] It is relatively uncommon, with its prevalence varying widely between regions. The global estimated prevalence ranges from 0.2 to 15 per 100,000 persons.[2] Prevalence rates in certain areas are lower than expected due to a lack of awareness about the significance of the symptoms. The symptoms are similar to those of respiratory tract infections, which can lead to a delayed diagnosis since the disease progresses gradually.[3]

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The etiology of bronchiectasis differs between children and adults. In children, it usually develops after recurrent pneumonia and inadequate treatment.[3] Immunodeficiency and cystic fibrosis are the common causes of bronchiectasis in developed countries,[4] while in developing countries, postinfectious bronchiectasis is the most common cause.[5,6] This type of bronchiectasis may result from persistent airway infection and inflammation due to poor sanitation and inadequate treatment.[7]

Bronchiectasis is generally suspected through the identification of symptoms, particularly a chronic recurrent wet or productive cough, which represents the earliest indication of the condition. Children may exhibit dyspnea and poor weight gain alongside other symptoms. Physical examination may reveal digital clubbing and abnormalities in the chest wall.[8] The gold standard for diagnosis is high-resolution computed tomography (HRCT) using Reid classification.[9] The management of bronchiectasis involves identifying and treating underlying causes. The goal of treatment is to prevent further progression and, in some cases, reverse the bronchiectasis. In addition, supportive treatment such as airway clearance therapy and antibiotic prophylaxis, if indicated, is needed to reduce lower airway inflammation or infection and prevent pulmonary exacerbations.[10]

Bronchiectasis is a serious condition in children, but it is often not diagnosed until it is quite advanced. This is because the symptoms are not always easy to recognize, which can delay treatment. The European Respiratory Society released comprehensive clinical practice guidelines for managing bronchiectasis in children and adolescents in 2021. However, it is important to note that the implementation of these guidelines may differ significantly across low- and middle-income countries due to varying healthcare resources, access to specialized care, and local practices. These disparities can lead to a wide range of management strategies for bronchiectasis, affecting the quality of care and outcomes for affected children and adolescents in those regions. To address these issues, our study aims to carefully review the clinical characteristics, causes, and long-term outcomes of non-cystic fibrosis bronchiectasis in children.

Methods and materials

Study area and period

This study was conducted at Srinagarind Hospital, a university-affiliated hospital in Northeastern Thailand. The data was collected from medical records of patients who attended Srinagarind Hospital from 1 January 2007 to 31 December 2021.

Study design

A retrospective cohort study was conducted.

Source population

The source population comprised all children diagnosed with bronchiectasis from 1 January 2007 to 31 December 2021. The diagnosis of bronchiectasis was identified using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Thai Modification (ICD-10-TM) code J47, A15.0, A16.0, A16.2, and Q33.4.[11] The main inclusion criteria for selection were diagnosis of bronchiectasis from chest HRCT and the age of less than 18 years at the time of diagnosis. Children who were diagnosed with bronchiectasis concordance with cystic fibrosis were excluded from our study.

Study population

All children diagnosed with bronchiectasis and their charts were available during the data collection period.

Eligibility criteria

Inclusion criteria. The study included all children less than 18 years of age who were diagnosed with bronchiectasis from chest HRCT.

Exclusion criteria. Children who were diagnosed with bronchiectasis concordance with cystic fibrosis were excluded from our study.

Sample size determination

All children less than 18 years of age who were diagnosed with bronchiectasis other than from cystic fibrosis between 01 January 2007 and 31 December 2021, were included in the study. The final sample size was 35.

Sampling technique and procedure

The medical registration charts of all children admitted with bronchiectasis between 01 January 2007, and 31 December 2021, were checked. Subsequently, all necessary information was extracted from the medical charts of the children based on the data extraction format prepared for the present study.

Variables

Dependent variable. The number of exacerbations, hospitalizations, mechanical ventilators, and mortality rates were collected.

Independent variables

- Demographic characteristics: age at symptoms onset, gender, body weight, height, and body mass index.
- Clinical-related characteristics of pediatrics: symptoms at once, physical examination findings, recurrent/persistent pneumonia episodes, radiographic data, pulmonary function test results, management, and disease outcomes.

Table 1. Cause of non-cystic bronchiectasis.

Cause of non-cystic bronchiectasis	*n* (N = 35)	Percentage (%)
Postinfection (*n* = 13)		
TB	4	11.4
Other organism	9	25.7
Noninfection cause (*n* = 22)		
Primary immune deficiency	9	25.7
Chronic aspiration	5	14.3
Congenital malformation	3	8.6
Primary ciliary dyskinesia	3	8.6
Asthma	1	2.9
Foreign body aspiration	1	2.9

Table 2. Clinical characteristics of patients at presentation.

Clinical characteristics	*n* (N = 35)	Percentage (%)
Fever	31	88.6
Wet cough	30	85.7
Poor weight gain	29	82.9
Dyspnea	21	60.0
Cyanosis/desaturation	9	25.7
Chest deformity	6	17.1
Dry cough	5	14.3

Operational definitions

Pulmonary exacerbation is characterized by any of the following symptoms: a change in cough quality from dry to wet and/or sputum production lasting for three or more days, breathlessness, chest pain, crepitation, wheezing, and/or an increase in values of infectious markers.[12]

Statistical analysis

The data was analyzed using STATA software version 10 (Stata Corp., College Station, TX, USA). Categorical data were presented as frequencies and percentages. To compare the differences between the two groups, we used the Chi-square test. The Shapiro–Wilk normality test was used to assess the normality of continuous data. Continuous variables were assessed for normality using the Shapiro–Wilk test and described as mean and standard deviation (SD) or median and interquartile range (IQR) depending on the normality of variables. We used the independent *T*-test to compare the differences between the two groups. Values of $p < 0.05$ were considered to indicate statistical significance between the two groups.

Ethical approval

This study was approved by the Khon Kaen University Ethical Committee (KKUEC), approval number HE651026, in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The written informed consent was waived by the Institutional Review Board of KKUEC as per Khon Kaen University's Announcement No. 2179/2563, the process of obtaining subjects' consent was waived as this is a study of existing data or biological specimens without further prospective data collection from or direct interactions with the subjects.

Results

During the study period, 38 children were diagnosed with bronchiectasis. However, three children were excluded from the study as they had cystic fibrosis. Therefore, the study included a total of 35 children who were diagnosed with non-cystic fibrosis bronchiectasis. The median age of diagnosis among these children was 36 months (IQR: 24–170 months). Out of the 35 children, 19 (54.3%) were diagnosed with non-cystic fibrosis bronchiectasis before the age of 5 years old. Among these 35 patients, 15 (42.9%) were male and 20 (57.1%) were female. In a diverse group of 16 children over 5 years of age at diagnosis, it was evident that 5 were male (31.3%), while 11 were female (68.7%).

In this study, the causes of non-cystic fibrosis bronchiectasis were classified into two categories: noninfectious and infectious. Among the children studied, 22 (62.9%) were found to have noninfectious causes. These were primarily attributed to primary immunodeficiency (*n* = 9, 25.7%), chronic aspiration (*n* = 5, 14.3%), congenital malformation and primary ciliary dyskinesia each (*n* = 3, 8.6%), asthma with right middle lobe syndrome (*n* = 1, 2.9%), and foreign body aspiration (*n* = 1, 2.9%). On the other hand, postinfection was identified as a secondary cause of bronchiectasis. Some cases were associated with post-TB infection (*n* = 4, 11.4%), while others were linked to other organisms (*n* = 9, 25.7%). For further details, Table 1 presents a summary of the baseline characteristics data.

According to Table 2, the most common symptom observed at the initial presentation was fever, which was reported by 31 patients (88.6%). This was followed by productive cough, which was reported by 30 patients (85.7%). Other clinical presentations included poor weight gain (29 patients, 82.86%), dyspnea (21 patients, 60%), cyanosis (9 patients, 25.7%), and chest deformity (6 patients, 17.1%), dry cough (5 patients, 14.3%).

Nine patients (25.7%) underwent pulmonary function tests, out of which three patients (33.3%) had normal test results. Among the rest, four patients (44.4%) were diagnosed with mixed obstructive and restrictive pulmonary disease, while two patients (22.2%) had restrictive lung disease (Table 3). Based on chest HRCT findings, most patients (*n* = 17, 48.6%) had cystic bronchiectasis, which is the most severe form of bronchiectasis, based on the Reid classification. This was followed by varicose bronchiectasis (*n* = 13, 37.1%), and cylindrical bronchiectasis (*n* = 5, 14.3%).

The majority of patients (31, 88.6%) received yearly influenza vaccines to prevent severe infections. In addition,

Table 3. Pulmonary function test at diagnosis.

Pulmonary function test at diagnosis	*n* (N = 9)	Percentage (%)
Normal	3	33.3
Obstructive lung defect	0	0
Restrictive lung defect		
Mild	1	11.1
Severe	1	11.1
Mixed lung defect	4	44.4

16 patients (45.7%) received pneumococcal vaccines. To reduce inflammation and prevent infections, 22 patients (62.9%) were administered azithromycin as an immunomodulator. Inhaled corticosteroids were administered to 11 children diagnosed with clinically reversible airway obstruction. All participants were under 6 years old, making it difficult to perform spirometry tests effectively. To enhance mucociliary clearance and prevent airway damage, a total of 17 children (48.6%) diagnosed with cystic bronchiectasis required airway clearance therapy. Interventions such as airway oscillating positive expiratory pressure and airway hydration techniques, including hypertonic saline nebulization, were employed. A significant number of patients, specifically 20 (79.6%) required oxygen support.

Clinical outcomes

Among 35 children who were diagnosed with bronchiectasis, 28 children (80%) had experienced exacerbations at least once after the diagnosis. All the exacerbations were associated with infected bronchiectasis. During the flexible bronchoscopy, microorganisms were collected by tracheal cultures and bronchoalveolar lavage. It resulted in the identification of 32 microorganisms in total. The most common microorganism identified was *Pseudomonas aeruginosa* (n=10, 31.2%). Other commonly identified microorganisms include *Staphylococcus aureus* (n=4, 12.5%), *Acinetobacter baumannii* (n=3, 9.4%), and *Haemophilus influenzae* (n=3, 9.4%).

To compare the outcomes between patients with bronchiectasis due to postinfection causes and those with bronchiectasis due to other causes, it was observed that the latter group experienced significantly more pulmonary exacerbations and hospitalizations. The group with other underlying causes had a higher pulmonary exacerbation rate (90.9%) compared to the postinfection group, which had a lower rate (61.5%) with a significant difference (p = 0.036). Regarding the hospitalization rate, the group with other underlying causes had a rate of 86.3%, whereas the postinfection group had a lower rate of 53.8% (p = 0.033) (Table 4).

Discussion

Bronchiectasis is a frequent complication of lower respiratory tract infections in children from developing countries, which remains a major problem in these parts of the world.[13] Improved social circumstances, the development of broad-spectrum antibiotics, and the effective treatment of bacterial pneumonia have contributed to the decreased incidence of bronchiectasis in developed countries.[14] Our study was conducted at a tertiary care center in Thailand, a developing country in Southeast Asia. We found that noninfection bronchiectasis was more frequent (62.9%) than postinfection. This shift can be attributed to improvements in medical access and sanitation, which aid in early diagnosis and optimal treatment. According to this study, primary immunodeficiency is the top cause of noninfectious bronchiectasis, accounting for 25.7% of cases. According to our research, the leading cause of bronchiectasis in Thailand has changed over the years. Improved diagnostic tools and technologies have aided in identifying the disease's etiology.[14]

Most clinical studies have found that symptoms of bronchiectasis in children appear in their early childhood years. In our study, we found that the median age for diagnosis of bronchiectasis in children was 36 months, which is consistent with previous studies.[15] The most common symptoms reported in these children were fever (88.5%) and wet cough (85.7%), which is also consistent with findings from other studies in the literature.[3,13] Other common clinical presentations included poor weight gain and dyspnea were consistent with the previous study.[3] Chest deformities were found to be a common presentation of non-cystic fibrosis bronchiectasis in our study. They developed due to chronic airway obstruction prior to diagnosis. A previous study also reported chest deformities in children with non-cystic fibrosis bronchiectasis.[16]

During diagnosis in this study, cystic bronchiectasis is the most observed radiologic finding. This condition is considered the most severe form of bronchiectasis, as per the Reid classification, and is linked with a poor prognosis.[9] Often, delayed diagnosis occurs due to a failure to recognize the significance of symptoms in children. These symptoms can resemble clinical respiratory tract infections, and when combined with the gradual natural progression of the disease, it results in poor outcomes. Although there have been some predictions of outcomes based on radiologic findings in bronchiectasis patients, evidence is still limited in children.[17]

The results of spirometry tests for bronchiectasis vary between developed and developing countries. Children in developed countries show normal or near-normal lung function during diagnosis and this remains stable over time. Early diagnosis leads to better lung function and milder symptoms.[18] In our research, the majority of the children were too young to undergo spirometry tests. Only nine patients took the test, and out of them, six showed abnormal results. Mixed obstructive and restrictive symptoms were the most common, similar to the findings of the previous study.[19]

It was found that children with bronchiectasis frequently experience pulmonary exacerbation. According to our study, 80% of children had at least one exacerbation after diagnosis. Pulmonary infection was identified as the main cause of

Table 4. Clinical outcome of children with bronchiectasis from postinfection and noninfection cause.

Outcome	Total ($N = 35$)	Etiology of bronchiectasis		p-Value
		Postinfection ($n = 13$)	Noninfection ($n = 22$)	
Number of exacerbations, *n* (%)	28 (80.0)	8 (61.5)	20 (90.9)	0.036
Number of hospitalizations, *n* (%)	26 (77.1)	7 (53.8)	19 (86.3)	0.033
Mechanical ventilator, *n* (%)	11 (31.4)	3 (23.0)	9 (45.4)	0.282
Mortality rate, *n* (%)	5 (14.2)	1 (7.6)	4 (18.1)	0.630

these exacerbations, with Pseudomonas aeruginosa being the most common microorganism, similar to previous studies.[20] Children with underlying conditions had a higher rate of pulmonary exacerbation and hospitalization compared to those with postinfection bronchiectasis. One of the noninfection causes of bronchiectasis in our study is primary immunodeficiency. This condition weakens the immune system, making it more vulnerable to infections. As a result, individuals with this condition experience pulmonary exacerbations more frequently than those with other causes.[21]

The majority of patients (62.9%) in our study were given azithromycin as an immunomodulator to reduce inflammation and prevent infections. A meta-analysis of long-term macrolide treatment in children with non-cystic fibrosis bronchiectasis discovered that prolonged azithromycin use significantly reduces the frequency of acute exacerbations and sputum purulence scores, despite an increased risk of azithromycin-resistant bacteria, but did not show significant improvements in pulmonary function or cytokine levels.[22] Thus, while long-term macrolide therapy can reduce exacerbations and improve some clinical outcomes, the danger of antibiotic resistance must be carefully assessed on an individual patient basis.[23]

This study has several important limitations. First, it was carried out in a single center, which may limit the generalizability of the findings to other centers or regions. Second, the study included children categorized under postinfectious bronchiectasis based on their history of recurrent lower respiratory tract infections. However, despite multiple diagnostic tests, no underlying organisms were identified in these cases. This suggests that diagnostic limitations may have contributed to an incomplete understanding of the infectious agents involved. Third, there is a lack of national data in Thailand that identifies the primary causes of bronchiectasis. As our center functions as a super-tertiary care and referral facility, the data gathered reflects the experience of children with bronchiectasis in the Northeastern region of Thailand rather than the entire country. This underscores the need for future research aimed at establishing a comprehensive national perspective on the condition. In addition, the study's retrospective design encompassed all children who met the inclusion criteria throughout the designated study period, but a formal sample size calculation was not conducted. Lastly, the tertiary care setting may have introduced a selection bias toward more severe or complicated cases. Further multicenter prospective studies are needed to validate and expand upon these findings.

Conclusion

The most common noninfectious cause of bronchiectasis is primary immune deficiency, followed by chronic aspiration. Bronchiectasis resulting from noninfectious causes is associated with a higher frequency of exacerbations and hospitalizations when compared to cases resulting from postinfectious causes.

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Author contributions

PS, AA, and RU conceptualized and designed the study, collected all the data, carried out analyses, drafted the manuscript, revised the final manuscript, and agreed to be accountable for all aspects of the work. SN conceptualized and designed the study, collected all the data, carried out analyses, drafted the manuscript, and revised the final manuscript. LT and SS conceptualized the study and revised the final manuscript. All authors have read and agreed to the published version of the manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

This study was approved by the Khon Kaen University Ethical Committee (KKUEC), approval number HE651026, in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Informed consent statement

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Trial registration

Not applicable.

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