ORIGINAL ARTICLE

Diagnostic Utility of Flexible Bronchoscopy in Young Children with Treatment-Refractory Wheeze. A 5-Year Retrospective Study

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ABSTRACT

Background: Wheezing is common in young children and is usually self-limiting, with most children responding to standard medical therapy. However, a subset of children develops treatment-refractory wheeze, in whom underlying structural airway abnormalities may contribute to persistent symptoms, which can be identified by flexible bronchoscopy.

Aim: To identify the dynamic airway abnormalities in children presenting with wheeze that was persistent or inadequately responsive to standard medical therapy.

Materials and Methods: This retrospective audit was conducted at the pediatric bronchoscopy service of a tertiary care center and included children aged ≤5 years who underwent flexible bronchoscopy (FB) for persistent or poorly responsive wheeze between January 2020 and December 2024. Clinical, demographic, bronchoscopic, and procedural data were retrieved from medical records. Structural and dynamic airway abnormalities were recorded.

Results: A total of 42 children were included. Mean age was 27.6±12.6 months and mean symptom duration was 10.1±6.5 months. Generalized wheeze was present in 33 (78.6%) children, localized wheeze in 7 (16.7%), and inspiratory stridor with expiratory wheeze in two (4.76%) children. Dynamic airway abnormalities were identified in 14 (38.1%). Tracheomalacia (TM) was found in seven (16.7%), bronchomalacia (BM) in 3 (7.1%). Isolated Laryngomalacia was seen in two (4.76%), whereas it was associated with TM in 4 children. No major procedural complications occurred. Minor complications included transient hypoxia in 8 (19.0%) and epistaxis in 4 (9.5%).

Conclusions: FB identified dynamic airway abnormalities in a substantial proportion of young children with treatment-refractory wheeze.

Key Words: Flexible Bronchoscopy, Refractory Wheeze, Children, Tracheomalacia

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INTRODUCTION

Wheezing is a common respiratory symptom in early childhood, with a significant proportion of children experiencing at least one wheezing episode during the first years of life[1]. Although recurrent wheeze in young children is frequently attributed to asthma or viral-associated airway disease, persistent or poorly responsive wheeze despite standard medical therapy may indicate an alternative or additional underlying pathology, including structural airway abnormalities[2]. The differential diagnosis of recurrent or persistent wheeze is broad and includes airway malacia and other congenital airway abnormalities, aspiration, bronchopulmonary dysplasia, cystic fibrosis, vascular or cardiac compression, foreign body aspiration, infection, immunodeficiency, and less common parenchymal or mediastinal disorders[3-6]. Consequently, identifying the cause of recurrent or treatment-refractory wheeze in children can be challenging, particularly when clinical features overlap with those of common obstructive airway diseases.

Flexible bronchoscopy (FB) provides direct visualization of the upper and central airways and can identify structural and dynamic abnormalities that may not be apparent on routine clinical or radiological

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assessment[7]. Many studies have found central airway malacia as an important cause of treatment resistant wheeze in young children[8]. The present study was undertaken to identify the dynamic airway abnormality in children presenting with wheeze that was persistent or inadequately responsive to standard medical therapy.

METHODS

This retrospective audit included children upto five years of age, who underwent FB as part of the diagnostic evaluation for refractory or poorly responsive wheeze, primarily to identify an underlying dynamic airway abnormality. Refractory/poorly responsive wheeze was defined as persistent wheeze despite optimal use of controller inhalers and with proper technique and compliance. Data from January 2020 to December 2024 was reviewed. Demographic and clinical variables extracted from the medical records included age, sex and weight. Duration of symptoms, previous treatment history, site of wheeze, family history of atopy, and history of feeding-related regurgitation or choking were also captured. An ethical waiver was sought from the Institutional Ethics Committee (SKIMS-IEC) for this retrospective study.

Flexible bronchoscopy

FB was performed after taking written informed consent from the parents/guardians of the enrolled children, in the dedicated bronchoscopy suite by a team comprising a bronchoscopist, bronchoscopy technologist, and pediatric resident. Children were pre-oxygenated, with a target oxygen saturation of >90% maintained throughout the procedure. Most procedures were performed via the trans-nasal route using an Olympus BF-XP160F flexible bronchoscope (Olympus Corporation, Japan; outer diameter 2.8 mm; working-channel diameter 1.2 mm).

Continuous electrocardiographic and pulse oximetry monitoring was performed throughout the procedure, while non-invasive blood pressure was recorded every 3–5 minutes. Supplemental oxygen was administered through a nasal cannula. Desaturation to ≤90% was managed by increasing oxygen supplementation and, when required, by administration through an oxygen mask.

Topical anesthesia was achieved using 2% lidocaine gel applied to the nasal mucosa, followed by 1-mL aliquots of 2% lidocaine diluted 1:1 with normal saline using the spray-as-you-go technique. Additional topical lidocaine was administered when required. The total dose of lidocaine did not exceed 5–6 mg/kg in any patient. All procedures were performed under conscious sedation using intravenous midazolam (0.1 mg/kg) and/or ketamine (1 mg/kg), with the child breathing spontaneously. No endotracheal tube, laryngeal mask airway, or positive-pressure ventilation was used during assessment of dynamic airway collapse.

The bronchoscopic examination was systematically reviewed for structural and dynamic airway abnormalities, including laryngomalacia (LM), tracheomalacia (TM), bronchomalacia (BM), and other associated upper and central airway abnormalities. TM and BM were defined according to the working definition of the European Respiratory Society as an expiratory reduction of >50% in the cross-sectional luminal area during spontaneous, quiet respiration. LM was diagnosed by criteria laid down by Olney et al.[9,10]. Dynamic airway collapse was assessed by direct visual bronchoscopic observation. The assessment was performed during spontaneous breathing, and the degree of airway collapse was estimated visually by a single experienced pediatric bronchoscopist who performed and interpreted all bronchoscopic examinations. Procedural complications and adverse events occurring during the procedure or within one hour after bronchoscopy were also recorded and analyzed.

Statistical Analysis.

A standardized data-extraction form was used to collect demographic characteristics, clinical variables, indication for bronchoscopy, hemodynamic parameters, oxygen saturation, and procedural adverse events. Statistical analysis was performed using SPSS version 25.0. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean (SD) or median (IQR), as appropriate.

RESULTS

During the five-year audit period, 623 bronchoscopy procedures were performed, of which 65 procedures were conducted for evaluation of treatment-refractory wheeze. Twenty-three children were excluded from the retrospective analysis because of insufficient clinical or procedural data. Thus, 42 children were included in the final analysis. The clinico-demographic and bronchoscopic findings of the study population are summarized in Table 1.

Table 1 : Baseline Demographic and Clinical Data of the Study Population (N=42)

Variable	Value
Age in months (Mean ± SD)	27.57 ± 12.6
Duration of symptoms in months (Mean ± SD)	10.05 ± 6.5
Weight in kg (Mean ± SD)	12.09 ± 3.06
Females. No (%)	20 (47.6)
GERD. No (%)	3 (7.14)
Recurrent choking during feeding. No (%)	1 (2.38)
Tracheomalacia. No (%)	7 (16.66)
Bronchomalacia. No (%)	3 (7.14)
Laryngomalacia. No (5)	2 (4.76)
Both upper and central airway abnormality. No (%)	4 (9.52)

Generalized wheeze was the most common presenting feature, documented in 33/42 (78.6%) children, followed by localized wheeze in 7/42 (16.7%) children. Among the seven children with localized wheeze, 3 (7.1%) had left-sided wheeze, while 4 (9.5%) had right-sided wheeze. Two children (4.8%) presented predominantly with inspiratory stridor in addition to expiratory wheeze.

TM was identified in 7/42 (16.7%) children. Among the seven children with TM, 3 (42.9%) had an associated double aortic arch confirmed by contrast-enhanced CT angiography, while the remaining 4 (57.1%) had primary TM. Of the three children with double aortic arch, one underwent surgical correction and demonstrated resolution of TM on repeat bronchoscopy done after one year of surgical intervention. The second child was managed conservatively, while the third was lost to follow-up. BM was identified in 3/42 (7.1%) children, involving the left main bronchus in 2/3 (66.7%) and the right main bronchus in 1/3 (33.3%). All three children with BM had underlying congenital heart disease. Laryngomalacia was identified in 6 (14.3%) patients; 4 (9.5%) had associated tracheomalacia, while 2 (4.8%) had isolated LM. No child required airway stenting or long-term/home oxygen therapy. No major procedural complications were recorded. Minor procedural adverse events included transient hypoxia in 8/42 (19.0%) children, epistaxis in 4/42 (9.5%), and transient ST-segment elevation in 1/42 (2.4%).

DISCUSSION

In this five-year retrospective study, we evaluated 42 children who underwent FB as part of the diagnostic evaluation of treatment-refractory wheeze. Dynamic airway abnormalities were identified in 16 (38.09%) children, with tracheomalacia being the most frequent finding. TM was present as an isolated abnormality in seven children and in association with laryngeal abnormalities in two children. Isolated BM was identified in three children. All three children with BM had underlying congenital heart disease. Among seven children diagnosed with TM three had double aortic arch as the underlying cause of TM. These findings support the importance of considering structural and dynamic airway abnormalities in children with persistent wheeze that does not respond adequately to conventional therapy. Previous studies have similarly demonstrated a substantial diagnostic yield of flexible bronchoscopy in children with refractory wheezing disorder. In a study by Aslan et al[11] in 34 children with persistent or recurrent wheeze despite treatment for asthma, bronchoscopy established a definitive diagnosis in 85%, with airway airway malacia seen in 12 (35.3%) children.

In our study cohort, FB was used to diagnose TM and BM, as it permits direct, real-time assessment of dynamic airway collapse during spontaneous breathing and provides information regarding the location, extent and severity of airway involvement. The ERS statement recognizes flexible bronchoscopy as the standard diagnostic method for evaluating pediatric TM and BM[9]. Conventional static CT provides valuable anatomical information but has limited sensitivity for detecting

dynamic airway collapse and may therefore not reliably exclude TM. CT and MRI nevertheless have an important complementary role in identifying extrinsic causes of airway compression, particularly vascular rings and other mediastinal or cardiovascular abnormalities. Dynamic airway CT has also been evaluated for diagnosing airway malacia in children and has demonstrated high specificity and positive predictive value, although its sensitivity may be insufficient to reliably exclude TM [12]. Virtual bronchoscopy (VB), derived from multidetector CT datasets, provides a non-invasive three-dimensional representation of the tracheobronchial lumen and has the additional advantage of demonstrating the airway distal to a stenotic segment as well as the surrounding vascular and mediastinal structures. However, unlike FB, VB does not permit real-time visualization of dynamic airway collapse. In a comparative study of 53 children, FB detected TM in 37 (70%) children, whereas VB identified TM in only 20 children, with a sensitivity of 54.1% and specificity of 87.5%; the sensitivity for BM was even lower at 45.2%[13]. The authors concluded that VB could not replace FB for the diagnosis of tracheobronchomalacia. Thus, VB may serve as a useful complementary investigation, particularly when assessment of extrinsic airway anatomy is required, but its relatively low sensitivity limits its role as a stand-alone modality for diagnosing dynamic airway malacia[13].

Both flexible and rigid bronchoscopy have roles in the evaluation of pediatric TM. FB is particularly suited to dynamic assessment because it can be performed during spontaneous breathing and permits evaluation of more distal bronchial segments, making it particularly useful for detecting BM. Rigid bronchoscopy, generally performed under deeper anesthesia, provides excellent visualization of the central airway and may be advantageous when therapeutic intervention, foreign-body removal or detailed assessment of the proximal airway is required. Comparative studies have demonstrated broadly comparable assessment of tracheal collapse with the two techniques, although differences in the assessment of the location and severity of airway collapse have also been reported[14,15]. Therefore, the choice of bronchoscopic technique should be guided by the clinical indication, suspected site and extent of airway involvement, and the potential need for therapeutic intervention.

The association between airway malacia and cardiovascular or vascular abnormalities observed in our cohort is consistent with previous literature. In children with congenital heart disease, airway compression and malacia may result from the close anatomical relationship between the tracheobronchial tree and cardiovascular structures. In a study by Lee et al[16] in children with congenital heart disease who underwent flexible bronchoscopy, airway abnormalities were identified in 92%, with extrinsic compression being the predominant lower-airway abnormality; BM was also identified in a subset of children. Similarly, studies have demonstrated that vascular rings and other cardiovascular abnormalities may produce airway compression and dynamic collapse, sometimes presenting predominantly with respiratory symptoms rather than classical stridor[17,18]. The identification of double aortic arch in three children in our cohort is clinically important, as recognition of an underlying vascular cause may alter subsequent management and prevent inappropriate escalation of asthma-directed therapy. In our cohort, one child with a double aortic arch underwent surgical correction, and repeat flexible bronchoscopy performed one year after surgery demonstrated complete resolution of the previously documented tracheomalacia. This observation supports the potential for progressive recovery of tracheal airway dynamics following relief of chronic vascular compression. Previous studies have similarly reported improvement of tracheomalacia following complete vascular ring division, although persistent tracheomalacia has been documented in a subset of children[19]. The natural history of pediatric tracheobronchomalacia should also be considered when interpreting bronchoscopic findings. Primary or congenital tracheomalacia may improve spontaneously with maturation and increasing rigidity of the tracheal cartilage, with many children becoming asymptomatic by the second year of life. However, the evidence

regarding the natural history and rate of resolution is limited, and spontaneous improvement should not be assumed in children with severe or secondary disease. Malacia associated with bronchopulmonary dysplasia, esophageal atresia/tracheoesophageal fistula, chronic airway injury or extrinsic vascular compression may have a more prolonged course and may require targeted treatment. Therefore, the clinical significance of bronchoscopically demonstrated malacia should be interpreted in relation to its severity, underlying cause and clinical course rather than on the bronchoscopic finding alone[20,21].

Flexible bronchoscopy was also well tolerated in our cohort, with no major procedural complications. This is consistent with contemporary pediatric data supporting the overall safety of flexible bronchoscopy when performed with appropriate monitoring, although complications such as hypoxemia and other respiratory events can occur. A recent Indian series of 869 pediatric bronchoscopies reported complications in 6.7% of procedures, with severe events in 3.2%, emphasizing the importance of appropriate patient selection and procedural monitoring[22].

This study has several limitations. Its retrospective, single-center design and relatively small sample size limit the generalizability of the findings and introduce the possibility of referral and selection bias, as bronchoscopy was performed only in children considered sufficiently refractory to standard treatment to warrant invasive evaluation. The absence of a control group also prevents comparison with children with wheeze who respond to conventional therapy. Furthermore, BAL findings were not consistently documented in the available records and were therefore excluded from the present analysis. Because the study primarily evaluated bronchoscopic abnormalities, it cannot establish that every abnormality identified was the sole cause of wheeze.

CONCLUSION

Our findings suggest that FB has a role to diagnose airway malacia in children with persistent or treatment-refractory wheeze, particularly when an underlying structural or dynamic airway abnormality is suspected. Identification of airway malacia, laryngeal abnormalities, or vascular compression may redirect further investigation and management rather than repeated escalation of asthma-directed therapy.

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