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Airway Resistance and Reactance Assessed by Impulse Oscillometry in Children with Osteogenesis Imperfecta: A Case-Control Study

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Abstract

Background

Respiratory impairment is an important complication of osteogenesis imperfecta (OI), traditionally attributed to thoracic deformities and skeletal abnormalities. However, oscillometric airway function in children with well-controlled OI have been insufficiently investigated using impulse oscillometry (IOS). This study aims to evaluate airway function in children with OI and compare oscillometric findings with those of healthy controls.

Methods

In this single-center case-control study, 20 children with OI and 20 age- and sex-matched healthy controls underwent IOS according to European Respiratory Society technical standards. Airway resistance (R5, R20, R5–R20) and reactance parameters (X5, X20, AX, and Fres) were analyzed. Oscillometric z-scores were calculated using the reference equations incorporated into the device software, and abnormal values were defined according to the corresponding upper and lower limits of normal. Demographic, clinical, laboratory, and treatment characteristics were also recorded.

Results

The two groups were comparable in age, sex, passive smoking exposure, and asthma prevalence. Children with OI had significantly lower height and weight z-scores than controls (both $p < 0.001$). Among IOS indices, only reactance area (AX) was significantly higher in the OI group than in healthy controls (1.62 vs. 1.10 kPa/L, $p = 0.031$). Although R5, R20, and R5–R20 were consistently higher in children with OI, none reached statistical significance, while R5–R20 showed a borderline difference ($p = 0.060$). X5, X20, and Fres were comparable between groups. Abnormal IOS findings were uncommon; Fres was the most frequently abnormal parameter (15%), whereas abnormal AX and X20 values were identified in 10% of patients each.

Conclusions

Well-treated children with OI demonstrated largely preserved oscillometric airway function despite significant skeletal involvement. The isolated increase in AX may indicate subtle alterations in respiratory system elastance that precede measurable abnormalities in airway resistance. IOS may represent a sensitive, non-invasive tool for detecting early functional respiratory changes in pediatric OI and warrants further evaluation in larger longitudinal studies.

1. Introduction

Osteogenesis imperfecta (OI) is an inherited connective tissue disorder characterized by bone fragility, primarily resulting from quantitative or qualitative defects in type I collagen. In many patients, pathogenic variants in the COL1A1 and COL1A2 genes are responsible, and the prevalence of the condition is reported to be approximately one in 15,000–20,000 live births. The clinical spectrum is quite broad; whilst mild cases may present with only recurrent fractures, severe forms can lead to progressive skeletal deformities, short stature and life-threatening complications. In recent years, it has become increasingly clear that OI is not merely a disease affecting the skeletal system, but rather a multisystemic connective tissue disorder that also involves the respiratory, cardiovascular, auditory and dental systems [1, 2].

Respiratory involvement is one of the leading causes of morbidity and mortality, particularly in patients with moderate-to-severe OI. For many years, it was accepted that respiratory dysfunction in OI primarily resulted from a restrictive ventilatory pattern caused by scoliosis, chest wall deformities, recurrent rib fractures and reduced thoracic compliance. However, clinical and experimental data obtained in recent years indicate that chest wall deformities alone are insufficient to explain the respiratory abnormalities observed [3, 4].

Type I collagen is a fundamental component not only of the bone matrix but also of the alveolar septa, the pulmonary interstitium, the bronchial walls and the pulmonary vascular structure. It is therefore thought that abnormalities in collagen synthesis or structure may directly affect lung development, elasticity and respiratory mechanics. Indeed, studies have demonstrated abnormalities in the intrinsic lung structure even in patients without obvious thoracic deformities; it has therefore been suggested that the loss of respiratory function in OI is attributable not only to skeletal deformities but also to primary connective tissue pathology [4, 5].

To date, pulmonary function in OI has largely been assessed using conventional spirometry. In the largest multicenter study, Tam and colleagues demonstrated that forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1) values decreased significantly as disease severity increased, and that restrictive ventilatory impairment was particularly pronounced in severe OI phenotypes [3]. Similarly, other studies in children have reported an association between reduced lung volumes, impaired respiratory muscle strength, thoracic deformities and respiratory function. However, spirometry is largely dependent on the patient's active cooperation and forced expiratory maneuvers. This can make it difficult to detect early or mild respiratory mechanical abnormalities, particularly in children and in patients with significant musculoskeletal involvement [3, 5].

Impulse oscillometry (IOS) is an oscillometric method that assesses airway resistance and reactance during tidal breathing without requiring forced respiratory maneuvers and is independent of forced exertion. Thanks to the resistance and reactance parameters obtained at different frequencies, the mechanical properties of both the central and peripheral airways can be assessed in detail, and early airway changes that cannot be detected by spirometry can be identified. Due to these characteristics,

IOS is being used increasingly, particularly in the pediatric age group and in patients in whom reliable spirometry cannot be performed.

However, the literature on the use of oscillometry in osteogenesis imperfecta is extremely limited. To date, only one study, conducted by Storoni and colleagues, has evaluated spirometry, plethysmography and the Forced Oscillation Technique (FOT) in 12 patients with OI; it was reported that oscillometric measurements could demonstrate bronchial obstruction and the bronchodilator response. However, this study had a small sample size, primarily included adult patients, lacked a healthy control group, and used the conventional FOT method rather than IOS. Consequently, the generalizability of the findings to the pediatric population is limited [6].

To the best of our knowledge, no previous study has assessed respiratory function in pediatric patients with osteogenesis imperfecta using impulse oscillometry in comparison with healthy controls. Consequently, whether IOS can identify subclinical alterations in airway resistance and reactance in clinically stable children with OI remains uncertain. The aim of this study was to compare impulse oscillometry parameters between children with osteogenesis imperfecta and age- and sex-matched healthy controls and to determine the prevalence of abnormal IOS findings based on z-scores derived from the reference equations incorporated into the device software. We hypothesized that, even in the absence of clinically evident respiratory disease, subtle alterations in airway function, particularly in reactance-derived parameters, may be detectable using IOS in children with OI.

2. Materials and Methods

2.1. Study Design and Patient Population

This study is a single-center, case-control study in which airway function was assessed using impulse oscillometry (IOS) in children being monitored for a diagnosis of osteogenesis imperfecta. The study was conducted in collaboration between the Department of Pediatric Endocrinology and the Department of Pediatric Immunology and Allergic Diseases at the Faculty of Medicine, Inonu University. Immediately after obtaining ethics committee approval, potentially eligible patients were identified from the pediatric endocrinology outpatient clinic database and contacted by telephone. Families willing to participate were invited to the clinic for evaluation. During the study visit, demographic and clinical data were recorded using standardized case report forms, and all respiratory assessments were completed on the same day under the supervision of the same study investigator.

2.2. Assessment of Clinical, Laboratory, and Treatment Characteristics

Patients' demographic characteristics, including age, sex, height and weight were recorded. Height and weight were measured using standardized methods, and height and weight Z-scores were calculated according to age- and sex-specific national reference standards [7]. Demographic and clinical information, including age at diagnosis, disease duration, osteogenesis imperfecta (OI) type, parental

consanguinity, family history of OI, exposure to passive smoking, history of long-bone deformity, vertebral compression fractures, previous orthopedic surgery, thoracic deformities (pectus deformity and scoliosis), lifetime fracture number, mobility status, walking limitation, prolonged immobilization, and regular physical activity were obtained from patient records and parental interviews.

Atopic comorbidities, including physician-diagnosed asthma, allergic rhinitis, atopic dermatitis, food allergy, and drug allergy, were recorded. Lumbar spine bone mineral density (BMD) Z-scores and available laboratory findings, including serum calcium, phosphorus, alkaline phosphatase (ALP), and parathyroid hormone (PTH) levels, were retrospectively retrieved from the patients' medical records.

Regarding treatment characteristics, the use of bisphosphonate therapy at the time of evaluation was recorded. The type of bisphosphonate treatment, including zoledronic acid was documented and patients' current treatment regimens were assessed. Children with a history of chronic respiratory disease (except physician-diagnosed asthma), congenital heart disease, neuromuscular disorders, acute respiratory tract infection within the preceding four weeks, inability to perform acceptable impulse oscillometry measurements according to ERS quality criteria, or unwillingness to participate in the study were excluded.

2.3. Assessment of Airway Functions Using Impulse Oscillometry System

Airway resistance and reactance were assessed using an impulse oscillometry system [Jaeger MasterScreen IOS system using SentrySuite software, version 3.20 (Vyaire Medical GmbH, Höchberg, Germany)]. The device was calibrated daily prior to testing using a standard 3-L syringe and reference resistance, in accordance with the manufacturer’s instructions. All IOS parameters were expressed as absolute values and, where available, as percent-predicted values generated by the Jaeger MasterScreen IOS software using age-, sex-, height-, and ethnicity-specific reference equations.

All measurements were performed in accordance with the ERS Technical Standards for Respiratory Oscillometry. [8]. Participants were instructed to avoid heavy meals, vigorous exercise, and short-acting bronchodilators for at least 4–6 hours prior to testing. Measurements were conducted in a quiet environment with participants in a seated position, wearing a nose clip and maintaining a neutral head position. To minimize upper airway artifact, participants firmly supported their cheeks and the floor of the mouth with their hands.

During the procedure, subjects were asked to breathe normally (tidal breathing) through a mouthpiece connected to the IOS device for approximately 30–45 seconds, ensuring a tight seal around the mouthpiece. At least three technically acceptable measurements were obtained from each participant. Measurement reproducibility was assessed using the coefficient of variation (CV) of R5, and only measurements with an R5 CV < 15% were accepted for analysis. Measurements were considered acceptable if they met the following criteria: absence of artifacts such as coughing, swallowing, vocalization, air leakage, or irregular breathing; a stable tidal breathing pattern; and coherence values of

≥ 0.80 at 5 Hz and ≥ 0.90 at frequencies ≥ 10 Hz. The mean values of the acceptable measurements were used for analysis.

The IOS parameters evaluated included total airway resistance at 5 Hz (R5), central airway resistance at 20 Hz (R20), and the difference between R5 and R20 (R5–R20), which reflects peripheral (small airway) resistance. Reactance parameters included reactance at 5 Hz (X5), reactance area (AX), and resonance frequency (Fres). Negative X5 values indicate reduced elastic recoil and peripheral airway involvement [9]. In addition to the absolute oscillometric values, z-scores were calculated using the reference equations implemented in the device software, considering age, sex, height, and ethnicity where applicable. Abnormal values were defined according to the upper limit of normal (ULN) or lower limit of normal (LLN). For resistance and impedance-derived parameters (R5, R20, R5–R20, AX, and Fres), values with z-scores > + 1.645 were considered abnormal, whereas for reactance parameters (X5 and X20), values with z-scores < − 1.645 were considered abnormal. The frequency of abnormal oscillometric findings was subsequently determined for each parameter.

2.4. Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows (Version 25.0, IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test. Variables showing a normal distribution were presented as mean ± standard deviation, whilst those not following a normal distribution were presented as the median (interquartile range; IQR). Categorical variables were expressed as frequencies and percentages. When comparing two independent groups, the the Mann–Whitney U test was used for those not following a normal distribution. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test. A two-tailed p-value of < 0.05 was taken as the threshold for statistical significance.

3. Result

3.1. Demographic and clinical characteristics

A total of 20 children with osteogenesis imperfecta were included in the study, of whom 11 (55%) were male. Consanguineous marriage was reported in 6 patients (30%), a family history of osteogenesis imperfecta in 9 (45%), and passive smoking exposure in 4 (20%). According to disease subtype, 15 patients (75%) had type I, 2 (10%) had type III, and 3 (15%) had type IV osteogenesis imperfecta. Thoracic deformities were present in a subset of patients, including pectus deformity in 4 (20%) and scoliosis in 5 (25%). A history of long-bone deformity was observed in 17 patients (85%), vertebral compression fractures in 8 (40%), and previous orthopedic surgery in 12 (60%). Regarding functional status, mobility was classified as low in 5 patients (25%), moderate in 6 (30%), and good in 9 (45%). Walking limitation was present in 6 patients (30%), while prolonged immobilization had occurred in 5 (25%); none of the participants engaged in regular sports activities. Atopic comorbidities were uncommon, with asthma and allergic rhinitis each reported in only one patient (5%), whereas no patient had a history of eczema, food allergy, or drug allergy.

The median lumbar spine bone mineral density (BMD) Z-score was −1.3, indicating generally preserved bone mineralization under current management. Laboratory parameters were also within the expected range, with mean serum parathyroid hormone, calcium, phosphate, and alkaline phosphatase levels of 40.8 ± 21.6 pg/mL, 9.8 ± 0.57 mg/dL, 4.3 ± 0.74 mg/dL, and 182.5 ± 60.8 U/L, respectively. At the time of the study, all patients (100%) were receiving ongoing bisphosphonate therapy, with 19 (95%) treated with pamidronate and 1 (5%) with zoledronic acid. The demographic, clinical, treatment, and laboratory characteristics of children with osteogenesis imperfecta are summarized in Table 1.

Table 1: Demographic, clinical, treatment, and laboratory characteristics of children with osteogenesis imperfecta (n=20)

Variables	n (%)
Sex, male	11 (55)
Age, median (IQR), years	12 (7.5)
Age at diagnosis, median (IQR), years	3 (6.25)
Disease duration, median (IQR), years	6.5 (7)
Height z score, median (IQR)	-1.7 (1.35)
Weight z score, median (IQR)	-1.45 (1.33)
Consanguineous marriage	6 (30)
Family history of osteogenesis imperfecta	9 (45)
Smoking exposure	4 (20)
Osteogenesis imperfecta type	
Type 1	15 (75)
Type 3	2 (10)
Type 4	3 (15)
Thorax deformity	
Pectus deformity (excavatum/carinatum)	4 (20)
Scoliosis	5 (25)
History of long bone deformity	17 (85)
Vertebral compression fracture	8 (40)
Previous orthopedic surgery	12 (60)
Lifetime fracture number, median (IQR)	7 (12.5)
Lumbar spine BMD Z-score, median (IQR)	-1.3 (1)
Daily activity level	
Low	5 (25)
Moderate	6 (30)
Good	9 (45)
Walking restriction	6 (30)
Long-term immobilization	5 (25)
Regular exercise	-

Presence of atopy in the patient	
Asthma	1 (5)
Allergic rhinitis	1 (5)
Eczema history	-
Food allergy history	-
Drug allergy history	-
Laboratory findings	
Parathyroid hormone (pg/mL)	40.8±21.6
Calcium (mg/dL)	9.8±0.57
Phosphate (mg/dL)	4.3±0.74
Alkaline phosphatase (U/L)	182.5±60.8
Current bisphosphonate therapy	
Pamidronate treatment	19 (95)
Zoledronic acid treatment	1 (5)

3.2. Comparison of demographic characteristics and oscillometric parameters

The OI and healthy control groups were comparable with respect to sex distribution (55% vs. 50%, p=0.752), age (p=0.620), passive smoking exposure (20% vs. 25%, p=1.000), and the prevalence of asthma (5% vs. 10%, p=1.000). Children with OI had significantly lower height and weight Z-scores than healthy controls (height Z-score: −1.7 vs. 0.87, p<0.001; weight Z-score: −1.45 vs. 0.75, p<0.001).

Children with OI demonstrated consistently higher resistance-derived IOS parameters (R5, R20, and R5–R20) than healthy controls. Although these differences were not statistically significant, R5–R20 approached statistical significance (p=0.060), suggesting a tendency toward increased peripheral airway resistance. In contrast, AX was the only oscillometric parameter that differed significantly between the groups (1.62 vs. 1.10 kPa/L, p=0.031). Likewise, X5, X20, and Fres were similar between the groups (all p>0.05). Table 2 summarizes the demographic characteristics and oscillometric findings of the OI and healthy control groups.

Table 2. Comparison of Demographic Characteristics and Distribution of Oscillometric Measurements in Osteogenesis Imperfecta and Healthy Control Groups

Variables	Osteogenesis Imperfecta Group (n=20)	Healthy Control Group (n=20)	p-value
Gender, male, n (%)	11 (55)	10 (50)	0.752
Age, median (IQR), years	17 (7.5)	12 (2)	0.62
Height z score, median (IQR)	-1.7 (1.35)	0.87 (1.47)	<0.001
Weight z score, median (IQR)	-1.45 (1.33)	0.75 (1.27)	<0.001
Exposure to smoking, n (%)	4 (20)	5 (25)	1.0
Asthma, n (%)	1 (5)	2 (10)	1.0
R5 (kPa·s/L), median (IQR)	0.51 (0.30)	0.44 (0.12)	0.142
R20 (kPa·s/L), median (IQR)	0.30 (0.15)	0.31 (0.18)	0.738
R5–R20 (kPa·s/L), median (IQR)	0.18 (0.20)	0.12 (0.11)	**0.06**
X5 (kPa·s/L), median (IQR)	-0.09 (0.19)	-0.09 (0.06)	0.512
X20 (kPa·s/L), median (IQR)	-0.04 (0.08)	0.02 (0.06)	0.253
AX (kPa/L), median (IQR)	1.62 (1.68)	1.10 (0.52)	**0.031**
Fres (Hz), median (IQR)	21.3 (8.91)	21.91 (9.24)	0.183

3.3. Abnormal oscillometric findings

The distribution of oscillometric parameters and the frequency of abnormal impulse oscillometry (IOS) findings in children with osteogenesis imperfecta are summarized in Table 3. Based on z-scores derived from the reference equations incorporated into the device software, abnormal R5, R5–R20, and X5 values were each identified in 1 patient (5%), whereas abnormal X20 and AX values were observed in 2 patients (10%) each. Fres was the most frequently abnormal IOS parameter, with 3 patients (15%) demonstrating values above the upper limit of normal. No patient had an abnormal R20 value.

Table 3. Oscillometric Measurements, Abnormality Criteria, and Frequency of Abnormal IOS Findings in Children with Osteogenesis Imperfecta (n=20)

Variables	Impulse oscillometry parameters	Abnormality criterion (ULN/LLN z score)	Abnormal results, n (%)
R5 (kPa·L^{-1} s), median (IQR)	0.51 (0.30)	z > +1.645	1 (5)
R20 (kPa·L^{-1} s), median (IQR)	0.30 (0.15)	z > +1.645	-
R5–R20 (kPa·L^{-1} s), median (IQR)	0.18 (0.20)	z > +1.645	1 (5)
X5 (kPa·L^{-1} s), median (IQR)	-0.09 (0.19)	z < –1.645	1 (5)
X20 (kPa·L^{-1} s), median (IQR)	-0.04 (0.08)	z < –1.645	2 (10)
AX ((kPa·L^{-1}), median (IQR)	1.62 (1.68)	z > +1.645	2 (10)
Fres (Hz), median (IQR)	21.3 (8.91)	z > +1.645	3 (15)

ULN: Upper limit of normal; LLN: Lower limit of normal. Abnormal values were defined as z-scores > +1.645 for R5, R20, R5–R20, AX, and Fres, and z-scores < −1.645 for X5 and X20.

4. Discussion

To our knowledge, the present study is the first pediatric case–control study to evaluate airway resistance and reactance in children with osteogenesis imperfecta (OI) using impulse oscillometry (IOS). The principal findings were that airway resistance parameters (R5, R20, and R5–R20) and most reactance indices remained comparable to those of healthy controls, whereas AX was significantly increased in the OI group. Furthermore, the generally low prevalence of abnormal IOS findings suggests that airway resistance and reactance are largely preserved in this predominantly mild pediatric OI cohort, although the higher AX observed in the OI group may indicate subtle alterations in reactance that warrant further investigation.

The demographic characteristics of our cohort were consistent with previous pediatric OI studies. As expected, children with OI had significantly lower height and weight Z-scores than healthy controls, reflecting the well-recognized effects of type I collagen defects on skeletal growth [1, 2]. Despite these anthropometric differences, most patients had preserved mobility, relatively few had severe thoracic deformities, and the majority were receiving regular bisphosphonate therapy. Collectively, these findings indicate that our cohort represents a relatively well-controlled pediatric OI population. Although causal inference is not possible in this case-control study, the largely preserved airway resistance and reactance observed in our cohort should be interpreted in the context of the predominantly mild disease profile and contemporary clinical management of these children with OI.

The most notable finding was the isolated increase in AX despite the absence of significant differences in other IOS parameters. AX reflects the integrated area of low-frequency reactance and is considered particularly sensitive to changes in peripheral lung mechanics, respiratory system elastance, and lung compliance. Previous studies have demonstrated that AX may become abnormal before conventional resistance parameters in both obstructive and restrictive lung diseases [10, 11]. Accordingly, the elevated AX observed in our cohort may reflect subtle alterations in reactance rather than clinically

significant airway obstruction. The absence of significant changes in R5, R20, and R5–R20 further supports the notion that central and peripheral airway resistance remains largely preserved in these children. Although R5–R20 tended to be higher in the OI group, the difference narrowly missed statistical significance, suggesting that larger multicenter studies may better define whether subtle peripheral airway involvement exists in pediatric OI.

Our findings should also be interpreted in the context of previous pulmonary function studies. The multicenter study by Tam et al. demonstrated progressive reductions in FVC and FEV_1 with increasing disease severity, particularly among patients with severe skeletal involvement [3]. Similar observations have been reported by other investigators, who found that thoracic deformity and reduced chest wall mobility were associated with restrictive ventilatory impairment [5, 12, 13]. At first glance, these findings may appear inconsistent with our results. However, important differences exist between study populations and assessment methods. Most previous investigations included patients with more severe skeletal deformities or older age groups and relied primarily on spirometry, which evaluates global ventilatory capacity during forced respiratory maneuvers. In contrast, IOS assesses respiratory impedance during tidal breathing and may detect more subtle alterations in lung mechanics. Therefore, the preserved IOS parameters observed in our cohort likely reflect the relatively mild respiratory involvement of well-treated pediatric patients rather than contradicting previous spirometric evidence.

Only one previous clinical study has specifically investigated oscillometric assessment in OI. Storoni et al. evaluated 12 patients using forced oscillation techniques (FOT), spirometry, and body plethysmography, demonstrating that oscillometry could detect bronchial obstruction and bronchodilator responsiveness during quiet breathing [6]. Nevertheless, that study included predominantly adult patients, lacked a healthy control group, and used conventional FOT rather than IOS. In contrast, our study included only children, incorporated matched healthy controls, and interpreted IOS findings using z-scores derived from the reference equations incorporated into the device software. Consequently, our findings substantially extend the existing evidence and suggest that, in children with OI, oscillometric abnormalities may initially involve reactance rather than airway resistance.

The underlying mechanisms responsible for these findings are probably multifactorial. Respiratory dysfunction in OI has traditionally been attributed to scoliosis, rib cage deformities, and reduced thoracic compliance. However, increasing evidence indicates that intrinsic pulmonary abnormalities also contribute to respiratory impairment. Type I collagen is an essential structural component of the pulmonary interstitium, alveolar septa, and bronchial walls; therefore, collagen defects may directly alter lung elastic properties independently of skeletal deformities [14, 15].

The isolated increase in AX observed in our study suggests that subtle alterations in respiratory system elastance may occur before measurable changes in airway resistance become evident. Increasing evidence indicates that reactance-derived parameters, particularly AX, are sensitive markers of peripheral lung mechanics and respiratory system stiffness and may identify early physiological abnormalities that remain undetected by conventional resistance measurements [11, 16]. Therefore, the

observed increase in AX may reflect early impairment of lung elastic properties rather than clinically significant airway obstruction. This interpretation is biologically plausible in OI, in which abnormalities of type I collagen may affect not only the thoracic cage but also the pulmonary interstitium and alveolar connective tissue [15]. Because children with OI had significantly lower height Z-scores than healthy controls, anthropometric differences could theoretically influence oscillometric measurements. However, all IOS findings were interpreted using z-scores derived from the reference equations incorporated into the device software, and abnormal oscillometric findings were defined according to the corresponding upper and lower limits of normal. Consequently, although differences in body size cannot be entirely excluded, the isolated increase in AX may reflect subtle alterations in reactance associated with OI. Nevertheless, future prospective studies integrating IOS with spirometry, high-resolution computed tomography, and longitudinal follow-up are needed to clarify the underlying mechanisms and clinical significance of these findings.

From a clinical perspective, these findings suggest that routine respiratory impairment may not be expected in clinically stable, well-treated children with OI. Nevertheless, IOS, particularly AX, may provide additional information regarding subtle alterations in reactance that are not reflected by resistance-derived IOS parameters.

Another notable finding was the low overall prevalence of abnormal IOS parameters in children with OI. Although Fres was the most frequent abnormal parameter, it exceeded the upper limit of normal in only three patients (15%), while abnormal AX and X20 values were identified in two patients (10%) each. Abnormal R5, R5–R20, and X5 values were each observed in only one patient (5%), and no patient demonstrated an abnormal R20 value. Collectively, these findings indicate that abnormal oscillometric findings were uncommon in this relatively well-managed pediatric cohort and further support the overall preservation of airway resistance and reactance, despite the isolated increase in AX.

The present study has several strengths. To the best of our knowledge, this is the first pediatric case–control study to evaluate airway resistance and reactance in children with osteogenesis imperfecta using impulse oscillometry, with findings interpreted using z-scores derived from the reference equations incorporated into the device software. The inclusion of an age- and sex-matched healthy control group and the use of a standardized IOS protocol further strengthen the internal validity of our findings.

Several limitations should also be acknowledged. First, the relatively small sample size and single-center design may limit the generalizability of our findings. Second, spirometry, lung diffusion capacity, and high-resolution chest imaging were not available for all participants, precluding direct correlations between oscillometric abnormalities and structural pulmonary changes. Third, because most patients had mild disease and were receiving regular bisphosphonate therapy, our findings may not be generally generalized to children with severe OI phenotypes. Fourth, given the exploratory nature and small sample size of the study, no formal adjustment for multiple comparisons was applied; therefore, the isolated significant difference in AX should be considered hypothesis-generating In addition, subgroup analyses according to OI subtype or disease severity could not be performed because of the limited sample size.

Finally, the case-control design precluded assessment of longitudinal changes in IOS parameters and their potential associations with disease progression or bisphosphonate therapy.

5. Conclusion

In conclusion, airway resistance and reactance appear to be largely preserved in clinically stable children with predominantly mild osteogenesis imperfecta. Nevertheless, the isolated increase in AX suggests that subtle alterations in respiratory system elastance may already be present before measurable changes in airway resistance or conventional pulmonary function tests become evident. These findings suggest that reactance-derived IOS parameters, particularly AX, may provide additional insight into subtle alterations in airway function in pediatric OI. As a simple, non-invasive, and effort-independent technique, impulse oscillometry may complement conventional pulmonary function assessment during the longitudinal follow-up of children with OI. Larger prospective multicenter studies integrating IOS with spirometry and structural lung imaging are warranted to determine the prognostic significance of these oscillometric abnormalities and to establish the role of IOS in the long-term respiratory monitoring of this population.

Declarations

This manuscript is not under simultaneous consideration by any other publication. An honorarium, grant, or other form of payment was not given to any author to produce the manuscript. All authors significantly contributed to the work, have approved the final manuscript and takes full responsibility for the manuscript. There are no conflicts of interest statements for each author.

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Ethical approval was obtained from the Non-Invasive Clinical Research Ethics Committee of Inonu University (approval no. 2026/10695; approval date: 14 July 2026). Written informed consent to participate was obtained from all participants and/or their parents or legal guardians, as appropriate, prior to enrollment in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

E.Y., E.T., and I.D. contributed to the conceptualization of the study. E.T., N.K.O., and I.D. contributed to the methodology. Z.Y.Y. performed data acquisition and clinical data curation. E.T. and E.C. performed the formal statistical analysis. E.T. and N.K.O. contributed to drafting the original manuscript, and Z.Y.Y. contributed to the interpretation of laboratory data. All authors contributed to the critical revision of the manuscript for important intellectual content, read and approved the final manuscript, and agreed to be accountable for all aspects of the work.

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