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#### Original Article

# **Reference Values for Respiratory System Impending Using Impulse Oscillometry in Healthy Sharkia Government's Children**

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Corresponding author*:		ABSTRACT				
Elham Elsayed	Earaby	Background: Unlike spirometry, impulse oscillometry (IOS) may				
Mahmoud		provide more particular data on the respiratory tract's resistive and elastic				
		features. This study aimed to create our reference equations of IOS parameters				
		of healthy children collected from the AL-Sharkia governorate. Egypt, as this				
Email:		has not been found till now.				
Drelhamelaraby	v88@gmail.com	Methods: This cross-sectional investigation was performed on 249 healthy				
	) 8	children aged 3 to 15 years in Pediatric Chest, Allergy, and Immunology units				
		in Zagazig University Hospitals All subjects underwent full history taking				
Submit Date	28-02-2024	and their body weight height and body mass index (BMI) were calculated as				
Revise Date	24-03-2024	well as a thorough clinical and pulmonary examination. The IOS method was				
Accent Date	30-03-2024	performed for all cases and each case had three attempts with less than 10%				
necept Dute		variability				
		<b>Results:</b> All IOS factors had a substantial negative connection with weight				
		height and age except pred X 5Hz which had a positive relationship (P $<$				
		0.05) For girls, all IOS factors had a notable negative connection with age and				
		weight except for X5 Hz which had a positive relationship ( $P < 0.05$ ). Results				
		of various linear regression equations were reported with standard error of the				
		estimate (SEE) modified $R_2$ and coefficients of determination ( $R_2$ ) for all				
		IOS components in both girls and boys. Height was the greatest predictive				
		indicator for modeling all IOS characteristics in hous and most of the factors				
		in girls				
		III gills.				
		conclusions: Our research revealed that weight, height, and age were				
		substantially associated with IOS values, as a remarkable negative association				
		was found between all IOS factors and neight, age, and weight, while				
		Reactance (A) had a positive association. Height had the highest predictive				
		potential for models of all IOS factors in boys and most in girls.				
		Keywords: Impulse Oscillometry, Respiratory System, Reference Values				

#### INTRODUCTION

Chronic respiratory conditions, such as asthma, are becoming more common for children in developing nations, and respiratory conditions possess the highest morbidity and mortality rates overall systemic conditions in pediatrics [1].

Lung function is a crucial feature that can help identify and manage respiratory illnesses. Despite spirometry being the most frequent of these assessments, it requires complete cooperation from the participant, which is not always attainable, particularly in infants. The impulse oscillometry system (IOS) has been widely adopted owing to its practical ease. Assessments are obtained when the participant breathes at tidal volume [2].

IOS depends on the user's work because it needs to breathe normally. The device produces sound waves that are superimposed on regular tidal breathing. The apparatus uses changes in flow and pressure to identify reactive variables and airflow resistance over frequencies ranging from 5-20 Hz. The impedance is defined by both reactance and airway resistance [3].

Unlike spirometry, the IOS provides more specific data about the respiratory system's resistive and elastic features. Plethysmography reveals a substantial relationship between IOS resistance and resistance [3].

The best IOS findings obtained by cases are typically compared to the predictive standard score for cases with the same age, gender, body mass index (BMI), height, and weight. These standard values vary for children of varied races. Thus, investigations try to generate local reference values [4].

The absence of standard equations and normal IOS levels for Egyptian children significantly impacts evaluation accuracy and hinders the clinical use of the OS technique. Therefore, due to the presence of several factors in terms of gender, nationality, and physical formation that affect the results of pulmonary function (PF), we must modify the device reference to suit our children. The present investigation aims to construct reference equations of IOS factors employing information from healthy Egyptian children recruited from a broad region with quality control standardization to offer the basis for the reasonable therapeutic usage of IOS.

## METHODS

From March 2023 to December 2023, this crosssectional study was carried out on 249 healthy children aged 3 to 15 years in Pediatric Chest, Allergy, and Immunology units in Zagazig University Hospitals.

Inclusion Criteria: All subjects who were healthy children above three years up to 15 years old came to the outpatient clinic during the study period.

We excluded children aged less than two years or above 15 years old, children who suffered a respiratory tract illness for four weeks before the study, congenital heart disease, history of prematurity or respiratory, immune, neuromuscular, and other conditions, or who had a family history of rhinitis, asthma, or other hereditary allergic disorders. Also, we excluded patients who could not contribute to pulse oscillation lung function assessment or those with abnormal pulmonary ventilation function.

This study followed the guidelines [the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies]. All participants' legal guardians provided informed and written consent. The Institutional Review Board has approved this research (#9641/16-4-2022).

All the included children were subjected to full history taking; the BMI (kg/m<sup>2</sup>) was assessed by measuring the body weight and height without footwear or heavy outer clothes. Clinical examination was done to determine respiratory disease manifestations such as fever, respiratory distress, and tachypnea; auscultation of the chest was to identify the reduced sound of breathing, bronchial breath sounds, wheezing, and crepitation, complication signs such as pleural effusion, pneumothorax, respiratory failure and lung abscess, and cardiac examination to exclude cardiac problem.

## **IOS measurements**

IOS evaluates a subject's pulmonary impedance (Zr) during regular rhythmic breathing. Zr comprises reactance (X) and resistance (R),  $90^{0}$  out of phase. Resistance represented the degree of energy necessary to convey the pressure wave throughout the airways, whereas reactance reflected the quantity of recoil produced by that pressure wave. The reactance included inertia forces caused by airflow in the interconnecting airways and elastic recoil in the lung tissue. R and X were assessed in the units of cmH2O/L/s or KPa/L/s [5].

In the present investigation, all children performed the IOS technique with VIASYS Healthcare GmbH (Leibnizstrasse 7, Jaeggar, Germany) corresponding to the American Thoracic Society (ATS) and European Respiratory Society's (ERS) guidance [6]. We adjusted the device and entered the case's data. The child was given instructions on how to do well on the IOS. The case was urged to sit in a comfortable chair. The case was fitted with a nasal clip and instructed to breathe from the mouth using a sterile mouthpiece tightly gripped by lips and not obstructed by the tongue. When IOS is turned on, a loudspeaker produces a pulse-shaped pressure wave in front of the lips, with alternative pulses (at varying cycles per second [5 Hz, 10 Hz, 20 Hz, 25 Hz]). The patient was asked to perform regular breathing with his cheeks held by his pediatrician's hands. Utilizing the instrument's software, R5 Hz, Z5 Hz, R20 Hz, X5 Hz, AX, and Fres were assessed.

Each case completed three trials with <10% variability. The time for the consistent breathing rhythm was 90 seconds. The impedance-time curve was followed throughout the assessment to look for any signs of abnormalities. Approved cases

performed the procedure correctly, with coherence of at least 0.8 at 5 Hz and 0.9 at 20 Hz [4].

## **Regression equations**

Regression analysis was utilized to determine the Reference Equations for this group. Outperforming multivariate linear equations, bivariate linear regressions generated the finest prediction patterns with greater independent variable impact. Making unique basic regression equations (REs) for every age group is one method of executing regression analysis. The most widely used metrics for assessing RE's ability to fit the data they represent are the correlation coefficient square (r2) and the standard error of the estimate (SEE). The ratio of variance in the observed data to that which the independent variables can account for is expressed as R2. The SEE shows the data's average Standard Deviation (SD) around the regression line. Regression methods reduce the variations between the measured and anticipated pulmonary function values in the control population; as a result, r2 increases and SEE outcomes decrease.[5].

#### **Statistical Analysis**

The data were analyzed using the Statistical Package for Social Science (SPSS) application for Windows (Standard version 26). The data's normality was initially assessed using the onesample Kolmogorov-Smirnov test. Qualitative data were defined using numbers and percentages. Continuous variables were given as mean  $\pm$  SD for normally distributed data. The two paired groups were compared using a paired t-test. The student ttest was used to examine quantitative factors between males and females. Pearson's correlation coefficient was utilized to assess the relationship between IOS parameters and other variables. Multiple linear regression (MLR) was used to create multivariate models with predictor variables correlated with the dependent variable. The coefficient of determination (adjusted R2) was utilized to select the optimal model. The significance level was 5% (P value < 0.05).

#### RESULTS

Table (1) shows that out of a total of 249 children enrolled in the investigation, 144 were males (57.8%) and 105 were females (42.2%). Their mean age was  $9.08 \pm 3.21$  years, ranging from 3-15 years. The descriptions of their anthropometric measures of weight, height, and BMI were 31.3 Kg, 130.2 Cm, and 18.45, respectively. No significant differences were found between the boys and girls studied concerning age and anthropometric factors.

A description of IOS parameters among the studied group is demonstrated in Table (2). No remarkable variance was found between males and females in both studies concerning IOS factors except for Pred Z at 5 Hz (p<0.001).

Table (3) illustrates the relationship between various IOS characteristics, age, and anthropometric variables in the examined boys. All IOS factors (except for Actl X at 5 Hz) had a substantial adverse connection with age, height, and weight, except pred X 5Hz, which had a positive correlation (P< 0.05).

Table (4) demonstrates the association between several IOS factors, anthropometric characteristics, and age among females. All IOS factors (except for Actl X at 5 Hz and resonant) had a remarkable association with weight and age, except for X5 Hz, which had a positive association (P < 0.05).

The results of MLR equations involving R2 adjusted R2 and SEE were displayed for all IOS factors in both males and females in Table (5). The greatest predictive power for models with most female traits was height. Height had the highest predictive power across all IOS factors in boys.

	Minimum	Maximum	Mean	S.D
Age (years)	3	15	9.08	3.21
Weight (Kg)	14	66	31.3	10.17
Height (Cm)	93	165	130.2	14.89
BMI	10.7	117.6	18.45	6.92
Gender	N (%)			
Boys	144 (57.8%)			
Girls	105 (42.2%)			

**Table 1:** Basic characteristics of the studied group.

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Volume 30, Issue 9.1, December. 2024, Supplement Issue

	Boys N=144	Girls N=105	Test	Р
	Mean $\pm$ SD	Mean $\pm$ SD		
Age	$9\pm2.27$	$9.2 \pm 2.13$	0.486	0.628
Weight	$30.9\pm9.56$	$31.9\pm10.98$	0.754	0.455
Height	$130.1\pm15.26$	$130.5\pm14.45$	0.260	0.795
BMI	$18.6\pm8.65$	$18.3\pm3.35$	0.283	0.769

BMI: body mass index,

**Table 2:** description of IOS parameters among studied group and difference between boys and girls regarding IOS parameters

	Minimum	Maximum	Mean	S.D
Pred Z at 5 Hz	0.26	1.26	0.674	0.269
Actl Z at 5 Hz	0.32	3.69	0.952	0.371
Pred R at 5 Hz	0.25	1.16	0.637	0.243
Actl R at 5 Hz	0.10	3.44	0.909	0.361
Pred R at 20 Hz	0.21	0.75	0.453	0.139
Actl R at 20 Hz	0.27	1.53	0.616	0.191
Pred X at 5 Hz	-0.43	0.20	-0.196	0.129
Actl X at 5 Hz	-27.00	0.60	-0.416	2.11
Resonant	2.39	35.76	21.37	4.86
	Boys N=144	Girls N=105	Test	Р
	Mean $\pm$ SD	Mean ± SD		
Pred Z at 5 Hz	$0.684\pm0.277$	$0.955\pm0.424$	0.664	< 0.001
Actl Z at 5 Hz	$0.955\pm0.426$	$0.948 \pm 0.281$	0.163	0.833
Pred R at 5 Hz	$0.644\pm0.254$	$0.628 \pm 0.228$	0.513	0.608
Actl R at 5 Hz	$0.915\pm0.405$	$0.902\pm0.292$	0.282	0.778
Pred R at 20 Hz	$0.452\pm0.144$	$0.456\pm0.204$	0.241	0.810
Actl R at 20 Hz	$0.597 \pm 0.204$	$0.642 \pm 0.169$	1.83	0.07
Pred X at 5 Hz	$-0.204 \pm 0.129$	$-0.186 \pm 0.129$	1.11	0.276
Actl X at 5 Hz	$-0.569 \pm 2.77$	$-0.207 \pm 0.168$	1.33	0.183
Resonant	$21.4\pm4.91$	$21.4\pm4.82$	0.047	0.963

R5 = resistance at 5 Hz, R20 = resistance at 20 Hz, X5 = reactance at 5 Hz, Z 5= impedance at 5 Hz, SD= Standard deviation

Table 3: Correlation	between IOS parameter	s with both age and	l anthropometric	measures among stud	lied boys
(n=144)					

		Age	Weight	Height	BMI
Pred Z at 5 Hz	r	-0.728**	-0.561**	668**	0.041
	P value	<0.000	<0.001	<0.001	0.628
Actl Z at 5 Hz	r	-0.414**	-0.303**	-0.367**	0.030
	P value	<0.000	<0.001	<0.001	0.725
Pred R at 5 Hz	r	-0.652**	-0.479**	-0.581**	0.046

Elbehedy, R., et al

https://doi.org/10.21608/zumj.2024.273478.3211

Volume 30, Issue 9.1, December. 2024, Supplement Issue

	P value	<0.000	<0.001	<0.001	0.580
Actl R at 5 Hz	r	-0.395**	-0.284**	-0.342**	0.032
	P value	<0.001	0.001	<0.001	0.702
Pred R at 20 Hz	r	-0.648**	-0.473**	-0.574**	0.040
	P value	<0.001	<0.001	<0.001	0.636
Actl R at 20 Hz	r	-0.452**	-0.359**	-0.418**	0.066
	P value	<0.001	<0.001	<0.001	0.434
Pred X at 5 Hz	r	0.675**	0.488**	0.590**	-0.047
	P value	<0.001	<0.001	<0.001	.573
Actl X at 5 Hz	r	0.163	0.154	0.156	0.020
	P value	0.051	0.065	0.062	0.809
Resonant	r	0.063	0.180*	0.091	0.037
	P value	0.452	0.03	0.281	0.661

R5 = resistance at 5 Hz, R20 = resistance at 20 Hz, X5 = reactance at 5 Hz, Z 5= impedance at 5 Hz, r= Pearson's correlation coefficient, \*=Significant  $\leq 0.05$  level, \*\*=Highly significant  $\leq 0.001$  level

**Table 4:** Correlation between IOS parameters with both age and anthropometric measures among studied girls (n=105)

		Age (years)	Weight (kg)	Height (m)	BMI
Pred Z at 5 Hz	r	-0.613**	-0.506**	-0.593**	-0.280**
	Р	<0.001	<0.000	<0.000	0.004
Actl Z at 5 Hz	r	-0.407**	-0.377**	-0.447**	-0.175
	Р	<0.000	<0.000	<0.000	0.073
Pred R at 5 Hz	r	-0.515**	-0.432**	-0.458**	-0.291**
	Р	<0.001	<0.000	<0.000	0.003
Actl R at 5 Hz	r	-0.327**	-0.287**	-0.393**	-0.093
	Р	0.001	0.003	<0.000	0.345
Pred R at 20 Hz	r	-0.539**	-0.454**	-0.493**	-0.296**
	Р	<0.000	<0.000	<0.000	0.002
Actl R at 20 Hz	r	-0.301**	-0.322**	-0.349**	-0.245*
	Р	0.002	0.001	<0.000	0.012
Pred X at 5 Hz	r	0.477**	0.417**	0.434**	0.299**
	Р	<0.001	<0.000	<0.000	0.002
Actl X at 5 Hz	r	0.134	0.085	0.143	0.002
	Р	0.174	0.388	0.146	0.981
resonant	R	-0.182	-0.011	-0.104	0.037
	Р	0.063	0.911	0.291	0.705

R5 = resistance at 5 Hz, R20 = resistance at 20 Hz, X5 = reactance at 5 Hz, Z 5= impedance at 5 Hz, r= Pearson's correlation coefficient, \*=Significant  $\leq 0.05$  level, \*\*=Highly significant  $\leq 0.01$  level

<b>Reference equations obtained by IOS for Boys.</b>								
Parameter	Equation	<b>R</b> <sup>2</sup> , %	Adjusted R <sup>2</sup>	SEE				
Pred Z 5 Hz	1.43 - (0.522 x age) – (0.093x height)	0.733	0.540	0.322				
Actl Z 5 Hz	4.21 - (0.221x age)- (0.003x height)	0.662	0.418	0.443				
Pred R 5Hz	11.1- (0.004x age)- (0.022x weight)-	0.663	0.321	0.221				
	(0.211x  height)							
Actl R 5Hz	2.12 -(0.098x height)	0.570	0.133	0.404				
Pred R 20Hz	6.11 - (0.995x age)- (0.004x weight)-	0.597	0.433	0.304				
	(0.176x height)							
Actl R 20Hz	11.3 - (0.997x age)- (0.003x height)	0.455	0.088	0.166				
Pred X 5Hz	1.27- (0.019x height)	0.544	0.402	0.211				
Actl X 5HZ	2.65- (0.003x height)	0.452	0.280	0.197				
	<b>Reference equations obtained by</b>	IOS for Girl	S					
Parameter	Equation	<b>R</b> <sup>2</sup> , %	Adjusted R <sup>2</sup>	SEE				
Pred Z 5 Hz	1.65 - (0.902 x age) – (0.003x height)	0.788	0.577	0.322				
Actl Z 5 Hz	1.71 - (0.021x age)	0.521	0.188	0.883				
Pred R 5Hz	1.99- (0.101x height)	0.753	0.519	0.821				
Actl R 5Hz	1.82 -(0.002x height)	0.625	0.199	0.796				
Pred R 20Hz	1.28 - (0.615x age)- (0.356x height)	0.521	0.253	0.487				
Actl R 20Hz	1.93 - (0.996x age)- (0.004x height)	0.599	0.308	0.249				
Pred X 5Hz	2.65- (0.995x age) -(0.011x height)-	0.494	0.308	0.344				
	(0.005x weight							
Actl X 5HZ	1.16- (0.004x weight)	0.526	0.178	0.433				

Table 5: Reference equations obtained by IOS for boys and Girls

**Figure 1**: Regression curves for age and IOS parameters among studied boys (A): age and Pred Z at 5 Hz, (B): age and Actl Z at 5 Hz, (C): age and Pred R at 5 Hz, (D): age and Actl R at 5 Hz, (E): age and Pred R at 20 Hz, (F): age and Actl R at 20 Hz, (G): age and Pred X at 5 Hz, (G): age and Actl X at 5 Hz





Elbehedy, R., et al

5179 | Page

**Figure 2**: Regression curves for weight and IOS parameters among studied girls (A): weight and Actl X at 5 Hz, (B): weight and Pred X at 5Hz, (C): weight and Actl R at 20 Hz, (D): weight and Pred R at 20 Hz, (E): weight and Actl R at 5Hz, (F): weight and Pred R at 5Hz, (G): weight and Actl Z at 5Hz, (G): weight and Pred Z at 5Hz





#### DISCUSSION

Pediatricians commonly use IOS to diagnose and treat respiratory and allergy illnesses. Like other PF measures, IOS measurements have variable normal guideline levels depending on race and age group [11].

Our study aimed to develop local reference values because the device references are registered according to the country of origin, which does not agree with our children in terms of the difference in height, weight, and lung volume and given the importance of that device in assessing the level of the respiratory system, we need to create a tyre that fits with our children.

In the present investigation, we measured IOS values in 249 healthy youngsters for whom spirometry is challenging. We acquired valid IOS values for the recruited youngsters at a greater success rate than indicated by Ducharme et al. [12]. This variation could be attributed to changes in inclusion and exclusion characteristics, IOS methodologies, and our usage of a single skilled operator for all assessments.

Park et al. [10] indicated that, in line with our findings, it is quite easy to do IOS in healthy infants under the age of six.

European Respiratory Society (ERS) and American Thoracic Society (ATS) recommended that a normal population be used for standard values for respiration evaluations, with healthy infants chosen using a questionnaire that displays asthma and allergy history and family allergies.

We assessed during the study period 144 boys (57.8%) and 105 girls (42.2%) with a mean age of

 $9.08 \pm 3.21$  years, with no significant difference between both studied girls and boys concerning anthropometric data, age, or any of the IOS parameters. Consistent with the results of Ishak and Hassan [4], they found that there was no substantial variation between males and females in anthropometric data, age, and IOS factors, except X5 Hz, R20 Hz, and Z5 Hz (P < 0.05). In contrast to our results, Amra et al. [13] found remarkable variance between both genders concerning IOS factors.

Our study revealed that there was a remarkable inverse association between all IOS factors (except for Actl X at 5 Hz) among studied boys with age, height, and weight except for pred X 5Hz, where the association was statistically remarkable (P< 0.05). Still, for Actl X5Hz, the correlation was not significantly positive. In a study held in 2020 by Ishak and Hassan [4], They also found a substantial inverse association between all IOS factors and both weight and age, except X5Hz, in which the relationship was positive, and a significant relationship between IOS factors (AX, R20 Hz, R5 Hz, and Z5 Hz) and height, except X5 Hz.t (it was a positive relationship).

With these results, Park et al. [10] also found a statistically substantial inverse relationship between Rrs5 values and height for all cases. At the same time, Xrs was positively associated with the height of the studied children. Another study held on 509 Iranian adolescents (aged 6-19 years) by Amra et al. [13] revealed that age and height had a negative correlation with resistance (Rrs). In contrast, age and height positively affected reactance (Xrs). The

same results were found among North American children by Frei et al. [14] and Finnish children by Malmberg et al. [15]

There was a substantial inverse association between all IOS factors and age, height, and weight among girls, except X5 Hz, which had a positive relationship (P< 0.05). Our results were in line with reports of Oostveen et al. [16], Frei et al. [14], and Ishak and Hassan [4], among different ethnicities, which could be attributed to that oscillation technique, does not modify the airway smooth muscle tone.

In our investigation, we noticed that in Z5 Hz, height and age influenced the prediction equation for both sexes, whereas in pred R5 Hz and R20 Hz, height, weight, and age affected the equation of boys; however, only height influenced pred R5 Hz for females, and both height and age influenced pred R20. Regarding the X5 Hz prediction equation, height was the most important parameter in males, whereas height, weight, and age all impacted females. Therefore, most of the predictive equations for IOS were affected by age, height, or both. Only R5 Hz and R20 Hz in boys and X5 Hz in girls were influenced by children's weight, but none of the equations were influenced by BMI, maybe due to the relationship of height and age with an exponential rise in lung volumes.

Comparing our results with a study of de Assumpção et al. [17], height was discovered to be the strongest predictive factor in the equations for males in all the variables of IOS, but age had a high impact on Fres and AX for ladies. Also, in another report by Gochicoa-Rangel et al. [18] on Mexican adolescents and children, height was the major variable impacting the equation; nevertheless, age affected the REs of many IOS factors; body weight did not affect any of the IOS factors.

While Frei et al. [14] proved that height was the only remarkable predictor for all IOS factors.

Dencker et al. [19] found that height was the major factor influencing the various oscillometric characteristics. While body surface area, age, and gender did not affect IOS factors, adding weight increased the coefficient of determination of several components. For both sexes, height and weight were therefore included in the RE.

Age and height influenced the prediction equations of Korean and Mexican cases, while the IOS factors of Korean females were affected by the height only by Park et al. [10] and Gochicoa-Rangel et al. [18]

Studies held by de Assumpção et al. [17], Frei et al. [14], and Dencker et al. [19] indicated non-

remarkable variance between both genders in the predictive equations, which is consistent with our findings. At the same time, Amra et al. [13] revealed a substantial variance between genders.

Upon analysis of the R2 values of our study to compare it with other investigations performed on variable races, we noticed that our R2 was greater than the equations of Taiwanese and North American researchers [8, 14]. At the same time, it was less than R2 of the Korean and Brazilian reports [10, 17].

In agreement with previous research, we found that IOS is an efficient and noninvasive approach for measuring lung function in infants. Standard values for IOS are significant for analyzing PFT data and for detecting and treating respiratory disorders [7]. The evaluation of respiratory input impedance with IOS has great clinical significance in infants with a range of respiratory diseases [20].

## Limitations

Firstly, the sample size might be relatively small, with 249 subjects. Secondly, since the study was conducted in a single outpatient clinic of a specific hospital, there is a potential for selection bias. The patient population might not fully represent the diversity and characteristics of all individuals with pulmonary conditions. This could affect the external validity of the study.

Points of Strength .IOS is a precise PFT for pulmonary recognizing problems in older and younger children. Our standard equations were created for the IOS assessment in adolescents and children. Compared to other prediction equations, ours were more appropriate for Egyptian children. These equations could be utilized in the future to offer a mathematical framework for indicating disease progress or as a guide for identifying the degree of respiratory system abnormalities in children between the ages of three and fifteen.

## CONCLUSION

In Egyptian children, height and age influenced the RE for IOS factor values. Our investigation discovered that age, height, and weight were closely associated with IOS values, with all IOS parameters showing a substantial negative connection with age, height, and weight, except Reactance (X), which showed a positive relationship. Height was the greatest predictive predictor for models of all IOS characteristics in males and most of the factors in females.

No potential conflict of interest was reported by the authors.

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