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Impulse oscillometry reference values and correlation with predictors in Turkish preschool children

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Impulse oscillometry (IOS) is a noninvasive, rapid technique requiring passive cooperation that allows for evaluation of lung function through the measurement of airway resistance and reactance. There are no available reference values for Turkish children. This study is aimed to determine the reference values of IOS parameters and to study their correlation with height, weight, body mass index, and age as predictors in healthy Turkish preschool children. Healthy children between 3-7 years of age who were selected according to ERS/ATS criteria and followed at Kocaeli University outpatient clinic performed IOS. The correlation between the anthropometric predictor variables and resistance and reactance at 5-20 hertz (R5-R20 and X5-X20), the respiratory impedance at 5 hertz (Z5), resistance area (AX) and resonance frequency (Fres) were assessed by regression analysis and stepwise method. 151 children (93 female) with the mean age of 67.9±16.2 months participated in the study. Multilinear regression analysis for IOS values of all children revealed that resistance was significantly correlated with height and reactance was significantly correlated with age ($p<0.05$). For girls, height had a negative effect on R5-20, Z5, AX values, while age had a positive effect on X5-20 and a negative effect on Fres ($p<0.05$). For boys, weight had a negative effect on R5-20, Z5 values, while age had a positive effect on X15-20 and a negative effect on AX, Fres ($p<0,05$). This study provided reference values of IOS in healthy Turkish children that would be a useful guide for diagnosing and following respiratory diseases in preschool children.

***Key words:** impulse oscillometry (IOS), reference values, preschool children.*

Pulmonary function tests allow monitoring of the respiratory system for the diagnosis and treatment of acute or chronic lung diseases by evaluating respiratory tract mechanics and physiology in both children and adults. Spirometry is the most commonly used pulmonary function test; but for some children performing the test can be challenging. In contrast to spirometry, impulse oscillometry (IOS) requires less cooperation and young children can easily perform it because only tidal volume breathing is needed. It also provides more specific information related to resistance and elastic properties of the respiratory system. Hence, today IOS serves as a good alternative method for the assessment of lung function in preschool children with suspected respiratory disease.[1,2]

Reference values from healthy children for IOS are needed to diagnose and evaluate treatment outcome of respiratory diseases.[3] Several studies from different ethnicity and age groups have recently reported the normal reference values of IOS.[4-11] However, reference values are not available for Turkish children.

The aim of this study is to determine the reference values of IOS parameters and to study their correlation with height, weight, body mass index, and age as predictors in healthy Turkish preschool children.

Material and Methods

Participants

We collected IOS data of healthy 3-7 years old Turkish preschool children who were recruited as controls for the IOS studies performed during the last five years at Kocaeli University Hospital.[12-14]

They were selected through a health screening questionnaire that was designed according to European Respiratory Society (ERS)[15] and American Thoracic Society (ATS)[16] criteria. Those with the following charecteristics were excluded from the study: Premature birth, low birth weight, history of mechanical ventilation or bronchopulmonary dysplasia, obesity, presence of congenital cardiac or neuromuscular diseases, exposure to cigarette smoke at home, personal or family history of wheezing or asthma, personal or family history of allergic rhinitis or atopic dermatitis and upper respiratory tract infection within the last two weeks.

All previous IOS studies were approved by the ethics committee of Kocaeli University (KAEK 3/12[12], 2013/138[13], 2012/156[14]) and written informed consent was obtained from the parents of all participating children.

Impulse oscillometry

A Jaeger Master screen IOS system (Wurzburg, Germany) was used to measure the input impedance of the respiratory system. The system was calibrated with a special 3-L metal syringe daily prior to the measurements of room temperature and humidity. Gender, height and weight of each child were recorded on the computer. The children were introduced to the instrument of IOS and the procedure was explained thoroughly.

IOS was performed using a nose-clip while the child was sitting, holding his/her head in a neutral position, and breathing quietly through a mouthpiece. The chin and cheeks were supported by the hands. Thirty-second intervals were used during the test. A series of three measurements were performed and the best measurement with a regular breathing process was used for analysis.

While the patient is breathing normally, IOS apparatus generates small pressure oscillations to determine impedance (Z) of the respiratory system. Pulmonary resistance (R) and reactance (X) are components of Z. R represents energy required to propagate pressure wave through airways and measures central and peripheral airway caliber. X is the amount of recoil generated against that pressure wave and indicates the elastic recoil properties of the lung tissue. IOS measures R and X in the frequency range of 5-20 Hz (kPa/(L/s)). A lower frequency oscillation that could reach the peripheral lung is used as an index of the airway status. Thus, when either proximal or distal airway obstruction occurs, R5 and X5 may be increased. Higher frequency oscillations provide information for the central airways and central airway obstruction will be reflected by increased R20. However, diseases isolated to distal airways are associated with increase in R5 to a greater extent than R20 while diseases isolated to proximal airways will be reflected as a similar increase in R5 and R20. The difference between R5-R20 (R5 minus R20) is referred to as frequency dependence of resistance and used as a sensitive index of distal airway obstruction. The reactance is equal to zero at a point where there is a transition in the lungs from passive distention to active stretch, this point is graphically referred to as resonant frequency (Fres, L/s). Fres is dependent on physical properties of chest size and tissue component. The area of reactance (AX) which is another parameter of IOS represents the total reactance area under the curve at all frequencies between 5 Hz and Fres and reflects a composite index for reactance. In addition to R5 minus R20, X5, Fres and AX can be used to demonstrate the degree of distal airway obstruction.[1,2,15]

Coherence is the correlation between airflow and pressure, and indicates the reliability of the IOS measurements. For 30-second testing, acceptable coherence values are ≥ 0.6 at 5 Hz and ≥ 0.8 at 10 Hz.[5,16]

Statistical analysis

All statistical analyses were performed using IBM SPSS for Windows® version 20.0 (IBM Corp., Armonk, NY, USA). Kolmogorov-Smirnov tests were used to test the normality of data distribution. Continuous variables were expressed as mean (±standard deviation) or median (25^{th}-75^{th} percentiles), and categorical variables were expressed as counts (percentages). Comparisons of non-normally distributed continuous variables between the groups were performed using the Mann-Whitney U Test. The relationship between IOS pulmonary function measures as dependent variables and anthropometric data: height, weight, body mass index and age as predictive variables were assessed by linear regression analysis. Log-transformation was done for non-normally distributed IOS variables before the analysis. They were first regressed individually against the mentioned independent predictive factors and then multiple linear regression analyses (stepwise method) were used to identify which combination would best fit for the model. Predictors were retained in regression model only if they showed statistically significant relation with the dependent variables ($p<0.05$). The equations with coefficient of determination (R^2), residual standard deviation (RSD), and standard error of estimate (SEE) were created.

Results

IOS pulmonary function test measurement of 151 healthy Turkish preschool children were collected for the study. Table I shows anthropometric data of them. There were no differences between girls and boys in age, height, weight and body mass index (BMI).

Median (25^{th}-75^{th} percentiles) IOS values of the 151 healthy Turkish preschool children are presented in Table II.

Relationships of IOS values (dependent variables) and predictive factors (independent variables)

The multiple linear regression analysis revealed height and age as the independent predictive powers for IOS values in both genders. Table III, Figure 1 and 2 show the regression equations for IOS values versus predictive factors in 151 healthy Turkish preschool children.

Multilinear regression analysis results for all IOS values of 151 healthy Turkish preschool children revealed that while R5-20 and Z5 were significantly negatively correlated with height, X5-20, R5-R20 (R5 minus R20) were positively and Fres, AX significantly negatively correlated with age ($p<0.05$). There was no correlation between BMI and IOS values ($p>0.05$).

IOS predictive equations for girls and boys:

IOS predictive equations for 93 girls and 58 boys are presented in Table IV. Height had a negative effect on R5-20, Z5, AX values, while age had a positive effect on X5-20 and a negative effect on R5-R20 (R5 minus R20), Fres values for Turkish healthy preschool girls ($p<0.05$).

Weight had a negative effect on R5-20, Z5 values, while age had a positive effect on X15-20 and a negative effect on AX, Fres values for Turkish healthy preschool boys ($p<0,05$). In the model, no statistically significant variable was found among the independent variables for the IOS values of X5, X10 and R5-R20.

Table I. Anthropometric Data of 151 Healthy Turkish Preschool Children.

	Girls (n=93)	Boys (n=58)	p
Age, months	68.37±16.59	67.43±15.81	0.70
Height, cm	112.86±10.91	113.41±10.16	0.81
Weight, kg	20.96±5.37	20.69±4.77	0.89
BMI, kg/m^2	16.23±2.05	16.00±2.57	0.36

Data is presented as mean ± standard deviation. BMI: body mass index

Table II. Impulse Oscillometry (IOS) Values of 151 Healthy Turkish Preschool Children.

IOS	All children (n=151)	
	Median	25th -75th percentiles
R5, kPa/(L/s)	0.86	0.70 – 1.03
R10, kPa/(L/s)	0.72	0.63 – 0.86
R15, kPa/(L/s)	0.69	0.64 – 0.94
R20, kPa/(L/s)	0.65	0.56 – 0.79
R5-R20, kPa/(L/s)	0,19	0,11 – 0,27
X5, kPa/(L/s)	-0.25	-0.34 – -0.18
X10, kPa/(L/s)	-0.13	-0.17 – -0.08
X15, kPa/(L/s)	-0.08	-0.11 – -0.02
X20, kPa/(L/s)	0.01	-0.04 – 0.05
Fres, 1/s	19.36	16.90 – 21.99
Z5, kPa/(L/s)	0.88	0.75 – 1.08
AX, kPa/(L)	1.53	0.86 – 1.95

AX: area of reactance curve less than zero, Fres: resonant frequency, R: resistance, R5-R20: R5 minus R20, X: reactance, Z: pulmonary impedance at 5 Hz,

Table III. Regression Equations for Impulse Oscillometry (IOS) Values versus Predictive Factors in 151 Healthy Turkish Preschool Children.

Equations	R^2	SEE
R5* = 0.527-0.005×Height	0.262	0.094
R10* = 0.387-0.005×Height	0.249	0.085
R15* = 0.360-0.005×Height	0.230	0.089
R20* = 0.299-0.004×Height	0.205	0.090
R5-R20= -0.307-0.084×Age	0.169	0.242
X5 = -0.476+0.042×Age	0.143	0.136
X10 = -0.283+0.028×Age	0.190	0.076
X15 = -0.208+0.025×Age	0.203	0.064
X20 = -0.113+0.024×Age	0.113	0.088
Fres = 1.405-0.024×Age	0.143	0.077
Z5 = 2.278-0.012×Height	0.283	0.204
AX = 3.012-0.282×Age	0.238	0.663

AX, area of reactance curve less than zero, Fres: resonant frequency, R: resistance, R2: coefficient of determination; R5-R20: R5 minus R20, SEE: standard errors of estimate, X: reactance, Z: pulmonary impedance at 5 Hz
*: logarithmic transformation

Discussion

Respiratory function testing is essential to diagnose and follow children with respiratory disorders. Reference values that are derived from the healthy children from the same population are important to appropriately evaluate the results of these tests.[1] IOS is a popular lung function test for children who are less cooperative to perform spirometry. The measurement of pulmonary input impedance using IOS has a significant clinic value in young children with chronic respiratory diseases.[1,2] So far, most countries and ethnicities have provided their reference values of IOS in preschool children and/or adolescents.[4-11] This study is the first report for the reference values of IOS parameters and their correlation with predictive factors in healthy Turkish preschool children.

IOS data of 151 children were collected for this study. The assessment of relationship between IOS parameters and predictive variables by Linear Regression Analysis revealed that height and age were independent predictive factors in both genders. This result was different from most previous studies[4-8,11] where only height was the main anthropometric determinant of the IOS variables. On the other hand, similar to previous studies, we found that the resistances were negatively correlated with height for all participants in our study (Table III, Fig. 1 and 2). The downward trend of resistances with height is attributed to growth by age and has been explained with progressive widening of bronchi and bronchioles during childhood while growing up, which is expected to stabilize in early adulthood.[2]

Lower frequency oscillation in IOS measurement can be transmitted into the peripheral lung and used as an index of the airway status in the entire pulmonary system. Therefore, R5 reflects total respiratory system resistance and offers more useful clinical information about lung physiology.[2] In some reference data[4,7], the correlation between resistance and height was most noticeable at 5 Hz. Table V shows the comparison of reference values of R5 between the present study and previous studies in healthy children. It was remarkable that although the ages of the population are nearly similar in the studies published by Frei et al.[5], Park et al.[7] and Lai et al.[8], our regression equation of R5 indicate lower resistance than theirs.

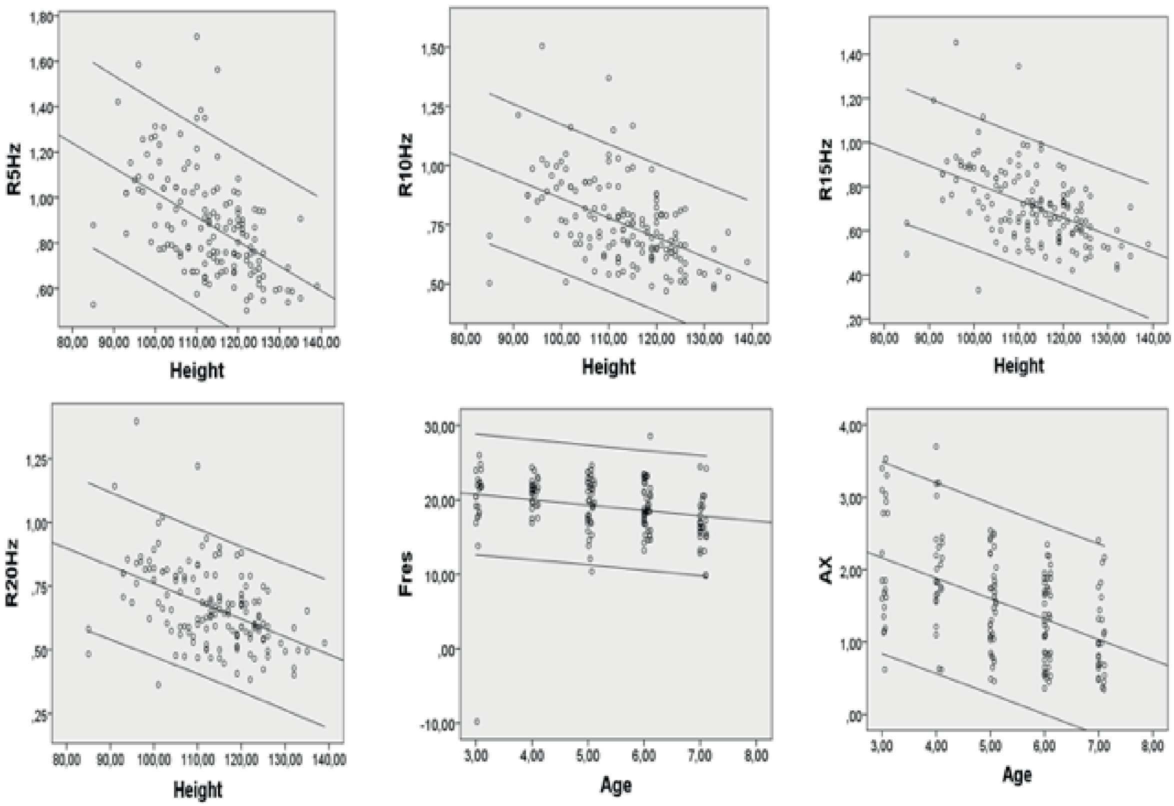

Fig. 1. Respiratory resistance (R) at 5 Hz to 20 Hz versus height (cm) and resonant frequency (Fres), area of reactance (AX) curve less than zero versus age (years) in 151 healthy Turkish preschool children.

Table IV. Impulse Oscillometry (IOS) Predictive Equations for Turkish Healthy Preschool Girls and Boys.

Girls, n=93			Boys, n=58		
Equations	R^2	SEE	Equations	R^2	SEE
R5* = 0.708-0.007×Height	0.411	0.009	R5 = -0.006× Weight	0.089	0.009
R10* = 0.526-0.006×Height	0.360	0.009	R10 = -0.007× Weight	0.143	0.079
R15* = 0.485-0.006×Height	0.310	0.093	R15 = -0.008 × Weight	0.231	0.074
R20* = 0.411-0.005×Height	0.278	0.093	R20 = -0.008 × Weight	0.218	0.077
R5-R20= -0.206-0.103×Age	0.288	0.222	R5-R20= -	-	-
X5 = -0.533+0.048×Age	0.297	0.101	X5 = -	-	-
X10 = -0.317+0.035×Age	0.360	0.063	X10 = -	-	-
X15 = -0.219+0.027×Age	0.267	0.061	X15 = -0.185+0.020×Age	0.115	0.069
X20 = -0.110+0.023×Age	0.139	0.079	X20 = 0.025×Age	0.086	0.102
Fres = 1.413-0.026×Age	0.171	0.076	Fres = 1.391-0.021×Age	0.100	0.079
Z5 = 2.629-0.015×Height	0.450	0.182	Z5 = 1.278-0.019 × Weight	0.153	0.215
AX = 5.890-0.038× Height	0.304	0.635	AX = 2.855-0.261×Age	0.177	0.694

AX, area of reactance curve less than zero, Fres: resonant frequency, R: resistance, R2: coefficient of determination; R5-R20: R5 minus R20, SEE: standard errors of estimate, X: reactance, Z: pulmonary impedance at 5 Hz
*: logarithmic transformation

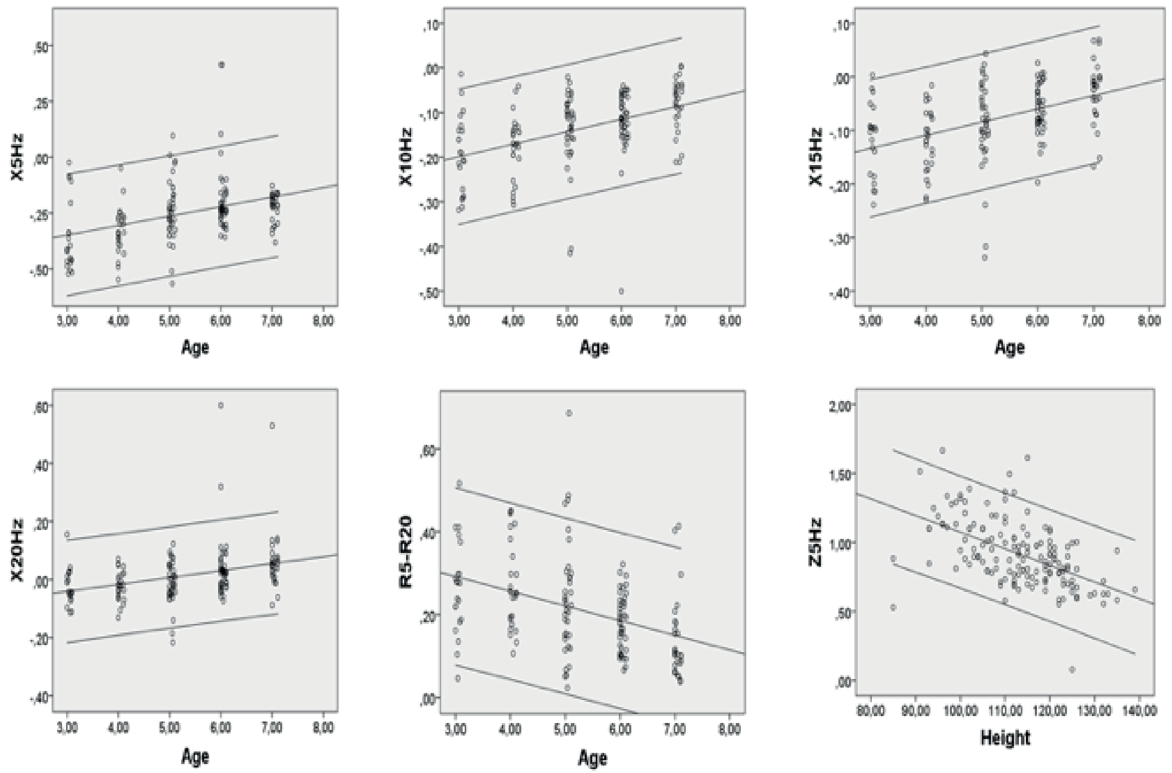

Fig. 2. Reactance (X) at 5 Hz to 20 Hz; R5-R20 (R5 minus R20) versus age (years) and pulmonary impedance (Z5) at 5Hz versus height (years) in 151 healthy Turkish preschool children.

Table V. Comparison of Reference Values of R5 Between the Previous Studies and Present Study on Healthy Preschool Children.

Published data/children number, age and ethnicity	R5 Equations
Malmberg LP, 2002[4]/ n=109, 2.1-7.0 years Finish children	8.286-1.786xlogHeight
Frei, 2005[5]/ n=222, 3-10 years North American children	2.11679-0.099xHeight
Denker,2006[6]/ n= 360, 2.1-11.1 years Finish and Swedish children	0.266+0.759xHeight^-3 +0.004xWeight
Park, 2011[7]/ n= 119, 3-6 years Korean children	1.934-0.009xHeight
Lee, 2012[17]/ n=390, 3-7 years Korean children	2.242-0.008 xHeight-0.005xAge
Lai, 2015[8]/n=150, 2-6 years Taiwanese children	2.4395-0.0134xHeight
Present study/ n=151, 3-7 years Turkish children	0.527-0.005xHeight

As anthropometric independent variables; height and weight had a negative effect on resistance values for boys and for girls, respectively. And the reactance values positively correlated with age in both genders. However, only a few studies have included different anthropometric variables such as age[9,10,17] and weight[6] in their reference equations. Most studies concluded that resistance negatively and reactance positively correlated with height.[4-8] Amra et al.[9] reported that height and age had negative effects on resistance but positive effect on reactance for the IOS regression equations of Iranian girls and boys aged 5-19 years. In the study of 2.7-15.4 years old Mexican children and adolescents published by Gochicoa-Rangel et al.[10], IOS variables had good correlation with age, height and weight. While multiple linear analysis identified height as the most influential variable in the majority of IOS variables, age also showed a moderate-tolarge influence in the regression models for many IOS variable. Therefore, reference values in Mexican children and adolescents were constructed considering age and height. Denker et al.[6] found that all IOS variables were related to height, most of them were also weakly related to weight for 2.1-11.1 years old Finish and Swedish children. These studies showed that the IOS reference values may also be related to variables other than height as our study.

The mean alveolar count of term born babies is 150 million which increases to approximately 300 million at 8 years of age and the size of the lungs is dependent upon the final body size.[18] According to results of previous studies[7,8], different results may be caused by racial features and/or age distribution and it is emphasized that independent from height, the additional mechanism by which age can modify lung function is not fully known and the main variable determining changes in lung function is age.[10]

Age related other parameters were Fres and AX. The correlation between Fres, AX and age may be due to the impact of Fres on AX. The AX area is a summation of reactance values that are graphically below Fres and enables to assess peripheral airway obstruction in low frequency system more clearly. The value of Fres also tends to decrease by age, because this parameter is inversely related to the size of the airway.[1,2] Except AX in girls group, Fres and AX were found negatively correlated with age, corroborating the findings of Frei et al.[5] and Assumpção et al.[11] In these studies, the relationship between Fres, AX and age was statistically greater than that for height and weight.

There are some limitations of the current study, especially in the group of Turkish boys. The proportion of variation in the data represented by the independent variables is measured by R^2. In our study, most R^2 of regression equations in boys was ≤20% which is less than in the previous studies. Additionally, we did not find any statistically significant variable among the independent variables for the IOS parameters of X5, X10 and R5-R20. Hence, we could not present the equations for those parameters. This may be due to the small number of boys involved in our study.

In conclusion, this is the first report for reference values of respiratory resistance and reactance using IOS in a group of healthy Turkish preschool children which can be used to diagnose and monitor respiratory disorders. Our results showed that variables other than height might have effect on IOS parameters. Future studies with increased number of healthy Turkish preschool children and in other age groups are needed to confirm our findings and to enlarge the involved population.

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