Respiratory Resistance by Impulse Oscillometry in Healthy Iranian Children aged 5-19 Years.

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ABSTRACT

The impulse oscillation system (IOS) measures respiratory impedance (Zrs) in terms of resistance (Rrs) and reactance (Xrs) at multiples of 5 Hz. These measurements can be used clinically to help diagnose and monitor respiratory disorders, independent of effort. There is, as yet, no information on reference values for IOS in Iranian adolescents.

The predictive equation for resistance and impedance at 5 and 15 and 25 Hz, for the first time, in 509 Iranian adolescent subjects (265 boys (aged 6–19 years) and 253 girls (aged 5–19 years) were determined. Gender-specific linear prediction equations were developed by multiple regression analysis; with measuring (R5, R15, R25, X5, X15, X25) as dependent variables regressed against age (A) and height (H).

For both genders, age and height had negative effects on resistance, while age and height had a positive effect on reactance. The prediction equations for R5 and X5 are as follows:

R5: -1.35×10⁻⁵ × age×2.823 – 0.001 × height ×1.022 + 0.547 for girls
X5: 1.78×10⁻⁷× age ×1.08 + 0.002 height ×4.150 – 0.539, for girls
R5: -6.19×10⁻⁷× age × 3.820 - 6.78E-005 ×height ×1.651 + 0.691 for boys
X5: 6.95×10⁻²₃ × age ×16.226 + 0.004height × 0.846– 0.430, for boys, respectively.

Our results therefore provide an original frame of reference for R5, R15, R25, X5, X15, X25 in Iranian adolescents population, obtained from a standardized forced oscillation technique.

Key word: Airway resistance; Airway reactance; Impulse oscillometry; Iranian Children

INTRODUCTION

As a noninvasive and effort independent technique, respiratory resistance obtained by forced oscillation technique is well suited for lung function measurement in young children.¹

The measurement of respiratory input impedance (Zrs) using the forced oscillation technique (FOT) has many advantages, especially in measuring resistance (Rrs) and reactance (Xrs).² Using the commercially available impulse oscillation system (IOS), which is one type of FOT, Rrs and Xrs can be obtained at multiples of 5 Hz. There are numerous publications
reporting the merit of using IOS at multiple frequencies.3,4

The resistive component of IOS parameters (Rrs) mainly reflects the frictional loss occurring during airflow in the bronchus, while the non-resistive component of IOS parameters (Xrs) reflects the energy stored by the more peripheral components of the respiratory system.3 An increase in Rrs at lower frequencies (5 Hz, R5) without a change in resistance at higher frequencies (20 Hz, R20) (frequency dependence of resistance) and a decrease in reactance at lower frequencies (X5) represents an increased resistance of peripheral airways, while an increase in Rrs both at lower (R5) and higher (R20) frequencies (frequency independence of resistance) without a change in reactance represents increased resistance of the central airways. These patterns have been identified with the use of mechano-electrical models consisting of seven components of a lung and chest model.5

One of the limitations of FOT/IOS in a clinical setting is the lack of definitive predictive equations in Iranians. There has been a limited number of studies assessing predictive equations2,6 and their clinical application, and there is one published study on the predictive equations for Asian adults.5 Ethnic variations should be considered when using predictive equations for IOS, as is the case for conventional pulmonary function tests such as spirometry.7

In this study, predictive equations for IOS for healthy Iranian children were developed.

MATERIALS AND METHODS

The Institutional Review Board for medical ethics at Isfahan Medical School approved the research protocol. During a 15-months period from January 2004 to April 2005, every 20th patient of a general medical clinic in Isfahan, Iran, was invited to bring his family members (children) for medical evaluation including a meticulous medical history, physical examination and impulse oscillometry.

The subjects excluded were those who had a past or ongoing history of respiratory disease (including bronchial asthma) and who had a lifelong history of smoking more than a hundred cigarettes and those who were unable to perform the appropriate procedures required for IOS. Informed consent was obtained from all enrolled subjects. Subjects were included in the study if they did not meet any of the exclusion criteria.

Their heights were measured, without shoes, standing against a wall (buttocks, back and head against the wall) with their head erect in the Frankfort horizontal plane. A carpenter's square was placed against the wall and the head. The subject was asked to step away from the wall, and height was measured to the nearest centimetre from the floor to the bottom of the square with a metal ruler attached to the wall.

Age was obtained by asking the subjects and parents. In most cases, insurance cards, or identity documents were checked which confirmed the accuracy of the stated age. Weight was also measured with feet wearing stockings and empty pockets.

Measurement of the Impulse Oscillatory System Parameters

The measurement of respiratory impedance by IOS was conducted with a commercially available oscillatory system (MS-IOS; Masterlab-IOS, Erich Jaeger, Germany), which has been described elsewhere,5 and fulfilled standard recommendations.8,9 Simply described, brief rectangular electrical pulses containing a continuous power spectrum ranging from 0 to 100 Hz were generated by a simple on/off control switch on a loudspeaker, at intervals of 0.2 s. These pressure pulses were superimposed on the spontaneous tidal breathing of the subjects, who were seated and wearing a nose clip with their cheeks supported, for approximately five breaths. To reduce loss of energy in the upper airways, their cheeks and chins were supported by the hands of the investigator. However, the parameters that we have investigated in this study have been reported to be less influenced by artifacts from the upper airway when lower frequencies are used.8 Pressure and airflow were recorded simultaneously at the subject's mouth. Frequency analysis was calculated using Fast Fourier transformation. The ratio of pressure to the resulting airflow constitutes the impedance of the respiratory system (Zrs), which is characterized by its two components: resistance (Rrs) and reactance (Xrs). IOS data were accepted if the coherence (correlations between oscillatory pressures and flows used to calculate all Rrs and Xrs values) were >0.8.

Data and Statistical Analysis

Data were analysed using the statistical package for the social sciences (SPSS for windows ver.13, SPSS, Chicago, IL, USA).
Data were analysed by stepwise multiple regression techniques. Dependent variables (R5, R15, R25, X5, X15, X25) were regressed against age, height, weight, BMI and body surface area (BSA) in different gender categories. They were first regressed individually against the mentioned independent variables, and then stepwise multiple regression analyses were used to determine which combination of variables would best fit the model. Predictor variables were retained in the regression model only if they significantly improved the explained variance of the dependent variable. The equations with the lowest standard errors of estimate (SEE) and highest coefficients of determination ($r^2$) were considered acceptable, if each included variable contributed significantly to the model ($p < 0.05$).

RESULTS

The age of the children in this study for girls ranged from 5 to 19 years (14.92 ± 3.07) and for boys ranged from 6-19 years (14.96 ± 3.44).

Means ± SD values of the variables are presented in Table 1. When these variables were more properly considered in a multiple regression analysis, only height and age remained with an independent predictive power in both genders (Table 2). However, we found a negative effect of height on the prediction of this variable, independent of gender.

Table 2 shows the predictive equations for R5, R15, R25 and X5, X15, X25, as determined by multiple linear regression analysis, for the healthy boys and girls.

### DISCUSSION

This study presents reference values for respiratory resistance, between 5 Hz and 25 Hz, along with data on reactance in Iranian children and adolescents.

In concordance with other investigators, we found that there was frequency dependence of resistance throughout the population examined, with resistance falling with increasing height, and with increasing oscillating frequency.

The equations generated in this study, however, are at variance with some of the frequently cited previous reports which used predominantly European and/or American population samples.1,2

Contrary to most previous studies where only height was main anthropometric determinant of the oscillometric results in our study standing height and age were the main determinants of the oscillometric results.

It may be due to broader range of age in our study. Indeed, in some studies the sole significant predictor for Resistance was height, a finding consistent of normal children in specific age range (3 to 10 years). Furthermore, within this age range there was no relationship between Resistance and gender, in the previous studies of oscillatory resistance in prepubescent children.1,2

In some previous studies, no difference between males and females was found.1,2,10

In disagreement with some observations,1,2,10 a significant gender related difference was found for respiratory resistance and reactance in our study. No agreement exists in the literature on this point: Duiverman et al11 reported a higher resistance in males up to 8 years, whereas Clement et al12 reported a higher resistance in females up to 7.5 yrs, both measured with FOT. The range of normal values for a given height is large. This is not a consequence of the variability of the test, as the repeatability of the test is acceptable. The reason for the range is that, similar to FOT, other factors unrelated to age, height, weight and sex have an important influence on the values.

Not only the overall airway diameter is important, but the circumference at specific "choke points" and the compliance of the airway, especially of the upper airway, also have an influence.

### Table 1. Anthropometric characteristics of the population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Boys(n=256)</th>
<th>Girls(n=211)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year)</td>
<td>14.96±3.44</td>
<td>14.92±3.07</td>
</tr>
<tr>
<td>Height(cm)</td>
<td>162.14±17.60</td>
<td>154.79±13.05</td>
</tr>
<tr>
<td>Weight(kg)</td>
<td>53.44±16.80</td>
<td>49.60±14.16</td>
</tr>
<tr>
<td>BMI</td>
<td>19.75±3.56</td>
<td>20.29±3.84</td>
</tr>
<tr>
<td>R5hz(KPa/L/s)</td>
<td>0.36±0.12</td>
<td>0.40±0.10</td>
</tr>
<tr>
<td>R15hz(KPa/L/s)</td>
<td>0.28±0.09</td>
<td>0.32±0.09</td>
</tr>
<tr>
<td>R25hz KPa/L/s)</td>
<td>0.26±0.08</td>
<td>0.30±0.09</td>
</tr>
<tr>
<td>X5hz(KPa/L/s)</td>
<td>-0.10±0.08</td>
<td>-0.14±0.07</td>
</tr>
<tr>
<td>X15hz(KPa/L/s)</td>
<td>-0.02±0.05</td>
<td>-0.02±0.04</td>
</tr>
<tr>
<td>X25hz(KPa/L/s)</td>
<td>0.04±0.06</td>
<td>0.04±0.04</td>
</tr>
</tbody>
</table>
Table 2. Prediction equations

<table>
<thead>
<tr>
<th>Parameter</th>
<th>equation</th>
<th>$r^2$</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Boys</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R5</td>
<td>$-6.19 \times 10^{-7} \times \text{age} \times 3.820 - 6.78 \times 10^{-5} \times \text{height} \times 1.651 + 0.691$</td>
<td>0.27</td>
<td>0.001</td>
</tr>
<tr>
<td>R15</td>
<td>$-2.04 \times 10^{-6} \times \text{age} \times 3.49 - 9.23 \times 10^{-9} \times \text{height} \times 3.16 + 0.412$</td>
<td>0.22</td>
<td>0.000</td>
</tr>
<tr>
<td>R25</td>
<td>$-6.71 \times 10^{-7} \times \text{age} \times 3.75 - 8.73 \times 10^{-10} \times \text{height} \times 3.57 + 0.362$</td>
<td>0.18</td>
<td>0.0000</td>
</tr>
<tr>
<td>X5</td>
<td>$6.95 \times 10^{23} \times \text{age} \times 16.226 + 0.004 \times \text{height} \times 0.846 - 0.430$</td>
<td>0.23</td>
<td>0.061</td>
</tr>
<tr>
<td>X15</td>
<td>$-1.40 \times 10^{-22} \times \text{age} \times 16.44 + 0.008 \times \text{height} \times 0.724 - 0.358$</td>
<td>0.27</td>
<td>0.08</td>
</tr>
<tr>
<td>X25</td>
<td>$0.573 \times \text{age} + 0.056 + 0.083 \times \text{height} - 0.129 - 0.779$</td>
<td>0.04</td>
<td>39.14</td>
</tr>
<tr>
<td><strong>Girls</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R5</td>
<td>$-1.35 \times 10^{-5} \times \text{age} \times 2.823 - 0.001 \times \text{height} \times 1.022 + 0.547$</td>
<td>0.04</td>
<td>0.049</td>
</tr>
<tr>
<td>R15</td>
<td>$0.000 \times \text{age} \times 1.74 + 0.001 \times \text{height} \times 0.921 - 0.155$</td>
<td>0.20</td>
<td>0.036</td>
</tr>
<tr>
<td>R25</td>
<td>$0.14 \times \text{age} \times 0.254 - 8.66 \times 10^{-6} \times \text{height} \times 1.759 - 0.341$</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>X5</td>
<td>$1.78 \times 10^{-5} \times \text{age} \times 4.15 + 0.002 \times \text{height} \times 1.08 - 0.539$</td>
<td>0.03</td>
<td>0.022</td>
</tr>
<tr>
<td>X15</td>
<td>$-1.40 \times 10^{-22} \times \text{age} \times 16.44 + 0.008 \times \text{height} \times 0.724 - 0.358$</td>
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<td>0.036</td>
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<td>39.14</td>
</tr>
</tbody>
</table>

$^1 r^2=$coefficient of determination

$^2$ SEE= Standard Error of the Estimate

Despite the similarities of these study findings, normative values for Asian children and young adult have not been published. Four pediatric reference samples have previously been published using impulse oscillometry. The diversity of measurement techniques probably contribute to difference values, the difference may be explained in part by minor difference in measurement technique as face mask, rather than a mouthpiece, was used. In our study all subjects used mouthpiece.

Also in the wide variability for resistance values predicted from different published equations, poor standardization and different computational algorithm could be involved. However, it is difficult to compare our results with previous studies. Since some authors generated predictive equations for the volume gradient of resistance (dR/dV) and reactance (dX/dV), the other published predictive equations for children and adolescents utilize the log (e) height to predict Rrs and Xrs.

Using a pseudo-random pulse, the most important factor influencing the prediction of adult reference values for Rrs and Xrs was reported to be height.

Although reference values for resistance and/or reactance for children and adolescents using sinusoidal pulse, rectangular pulse, and pseudo-random pulse have been published, predictive equations for IOS measurements are relatively scarce for children, adolescents. We used rectangular pulse for measuring reference values in children and adolescents. However the form of pulse may have a minor difference among studies. Although pseudorandom noise method and IOS give comparable results, the diversity of measurement techniques probably contribute to differences in reference values.

Our results further confirm the statistical notion that reference values for some biological measurements should be obtained ideally from a randomly selected sample with a general profile similar to that of the population to which these values will be applied. Compared with two famous prediction equations, our results are minimally higher than those of Denker and Hellinickx. In these studies different age range and frequency were used for measurement.

Also the baseline values for Rrs with the IOS in children are slightly higher than those of Duiverman and Clement et al with FOT, but in those studies most of the collected data were obtained in somewhat younger children and Rrs at 6 Hz (Rrs, 6) was measured.

In conclusion, we present reference values for oscillatory resistance measurements for the MasterScreen IOS System generated from a group of Iranian children and young adults.

In summary, predictive equations for IOS parameters in Iranian children and adolescents have been derived for the first time.
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REFERENCES