Prediction Equations for Spirometry parameters of Healthy School-Going Children in South India

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Abstract:

Introduction: Spirometric reference ranges reported from India and other parts of the world exhibit considerable diversity but is limited by lack of pediatric subjects. This study investigated the association of age, weight and height with spirometric values in children aged 5 – 15 years to develop more appropriate predictive equations that could describe the relationship.

Materials and Methods: A total of 790 healthy school-going boys and girls aged 5 – 15 years from Tamil Nadu participated in this cross-sectional study between September 2018 and October 2019. Spirometry was carried out according to the American Thoracic Society criteria. Multiple stepwise linear regression analysis was performed for each parameter against age, height and weight for males and females separately.
**Results:** No significant differences were observed among both the groups in terms of age, height, weight and BMI. All spirometry data (FVC, FEV1 and PEF) were significantly higher in males than in females except FEV1/FVC where it was otherwise. All measured PFT strongly correlated to age, height and weight however the relationship with age was non-linear with sudden rise of FVC, FEV1, PEF and FEF25-75% observed during pubertal stage.

**Conclusion:** Changes in lung function have distinct phases that cannot be explained by a single linear relationship. The equations derived in this study provide a newer perspective to the spirometry values; fitting age, weight and height trends and have the potential to be a foundation from which future studies can be developed to continue to improve the accuracy of reference data for spirometry.

**Keywords:** Reference equations; Healthy children; spirometric values


**Introduction:**

Normal spirometry values are influenced by many factors, including age, height, weight, body mass index (BMI), sex, ethnic origin, physical activity, environmental conditions, altitude, tobacco smoking, and socioeconomic status(1–4). For interpreting spirometry range, reference values are important and these can aid in the management of respiratory diseases (5). There is a concurrent need to keep reference data up-to-date as measurement techniques, equipment, and population characteristics evolve to reflect the changes.

The lung function tests reported from India (6–9) and other parts of the world (10,11) exhibit considerable diversity. These references are limited by a lack of pediatric subjects, and reference data has often being extrapolated to younger ages. The American Thoracic Society (ATS) strongly discourages extrapolation of reference data beyond the intended age/height range (12,13). Also the selection of explanatory factors used to predict lung function led to inconsistent findings in pediatric reference data. Though evidence supporting relation of spirometric values to BMI and age in adults is plenty, however, in children, some references have chosen to omit age from prediction models. The studies that adjusted for both height and age in children tend to either describe an absolute association (10,14,15)or a proportional one (4) and, in some cases, develop only age-specific equations (14,16). Adjustment for age using a proportional model is especially important during periods of rapid growth, such as puberty (4,17).

Spirometric data in children vary with increasing age and pubertal changes influence the measurements considerably due to hormonal changes and genetic predispositions (3). These measurements are further complicated because the variability of individual measurements around the median is skewed in relation to the age/height range, which questions the validity of conventional multiple regression analysis. Moreover, weight is also a potential confounder.
which hasn’t been addressed in the studies. This study investigated the association of age, weight and height with spirometric values in children aged 5 – 15 years to develop predictive equations that could describe the relationship.

**Materials & Methods:**

**Study Population**
Using the stratified-multi-steps-cluster sampling method, 1127 males and females aged 5 – 15 years Tamil Nadu were screened in this cross-sectional study between September 2018 and October 2019. Then, the exclusion criteria were applied: history of upper respiratory tract infection; history of bronchodilators or antibiotics; history of asthma; or history of any lung disease, lung surgery (18). After applying these criteria, 790 healthy school children (336 males and 454 females) were available for analysis. The study was approved by the Institute Human Ethics Committee of Chettinad Hospital & Research Institute. Informed assent was obtained from the parents of all subjects before examination.

**Pulmonary function tests**
Height and weight were measured bare foot, with clothes, and with standardized equipment. Force expiratory volume in first second (FEV1), force vital capacity (FVC), FEV1/FVC, peak expiratory flow (PEF), and forced expiratory flow at 25–75% (FEF25–75) were measured by Easy One Air Ultrasonic portable Spirometer. Tests were performed in the sitting position according to ATS guidelines with nose clips after an oral instruction by the technician. The participants were assisted by a specially trained pulmonary function technician during the course of start, duration, and end (18,19). Three FVC maneuvers were performed to meet acceptability for each subject. Repeatability was checked once 3 acceptable FVC maneuvers were obtained and if not met, more FVC maneuvers were performed (not usually more than 8). The exclusion criteria were incomplete efforts or coughing by participants.

**Statistical Analysis:**
All data were analyzed using SPSS 20.0 for Windows (IBM, Armonk, NY). Continuous data were expressed as mean ± standard deviation. Sex-specific regression equations for predicted reference values of pulmonary function in various powers and interactions were formulated based on age, height, and weight. Two-sided P values <0.05 were considered statistically significant.

**Results:**

**Characteristics of study participants**
The characteristics of the study population along with spirometry test variables are outlined in Table 1. Of the 790 subjects, there were 42.53% were males and the rest were females with a mean age of 12.60 ± 1.72 years. There was no significant difference among both the groups in terms of age, height, weight and BMI. As for spirometric tests,
FVC (P<.0001), FEV1 (P<.0001), and PEF (P<.0001) were higher significantly in males than in females (Table 1). However, FEV1/FVC (P<.0001) was lower significantly in males than in females.

**Spirometry data and prediction equations**

Almost all the measured spirometry parameters were strongly correlated to age and BMI with FVC and FEV1 having the highest correlation among both males and females. However, FEV1/FVC was not found to be associated with any of the parameters (age, weight and height) in case of males and only age was a predicting factor for FEV1/FVC in females. Also, weight was observed to be an insignificant factor to predict PEF. (Table 02).

When scrutinizing the plots (Figure 01), most lung function variables were found to have a non-linear association with age. A sudden rise was observed for FVC in case of males after 12 years of age. Similar was the case for FEV1, PEF and FEF25-75%. However, the rise was comparatively gradual in case of females for FVC and FEV1; but PEF and FEF25-75% showed a rise after 8 years of age, but the curve wasn’t as steep as that in males.

On the other hand, FEV1/FVC decreased in case of males with a sudden drop observed after 14 years of age, while in females it showed a plateau beginning from 10 years of age.

**Table 01: Summary Characteristics and spirometry test variables between genders**

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 790)</th>
<th>Male (n = 336)</th>
<th>Female (n = 454)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>12.60 ± 1.72</td>
<td>12.69 ± 1.48</td>
<td>12.52 ± 1.88</td>
<td>0.17</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>150.17 ± 10.92</td>
<td>150.73 ± 12.54</td>
<td>149.76 ± 9.54</td>
<td>0.21</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>42.81 ± 12.09</td>
<td>42.93 ± 13.62</td>
<td>42.72 ± 10.84</td>
<td>0.80</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.44 ± 3.63</td>
<td>23.38 ± 4.11</td>
<td>23.48 ± 3.25</td>
<td>0.70</td>
</tr>
<tr>
<td>FVC</td>
<td>2.24 ± 0.55</td>
<td>2.37 ± 0.63</td>
<td>2.14 ± 0.47</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>FEV1</td>
<td>1.99 ± 0.48</td>
<td>2.08 ± 0.54</td>
<td>1.93 ± 0.42</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>89.47 ± 5.21</td>
<td>88.29 ± 4.89</td>
<td>90.35 ± 5.28</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PEF</td>
<td>4.77 ± 1.17</td>
<td>4.97 ± 1.28</td>
<td>4.62 ± 1.07</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>FEF 25-75</td>
<td>2.61 ± 0.73</td>
<td>2.57 ± 0.77</td>
<td>2.64 ± 0.70</td>
<td>0.18</td>
</tr>
</tbody>
</table>

*-p<0.05

Table 02: Prediction Equations of the spirometry test variables among males and females

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R^2</td>
<td>p-value</td>
<td>R^2</td>
<td>p-value</td>
</tr>
<tr>
<td>FVC</td>
<td>-3.023 + 0.064A + 0.012W + 0.027H</td>
<td>0.71</td>
<td>-2.435 + 0.051A + 0.006W + 0.025H</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-2.115 + 0.057A + 0.006W + 0.021H</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>96.150 – 0.0117A – 0.038W – 0.031H</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>92.972 + 0.578A</td>
<td>0.02</td>
</tr>
<tr>
<td>FEV1</td>
<td>-2.451 + 0.054A + 0.01W + 0.023H</td>
<td>0.68</td>
<td>-3.766 + 0.124A + 0.044H</td>
<td>0.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-1.554 + 0.016W + 0.021H</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-1.281 + 0.091A + 0.010W + 0.016H</td>
<td>0.27</td>
</tr>
</tbody>
</table>

* - p<0.05
A – Age; W – Weight; H - Height; FVC – Forced Vital Capacity; FEV1 – Forced Expiratory Volume in 1st second; PEF – Peak Expiratory Flow; FEF25-75 – Forced Expiratory Flow at 25 – 75%.
Figure 01: Spirometry data of all subjects across age.

FVC – Forced Vital Capacity; FEV1 – Forced Expiratory Volume in 1st second; PEF – Peak Expiratory Flow; FEF25-75 – Forced Expiratory Flow at 25 – 75%

Discussion:

The purpose of this study and its analysis was to derive predictive equations for spirometry in school going children aged 5 -15 years and to calculate regression equations which correctly reflected the values of reference population. However, it should be noted that these equations are only valid for children aged 5 – 15 years with height ranging from 105 cm to 177 cm. Extrapolation of these to test younger children

taller for their age or adults who are short must be done with utmost care as these might stand invalid under those circumstances.

The finding that a linear or power curvilinear relationship doesn’t exist between the spirometric values and age (Figure 01) was also noted by Dickman et al.\textsuperscript{[20]} The reason assumed for the discontinuity was pubertal stage, though it wasn’t assessed in that study. Similarly, Engstrom et al. related peak flow to pubertal stage and showed marked rise in PEF in late puberty.\textsuperscript{[21]} These findings were reverberated in our study where a sudden increase was observed in FVC, FEV1, PEF and FEF25-75% around the time of puberty. Males seemed to have earlier rises in lung function which was supported by Sherrill et al.\textsuperscript{[22]} In another longitudinal study by DeGroodt et al., the thoracic dimensions and height were measured in males and females and it was concluded that thoracic width in females didn’t change significantly during adolescence while in case of males it increased twice as fast.\textsuperscript{[23]} However, the thoracic dimensions were not assessed in the present study.

This study also confirms previous observations regarding the rapid decrease in the FEV1/FVC ratio with age.\textsuperscript{[24]} It was more pronounced in case of males, while it attained a plateau in females. The initial high values reflect the relatively large airways in relation to lung volumes in early life, which are associated with a short expiratory time constant and rapid lung emptying, whereas as age progresses, the rapid decline in FEV1/FVC probably reflects the different rates of lung and airway growth, which may be particularly marked in males, in whom lung growth continues for several years even after somatic growth has halted.\textsuperscript{[4,24]}

A key feature of the current study is the proportional model that adjusts for measures of body weight, height and age in a way that is biologically plausible. Inclusion of an age adjustment in addition to weight and height allows the complex changes during puberty to be accounted for without the need to undertake pubertal staging, which may be impractical in many clinical and research settings.

We have collated data from a large number of study participants using a stratified-multi-steps-cluster sampling method which as far as our knowledge concerns hasn’t been done in any study among Indian population in the pediatric age group. Thus a foundation has been established on which more comprehensive datasets can be built. From our findings we could deduce that each geographical area should develop its own reference ranges; however, in practice, this is rarely feasible.\textsuperscript{[25,26]} Nevertheless, as mentioned by Pellegrino et al. various organizations should continue to validate reference equations with a sample of healthy control subjects from their own population to test for any systematic biases.\textsuperscript{[13]}

As mentioned by Stanojevic et al. our reference data too is limited by the fact that we have not addressed the issue of whether FEV1 is the most appropriate outcome during early childhood.\textsuperscript{[3]} As young children
have relatively large airways compared with their lung volumes, during forced expiration, emptying may be virtually complete within 1 second. In such cases, FEV1 is equivalent to FVC, suggesting that FEV0.75 may be a more appropriate measure for young children.\textsuperscript{[27,28]} However, with the exception of the studies by Pesant et al.\textsuperscript{[27]} and Piccioni et al.\textsuperscript{[28]} on preschool spirometry, reference equations for FEV0.75 in children remain limited.

**Conclusion:**

Changes in lung function have distinct phases that cannot be explained by a single linear relationship. The pubertal stage is crucially important when comparing the participants. Our equations provide a newer perspective to the spirometry values; fitting age, weight and height trends. These normograms have the potential to be a foundation from which future studies can be developed to continue to improve the accuracy of reference data for spirometry in children of varying age groups.

**References:**


[Annals of Tropical Medicine & Public Health](http://doi.org/10.36295/ASRO.2020.231514)


