Short Communication

Regression Equations for Spirometry in Children Aged 6 to 17 Years in Delhi Region

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ABSTRACT

Background. Most of the studies carried out in India to develop regression equations for spirometry in children are now several years-to-decades old and had used equipment and measurement protocols that have since changed. Prediction equations using the current standardisation protocols for spirometry are not available. The lung health of the population may have changed too.

Objective. To develop regression equations for spirometry for children aged 6 to 17 years of north Indian origin in Delhi region.

Methods. School children of north Indian origin, as determined by mother tongue and parentage, aged 6 to 17 years were screened by a health questionnaire and physical examination and those found "normal" underwent spirometry according to the standardised procedure recommended by the American Thoracic Society/ European Respiratory Society (ATS/ERS) task force in 2005. Pearson's correlation analysis was carried out to identify the predictor variables for spirometric parameters. Prediction equations were developed using the multiple linear regression procedure. The independent variables were entered in sequence of height, age and weight. R^2, adjusted R^2 and R^2 change, standard errors of the estimate (SEE), and estimates of regression coefficients were obtained and the goodness of fit was examined.

Results. Data was obtained in 365 boys and 305 girls. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow rate (PEFR), forced expiratory flow rate at 50% and 75% exhalation of vial capacity (F_{50} and F_{75}) and mean forced expiratory flow rate over the middle 50% of the vital capacity (F_{25-75}) showed moderate to strong correlations with age, height and weight in both boys and girls. In both genders, the equations explained very high variability of FVC, FEV_1 and PEFR as shown by the R^2 values. The explained variability for flow rates was lesser, with that for F_{75} being the least.

Conclusions. Regression equations for spirometry variables for children of north Indian origin in Delhi region have been developed. These represent the first such effort from India after the publication of the ATS/ERS task force 2005 guidelines on standardisation of spirometry. **[Indian J Chest Dis Allied Sci 2012;54:59-63]**

Key words: Pulmonary function, Spirometry, Normals, Children, Delhi, Regression equations.

INTRODUCTION

Pulmonary function is influenced by anthropometric, gender, environmental, genetic, socio-economic and technical factors. To predict pulmonary function, variations with anthropometric variables, sex and race have been studied extensively and documented in the western literature. A few studies from different parts of India[1-9] have provided information on pulmonary function in children and its determinants and prediction equations have been described. The studies have varied in sample size, instrumentation and results. In general, boys have been found to have larger vital capacities and height is the most important determinant with variable contributions from age, weight and some other physical measurements.

Technological advancements have resulted in greater automation and newer methods of electronic measurements. The measurement protocols have been revised over time. The latest standardisation of spirometry was carried out by a joint task force of the American Thoracic Society and the European Respiratory Society (ATS/ERS) and published in the year 2005.[10] Most of the above Indian studies were carried out several years-to-decades ago with equipment and measurement protocols that have changed. Thus, these may no longer be valid. This is likely to affect interpretation of data. Correct interpretation of pulmonary function data requires

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use of locally developed prediction equations. Equations using the current standardisation protocols for spirometry have not been developed in India. Ethnic variations in pulmonary function are well known. This precludes development of a single equation for all Indians. There is an urgent need to develop these equations for different regions of the country. Delhi is a cosmopolitan city in the northern region of the country. We, therefore, carried out a study to develop regression equations for spirometry in children aged 6 to 17 years of north Indian origin in Delhi region. We present here a brief communication of the study carried so that these can be applied in practice at the earliest. A detailed evaluation and comparative analysis with previous Indian studies as well as with equations from other countries will be presented subsequently.

MATERIAL AND METHODS

The study was approved by the Institutional Ethics Committee. It was carried out in children in a school selected randomly from a list of schools in Delhi. The school caters to a wide area of Delhi and the children are drawn from a very wide socio-economic spectrum. Hence, it approximates a representative sample. All the children from ages 6 to 17 years were eligible for inclusion provided they had been in Delhi for more than half of their life. Additionally, the mother tongue was required to be Hindi, Urdu or Punjabi, the predominant languages in this region, and both parents had to be of north Indian origin to limit the confounding effects of ethnic variation. A demonstration of the testing procedure was given to familiarise the children with pulmonary function testing. For each age, a target of 15 to 20 boys and girls with technically acceptable tests was set and consecutive eligible children were included till the sample requirement was met. This number was based on statistical considerations of numbers required for linear regression procedures, previously published studies[1-9] and feasibility.

A questionnaire was designed in English and Hindi was answered by either parent. It had several sections as follows: cover letter from Principal, information sheet, consent form and questionnaire about the health status. Children with completely filled-up questionnaires with written consent for participation were included. Those judged to be "normal" from the questionnaire responses were again examined by the investigators in the school to confirm that they were eligible for inclusion. The *exclusion criteria* included current or past history of any chronic respiratory, cardiac or other system disease, thoracic cage abnormality, any current acute illness, recent chest infection (within 6 weeks), current smokers or with environmental tobacco smoke exposure, and unwilling parents/children.

Age in completed years, gender, standing height to the nearest centimeter without shoes and weight rounded off to the nearest kilogram were recorded at the time of the testing. Weight was measured wearing light clothing and no footwear to the nearest 0.5 Kg using an electronic scale that was calibrated on a weekly basis with known weights. Height was measured with the children standing erect with head in the Frankfurt plane and ankles pressed against a wall on which a measuring tape had been fixed.

Spirometry was carried out in accordance with the recommendations of the ATS/ERS task force.[10] The spirometer with a heated Lily screen pneumotach (Medisoft Micro 5000, Belgium) was calibrated daily. The manoeuvers were performed in the sitting position with a nose-clip applied. The children was asked to inhale completely and rapidly with a pause of <1 s at total lung capacity (TLC) and exhale with maximum force until no more air was expelled out while maintaining an upright posture. At the completion of expiration and on signal from the technician, the subject was asked to inhale completely. The manoeuvers was monitored on the computer screen. Throughout the procedure, loud verbal encouragement was given to obtain the expiratory and inspiratory manoeuvers completely with maximal force. The procedure was monitored for compliance with the acceptability and repeatability criteria recommended by the ATS/ERS task Force.[10] At least three acceptable and two repeatable efforts were obtained.

The highest values of FVC, FEV_1 and PEFR were selected. The flow rates, forced expiratory flow rate at 50% and 75% exhalation of vital capacity (F_{50} and F_{75}) and mean forced expiratory flow rates over the middle 50% of the vital capacity(F_{25-75}) were obtained from the "best" curve, i.e. the one with the highest sum of FVC and FEV_1.

Statistical Analysis

Statistical analysis was carried out using statistical package for the social sciences (SPSS) 16.0 and GraphPad Prism 4.01 softwares. Analysis was carried out separately in boys and girls. In the present study, the dependent variables were FVC, FEV_1, PEFR, F_{50}, F_{75} and F_{25-75}. Pearson's correlation analysis was carried out to identify the predictor variables. Prediction equations were developed using the multiple linear regression procedure. Linear and non-linear models were developed and the former was selected based on criteria of simplicity and ease of clinical application, high predictive capability (R^2) and yield of smallest residuals.

The independent variables were entered in the sequence of height, age and weight. Models were constructed including one (height), two (height and age) and three predictor variables (height, age and weight) and R^2, adjusted R^2 and R^2 change on entering each predictor variable were calculated for each model. If the R^2 change at each step was significant and there was a substantial improvement in the predictive ability, the model was accepted. If not, the model at the previous step was accepted. Standard errors of the estimate (SEE) were calculated and analysis of variance was carried out for each model to evaluate the significance of the regression equation. Estimates of regression coefficients were obtained and their significance was determined by student's 't' test.

The goodness of fit was examined by testing for independence of predictor variables (by examining the tolerance statistics and VIF values), normality and equal variances of the residuals (by residuals normality plot), and linear type relationship between the predictors and the outcome variable (by Q-Q plots). Unusual and influential observations were examined. These included outliers, points with high leverage and high influence. Analysis was repeated excluding these observations to determine their impact on the models and the original models were retained if the effect on the equations was small and inconsequential.

RESULTS

Acceptable data was obtained in 365 boys and 305 girls. The ages and the anthropometric data (mean±SD) in the two genders were respectively: age (years), 11.53±3.37 and 11.74±3.23 ($p>0.05$); height (m), 1.49±0.18 and 1.45±0.14 ($p<0.01$); weight (Kg), 44.56±18.42 and 40.97±13.82 ($p<0.01$); and body mass index (Kg/m^2) 19.04±4.43 and 18.75±3.91 ($p>0.05$). The age distribution is shown in table 1. The median, (range) and interquartile ranges (IQR) in boys were as follows: age (years): 11, (6 to 17), IQR: 9 to 14; height (m): 1.5, (1.09 to 1.91), IQR: 1.35 to 1.65; weight (Kg): 44, (15 to 98), IQR: 28 to 58. The median, (range) and IQR in girls were as follows: age (years): 11, (6 to 17), IQR: 9 to 15; height (m): 1.48, (1.09 to 1.7), IQR: 1.35 to 1.58; weight (Kg): 41, (15 to 78), IQR: 30 to 51.

Table 1. Age distribution of the children

Age (in years) (n)	Boys (n=365)	Girls (n=305)
6 (62)	40	22
7 (28)	16	12
8 (39)	21	18
9 (71)	36	35
10 (47)	25	22
11 (96)	51	45
12 (44)	22	22
13 (60)	30	30
14 (59)	37	22
15 (59)	33	26
16 (59)	30	29
17 (46)	24	22

The pulmonary functions of boys and girls were compared for the entire sample (Table 2). FVC, FEV_1 and PEFR were significantly higher among boys. However, the flow rates, F_{50}, F_{75} and F_{25-75} were not significantly different. Table 3 shows the correlations of FVC and FEV_1 with age, height and weight in boys and girls. Table 4 shows the correlations of PEFR, F_{25-75}, F_{50}, and F_{75} with age, height and weight in boys and girls. The regression equations developed are given in table 5. The equation is expressed as follows:

Spirometric parameter = Constant + (β Coefficient for height x height in cm) + (β Coefficient for age x age in years) + (β Coefficient for weight x weight in Kg)

The SEE is provided for calculation of the lower limits of normal. As FEV_1/FVC was found to be independent of age and height in boys, and had only a weak correlation with age in girls, no equations were developed for this parameter.

Table 2. Pulmonary function distribution in boys and girls for the whole sample

Spirometry Parameter	Gender	Mean±SD	Median	Range	Interquartile Range
FVC	Boys	2.88±1.09*	2.61	1.09 to 6.40	2.03 to 3.71
	Girls	2.42±0.72	2.41	0.83 to 4.320	1.84 to 2.93
FEV_1	Boys	2.43±0.94*	2.24	0.92 to 5.24	1.66 to 3.19
	Girls	2.14±0.65	2.14	0.81 to 3.96	1.60 to 2.64
PEFR	Boys	5.47±2.02**	5.04	1.75 to 12.00	3.90 to 6.86
	Girls	5.00±1.46	4.97	2.05 to 9.92	3.94 to 6.05
F_{25-75}	Boys	3.04±1.10^{ns}	2.82	0.97 to 6.60	2.21 to 3.70
	Girls	2.97±0.91	2.89	1.24 to 5.46	2.29 to 3.56
F_{50}	Boys	3.22±1.24^{ns}	2.86	1.04 to 7.13	2.32 to 3.99
	Girls	3.17±1.04	3.02	1.00 to 5.82	2.33 to 3.99
F_{75}	Boys	1.45±0.75^{ns}	1.22	0.34 to 4.43	0.92 to 1.84
	Girls	1.52±0.66	1.41	0.33 to 3.86	1.00 to 1.92

FVC=Forced vital capacity; FEV_1=Forced expiratory volume in one second; PEFR=Peak expiratory flow rate; F_{25-75}=Mean forced expiratory flow rate over the middle 50% of the vital capacity; F_{50} and F_{75}=Forced expiratory flow rates at 50% and 75% exhalation of vital capacity; *=p<0.001; **=p<0.01; ns=Not significant, p>0.05

Table 3. Pearson's correlation coefficients (r) for FVC and FEV_1 with age, height and weight

	Boys		Girls	
	FVC	**FEV_1**	**FVC**	**FEV_1**
Age	r=0.89 p<0.0001	r=0.89 p<0.0001	r=0.85 p<0.0001	r=0.87 p<0.0001
Height	r=0.92 p<0.0001	r=0.92 p<0.0001	r=0.88 p<0.0001	r=0.86 p<0.0001
Weight	r=0.86 p<0.0001	r=0.842 p<0.0001	r=0.84 p<0.0001	r=0.83 p<0.0001

Table 4. Pearson's correlation coefficients (r) for PEFR, $F_{25-75,}$ F_{50} and F_{75} with age, height and weight

	Boys				Girls			
	PEFR	**F_{25-75}**	**F_{50}**	**F_{75}**	**PEFR**	**F_{25-75}**	**F_{50}**	**F_{75}**
Age	r=0.87 p<0.0001	r=0.81 p<0.0001	r=0.77 p<0.0001	r=0.77 p<0.0001	r=0.82 p<0.0001	r=0.73 p<0.0001	r=0.70 p<0.0001	r=0.62 p<0.0001
Height	r=0.87 p<0.0001	r=0.82 p<0.0001	r=0.77 p<0.0001	r=0.69 p<0.0001	r=0.81 p<0.0001	r=0.76 p<0.0001	r=0.70 p<0.0001	r=0.64 p<0.0001
Weight	r=0.78 p<0.000	r=0.71 p<0.0001	r=0.69 p<0.0001	r=0.60 p<0.0001	r=0.74 p<0.0001	r=0.68 p<0.0001	r=0.66 p<0.0001	r=0.55 p<0.0001

Table 5. Regression equations for spirometry parameters

Spirometry Parameter	Constant	β Coefficient for Height	β Coefficient for Age	β Coefficient for Weight	Standard Error of Estimate	R^2
Boys						
FVC	–3.226	0.032	0.066	0.014	0.394	0.872
FEV_1	–2.763	0.026	0.080	0.008	0.360	0.856
PEFR	–5.043	0.050	0.267		0.926	0.790
F_{25-75}	–2.704	0.030	0.111		0.620	0.686
F_{50}	–2.540	0.027	0.145		0.772	0.618
F_{75}	–1.617	0.014	0.081		0.537	0.491
Girls						
FVC	–1.733	0.019	0.073	0.015	0.291	0.840
FEV_1	–1.633	0.017	0.078	0.010	0.256	0.847
PEFR	–2.474	0.030	0.211	0.014	0.771	0.725
F_{25-75}	–2.662	0.032	0.082		0.573	0.603
F_{50}	–1.229	0.017	0.118	0.014	0.708	0.544
F_{75}	–1.791	0.018	0.060		0.504	0.431

Equation: Spirometric parameter = Constant + (β Coefficient for height x height in cm) + (β Coefficient for age x age in years) + (β Coefficient for weight x weight in Kg)

Descriptive statistics for FEV_1/FVC is presented in table 6. The 5th percentile can be used to define the lower limit of normal.

Table 6. Descriptive statistics for FEV_1/FVC ratio

Gender	Mead±SD	5th percentile	50th percentile	95th percentile
Boys	84.41±5.86	73.96	84.57	94.11
Girls	88.45±5.86	79.24	88.48	97.32

DISCUSSION

We have presented prediction equations for various spirometry parameters for children of north Indian origin in Delhi region between the ages of 6 to 17 years. These are derived from spirometry carried out as per the current standardised protocol recommended by the ATS/ERS task force.[10] The FVC, $FEV_{1,}$ PEFR, $F_{50,}$ $F_{75,}$ and F_{25-75} showed moderate to strong correlations with age, height and weight in both boys and girls. The FEV_1/FVC was not correlated with age or height in boys, and with height in girls, though it showed a weak correlation with age in the latter.

In both boys and girls, the equations explained very high variability of FVC, FEV_1 and PEFR as shown by the R^2 values. However, the explained variability for flow rates was lesser, with that for F_{75} being the least. The very high values for R^2 for FVC and FEV_1 are also the reason why the interpretation algorithms for spirometry are based exclusively on these two parameters. The FVC and FEV_1 are the only parameters for which reproducibility criteria have been defined[10] and the flow rates have less precision. Effects of environmental exposures including environmental tobacco smoke and outdoor air pollution, physical activity and conditioning, nutritional factors, genetics and respiratory infections are extremely difficult to capture and therefore never factored in any model. In addition, pulmonary function has inherent variability on repeated testing. Therefore, pulmonary function parameters usually have a high standard deviation and consequently wide range of 95% confidence limits for defining normalcy.

It is remarkable that among all the predictors, height alone explained a major part of variability. Inclusion of age, and weight in some equations, explained a small additional variability as shown by the R^2 change. Thus, in boys, for FVC and FEV_1, all the three predictor variables were retained in the equations while for PEFR, $F_{50,}$ F_{75} and F_{25-75}, only height and age were included. For girls, weight was retained in the equations for FVC, FEV_1, PEFR and F_{50}. For all the parameters, the adjusted R^2 values were very close to R^2 implying that if the equation was derived from the population rather than the sample, we would get similar results.

These equations are the first effort from India after the recent standardisation of spirometry[10] and indeed one of the few available globally. Revision of prediction equations was long overdue as technology and measurement protocols have changed and also to determine if lung health in population is changing due to changes in nutritional status, environmental exposures and rates of early childhood respiratory infections. The previous studies from India, with city and year, were: Bhattacharya and Banerjee[1] (Delhi, 1966), Jain and Ramiah[2] (Delhi, 1967), Vohra *et al*[3] (Ahmedabad, 1984), Malik and Jindal[4] (Chandigarh, 1985), Kumar *et al*[5] (Patiala, 1992), Gupta *et al*[6] (Delhi, 1993), Chowgule *et al*[7] (Mumbai, 1995), RajKappor *et al*[8] (Rohtak, 1997) and Vijayan *et al*[9] (Chennai, 2000).

The present study has a few limitations. A wider selection from several schools would have provided a more representative sample. However, the selected school caters to a very wide socio-economic spectrum, and therefore, may be viewed as being fairly representative of Delhi. In order to ensure ethnic homogeneity, we included only children whose parents were of north Indian origin. A multicentric study with participation of other cities of the region was not feasible because of limited resources. Therefore, while the equations predict pulmonary function of children of north Indian origin, we suggest that the equations may also be validated in other north Indian states in further studies. A chest radiograph would have confirmed normalcy. However, this was not feasible in a field study. A careful and detailed history and examination by the physicians, however, ensured that only normal children were included.

These equations should be helpful in interpretation of spirometric data, and thus, in the management of respiratory diseases such as asthma in children. Equipments used in most pulmonary clinics use softwares that carry western prediction equations and are not valid for Indian population. These equations would allow manufacturers to provide Indian equations in the softwares. The equations described by us have been developed for northern parts of the country. As ethnic differences are important, each region needs to develop such equations following the standardised protocols and strict quality control.

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