Original Article

Prediction equations for pulmonary function values in healthy children in Mashhad city, North East Iran

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Background: Pulmonary function tests (PFTs) are used in assessing physiological to clinical status of the respiratory system, which is expressed as a percentage of predicted values. Predicted PFTs values are varies in different ethnics. Predicted PFTs values were studied in a sample of Iranian children. **Materials and Methods:** Prediction equations for PFTs were derived from urban children in the city of Mashhad (northeast Iran). Regression analysis using height and age as independent variables was applied to provide predicted values for both sexes. PFT values were measured in 414 healthy children (192 boy and 222 female, aged 4-10 years). Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), maximal mid-expiratory flow (MMEF), peak expiratory flow (PEF), MEF at 75%, 50% and 25% of the FVC (MEF_{75}, MEF_{50} and MEF_{25} respectively) were measured. **Results:** There were positive correlations between each pulmonary function variable with height and age. The largest positive correlations were found for FVC ($r = 0.712$, $P < 0.0001$) and FEV_1 ($r = 0.642$, $P < 0.0001$) in boys and girls respectively with height and for PEF (0.698, $P < 0.0001$) and MEF ($r = 0.624$, $P < 0.0001$) with age. Comparison of PFTs derived from the equations of the present study showed significant differences with those of several previous studies ($P < 0.001$ for most cases). **Conclusion:** A set of PFT reference values and prediction equations for both sexes has been derived using relatively large, healthy, Iranian children for the first time, which the generated results were differ from several prediction equations.

Key words: Children, Iranian population, predicted equation, pulmonary function test

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INTRODUCTION

Pulmonary function tests (PFTs) are used in assessing physiological and clinical status of the respiratory system. However, the results of PFTs should be interpreted relative to reference values, to judge whether they are within the normal range.[1]

The values of predicted pulmonary function tests are calculated according to gender, age, height and weight (for some tests) variables. In addition, predicted values of pulmonary function from different published studies vary by as much as 20% for an individual subject,[2] which some of these variations are due to ethnic differences.[3-6]

Therefore, local and native prediction equations for predicted values of PFTs will enhance the reliability of the interpretation of PFTs.[7] There is very little data in the literature to date regarding the PFT reference values for Iranian children and even middle east ethnic groups. In previous studies, prediction equations for pulmonary function values of a healthy, non-smoking, urban, Iranian, adult[8] and young adult[9] population were determined.

However, the result of our previous study is not appropriate for calculation of PFT predicted values in children of Iran and the region. Therefore, in the present study, prediction equations for pulmonary function values of a healthy urban, Iranian, children population of the Mashhad city were determined.

MATERIALS AND METHODS

Study area and population

The study area was the city of Mashhad, which has moderate industry and heavy traffic. Mashhad is a holy city located in the northeast of Iran with a population of 3.15 million people many of whom are immigrants from all over Iran. In addition, there is little or no difference in ethnicity of the inhabitants of the different areas of

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Iran. Therefore the population of Mashhad could well be considered as representative of the Iranian population.

Subjects

A total of 495 subjects including 248 boys and 247 girls participated in the study, but only 442 (215 boys and 227 girls) completed the pulmonary function measurements, which were included in the study. The rest of the subjects were not able to perform PFT precisely. The subjects were recruited from primary schools in 4 randomly selected educational regions of Mashhad by electoral roll. The city of Mashhad has 7 different educational regions. The students of randomly selected primary schools of 4 educational region were studied. Therefore, the studied subjects were of different socio-economic classes and all were ethnic Iranians. The ages of the subjects whose pulmonary function data were used for statistical analysis were between 4 and 10 years and their heights between 84 and 138 cm in the boy and 88 and 154 in female [Tables 1 and 2]. All subjects were with no history or symptoms of cardiovascular or respiratory diseases that required treatment (excluding the common cold, but those that recovered at least 1 month prior of study). The protocol was approved by the ethics committee of our institution and each subject gave informed consent.

Measurements

Expiratory flow-volume curves were recorded by a spirometer with a pneumotachograph sensor (model ZAN100, Germany). The spirometer was calibrated daily for a few days at the beginning and end of the study and at various intervals in the middle of the study with a 1 liter calibrating syringe. However, because there were no differences in daily calibration, calibration of the spirometer was carried out weekly for the rest of the study. All tests were conducted by a final year medical student, which was fully trained in the procedure of spirometry by a supervisor. Prior to testing, the required manoeuvre was demonstrated by the operator and subjects were encouraged and supervised throughout test performance. The required manoeuvre included tidal breathing for a while followed by a maximal inspiration and maximal expiration. Studies were performed using the standards outlined by the American Thoracic Society (ATS),[10] with subjects in a sitting position and wearing nose clips. All tests were carried out between 10.00 and 17.00 h. PFTs were measured at least three times in each subject with an acceptable technique. The highest level for FVC, forced expiratory volume in one second (FEV_1) and peak expiratory flow (PEF), was taken independent from the three curves. However, maximal mid-expiratory flow (MMEF), MEF at 75, 50 and 25% of the FVC (MEF_{75}, MEF_{50} and $MEF_{25,}$ respectively) were obtained from the single curve with the largest sum of FVC + FEV_1.[11] The height of studied subjects was measured as described previously.[11] The study was performed between March and June 2010.

Table 1: Age distribution of studied subjects

Age (years)	Boys number (%)	Girls number (%)
4	21 (9.8)	14 (6.2)
5	13 (6.0)	11 (4.8)
6	16 (7.5)	17 (7.5)
7	56 (26.0)	26 (11.5)
8	66 (30.7)	64 (28.2)
9	29 (13.5)	72 (31.7)
10	14 (6.5)	23 (10.1)
Total	215 (100)	227 (100)

Table 2: Range, mean and SD, of age, height, and pulmonary function variables for boys and girls subjects

Parameter	Range	Mean	SD
Boys			
Age (year)	4-10	7	1
Weight (kg)	14-44	25.10	5.65
Height (cm)	66.00-145.00	120.00	9.97
FVC (L)	0.57-2.55	1.41	0.36
FEV_1 (L)	0.57-2.38	1.33	0.34
PEF (L/S)	1.45-4.88	2.86	0.81
MEF_{75} (L/S)	0.19-4.84	2.67	0.86
MEF_{50} (L/S)	0.63-3.96	2.23	0.64
MEF_{25} (L/S)	0.43-2.72	1.42	0.48
MEF_{25-75} (L/S)	0.34-3.50	2.04	0.62
Girls			
Age (year)	4-10	7	1.59
Weight (kg)	15.00-62.00	27.52	7.47
Height (cm)	88-154	124.00	9.84
FVC (L)	0.55-2.30	1.365	0.27
FEV_1 (L)	0.55-2.30	1.340	0.267
PEF (L/S)	0.97-6.94	2.950	0.874
MEF_{75} (L/S)	0.74-6.77	2.780	0.888
MEF_{50} (L/S)	0.79-5.31	2.416	0.750
MEF_{25} (L/S)	0.36-3.50	1.538	0.577
MEF_{25-75} (L/S)	0.73-5.04	2.215	0.728

SD = Standard deviation; FVC = Forced vital capacity; FEV_1 = Forced expiratory volume in one second; MMEF = Maximal mid-expiratory flow; PEF = Peak expiratory flow; MEF_{75}, MEF_{50}, and MEF_{25} = Maximal expiratory flow at 75%, 50%, and 25% of the FVC, respectively

Data analysis

Data were analyzed using the statistical package for social science version windows 16 software (SPSS Inc., Chicago, IL, USA). The data of height, age and pulmonary function parameters were expressed as means ± standard deviation Scatter plots of pulmonary function variables against height and age were examined initially for each gender. Normal distribution of the residuals was examined using Kolmogorov and Smirnov test. Consistency of variance of the error term was examined by the plot of absolute residuals against fitted values. Multiple regression analysis was used to produce prediction equations for each pulmonary function variable with the independent variables and a constant. Agreements between observed and predicted values were examined using Intra-class correlation coefficient (ICC). In addition, the predicted PFTs of the population (215 boys and 227 girls) derived from the predicted equations of the present study and from the various other studies[12-16] were compared with the measured PFTs using paired *t*-test. The age distribution of the above studies were 6-11, 5-14, 6-11, 6-16 and 5-11 years for Tsai *et al.*,[12] Kaditis *et al.*,[13] Budhiraja *et al.*,[14] Knudson *et al.*,[15] and Golshan *et al.*[16] respectively. In addition the prediction values for each set of the equation, were calculated and compared using the presence age population of the studied subjects (e.g. for equations, the predicted PFT values for studied children aged 6-10 years were calculated and compared with the PFT of the same aged children). The criterion of significance was $P < 0.05$.

RESULTS

A total of 442 subjects, including 215 boys and 227 girls, completed the pulmonary function measurements. Mean, median and also skew values, indicated a normal distribution of height and age among the population studied. The age distribution is detailed in Table 1. Mean values, ranges, medians and standard deviations values for height, age and each pulmonary function variable are shown in Table 2. The regression coefficients and constants for the prediction equations of PFTs are described in Table 3. Figure 1 gives an example of FEV_1 showing how PFTs varied with height and age among male and female subjects.

All PFT variables correlated positively with height and age. The largest positive correlations were found in boys for FVC ($r = 0.712$, $P < 0.001$) and girls for FEV_1 ($r = 0.580$, $P < 0.001$) with height and in boys for PEF (0.698, $P < 0.001$) and girls for MEF ($r = 0.624$, $P < 0.001$) with age. However, the lowest correlation was observed between MEF 25% ($r = 0.493$, $P < 0.001$) with age and MEF 75% ($r = 0.405$, $P < 0.001$) with height in boys but in girls, for FVC ($r = 0.499$, $P < 0.001$) with age and MEF 25% ($r = 0.556$, $P < 0.001$) with height.

ICC of observed and predicted values for FVC, FEV_1, PE, MEF_{75}, MEF_{50}, MEF_{25} and MEF_{25-75} were 0.854, 0.852, 0.801, 0.783, 0.754, 0.618 and 0.773 for boys and 0.691, 0.760, 0.769, 0.744, 0.761, 0.637 and 0.764 for girls respectively.

A comparison of PFTs derived by prediction equations from the present study with those calculated by some previous equations for the studied children revealed significant differences between most of the PFTs derived from the

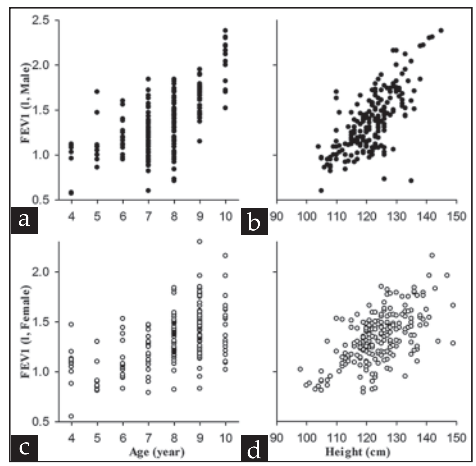

Figure 1: Scatter gram of measured FEV_1 against age (a and c) and height (b and d) in boy and girl subjects. The equations derived by linear regression are:
Boy: 0.090 (A) + 0.016 (H) − 1.233
Girl: 0.039 (A) + 0.013 (H) − 0.612

Table 3: Regression coefficients and constants for prediction equations of pulmonary function tests

Parameter	Boys					Girls				
	Height (cm)	Age (year)	Constant	RSD	R^2	Height (cm)	Age (year)	Constant	RSD	R^2
FVC (L)	0.020	0.081	−1.628	0.202	0.595	0.012	0.035	−0.449	0.226	0.359
SE	0.0019	0.0119	0.0808			0.0020	0.0124	0.1982		
FEV_1 (L)	0.016	0.090	−1.233	0.206	0.590	0.013	0.039	−0.612	0.203	0.442
SE	0.0018	0.011	0.1850			0.0018	0.0112	0.1802		
PEF (L/S)	0.011	0.319	−0.830	0.576	0.502	0.029	0.225	−2.409	0.638	0.454
SE	0.0046	0.029	0.4860			0.0059	0.0363	0.5821		
MEF_{75} (L/S)	0.007	0.350	−0.688	0.644	0.469	0.028	0.225	−2.402	0.685	0.421
SE	0.0050	0.031	0.5310			0.0061	0.0379	0.6084		
MEF_{50} (L/S)	0.009	0.230	−0.583	0.434	0.345	0.026	0.184	−2.221	0.568	0.443
SE	0.0030	0.0240	0.4090			0.0051	0.0314	0.5046		
MEF_{25} (L/S)	0.012	0.109	−0.804	0.392	0.288	0.020	0.097	−1.670	0.478	0.305
SE	0.0032	0.0200	0.3410			0.0044	0.0270	0.4333		
MEF_{25-75} (L/S)	0.006	0.242	−0.501	0.462	0.452	0.024	0.186	−2.221	0.549	0.447
SE	0.0037	0.0230	0.3880			0.0049	0.0304	0.4877		

FVC = Forced vital capacity; FEV_1 = Forced expiratory volume in one second; MMEF = Maximal mid-expiratory flow; PEF = Peak expiratory flow; MEF_{75}, MEF_{50}, and MEF_{25} = maximal expiratory flow at 75%, 50%, and 25% of the FVC, respectively; RSD = Standard deviation of residuals; SE = Standard error; R^2 = square regression prediction equations of present compared with those of previous studies [Table 4].

DISCUSSION

The results of this study present the PFT variables and predicted equations derived from 442 healthy boys and girls (aged 4-10 years) from an urban area in the northeast of Iran. The subjects have no history of cardiorespiratory disease and with a normal distribution of height and age among the study population and were drawn from various social classes. The prediction equations produced from these data provide normal values and ranges for PFTs, which have rarely been accurately examined for an Iranian population previously. Therefore, the prediction equations derived from the present study are suitable for low aged children.

The results of the present study showed that there are significant differences between predicted pulmonary function variables in Iranian children and those derived from most international studies.[12-16] Most of the PFT variables were higher than East Asian countries, but most PFTs were smaller than those calculated by European equations. Most of the studies evaluating PFT in non-European populations have shown greatly reduced lung volumes when compared to European-published reference values.[3,5-7]

Discrepancies observed among the different sets of prediction equations[12-16] with those of the present study may be due to various methodological factors influencing spirometric measurements, for example the equipment and technicians.[6,17] However, the most likely reason for the lower values of PFT derived from prediction equations of the present study may be due to ethnic differences among the study populations. In fact, significant differences in PFTs between race/ethnic groups of Caucasians, African-Americans and Mexican-Americans were demonstrated[7] but, reference equations from the mentioned study[5] were similar to those of other studies.[15,18,19] In fact, African-Americans with similar height for a particular age had lower values of FEV_1 than both Caucasians and Mexican-Americans[19,20] and among Asian-American male and female compared with European-Americans.[21]

Table 4: Comparison between PFT values of population undertaken in this study obtained by predicted equations of the present study with those of various other studies and measured pulmonary function tests

Study	FVC	FEV_1	MEF_{75}	MEF_{50}	MEF_{25}	MEF_{25-75}	PEF
Boys							
Measured	1.410±0.376	1.335±0.341	2.666±0.865	2.228±0.643	1.424±0.477	2.041±0.624	2.864±0.813
Present study	1.381±0.287	1.357±0.263	2.664±0.592	2.181±0.591	1.441±0.257	2.039±0.419	2.824±0.574
Statistical difference	0.341	0.586	0.946	0.146	0.519	0.942	0.306
Tsai *et al.*[12]	1.378±0.253	1.281±0.238	–	–	–	1.982±0.314	3.098±0.520
Statistical difference	*P*<0.001	*P*<0.001	–	–	–	*P*<0.001	*P*<0.001
Kaditis *et al.*[13]	1.608±0.334	1.353±0.267	–	1.952±0.316	0.996±0.126	1.788±0.260	–
Statistical difference	*P*<0.001	*P*<0.001	–	*P*<0.001	*P*<0.001	*P*<0.001	–
Budhiraja *et al.*[14]	1.158±0.312	–	–	–	–	1.137±0.402	2.203±0.401
Statistical difference	*P*<0.001	–	–	–	–	*P*<0.001	*P*<0.001
Knudson *et al.*[15]	1.437±0.342	1.307±0.201	–	–	–	1.943±0.265	2.743±0.582
Statistical difference	*P*<0.001	*P*<0.001	–	–	–	*P*<0.001	*P*<0.001
Golshan *et al.*[16]	1.694±0.110	1.052±0.040	0.997±0.065	2.151±0.140	3.218±0.274	1.823±0.119	3.282±0.213
Statistical difference	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001
Girls							
Measured	1.366±0.274	1.338±0.268	2.783±0.888	2.416±0.750	1.538±0.577	2.215±0.728	2.952±0.874
Present study	1.316±0.160	1.308±0.176	2.844±0.581	2.454±0.502	1.575±0.322	2.221±0.488	2.961±0.590
Statistical difference	0.274	0.236	0.173	0.311	0.234	0.875	0.854
Tsai *et al.*[12]	1.423±0.275	1.325±0.260	–	–	–	2.123±0.367	3.173±0.531
Statistical difference	*P*<0.001	*P*<0.001	–	–	–	*P*<0.001	*P*<0.001
Kaditis *et al.*[13]	1.557±0.368	1.385±0.312	–	2.088±0.388	1.065±0.142	1.846±0.255	
Statistical difference	*P*<0.001	*P*<0.001	–	*P*<0.001	*P*<0.001	*P*<0.001	–
Budhiraja *et al.*[14]	1.176±0.378	–	–	–	–	1.177±0.295	–
Statistical difference	*P*<0.001	–	–	–	–	*P*<0.001	–
Knudson *et al.*[15]	1.283±0.313	1.292±0.169	–	–	–	2.098±0.221	2.724±0.252
Statistical difference	*P*<0.001	*P*<0.001	–	–	–	*P*<0.001	*P*<0.001
Golshan *et al.*[16]	1.740±0.132	1.541±0.098	1.024±0.076	2.209±0.167	4.331±0.328	1.873±0.141	3.370±0.255
Statistical difference	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001	*P*<0.001

PFT = Pulmonary function tests; FVC = Forced vital capacity; FEV_1 = Forced expiratory volume in one second; MMEF = Maximal mid-expiratory flow; PEF = Peak expiratory flow; MEF_{75}, MEF_{50}, and MEF_{25} = Maximal expiratory flow at 75%, 50%, and 25%; NS = Non-significant

The PFT values derived from the equations of the present study were even different than those of other study of our country.[16] Although, MEF_{25} derived from Golshan *et al*. equation was higher the value of MEF_{25-75} was lower than the present study. Therefore, the most probable explanation for the differences between the PFT values derived from the present study and those of previous studies is probably the age distribution of the population of different studies. The age distribution of the studied population of the present study was 4-10 years old children. However, the age distribution of studied population of all other studies is children aged more than 6 years except that of Golshan *et al*. which was 5 years. In addition, the maximum age of other studies were 11 years or older. Therefore, the prediction equations derived from the present study are most suitable for low aged children.

Although there are negative correlations between different PFTs and age in adult populations, the results from the present study showed a positive correlation between PFTs and age. The cause of this observation is growing age in the studied population of the present study.

In previous studies, the predicted equations for PFT values of adult[8] and young adult (aged 10-18 years) population[9] in north-east region of Iran were obtained. In the present study these equations were obtained for very young children (aged 4-10 years). Measurement of PFT values in low old children are very difficult because cooperation of low old children for these measurements. However, in the present study, major efforts have been done to obtain the most accurate PFT values in studied population. The PFT measurements were done by a fully trained final year medical school. The children were fully trained before PFT measurement and thy encouraged to do their best during performance.

The novel findings of the present study are presenting predicted equations of spirometric variables for very young children (aged 4-10 years) from an urban area in the northeast of Iran. Although the study has performed in the city of Mashhad, the population of this city has immigrants from all over Iran and therefore it could represent Iranian population. The other limitation of the study is relatively low number of studied subjects, especially in age groups 4, 5 and 10. Although the population of the city of Mashhad are immigrants from all over Iran the population of this city could considered as representative of the Iranian population, more studies are needed to derive prediction equation of PFT values in children in a different part of Iran, combining the results of different part to obtain equations for predicted PFT values for Iranian population.

CONCLUSION

The results of this study provide PFT predicted equations derived from adequate number of healthy, Iranian low aged children with a relatively wide range of heights and ages. The small but significant differences between predicted equations of the present study compared with those of other studies indicate it is preferable to use PFT equations based on local data, which is supported by ATS and European Respiratory Society recommendations.

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