RESEARCH ARTICLE

Establishing age specific spirometry reference ranges for children/adolescents of Karachi, Pakistan: Randomized trials

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Abstract

Objectives: To establish age-specific normative spirometry reference range along with regression equation for children and adolescents.

Methods: The cross-sectional study was conducted from April to October 2017, and comprised children and adolescents aged 7-18 years at 8 educational institutions representing various socio-economic strata of Karachi. A modified version of the International Study of Asthma and Allergies in Childhood Questionnaire was used. Spirometry variables including forced vital capacity, forced expiratory volume in 1 second, ratio between the two, peak expiratory flow rate, forced expiratory flow between 25% and 75% expired volume were recorded and interpreted. By normal distribution curve the reference values were established, and mean ±2 standard deviation values were taken as significant. Pearson's correlation coefficient and linear regression models were calculated for all pulmonary variables with age.

Results: Of the 751 subjects, 484(64.4%) were boys and 267(35.5%) were girls. The overall mean age was 12.96±2.8 years. The mean lung volume for forced vital capacity was 2.21±0.75, forced expiratory volume in 1 second 2.08±0.73, ratio between the two 92.9±4.7, peak expiratory flow 231.3 ± 70.5 and forced expiratory flow between 25% and 75% expired volume was , , , 2.68±1.2. These lung volumes directly increased with age from children to adolescents ($p<0.05$). All variables showed a significant difference between boys and girls ($p<0.05$).

Conclusion: There was a linear positive correlation of age with lung function variables, while the boys presented higher values than the girls.

Keywords: Pulmonary function test, Spirometry, Forced vital capacity, forced expiratory volume, Regression analysis. (JPMA 69: 24; 2019)

Introduction

Respiratory diseases are responsible for the global increase in morbidity and mortality, especially among children and adolescents.[1] Focussing on the developing countries like Pakistan, the 2012 report of the World Health Organisation (WHO) showed that 34% of Pakistani population was under 15 years of age with high prevalence of respiratory diseases.[2] To diagnose these diseases, different pulmonary function tests are used and among them the spirometry is the gold standard one.[3]

Spirometry does not require either a complicated technique or the instrument and is a non-invasive procedure as well. It helps in easy evaluation of pulmonary function, describe the course of diseases that affect lung function and in measuring response to treatment.[4-6] An accurate diagnosis requires a good interpretation of results based on the availability of region-specific reference range as there are many modifiable as well as non-modifiable factors that can affect the lung function like age, gender, height, weight, ethnicity, socioeconomic status, cultural beliefs and biomass smoke exposure.[4,5,7]

To establish normative spirometry reference ranges, few studies have been done in South Asia and very few of them focus the children.[8,9] Literature review revealed only three studies in Pakistan that established the spirometry reference range in adults but there was no data for school-going children and adolescents.[6,10,11] Unfortunately, Pakistani children and adolescents are being diagnosed on the basis of Polgar and European Respiratory Society 1993 criteria in clinical practice.[12] On the other hand, studies reported that spirometry lung function of white children or adolescents are higher than the children or adolescents of South Asia, so Pakistani children and adolescents are being misdiagnosed.[13,14]

The current study was planned to establish age-specific normative spirometry reference range along with regression equation for children and adolescents in Pakistan.

Subjects and Methods

The descriptive cross-sectional study was conducted from April to October 2017, and comprised children and

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adolescents aged 7-18 attending primary, middle, secondary and higher secondary schools of Karachi. After approval was obtained from the ethics review committee of Ziauddin University and Hospital, Karachi, sample size was calculated using OpenEpi calculator.[15,16] Multistage sampling technique was utilised for selection of schools and subjects. In the first stage, 8 schools were randomly selected from all three socio-economic strata of Karachi. In the second stage, students were conveniently selected from those schools where entire sections corresponding to a particular age were selected for data collection. Consent was obtained from both school authorities and parents. Those children/adolescents outside the 7-18 year age limit, or who had history of trauma that can affect respiratory system, those diagnosed as a case of asthma, wheezing, allergic rhinitis, or any significant respiratory tract disease, or diagnosed for congenital heart diseases, or had muscular disorders like Duchene muscular dystrophy, those on bronchodilator therapy, those with chest wall deformity, and smokers were excluded. In addition, the International Study of Asthma and Allergies in Childhood (ISAAC) Questionnaire[17] was modified and used before performing the test. Height, weight and body measurements were recorded. Detailed general physical and systemic examination was done by a doctor. Spirometry was done using a spirometer (Vitalograph-alpha)which was calibrated before the test. American Thoracic Society/European Respiratory Society (ATS/ERS) Task Force 2005 standardisation guidelines[18] were used to assess lung volumes. Spirometry variables, including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1/FVC, peak expiratory flow rate (PEF), forced expiratory flow between 25% and 75% expired volume (FEF25-75), were recorded and interpreted.

Spirometry was performed in sitting position, and the noses of all subjects were pinched by using a nose clip. Minimum of three manoeuvres but not more than eight manoeuvres were taken. During the test, the investigator monitored the graph. From among the values, the best were taken for statistical analysis.

Data analysis was done using SPSS20.All quantitative variables were presented as mean and standard deviation (SD) while qualitative variables were presented as frequencies and percentages. By normal distribution curve, the reference values were established, and mean±2 SD were taken as significant. Pearson's correlation coefficient was calculated for all pulmonary variables with age (years). Linear regression models were calculated for all pulmonary variables with age. Data with $p<0.05$ was considered statistically significant.

Results

Spirometry was initially performed on 812 subjects, but data of 61(7.5%) subjects was excluded, and the final sample stood at 751(92.5%). Mean values for age, height, weight and pulmonary variables were noted (Table-1). The mean lung volume for FVC was 2.21±0.75, FEV1 was 2.08±0.73, FEV1/FVC ratio was 92.9±4.7, PEF was 231.3±70.5 and (FEF25-75) was 2.68±1.2 (Table-1).

Table-1: Mean Demographic and Pulmonary function variables.

Quantitative variables	Mean ± SD (n = 751)	Boys (n = 484)	Girls (n = 267)
Age	12.96 ± 2.8	13.1 ± 2.7	12.66 ± 2.8
Height (cm)	150.2 ± 15.8	152.3 ± 16.7	146.4 ± 13.3
Weight (Kg)	44.2 ± 16.6	45.3 ± 17.3	42.2 ± 15
BMI	19 ± 4.4	18.9 ± 4.3	19.2 ± 4.5
FVC	2.21 ± 0.75	2.28± 0.753	2.10± 0.74
FEV_1	2.08 ± 0.73	2.13± 0.726	1.97± 0.73
FEV_1/FVC	92.9 ± 4.7	92.93± 4.78	92.89± 4.49
PEF	231.3 ± 70.5	236.6± 73.59	221.6± 63.6
FEF_{25-75}	2.68 ± 1.2	2.78± 1.26	2.52± 1.06

SD: Standard deviation. BMI: Body mass index. FVC: Forced vital capacity
FEV_1: Forced expiratory volume in 1 second
PEF: Peak expiratory flow rate
FEF_{25-75}: Forced expiratory flow between 25% and 75% expired volume.

These lung volumes directly increased with age from children to adolescents and the eldest age group showed the highest range of lung volumes (Table-2).

All variables showed a significant difference between boys and girls except FEV1/FVC ratio which was higher than 90% among both genders (Table-3).

Discussion

Spirometry is used as a diagnostic test in clinical practice so area-specific normative reference values are essential for its authenticity.[19] The spirometry values progressively increase with age because of increase in muscular strength and the size of the chest[20] and the present study showed a strong positive correlation with age.

When comparing with the Global Lung Function Initiative (GLI) a multicentre study, the present study revealed that the mean FVC and FEV1values were lower than the values predicted by the team for South Asians.[21] Lung function values calculated in India showed lower values than the GLI reference values and supported the present study.[22] This may be due to the old data that was used by the GLI team in their study.

Table-2: Pulmonary function variables among different age groups.

Age	Variables	Mean±SD	Range
7 Years (n=13)	FVC	0.95± 0.13	0.69 - 1.21
	FEV_1	0.89± 0.15	0.61 - 1.19
	FEV_1/FVC	94.23± 4.34	---
	PEF	131.69± 15.04	101.9 - 162.0
	FEF_{25-75}	1.09± 0.059	0.97 - 1.21
8 Years (n=45)	FVC	1.13± 0.19	0.75 - 1.51
	FEV_1	1.03± 0.17	0.69 - 1.38
	FEV_1/FVC	91.53±5.08	---
	PEF	149± 13.54	121.9 - 176.1
	FEF_{25-75}	1.27± 0.18	0.91 - 1.63
9 Years (n=36)	FVC	1.27± 0.13	1.01 - 1.53
	FEV_1	1.16± 0.14	0.88 - 1.44
	FEV_1/FVC	91.06± 4.92	---
	PEF	150.94± 17.62	115.7 - 186.2
	FEF_{25-75}	1.36± 0.15	1.05 - 1.66
10 Years (n=52)	FVC	1.42± 0.25	0.93 - 1.91
	FEV_1	1.30± 0.25	0.8 - 1.81
	FEV_1/FVC	91.5± 4.19	---
	PEF	160.85± 16.47	127.9 - 193.8
	FEF_{25-75}	1.55± 0.20	1.15 - 1.95
11 Years (n=79)	FVC	1.65± 0.17	1.31 - 1.98
	FEV_1	1.51±0.18	1.14 - 1.88
	FEV_1/FVC	91.34± 5.18	---
	PEF	171.18± 26.72	117.7 - 224.6
	FEF_{25-75}	1.75± 0.28	1.20 - 2.31
12 Years (n=115)	FVC	1.91± 0.22	1.47 - 2.34
	FEV_1	1.78± 0.23	1.32 - 2.24
	FEV_1/FVC	93.23± 4.45	---
	PEF	195.5± 21.14	153.2 - 237.8
	FEF_{25-75}	2.11± 0.41	1.29 - 2.93
13 Years (n=82)	FVC	2.10± 0.21	1.69 - 2.51
	FEV_1	1.96± 0.23	1.50 - 2.42
	FEV_1/FVC	92.93± 4.55	---
	PEF	216.9± 19.58	177.7 - 256.1
	FEF_{25-75}	2.39± 0.22	1.95 - 2.83
14 Years (n=85)	FVC	2.41±0.23	1.95 - 2.88
	FEV_1	2.25±0.27	1.7 - 2.8
	FEV_1/FVC	93± 4.88	---
	PEF	249.58± 20.43	208.7 - 290.4
	FEF_{25-75}	2.82± 0.33	2.17 - 3.47
15 Years (n=77)	FVC	2.79± 0.22	2.35 - 3.23
	FEV_1	2.63± 0.23	2.16 - 3.10
	FEV_1/FVC	93.56± 4.62	---
	PEF	278.6± 17.42	243.8 - 313.4
	FEF_{25-75}	3.37± 0.35	2.67 - 4.10
16 Years (n=81)	FVC	3.05± 0.24	2.57 - 3.53
	FEV_1	2.90± 0.27	2.36 - 3.45
	FEV_1/FVC	94.44± 3.86	---
	PEF	310± 31.46	247.1 - 372.9
	FEF_{25-75}	3.87± 0.53	2.81 - 4.94
17 Years (n=68)	FVC	3.39± 0.27	2.85 - 3.94
	FEV_1	3.22± 0.23	2.76 - 3.68
	FEV_1/FVC	94.25± 4.22	---
	PEF	346.12± 41.25	263.6 - 428.6
	FEF_{25-75}	4.90± 0.74	3.43 - 6.37
18 Years (n=18)	FVC	3.52± 0.34	2.84 - 4.20
	FEV_1	3.29± 0.31	2.68 - 3.90
	FEV1/FVC	92.89± 4.86	---
	PEF	354.28± 59.89	234.5 - 474.1
	FEF25-75	5.17± 0.62	3.94 - 6.40

SD: Standard deviation. FVC: Forced vital capacity.
FEV_1: Forced expiratory volume in 1 second.
PEF: Peak expiratory flow rate.
FEF_{25-75}: Forced expiratory flow between 25% and 75% expired volume.

Table-3: Pearson's correlation coefficients of spirometry parameters with age.

Variables	R	R^2	Regression Equation	p-value
Boys (n= 484)				
FVC	0.944	0.892	(-1.154)+0.262(A)	0.000
FEV_1	0.937	0.878	(-1.156)+0.251(A)	0.000
PEF	0.892	0.796	(-80.725)+24.181(A)	0.000
FEF_{25-75}	0.898	0.806	(-2.699)+0.417(A)	0.000
Girls (n= 267)				
FVC	0.955	0.911	(-1.048)+0.249(A)	0.000
FEV_1	0.941	0.886	(-1.115)+0.244(A)	0.000
PEF	0.949	0.901	(-48.470)+21.343(A)	0.000
FEF_{25-75}	0.936	0.876	(-1.930)+0.352(A)	0.000
Total (n=751)				
FVC	0.948	0.898	(-1.123)+0.258(A)	0.000
FEV_1	0.939	0.881	(-1.147)+0.249(A)	0.000
PEF	0.908	0.825	(-69.027)+23.178(A)	0.000
FEF_{25-75}	0.906	0.821	(-2.416)+0.394(A)	0.000

FVC: Forced vital capacity, FEV_1: Forced expiratory volume in 1 second.
PEF: Peak expiratory flow rate
FEF_{25-75}: Forced expiratory flow between 25% and 75% expired volume.

Another study done in South India in the age group of 7-19 years showed a bit higher values in boys (FVC 2.43±0.07 and FEV1 2.14±0.06) but surprisingly lower values in girls (FVC 1.86±0.05 and FEV1 1.65±0.04) compared to the present study. The difference may be either due to the ethnicity, physical activity, cultural belief or the socioeconomic status.[23] On the other hand, a study in Gujrat region of India found overall lower spirometry values in the boys (FVC 2.0±0.46 and FEV1 1.76±0.38) as well as in the girls (FVC 1.91±0.47 and FEV1 1.69±0.40) compared to the present study.[24]

A comparison study on Caucasian and United Kingdom born Asians found that the spirometry values were lower in UK born Asians than the Caucasian, and concluded that ethnicity was the main reason behind the variation.[4]

The present study reported that pulmonary function values were higher in boys compared to girls. Multiple studies had similar this findings.[23-25] A possible explanation for this result is that the boys have larger lungs, more muscularity and different growth pattern so there should be a gender-based reference equation.[24] One study done on lung morphometry manifested that boys have larger lungs and more alveoli compared to girls.[26] One study mentioned sex hormone or the intracellular signalling pathway as a reason behind the gender difference in pulmonary function values.[27] On the other hand, a study in Taiwan showed no significant differences in lung function variables between the genders.[28]

Conclusion

Lung function variables are important for diagnosing obstructive and restrictive lung diseases as well as for therapeutic follow-up. The study found a linear positive correlation of age with lung function variables while the boys presented higher values than the girls. The spirometers used in hospital settings have western predictive values which are not valid for Pakistani population so the software in the equipment should be updated according to the present study.

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