ORIGINAL ARTICLE

SPIROMETRIC REFERENCE VALUES FOR CHILDREN/ ADOLESCENTS OF KARACHI

Sara Sadiq, Nadeem Ahmed Rizvi*, Syed Zaryab Ahmed, Moazzam Ali Shahid***, Zainab Rabail†, Arsalan Mehmood†**

Department of Physiology, CMH Institute of Medical Sciences Bahawalpur, *Department of Chest Medicine, Jinnah Postgraduate Medical Centre, **Department of Biochemistry, ***Research Department, †Physiology, Ziauddin University, Karachi, Pakistan

Background: Accurate diagnosis of respiratory disease requires region specific reference range. The objective of this study was to establish spirometry reference ranges for children and adolescents of Karachi, considering height as an independent variable. **Method:** This was a cross-sectional study conducted from Apr to Oct 2017. A questionnaire was referenced from the International Study of Asthma and Allergies in Childhood (ISAAC). Spirometry variables taken were Forced Vital Capacity (FVC), Forced Expiratory Volume in 1st second (FEV_1), FEV_1/FVC ratio, Peak Expiratory Flow Rate (PEF), Forced Expiratory Flow between 25% and 75% expired volume (FEF_{25-75}). The reference values were established using normal distribution curve; Mean±2SD was taken as significant. The linear regression models were calculated for all pulmonary variables with the age and height. Data with $p<0.05$ was considered as statistically significant. **Results:** The FVC, FEV_1, FEV_1/FVC, PEF and FEF_{25-75} were 2.21±0.75 L, 2.08±0.73 L, 92.9±4.7%, 231.3±70.5 L/min and 2.68±1.2 L/Sec, respectively. The lung volumes were directly increasing with height from children to adolescents. There was a strong positive correlation between height and pulmonary variables, including FVC, FEV_1, PEF and FEF_{25-75}. **Conclusion:** The current study establishes a normative reference range along with a prediction equation for children and adolescents of age group 7–18 years of Karachi. There was a strong positive correlation of height with the spirometry variables.

Keywords: Pulmonary function test, Spirometry, Forced vital capacity, Forced expiratory volume, Regression analysis

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INTRODUCTION

Respiratory diseases are one of the common causes of morbidity and mortality worldwide. Considering the children and adolescents, the most frequent reason among them for consulting a general practitioner are respiratory tract diseases.[1] For the diagnosis of these respiratory tract diseases, multiple pulmonary function tests are widely used to assess the lung function. Spirometry is considered as a gold standard technique.[2]

Spirometry is simple, safe and non-invasive technique widely used in clinical practice to assess lung function, diseased status and follow up after medications.[3–5] For correct diagnosis it is important to interpret the results appropriately which depend upon the population as well as area specific reference range. Literature revealed wide variations among reference ranges of different populations. The reason behind variation may be factors that affect pulmonary function, including age, sex, height, weight, ethnicity, socioeconomic status, cultural values and biomass smoke exposure.[3,4,6]

Looking over South Asia, few studies have focused on establishing a spirometry reference range for children and adolescents.[7,8] Considering developing countries, especially Pakistan, studies have established a reference range for an adult population. However, no study has been done for children and adolescents in Pakistan.[5,9,10] So in clinical practice, children and adolescents are diagnosed on Polgar reference ranges which is a reason behind false positive or false negative results.[11] Multiple studies revealed a higher spirometric reference range among Caucasian children and adolescents when compared with Asians.[12,13] Looking over the Global Lung Initiative (GLI 2012) reference values, it has been mentioned that there is a lack of reference values for South Asian population because the data provided by South Asians was not comparable with the mean results.[14,15] On the other hand, multiple studies reported differences among the GLI reference range and the measured range for that particular region.[8,14,16] The objective of this study was to establish spirometric reference values for children and adolescents of Karachi, considering height as an independent variable.

METHODS

This was a cross-sectional study carried out from April to October 2017. Data was collected from children and adolescents of primary, middle, secondary and higher secondary schools of Karachi. Ethical review committee of Ziauddin University and Hospital approved the study. Consent was taken from school authorities and parents; and from the subjects. Multistage sampling technique was used in which 8 schools were randomly selected from all three socioeconomic strata while in the second stage students of particular age groups were conveniently taken from those schools.

The children and adolescents were excluded from the study if the age of the child was less than 7, had history of trauma that can affect respiratory system, was a diagnosed case of asthma, wheezing, allergic rhinitis, or any significant respiratory tract disease, was diagnosed for congenital heart diseases, had muscular disorders, e.g., Duchenne muscular dystrophy, was on bronchodilator therapy, had chest wall deformity, or was a smoker. International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was modified, validated and used for the study.

Height of the subjects (in Cm) was recorded in standing position without shoes by using a wall scale. Weight (Kg) was taken bare-footed with light clothes. Detailed physical examination was performed.

Vitalograph-alpha®, was used for spirometry. The instrument was calibrated before the test. American Thoracic Society/European Respiratory Society (ATS/ERS) task force 2005 standardization guidelines[17] were followed. Forced vital capacity (FVC), Forced Expiratory Volume in 1st second (FEV_1), FEV_1/FVC ratio, Peak Expiratory Flow rate (PEF), Forced Expiratory Flow between 25% and 75% expired volume ($FEF_{25–75}$) were measured/calculated.

The spirometry was done at room temperature. Spirometric values were recorded in sitting position with a nose-clip applied to pinch the nose. A disposable mouth piece was attached to the hose pipe of spirometer. The participants were asked to take a deep breath, and to blow out air into the mouth piece as rapidly and completely as possible. Three to eight readings were taken to attain the reproducibility criteria. The operator monitored the graph and followed the repeatability as well as acceptability criteria of ATS/ERS task force 2005 standardization guidelines.

Descriptive analysis was done using SPSS-20. All quantitative variables were presented as Mean±SD. By normal distribution curve the normative reference range were established, taking Mean±2 SD as significant. Pearson's correlation coefficient was calculated for all pulmonary variables with height (Cm). The linear regression models were calculated for all pulmonary variables with the age and height. Data with $p<0.05$ was considered as statistically significant.

RESULTS

A total of 1085 participants were included in the study. Spirometry was performed on 751 participants. The demographic variables including age, height, weight and pulmonary variables are given in Table-1. There was a significant variation among boys and girls for all spirometric variables including FVC, FEV_1, PEF and $FEF_{25–75}$. Both genders had >90% FEV_1/FVC ratio.

The participants were divided into 8 groups at 10 Cm height intervals starting at a height of 108 Cm. Table-2 manifests the spirometry variables among different height groups. All variables are mentioned as mean ± standard deviation along with a normative range for that particular height group. The data reported that lung volumes were directly proportional with height; increasing from children to adolescents.

Table-1: Mean Demographic and Pulmonary Function variables

Quantitative variables	Mean±SD		
	Total (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 (Kg/m²)	19±4.4	18.9±4.3	19.2±4.5
FVC (L)	2.21±0.75	2.28±0.753	2.10±0.74
FEV_1 (L)	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 (L/Min)	231.3±70.5	236.6±73.59	221.6±63.6
FEF_{25-75} (L/Sec)	2.68±1.2	2.78±1.26	2.52±1.06

Table-2: Height based Mean±SD and Normative Range of Spirometric variables

	Group-A (108–117 Cm)	Group-B (118–127 Cm)	Group-C (128–137 Cm)	Group-D (138–147 Cm)	Group-E (148–157 Cm)	Group-F (158–167 Cm)	Group-G (168–177 Cm)	Group-H (178–187 Cm)
FVC (L)								
Mean±SD	1.0±0.18	1.16±0.18	1.51±0.34	1.86±0.43	2.35±0.47	2.76±0.51	3.02±0.47	3.29±0.45
Range	0.64–1.36	0.81–1.52	0.83–2.19	1.01–2.72	1.41–3.29	1.74–3.78	2.08–3.96	2.39–4.19
FEV_1 (L)								
Mean±SD	0.91±0.15	1.07±0.17	1.39±0.34	1.73±0.43	2.22±0.48	2.59±0.52	2.84±0.47	3.13±0.44
Range	0.61–1.21	0.73–1.41	0.71–2.07	0.87–2.59	1.26–3.18	1.55–3.63	1.9–3.78	2.25–4.01
FEV_1/FVC (%)								
Mean±SD	91.8±4.12	92.2±4.49	91.6±9.74	92.53±9.34	93.74±4.12	93.2±4.8	93.39±5.04	93.8±4.8
PEF (L/Min)								
Mean±SD	144.6±24.78	148.06±16.23	169.58±26.95	190.97±39.8	241.07±48.1	276.5±46.6	307.9±54.26	351.6±67.26
Range	95.0–194.2	115.6–180.5	115.7–223.5	111.4–270.6	144.9–337.3	183.3–369.7	199.4–416.4	217.1–486.1
FEF_{25-75} (L/Sec)								
Mean±SD	1.25±0.36	1.29±0.14	1.66±0.48	2.1±0.58	2.77±0.8	3.45±0.91	3.98±1,03	4.83±1.05
Range	0.53–1.97	1.01–1.57	0.72–2.62	0.94–3.26	1.17–4.37	1.63–5.27	1.92–6.04	2.73–6.93

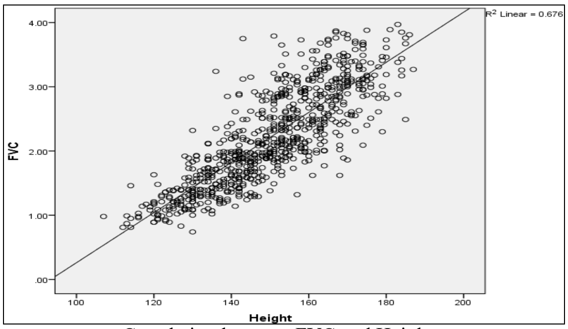
The distribution of data in relation to height is mentioned in the Figure-1. The scatter plots with regression lines displayed a linear correlation. All pulmonary variables including FVC, FEV_1, PEF and $FEF_{25–75}$ show strong positive correlation with height.

Considering all factors that can affect the spirometric reference range including age, sex, height, weight, socioeconomic status, cultural factors and biomass smoke exposure, the results show that age and height are the two main independent factors. Both of them have a direct correlation with spirometric variables.

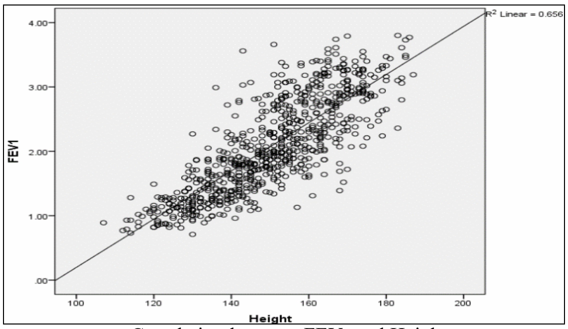
Table-3 shows Pearson's correlation coefficients of spirometry variables by putting age and height as an independent variable and this can be considered as the best predictor for lung function among children and adolescents. All spirometry parameters have strong positive correlation with age and height of the participants (p<0.000). Scatter plots with regression lines displayed a linear correlation. According to age and height the regression equations for FVC, FEV_1, PEF and $FEF_{25–75}$ are also mentioned in Table-3.

Table-3: Pearson's correlation coefficients of spirometric parameters with age and height

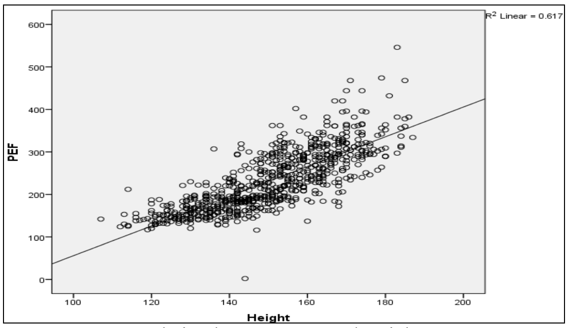
Variables	R	R^2	Regression Equation	*p*
FVC	0.949	0.901	(-1.537)+0.235(A)+0.005(H)	0.000
FEV_1	0.940	0.883	(-1.488)+0.23(A)+0.004(H)	0.000
PEF	0.909	0.827	(-103.465)+21.303(A)+0.391(H)	0.002
$FEF_{25–75}$	0.907	0.823	(-2.939)+0.365(A)+0.006(H)	0.005



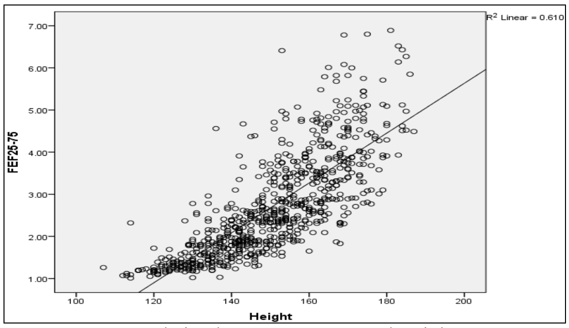
Correlation between FVC and Height



Correlation between FEV_1 and Height



Correlation between PEF and Height



Correlation between $FEF_{25–75}$ and Height

Figure-1: Linear correlation among spirometric variables and height

DISCUSSION

Spirometry is considered as a diagnostic tool in clinical practice and epidemiological work to assess lung function and environmental exposure. Area specific normative reference values are important for its reliability.[18,19] The current study establishes a normative reference range along with prediction equation for children and adolescents of Karachi in 7–18 years age group.

Multiple studies have reported that height has a linear correlation with lung volumes.[20,21] The current study supports this finding. Sonnappa *et al*[14] found that Indian children have lower spirometric volumes when compared with their age mates, who had the same ancestry but lived abroad. The reason behind this difference might be that children living in a developing country, are malnourished having less height and weight parallel to children living in a developed country with the same age and ancestry.

A Chinese study noted that lung size increases with height. Thus, lung capacities and volumes are directly correlated with height.[22] Height shows a linear type of relationship with lung volumes.[16] A few studies considered height as an independent variable having a high coefficient of correlation.[23,24] Due to this reason, one study excluded age from the prediction equation by keeping height as the main variable. Though this created bias, the problem was resolved by using height and age both as independent variables in the equation.[8] The current study also established the prediction equation by putting age and height as independent variables.

When comparing with the GLI multicentre study, the current study disclosed that the mean FVC and FEV_1 were 2.76 L and 2.59 L respectively. This is lower than the predicted values of GLI team for Asians (4.12 L and 3.61 L) among the individual with height up to 160 Cm. Individuals with height up to 180 Cm had a FVC of 3.29 L and FEV_1 of 3.13 L measured in current study compared to GLI values for Asians (5.47 L and 4.68 L respectively).[15] One Indian study supported our findings showing lower spirometry lung volumes as compared to the reference range given by GLI team.[14] A Gypsy study that concluded lower spirometry lung volumes as compared to those predicted by Quanjer's team also favoured our findings.[25] This shows that the reference range given by GLI team is not accurate for the Asian population. According to the GLI team, the data provided by Asians to them was not accurate.[14,15]

The limitation of the study is that participants were only from Karachi, so the equation developed is not suitable for all regions of Pakistan. There should be a multicentre study to update the current reference equation.

CONCLUSIONS

The current study establishes a normative reference range along with prediction equation for children and adolescents of age group 7–18 years of Karachi. There is a strong positive correlation of height with spirometric variables. The boys have higher spirometric values as compared to girls.

REFERENCE

1. Stanojevic S, Wade A, Stocks J. Reference values for lung function: past, present and future. Eur Respir J 2010;36(1):12–9.
2. Lum S, Bountziouka V, Quanjer P, Sonnappa S, Wade A, Beardsmore C, *et al*. Challenges in collating spirometry reference data for South-Asian children: an observational study. PloS One 2016;11(4):e0154336.
3. Strippoli MP, Kuehni CE, Dogaru CM, Spycher BD, McNally T, Silverman M, *et al*. Etiology of ethnic differences in childhood spirometry. Pediatrics 2013;131(6):e1842–9.
4. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Eur Respir J 1993;16(6 Suppl):5–40.
5. Nadeem M, Raza S, Malik M. Ventilatory function of healthy, urban, non smoking, Pakistani young adults aged 18–24 years. Respir Med 1999;93(8):546–51.
6. Mohammed J, Maiwada SaA, Sumaila FG. Relationship between anthropometric variables and lung function parameters among primary school children. Ann Niger Med 2015;9(1):20–5.
7. Kumar R, Seibold MA, Aldrich MC, Williams LK, Reiner AP, Colangelo L, *et al*. Genetic ancestry in lung-function predictions. N Engl J Med 2010;363(4):321–30.
8. Jiang M, Gao Y, Zhong NS, Chen WQ, Guan WJ, Zheng JP. Spirometric reference values for healthy Han children aged 5–15 years in Guangzhou, southern China. Pediatr Pulmonol 2015;50(10):1009–16.
9. Memon MA, Sandila MP, Ahmed ST. Spirometric reference values in healthy, non-smoking, urban Pakistani population. J Pak Med Assoc 2007;57(4):193–5.
10. Bhatti U, Rani K, Memon MQ. Variation in lung volumes and capacities among young males in relation to height. J Ayub Med Coll Abbottabad 2014;26(2):200–2.
11. Quanjer PH, Borsboom GJ, Brunekreef B, Zach M, Forche G, Cotes JE, *et al*. Spirometric reference values for white European children and adolescents: Polgar revisited. Pediatr Pulmonol 1995;19(2):135–42.
12. Whitrow MJ, Harding S. Ethnic differences in adolescent lung function: anthropometric, socioeconomic, and psychosocial factors. Am J Respir Crit Care Med 2008;177(11):1262–7.
13. Whittaker AL, Sutton AJ, Beardsmore CS. Are ethnic differences in lung function explained by chest size? Arch Dis Child Fetal Neonatal Ed 2005;90(5):F423–8.
14. Sonnappa S, Lum S, Kirkby J, Bonner R, Wade A, Subramanya V, *et al*. Disparities in pulmonary function in healthy children across the Indian urban-rural continuum. Am J Respir Crit Care Med 2015;191(1):79–86.
15. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, *et al*. Multi-ethnic reference values for spirometry for the 3–95 year age range: the global lung function 2012 equations. Eur Respir J 2012;40(6):1324–43.
16. Takase M, Sakata H, Shikada M, Tatara K, Fukushima T, Miyakawa T. Development of reference equations for spirometry in Japanese children aged 6–18 years. Pediatr Pulmonol 2013;48(1):35–44.
17. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, *et al*. Standardisation of the measurement of lung volumes. Eur Respir J 2005;26(3):511–22.
18. Falaschetti E, Laiho J, Primatesta P, Purdon S. Prediction equations for normal and low lung function from the Health Survey for England. Eur Respir J 2004;23(3):456–63.
19. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, *et al*. Interpretative strategies for lung function tests. Eur Respir J 2005;26(5):948–68.
20. Al-Riyami BM, Al-Rawas OA, Hassan MO. Normal spirometric reference values for Omani children and adolescents. Respirology 2004;9(3):387–91.
21. Chhabra SK, Kumar R, Mittal V. Prediction equations for spirometry for children from northern India. Indian Pediatr 2016;53(9):781–5.
22. Ma YN, Wang J, Dong GH, Liu MM, Wang D, Liu YQ, *et al*. Predictive equations using regression analysis of pulmonary function for healthy children in Northeast China. PloS One 2013;8(5):e63875.
23. Singh V, Kurrey V, Khandwal O, Phulijhele S. Evaluation of Lung Function by Spirometry in 12–14 years Adolescents in schools of Raipur city Chhattisgarh. Int J Med Sci Res Pract 2014;1(1):9–15.
24. Chhabra S, Vijayan V, Rahman M, Mittal V, Singh P. Regression equations for spirometry in children aged 6 to 17 years in Delhi region. Indian J Chest Dis Allied Sci 2012;54(1):59–63.
25. Kaditis AG, Gourgoulianis K, Tsoutsou P, Papaioannou AI, Fotiadou A, Messini C, *et al*. Spirometric values in Gypsy (Roma) children. Respir Med 2008;102(9):1321–8.

Address for Correspondence:

Dr Sara Sadiq, Department of Physiology, CMH Institute of Medical Sciences Bahawalpur, Pakistan. **Cell:** +92-335-2127642

Email: dr.sarabhatti@gmail.com

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