Lung Function Parameters in Healthy Libyan Children and Adolescents aged between 4-19 years

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Abstract:

***Background**:* No appropriate reference values of lung function parameters exist in healthy Libyan children with which the same parameters of pediatric respiratory patients of this country can be compared. Our aim; to asses lung function parameters in Libyan healthy children to use inassessment of lung function abnormalities in children with respiratory disease.

Methods:Spirometeric values were measured in a group of 449 healthy Libyan children and adolescents (226 boys and 223 girls), aged between 4-19 years old. Multiple linear analysis was performed for each spirometric parameter against age, weight, height and BMI.

Results: The values of the measured parameters increased nonlinearly and correlated significantly with body height (P< 0.05); the correlation was much lower with age. The best-fit regression equation relating the measured parameters values and body height was a simple power function providing the possibility to calculate the mean value with lower and upper limits for each parameter. No statistical significant differences of the studied functional parameters were found between boys and girls.

Conclusions:our reference values are close to those of the European children. These developed predictive values can be used in clinical practice in Libya and in other neighboring North African countries.

Keywords: lung function tests, Expiratory flow-volume curves

Introduction:

Lung function parameters have been shown to be race and ethnic specific in both children and adults. Values of spirometry are varying among subjects of similar age, gender, height and smoking status and between different ethnic groups (1).Lung function parameters have been shown to be race and ethnic specific in both adults and children (2-6). In various populations of healthy children the reference (predicted, standard, and normal) values and equations for their calculation have been established (5, 7-10). It is claimed that a reliable interpretation of lung function tests in different ethnic populations requires reliable (i.e. ethnic specific) reference values (2-6, 9).Among Arab populations of children peak expiratory flow was measured in healthywas significantly lower than in Swedish and British children (11-13). Spirometric reference values of forced vital capacity and forced expiratory volume in one second in Omani children and adolescents were also shown to be 5 to 10% lower than the respective values in Caucasian groups of children (14). The purpose of this study was to establish more recent, and reliable reference values in healthy Libyan children and adolescents against which pediatric respiratory patients of this country could be compared.Furthermore; low socioeconomic status in childhood is inversely related to lung function in adulthood (15).

Material and Methods:

In 449 healthy Libyan children and adolescents (226 boys and 223 girls, age range: 4-19 years. Lung function studies were performed in cross-sectional measurements. Children were of Arab origin and have lived in north-west of Libya. The subjects were recruited from schools. The study was carried out over the period of 2 years Informed consent was obtained from the parents of all studied children.Prior to lung function testing children and their parents were asked for medical history of children. Then the children were clinically examined. They were free of respiratory, cardiac or other diseases and considered as completely healthy subjects without smoking history. Body height was measured without shoes and socks.Experienced personnel measured lung function tests in the standing position of children whilewearing a nose clip. Before started of testing, the whole procedure of measurement was explained to each child, primarily how to perform the expiratory and inspiratory maneuvers. In our cohort; maximum expiratory flow-volume (MEFV) and inspiratory flow-volume curves were recorded with a Spirometer ZAN 100 Handy (Germany). From the curves were measured forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow (PEF), maximum expiratory flows at 75%, 50%, and 25% (MEF_{75}, MEF_{50}, and MEF_{25}), maximum mid-expiratory flow ($MMEF_{25-75}$), area delineated by MEFV curve (A_{ex}), and peak inspiratory flow (PIF). In each child 3-5 curves were obtained within the 5-20- min intervals. Maximum expiratory flows (MEFs),

PEF, and FEV_1 were also expressed per unit of FVC as a correction for lung size. In each child 3-5 curves were obtained. The best MEFV curve was automatically selected by a spirometric program according to ATS criteria (16) and to our criteria (reproducibility of the descendent portion of MEFV curve, elimination of curves with incomplete exhalation to residual volume level, and submaximal expiratory effort).

Statistical analysis:

All studied lung function parameters were correlated with body height and age. Single regression equation was calculated for each relationship between the measured parameter and body height or age (linear, power, and exponential) with standard deviation (SD) around regression by using the Statistical Program Statgraphics and Microsoft-Excel. By this manner the upper (+2SD) and lower (-2SD), 95% confidence limits from the regression line (mean value) were obtained. The choice of the best-fit model for each relationship was made according to the highest correlation coefficient. The statistical significance of correlation coefficient was set at $P<0.05$.

Results:

Our cohort is 449 healthy children (226 boys) from the middle socio-economic class, mean age: 11.4 years. Standing body height range was 97-182 cm, mean height: 141.2 cm, median height: 144 cm) (Table 1,2). We note that the correlation was better with body height than with age of children (Figs.1-3, Table 3) and the values of the measured lung function parameters significantly and nonlinearly increased with increasing standing body height in boys and girls ($P<0.0001$). In addition;the coefficient of variation around regression line was smaller for body height than for age of children. Therefore, we did not analyze further the data with respect to age.

The simple regression equation as a power function (**$y = a. x^b$**) was found as a best-fit model for expressing the relationship of functional parameters on body height. This mode of equation was transformed into a logarithmic one, i.e. **$\ln y = \ln a + b. \ln x$,** (**ln**: natural logarithm, **y**: functional parameter, **a**: intercept which equals ln a, **b**: slope of the regression line, **x**: body height in cm). From the anti-ln y value the mean absolute value of a given parameter was calculated. By adding or subtracting 2 standard deviations (±2SD) to the mean value, the 95% confidence limit (physiological variability) of the given functional parameter was computed. Based on the numbers of SD from the mean value (z-score) the grade of peripheral and central airway obstruction were classified into several categories (Table 4).Table 3 showed; the summarizes of 23 regression equations for calculation of the studied parameters on body height, standard deviation (SD) from the regression line, coefficient of variation around the regression line in negative (down) and positive (up) directions, and correlation coefficient (r). Figures 1-4 depict individual data, regression lines, and 95% confidence limits (±2SD) around regression lines. No significant differences in the measured parameters were found between boys and girls, statistically not significant (P= 0.17). Among the traditional functional parameters the new parameter of area delineated by the MEFV curve (A_{ex}) was introduced.The values of MEFs, PEF, and FEV_1 expressed per unit of FVC in order to correct these parameters for lung size significantly decreased with increasing body height (r = -0.37 to -0.52, P<0.0001), (Fig. 4, Table 5).

Discussion:

There is lake of recent data of lung function parameters in healthy Libyan children and adolescents, there is only one study of FVC and FEV_1 was published on 1988 (17). From North African Countries, Trabelsi et al. (11) was giving a larger number of spirometric reference values in healthy Tunisian Arab children.The basic requirement for getting reliable MEFV curve was the presence of a reproducible descending portion in a series of the MEFV curves. The representative MEFV curve in a given child was that one with the reproducible descending portion of the MEFV curve, largest FVC and FEV_1. We assume that such MEFV curve reflected expiratory airflow limitation and was appropriate for the analysis. Therefore the obtained lung function parameters could be considered as reference values for this group of children and adolescents. The representative peak inspiratory flow (PIF) in a child was that with the largest value of PIF in a series of forced inspiratory maneuvers.

A simple power function was a best fit regression equation; it showed a non-linear relationship between functional parameters and body height. This function was also advantageous since the coefficient of variation around the regression line (mean value) was the same for the entire range of body height in the studied subjects. Based on the coefficient of variation around the regression line the z-score (number of SD from the mean) for a given parameter was possible to calculate and the patency of airway passages to classify into 5 categories as normal and reduced, i.e.mild, moderate, severe, and very severe (Table 4). The coefficient of variation in the upper direction from the regression line fitted as power function was also larger than that in the lower direction (Table 3).

Since no significant differences in the measured parameters were found between boys and girls the present functional parameters can be used equally in both boys and girls. It makes the evaluation of lung function easier. This pattern is the same as in other similar studies (18, 19, 21, 22). The recently presented parameter of A_{ex} having a unit of l^2/sec was found to be very valuable in the assessment of induced bronchoconstriction and bronchodilation (20).

The significant decrease of the ratios MEF_{25}/FVC, MEF_{50}/FVC, MEF_{75}/FVC, PEF/FVC, and FEV_1/FVC characterizing the maximum expiratory flows, PEF, and FEV_1 as a fraction of FVC suggested a physiological reduction of airway caliber with regard to lung volume (lung size) with growth of children and adolescents (Fig. 4, Table 5). The latter ratios also suggested that lungs and airways as a whole do not grow isotropically as originally reported (21). These findings are similar to some already published (22). We considered FVC as a measure of lung size and all lung fuction parameters to be normal in our studied subjects. Since FVC was assumed to be normal and a measure of lung size the latter ratios suggested maximal flows, PEF, and FEV_1 to be corrected for lung size.

In obstructive lung conditions FVC can be abnormal and misleading in a lung size assessment. In this respect only total lung capacity has been considered as an appropriate functional assessment of lung size. In restrictive lung diseases lung size corrected MEFs, PEF, and FEV_1 play an important role in a proper evaluation of the reduced MEFs, PEF and FEV_1, i.e. airway obstruction. The absolute values of maximum expiratory flows, PEF, and FEV_1 can be reduced in such conditions not only from the reduction of airway diameter (constriction, inflammation of airways) but also from the reduction of lung volume and consequently from the deficient air supply for airflow in the airways. By using the ratios MEFs/FVC, PEF/FVC, and FEV_1/FVC in the evaluation of airway patency two groups of patients with lung restriction conditions can be distinguished. In a situation when the latter ratios are reduced the cause of decreased absolute values of MEFs, PEF, and FEV_1 is in the diminished airway diameter (airway obstruction). When the latter ratios are within normal limits then the reduction of absolute values of MEFs, PEF, and FEV1 is due to the reduced lung volume.

It was rather difficult to compare the present lung function parameters standards with those similar from other Arab ethnic populations. In the study of Shamssain et al (17) in Libyan childrenthe only measured parameters FVC and FEV_1 were 10% lower than our current lung function standards. Other lung function standards published in Arab children provided a limited number of parameters (12-14).

The difference in FVC between the present study and that from Tunisia et al (11); was less than 1%, and the difference in FVC with Czech study varied from less than 1% to 7% (18,19). Since no statistical significant differences were observed for FVC, FEV_1, and A_{ex}($P=0.06$) and minor differences were found for MEFs ($P<0.03$) between the present and Czech standards (Table 6); we might use both lung function standards in children in both countries. In addition; this current Libyan lung function standards are also suitable for Tunisian children because of non-significant differences between both groups of children.

Conclusion:

The obtained values increased most significantly with standing body height and were similar to those in Tunisian and in Central Europe children. The racial as well as gender differences were not observed. The maximum expiratory flows corrected for FVC (lung size) suggested larger airway patency in smaller chidren and non-isotropically growth of lungs.

This recent lung function parameters might serve as reference (predicted) values not only in Libyan children and adolescents but also in those of Arab origin from North Africa and white Caucasian children and adolescents from the Central Europe.

No conflict of interest

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Figures

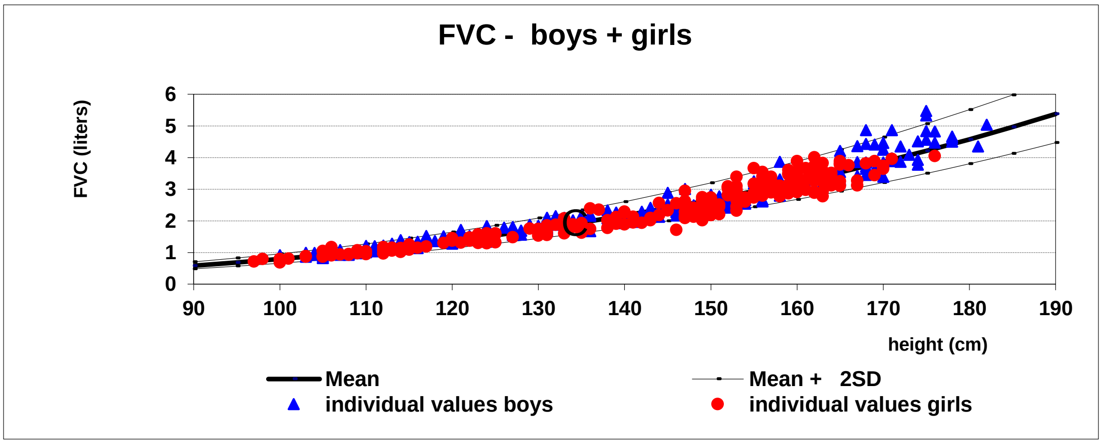

Fig. 1: Relationship of FVC (L) to body height (cm) in boys and girls. The heavy line indicates the mean value; the weak lines indicate ± 2 standard deviations from the mean

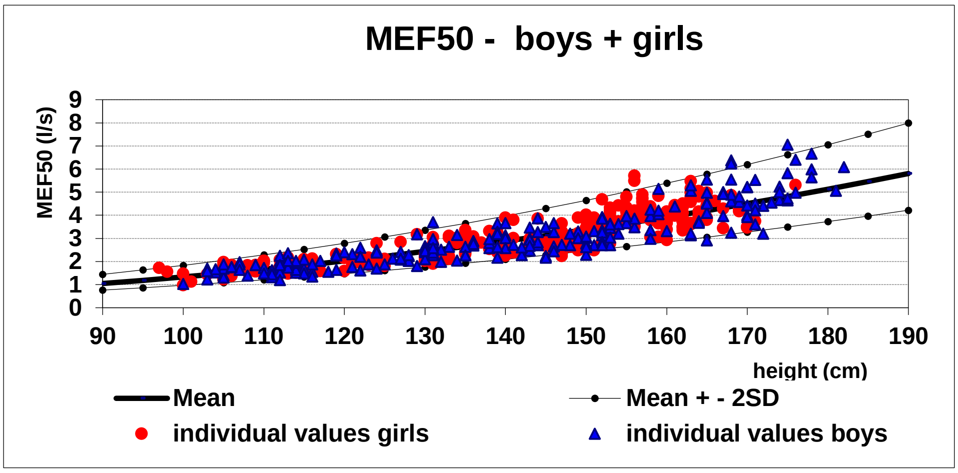

Fig. 2:Relationship of MEF_{50} (L/s) to body height (cm) in boys and girls

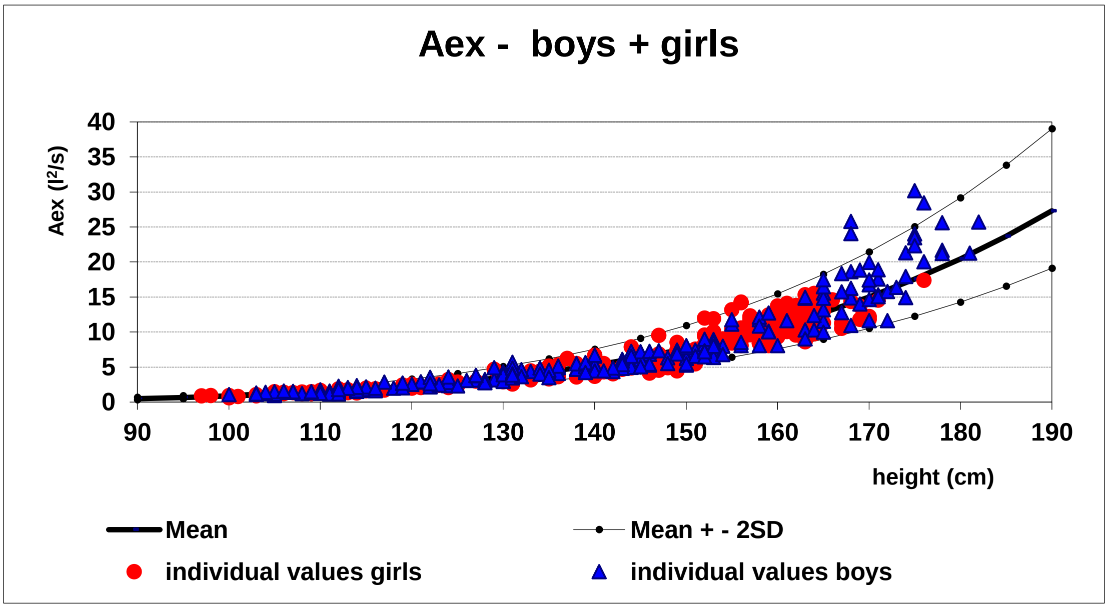

Fig.3: Relationship of A_{ex} (area under MEFV curve), (L^2/s) to body height (cm) in boys and girls

Height (cm)	70	171-182
No. of subjects		30

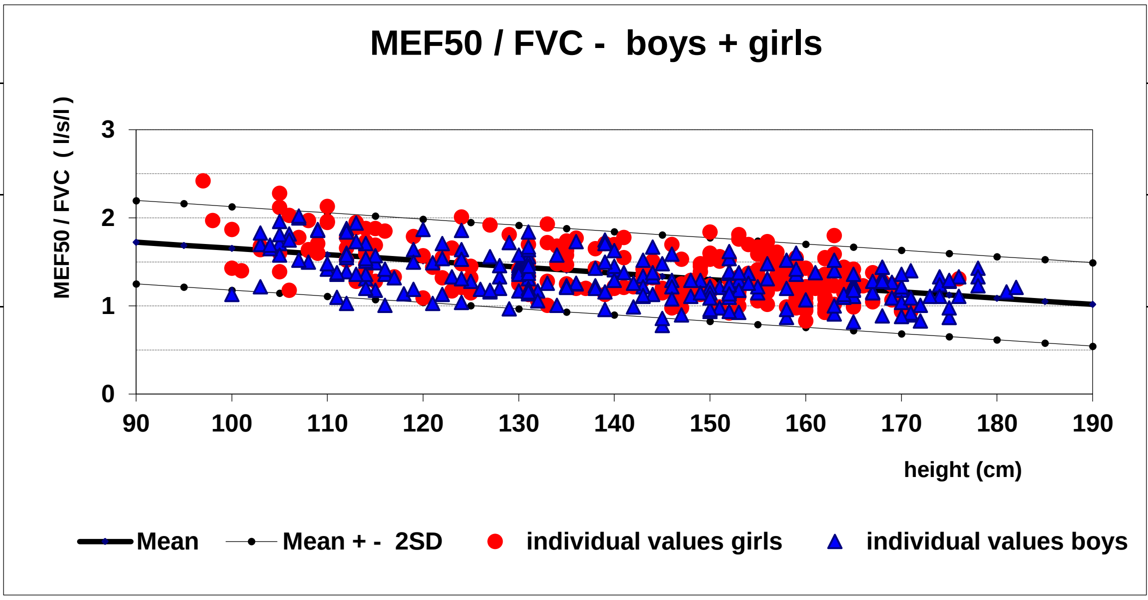

Fig.4: Relationship of MEF_{50}/FVC (L/s/L) to body height (cm) in boys and girls

Tables

Table 1- Frequency Distribution of Age in 449 Healthy Libyan children and Adolescents

Age (years)	**4-6**	**7-14**	**15-19**
No. of subjects	108	197	144

Table 2: Frequency Distribution of Body Height in 449 Healthy Libyan Children and Adolescents

Table 3: Regresion Equations of Functional Parametars in Relation to Body Height (Midline), Standard Deviation (SD) and Coefficient of Variation Around Regression

Regression equation	SD	CV (%) down/up	r
ln FVC (L), m= -13.7394 + 2.94169. ln height (cm)	0.0868	7.9/9.7	0.98
ln FVC (L), f = -14.2632 + 3.03736 . ln height (cm)	0.0910	8.2/10.0	0.98
ln FVC(L),m+f=-13.9452 + 2.97828 . ln height (cm)	0.0926	8.6/10.4	0.98
ln FEV_1 (L),m=-13.0461 + 2.78554 . ln height (cm)	0.0843	8.3/8.8	0.98
ln FEV_1 (L), f=-13.5158 + 2.87245 . ln height (cm)	0.0820	7.9/8.5	0.98
ln FEV_1(L),m+f=-13.2380 + 2.8203 . ln height (cm)	0.0856	7.8/9.4	0.98
ln PEF(L/s),m+f=-11.4261 + 2.6008 . ln height (cm)	0.1380	12.1/15.9	0.94
ln PEF (L/s), m=-11.5687+2.6326. ln height	0.1392	13.0/14.9	0.94
ln PEF (L/s), f= -11.3103+2.5745. ln height (cm)	0.1357	12.7/14.5	0.94
ln MEF_{75} (L/s), m+f= -11.0128+2.504. ln height (cm)	0.1421	12.7/16.2	0.94
ln MEF_{75}(L/s),m= -11.0376+2.5115. ln height (cm)	0.1460	13.5/15.7	0.94
ln MEF_{75}(L/s).f= -11.0092+2.5026. ln height(cm)	0.1382	12.9/14.8	0.94
ln MEF_{50}(L/s), m+f= -10.2571+2.2901. ln height (cm)	0.1594	13.8/18.5	0.90
ln MEF_{50}(L/s),m= -10.3498 +2.308. ln height(cm)	0.1630	15.0/17.7	0.91
ln MEF_{50}(L/s),f= - 10.1369 +2.2666. ln height (cm)	0.1564	14.5/16.9	0.90
ln MEF_{25}(L/s),m+f= - 10.182 + 2.1429. ln height (cm)	0.2074	16.3/25.8	0.84
ln MEF_{25}(L/s),m= -10.1375+2.1346. ln height(cm)	0.2115	19.0/23.5	0.84
ln MEF_{25}(L/s),f= -10.2443+2.1548. ln height(cm)	0.2042	18.4/22.6	0.84
ln $MMEF_{25-75}$(L/s),m+f = - 10.3231+2.2838. ln height (cm)	0.1548	14.3/16.7	0.91
ln A_{ex} (L^2/s),m+f = -24.9456+5.3845. ln height (cm)	0.1785	15.3/21.4	0.98
ln A_{ex} (L^2/s), m =-24.7711+5.3558. ln height (cm)	0.1802	16.4/19.7	0.98
ln A_{ex} (L^2/s), f=- 25.2523+5.4398. ln height (cm)	0.1709	15.7/18.6	0.98
ln PIF (L/s),m+f = -14.3645+3.0991. ln height (cm)	0.2296	20.5/25.8	0.90

(CV) Correlation Coefficient (r), in 449 Healthy Libyan Children 4-19 years of age

Abbreviations: ln : natural logarithm, m:male, f: female, down: negative directionregression line; up:positive direction from the regression line, L: liter, L/s: liter/sec.

r is significant at P<0.005-0.0001.

Table 4: Classification of Airways Obstruction According to the Reference Valuesin 449 Healthy Libyan Children (Age 4-19 Years)

Level and degree of obstruction	z-score	% of predicted
Peripheral airways:		
1. **Degree** based on MEF_{25} :		
Mild	<-2SD to -3SD	<67-54
Moderate	<-3SD to -4SD	<53-44
Severe	<-4SD to -5SD	<43-36
Very severe	<-5SD	<36%
2. **Degree** based on MEF_{50} :		
Mild	<-2SD to -3SD	<72-62
Moderate	<-3SD to -4SD	<61-53
Severe	<-4SD to -5SD	<52-45
Very severe	<-5SD	<45
Central airways:		
Degree based on PEF:		
Mild	<-2SD to -3SD	<75-68
Moderate	<-3SD to –4SD	<67-58
Severe	<-4SD to –5SD	<57-50
Very severe	<-5SD	<50

Table 5: Regression Equations of Functional Parameters Expressed per Unit of FVC in Relation to Body Height, Standard Deviation (SD) and Coefficient of Variation Around Regression line (CV), Correlation Coefficient (r), and P-Value in 449 healthy Libyan Children 4-19 Years of Age

Regression equation (m+f)	SD	CV (%) at mean body height	r	P<
FEV_1/FVC (l/l) = 1.08284- 0.001076.	4.07428	4.0	-048	0.0001

height (cm)				
PEF/FVC (l/s/l) = 2.69793-0.005319. height (cm)	0.27384	13.8	-0.37	0.0001
MEF_{75}/FVC (l/s/l) = 2.73547-0.006365. height (cm)	0.27284	14.6	-0.43	0.0001
MEF_{50}/FVC (l/s/l) = 2.35958-0.007059. height (cm)	0.23662	17.1	-0.52	0.0001
MEF_{25}/FVC (l/s/l) = 1.36774-0.004591. height (cm)	0.16364	22.2	-0.50	0.0001

m: male, f: female

Table 6: Comparison of Spirometric Reference Values

Healthy children	**Libyan (4 -19 yrs.) (present)**		**Tunisian (6-16 yrs.) (11)**		**Czech (3-18 yrs.) (16, 17)**	
Body height	***140 cm***	***180 cm***	***140 cm***	***180 cm***	***140 cm***	***180 cm***
FVC (L), m	2.22	4.65	2.27	4.61	2.38	4.99
FVC (L), f	2.11	4.53	2.20	4.31	2.21	4.48
FEV_1 (L), m+f	2.01	4.09	-	-	2.00	4.11
PEF (L/s), m+f	4.16	8.00	-	-	4.52	8.15
MEF_{75} (L/s), m+f	3.92	7.35	-	-	4.04	6.94
MEF_{50} (L/s), m+f	2.89	5.13	-	-	2.85	4.93
MEF_{25} (L/s), m+f	1.50	2.58	-	-	1.46	2.55
A_{ex} (L/s), m+f	5.27	20.41	-	-	5.18	20.27

Abbreviations: m: male, f: female,