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ORIGINAL ARTICLE

Spirometric values in healthy preschool children

Valores espirométricos en pre-escolares sanos

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Abstract

Introduction. Spirometry is the most commonly used test to evaluate lung function. Foreign reference standards are currently available for preschool children. **Objectives:** 1. To measure spirometric variables in healthy Chilean preschool children, 2. To compare these results with predictive ones according to GLI (Global Lung Initiative), Eigen (USA) and França (Brazil), and 3. If there is a significant difference with these, to develop reference equations. **Subjects and Method:** Questionnaires were distributed to parents in several schools and kindergartens in Santiago. Children with a history of prematurity, asthmatic symptoms, chronic lung disease (including asthma), and chronic non-respiratory disease were excluded. Spirometry was performed according to ATS/ERS 2007 guidelines, with MedGraphics equipment, USA. Family and environmental background, weight and height were recorded, as well as values obtained in forced vital capacity (FVC), forced expiratory volume in 0.5, 0.75 and 1 second (FEV0.5, FEV0.75, and FEV1, respectively). **Results:** 276 spirometries were performed, 202 met acceptability criteria, 112 girls, average age 5.01 ± 0.57 years, height 108.7 ± 5.6 cm. When comparing by gender, there was only a significant difference in FVC, which was higher in boys. The average values obtained in the total group were: FVC 1.22 ± 0.22 liters, FEV1 1.16 ± 0.18 liters, FEV0.75 1.07 ± 0.17 liters. These parameters were higher in percentage than the predictive ones according to GLI, Eigen, and França, except FVC with Eigen, therefore, predictive equations were developed. **Conclusions:** Spirometric values of preschoolers living in Santiago were higher than foreign reference values. We proposed these reference standards to be used in our country.

Keywords:
Spirometry;
preschoolers;
reference values;
lung function

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Introduction

Spirometry is the most commonly used method to assess lung function[1-5]. In 2007, the consensus of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) was published with recommendations for its implementation and interpretation in preschool age[1]. It proposes acceptability and repeatability criteria for this age based on its lower lung volume, and on the disproportion between the airway size in relation to this lower lung volume[4-6]. Some authors have already shown good results in applying these new criteria[4-11].

The guidelines discuss the most appropriate way to choose reference values, emphasizing that values made in subjects older than six years should not be extrapolated to preschoolers. If values are obtained in subjects with different characteristics, they should be validated by studying at least 300 healthy individuals. It is also emphasized that the results must be expressed as z score[1,12,13].

The reference values published to date have been obtained mainly in Caucasian, European or North American populations[2,4,14-17], which present ethnic, nutritional and body constitution differences regarding our population.

Our hypothesis is that the spirometric values of healthy Chilean preschoolers are higher than the reference values predicted by foreign formulas. The objectives are i) to measure volumes and forced expiratory flows, ii) to compare them with the theoretical values of the Global Lung Function Initiative (GLI) (14), Eigen et al. (2), and França et al. (10), iii) If the obtained values differ significantly, to elaborate reference equations.

Subjects and Method

Participants. Principals of 13 educational institutions (schools and kindergartens) located in different communes of Santiago were contacted. The children were from 23 communes. According to the socioeconomic level defined by the National Socioeconomic Characterization Survey (CASEN), 19.3% of them lived in high-income communes, 49.5% in middle-income communes, and 31.2% in low-income communes. They were all Chilean and of Chilean parents. Questionnaires were sent to parents of students aged between three years and five years, 11 months and 29 days requesting perinatal, general morbid and respiratory, family and environmental history. Exclusion criteria were: prematurity (newborn ≤ 37 weeks), birth weight ≤ 2.5 kg, chronic lung disease (bronchial asthma, bronchopulmonary dysplasia, cystic fibrosis, bronchiolitis obliterans, airways and lung malformations), history of hospitalization for respiratory cause (neonatal respiratory distress, pneumonia), use of permanent or intermittent inhaled medications, and chronic non-respiratory disease (neuromuscular, heart, or renal disease). Children with mild upper respiratory symptoms were accepted, without cough that would prevent them from performing the expiratory effort for the procedure[18]. The children had no previous preparation and were not trained to make a second attempt as they did not achieve acceptable curves on their first visit.

Procedure. Height was measured with the Seca® 213 portable stadiometer, Spain, standing, without footwear, and weight with the Medisana® PSD analog scale, Germany. Body mass index (BMI) was calculated, defining overweight a BMI in the range > P85 - < P95 and obesity a BMI ≥ P95.

Three operators (AM, LF, SC) performed spirometry. The used equipment was the CPFS/D USBTM spirometer (Medical Graphics, St Paul, Minnesota, USA) with pneumotachograph with pitot-like tubes, calibrated with 3 liters syringe in each visit, adjusted according to temperature, humidity and the barometric pressure of the room enabled for the procedure. The linearity of calibration measurements was reviewed. The children were accompanied by an assistant or a childcare teacher, in groups of two to three, and a maximum of 15 minutes was dedicated to each child. Spirometry was performed while the children were standing, initially with a nose clip and without incentive. In cases where the mouthpiece caused discomfort, an adapter was added. If the child had difficulty performing three to four initial maneuvers, the software incentive was used and/or removal of the nose clip.

Each child made at least three efforts and a maximum of 12. The back-extrapolated volume (BEV) reported by the software was observed and the expiratory time was measured with a millimeter ruler. The repeatability of FVC and FEV1 was determined (FEV0.5 or FEV0.75 if FEV1 was not obtained), considering a variability < 10% in cases where two or more acceptable efforts were obtained.

The recorded spirometric values were: Forced Vital Capacity (FVC), Forced Expiratory Volume (FEVt): FEV0.5, FEV0.75, and FEV1, Forced Expiratory Flows (FEF) at 50% and between 25% and 75% of the FVC (FEF50 and FEF25-75 respectively), and Peak Expiratory Flow (PEF), ratios: FEV1/FVC, FEV0.5/FVC, and FEV0.75/FVC. The best absolute values obtained in volumes and expiratory flows were used for descriptive, comparative, and predictive analysis. The spirometries quality was analyzed independently by two of the authors (AM and SC), based on the criteria of Gatto et al.[19]. Those that did not meet three or more acceptability criteria were considered poor quality and should be excluded from the study. In case of discrepancy, they reach an agreement.

Ethics Committee. This study was approved by the ethics committee of the Pontifical Catholic University of Chile (n° 15-326). Parents signed informed consent.

Statistical Analysis. The data are displayed as an average ± standard deviation. The percentage difference between the observed values and the predetermined theoretical values of FVC, FEV1, FEV0.5, and FEV0.75 is also presented. For the comparison with GLI formulas (FVC and FEV1), z score was also used, considering a significant difference if it was higher than 0.5 or if the SD was higher than 1.

In order to evaluate the data dispersion, the interindividual variation coefficient was calculated for each variable (V = 100xSD/average). Pearson correlation coefficient was used to determine the linear association degree between numerical variables. For the averages comparison between groups, Student's t-test was used for independent samples, and also for the comparison between observed and theoretical values for paired samples.

Predictive equations for volume and forced expiratory flows variables were developed using multiple regression analysis, and the lower limit of normal (LLN) was determined, which corresponds to the 5th percentile of the fitted regression line.

All analyses were performed using the statistical software SPSS 17, GLI theoretical values were obtained using macros available for the statistical software SAS. Any p-value lower than 0.05 was considered significant.

Results

Figure 1 shows the flowchart for obtaining spirometries.

Between May 2016 and August 2017, 276 basal spirometries were performed on children aged bet-

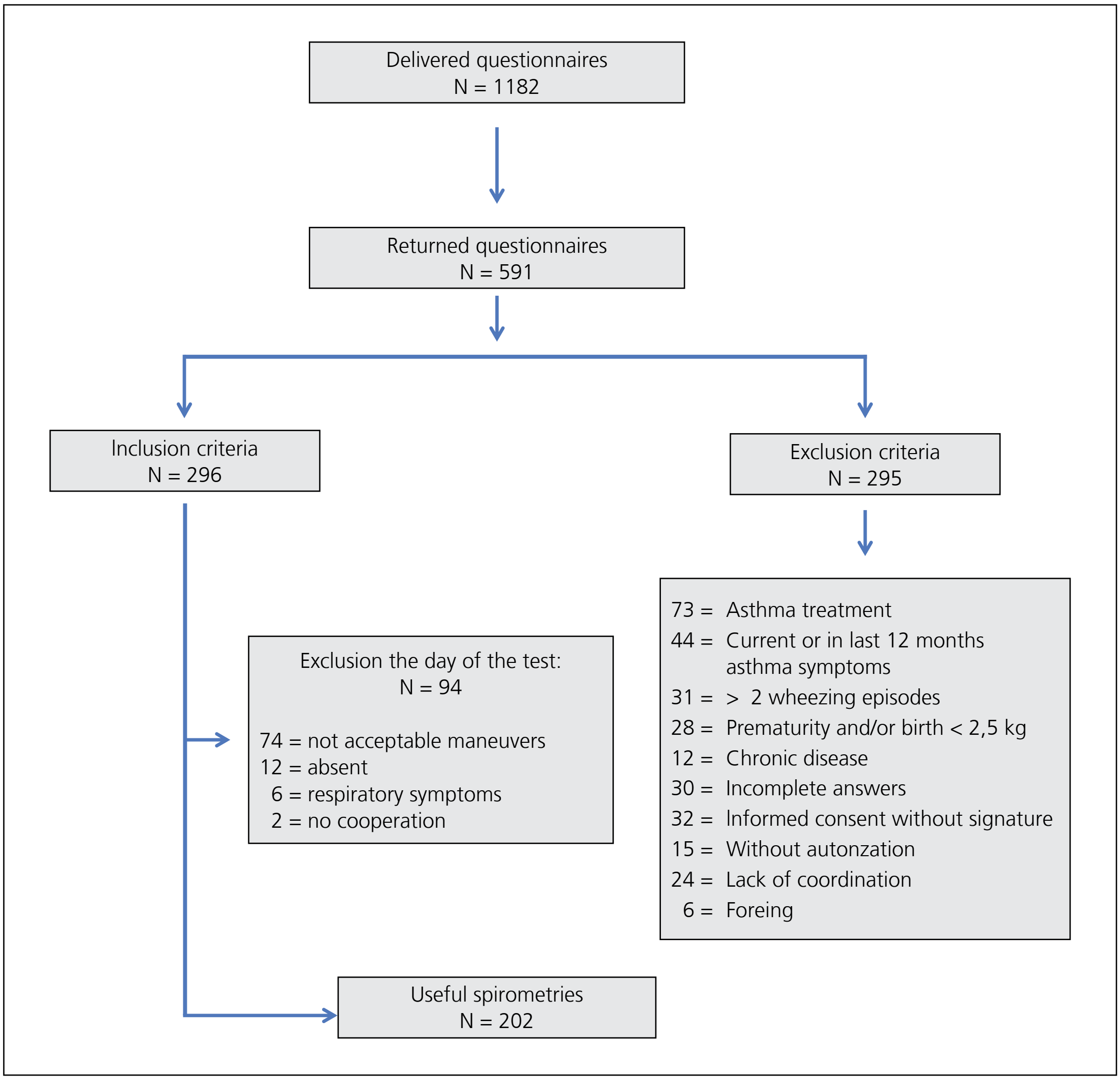

Figure 1. Flowchart for obtaining spirometries.

Table 1. General description of the study group (n = 202)

Variable	n, mean + SD, percentage (%)
Girls n (%)	112 (55.4)
Age (y.o., SD)	5.01 ± 0.57
3 - 3 y.o. 11 months: n (%)	7 (3.4)
4 - 4 y.o. 11 months: n (%)	86 (42.6)
5 - 5 y.o. 11 months: n (%)	109 (54)
Height (cm) (mean ± SD)	108 ± 5.6
Weight (kg) (mean ± SD)	20 ± 3.2
BMI (mean ± SD)	16.8 ±1.8
Nutritional status	
Normal n (%)	119 (58.9)
Overweight n (%)	38 (18.8)
Obesity n (%)	45 (22.3)
Tobacoo exposure n (%)	54 (26.7)
Familial asthma n (%)	25 (12.4)

SD: Standard Deviation. BMI: Body Mass Index.

Table 2. Succes spirometries according to age

Age	Performed spirometries (n)	Acceptable spirometries (n)	Succes percentaje*
3 - 3 y.o. 11 months	24	7	29%
4 - 4 y.o. 11 months	112	86	76.7%
5 - 5 y.o. 11 months	140	109	77.8%
Total	276	202	

*p < 0.001 between groups.

ween three years and three months, and five years, 11 months and 29 days, and with a height between 94 and 129 cm. Table 1 shows the general characteristics of the subjects. There were no differences in weight and height between the two sexes.

In relation to spirometric results, the average number of attempts was eight per child. More successful maneuvers were observed at older ages (table 2), 18 children (9%) achieved acceptable efforts in a second visit.

To verify agreement among evaluators, the initial 276 spirometries were analyzed. The 74 excluded had a poor quality according to both evaluators (100% concordance). There was a discrepancy in the following acceptability criteria: 1. The ascent of F/V curve 1%, 2. PEF defined 1%, 3. irregular descent 2.5%, and 4. End of expiration 0.5%. These spirometries were then reviewed by both evaluators together and included for analysis.

The back-extrapolated volume was less than 12.5% (or 80 ml) in the total of selected spirometries. The mean expiratory time was 1.4 seconds ± 0.46 (range 0.7-2.8) without gender difference. Children aged four to five years showed no significant difference in the expiratory time, while there was a difference between those aged four and five compared to those aged three years (p 0.04). Children who used nose clips exhaled less time than those who did not (1.37±0.44 vs 1.57±0.50 seconds, $p < 0.01$), however, there was no difference in the FVC value (1.23 ± 0.21 vs 1.21 ± 0.23 liters, p 0.55). With the use of incentive, the expiratory time was less than not using it (1.37 ± 0.43 vs 1.57 ± 0.52 seconds, $p < 0.01$), and the FVC also showed no difference (1.21±0.21 vs 1.26 ± 0.24 liters, p 0.17).

Twenty children did not reach a one-second expiration, therefore they did not register FEV1, and they were considered for calculations of FEV0.5 and FEV0.75 according to the obtained expiratory time.

In 56 subjects, only one acceptable effort was obtained, in 115 were two, and in 31 were three efforts which were acceptable and repeatable. In the cases where at least two acceptable efforts were available, the following coefficients of variation were calculated: FVC: 3.57%, FEV1 3%, FEV0.5 3.26%, and FEV0.75 3.1%.

Table 3 describes the average spirometric variables of the group. FVC was higher in 5-year-olds compared to 3- and 4-year-olds ($p < 0.001$). When comparing by gender, it was observed that only FVC showed to be significantly higher in men than in women (1.26±0.22 l vs 1.20 ± 0.21 l respectively, $p < 0.02$). In the rest of the variables, there was no difference by gender (Apendix 1). Figure 2 shows the relationship between height and forced expiratory volumes.

In the comparison with theoretical values according to GLI, Eigen, and França, it was observed that according to percentage, the ones obtained in our study were significantly higher, except CVF with Eigen (table 3). In the comparison with GLI using z score, the difference in FVC was 0.44 SD and with FEV1 0.62 SD. Following the objectives of our study, reference equations were elaborated for average and 5th percentile, which are shown in table 4. For FVC, formulas are made separated by gender due to the found differences.

Discussion

In this study, we obtained a sample of 202 spirometries performed on healthy Chilean pre-school children. When comparing their results with foreign theorists, significant differences were found in most of the spirometric variables. Predictive equations were elaborated and proposed to evaluate volumes and forced expiratory flows in this age group.

The evaluated children belonged to kindergartens and schools of several communes of Santiago and were of different socioeconomic levels. A high percentage of response to the surveys was obtained. Weight and height did not vary between men and women which is usual at preschool age. In relation to nutritional status, the group has a similar percentage of obesity, and regarding overweight, it was somewhat lower than described in national figures for 2016[20]. Despite this, we found that the FVC was higher than predicted by foreign formulas. In general, when measuring lung function in healthy children, it requires that they be asymptomatic for at least three weeks[1]. Our study included children with mild upper respiratory symptoms, based on a study by Lum et al.[18] which showed that their presence did not influence measurements.

In relation to our first objective, we achieved a success rate of 73.2% (202 of 276, Figure 1), similar to several cases previously described[3,5,7,8], however, there are publications that show values as high as 82-88%[9,21]. As expected, the older the child, the more successful the maneuver, as well as other experiences[10,23,24]. 91% of the children achieved acceptable curves in the first visit, higher than that described in other series[5]. This could be explained by the examination in groups of maximum three children, which allowed a personalized explanation of the maneuver and adapted to the age, in a pleasant environment[24]. On the other hand, it could also be explained by the use of incentive, in 75.7% of the children, when it was noted that the child required more stimulus or did not understand the instructions. The most used type of animation encouraged to reach an adequate Peak Expiratory Flow (PEF) and then to prolong the expiration until reaching the residual volume. However, its use shortened the expiratory time but did not affect the FVC measurement. This tool is still controversial, probably the child is distracted and the expiratory effort is affected. Gracchi et al. compa-

Table 3. Mean spirometric variables from study group, and percentage difference with respect to theoretical values by GLI, Eigen y França

Variable (theoretical mean)	Study group	GLI % difference	Eigen % difference	França % difference
CVF (l)	1.22 ± 0.22	1.15 ± 0.15 4.6 ± 10%	1.23 ± 0.19 * -1.2 ± 10.5%	1.16 ± 0.15 4.52 ± 10.4%
FEV_1 (l)	1.16 ± 0.18	1.07 ± 0.12 6.5 ± 8.9%	1.09 ± 0.14 5.6 ± 9%	1.07 ± 0.16 6.08 ± 9.47%
$FEV_{0,5}$ (l)	0.91 ± 0.15	- -	- -	0.80 ± 0.09 10.55 ± 10.34%
$FEV_{0,75}$ (l)	1.07 ± 0.17	0.99 ± 0.11 5.8 ± 9.6%	- -	- -

*p 0.8. Other comparisons p < 0.01. FVC: Forced Vital Capacity. FEV: Forced Expiratory Volume.

Table 4. Equations for define mean value and lower limit value of spirometric variables for children in pre-school age

	Equation for mean value			Equation for lower limit value	
Variable	Constant	Height	R^2	Constant	Height
FEV_1	-1.602	0.025	0.60	-1.794	0.025
FVC boys	-2.058	0.031	0.61	-2.304	0.031
FVC girls	-2.125	0.031	0.65	-2.320	0.031
FEV1/FVC	115.643	-0.204	0.05	107.4	-0.204
$FEV_{0.5}$	-1.151	0.019	0.51	-1.323	0.019
$FEV_{0.5}$/FVC	110.003	-0.323	0.06	98.262	-0.323
$FEV_{0.75}$	-1.446	0.023	0.57	-1.631	0.023
$FEV_{0.75}$/FVC	116.1	-0.264	0.05	105.728	-0.264
FEF_{25-75}	-1.100	0.025	0.15	-1.652	0.025
PEF	-2.943	0.051	0.36	-3.584	0.051

R^2: coefficient of determination. LLN: lower limit of normality, corresponds to Percentile 5. To calculate mean value, the following formula is used: Constant + (height coefficient x height [in cm]). To calculate LLN: Constant + (height coefficient x height [in cm]).FVC: Forced Vital Capacity. FEV: Forced Expiratory Volume. FEF: Forced Exiratory Flow.

red the use and non-use of incentive in 4-5-year-olds, finding that less repeatability was obtained in FVC and FEV1 when using it[25]. Chavasse et al. found that not using a nose clip does not affect FVC or FEV1 measurements in school-age children[26]. In our series, its use also shortened the expiratory time but was no difference in the measurement of FVC either. In a Spanish study, 69.2% used nose clip, without showing any decrease in expiratory time[4].

The spirometries used for the analyses met the acceptability criteria suggested by the ATS/ERS 2007[1] and showed very low coefficients of variation between the measurements. Only tests rated as "very good quality"[19] were selected for analysis; 20 spirometries with an expiratory time less than one second were also considered, using the values of FEV0.5 and FEV0.75 for their respective predictive formulas. Children under six years of age still have their lungs in growing stage, the airways are relatively larger than the pulmonary parenchyma, which would explain a rapid emptying with forced expiration, with a sudden and early end[8,11,27]. Children at this age can express their FVC with expirations less than one second, obtaining values of FEV0.5 and FEV0.75, which have good reproducibility and are useful to evaluate response to bronchodilator[28-30, 37].

We currently have numerous publications of reference standards for children in pre-school age[1,2,10, 14-17], however, in order to be able to apply them in our population, we would have to find similarity with some of them in the measurements of at least 300 children of the same age[1]. We decided to make comparisons with GLI because it is the current recommendation[31] and because it allows continuity to interpret the spirometries of a person as it ranges from three to 95 years. We also wanted to compare with Eigen[2] because they are the reference values used in our laboratory. This is due to having carried out a comparative exercise in 2011, and finding that these theoretical values were the ones that mostly resembled the measurements made in Chilean children (32, unpublished). We compared

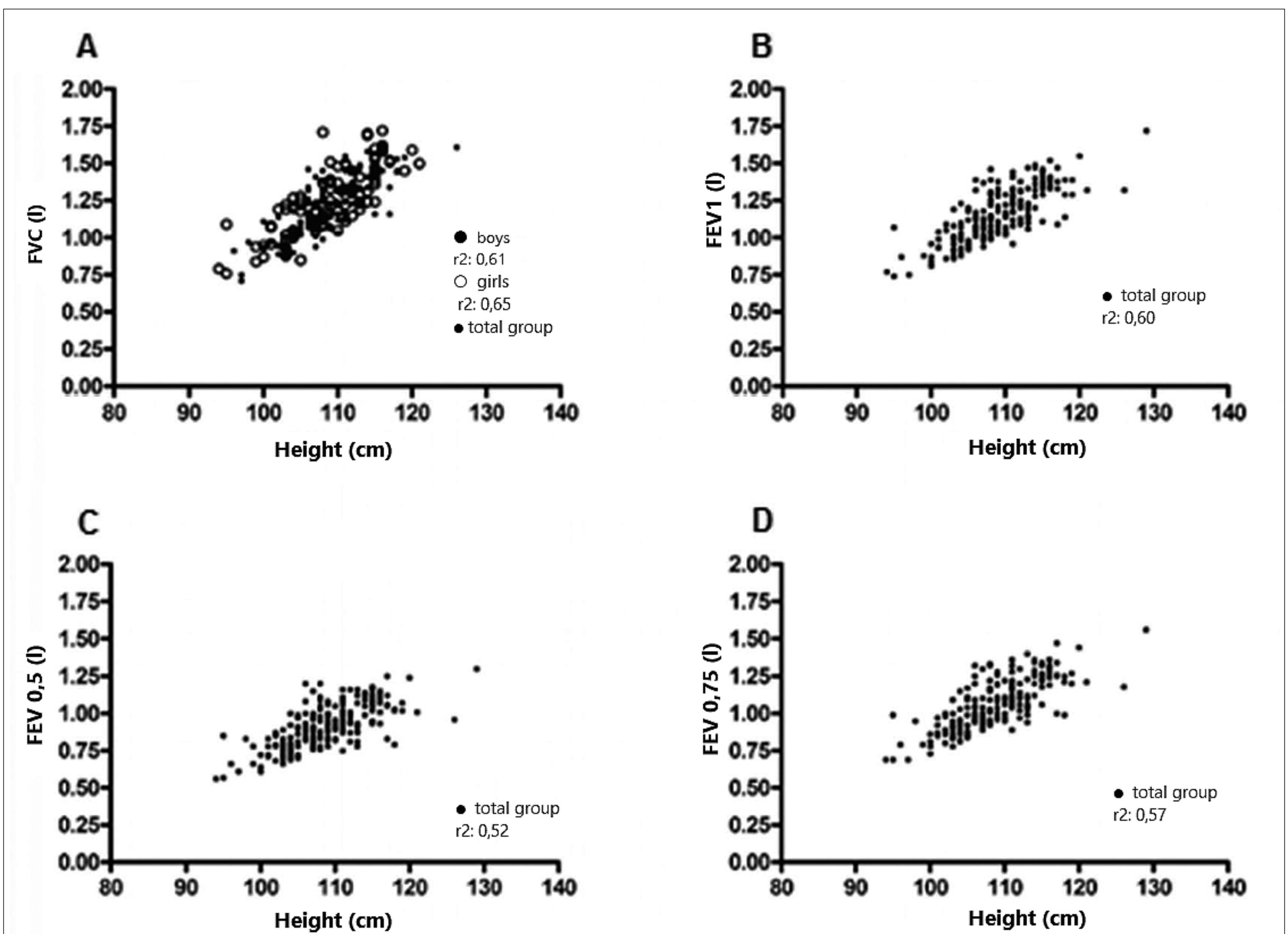

Figure 2. Height vs Forced Expiratory Volumes: A. Height vs FVC in boys and girls separately. B,C,D. Height vs FEV1, height vs FEV0,5 and height vs 0,75 respectively, in total group. FVC: Forced Vital Capacity, FEV1 Forced Expiratory Volume on one second, FEV0,5 Forced Expiratory Volume on 0,5 seconds, FEV0,75 Forced Expiratory Volume on 0,75 seconds.

with the Brazilian publication[10] because it is the series with the highest n to elaborate equations in South America. We found significant differences in all variables except FVC with Eigen. These differences could be explained by 1. the sample size[33], where our sample size was similar to that of Eigen and França, 2. By the used pneumotachograph, and the position when performing the spirometry, standing or sitting[34,35], and 3. Although in children of this age there are no studies, it could be explained by ethnic differences[35], since the theoretical values of GLI are based on measurements in Caucasian children, those of Eigen in North American children, and those of França in children of Sete Lagoas, Brazil. In the Spanish study by Martin et al. also find significant percentage differences between theoretical averages GLI and Candela[4]. In our study, it stands out that our values are higher in most variables than those measured by França and Eigen, although they include six-year children. However, it should be noted that the differences in absolute values are very small since these are lung volumes of approximately one liter in FVC. In this sense, we were able to compare with GLI formulas by z score, showing that there was no significant difference. When performing multiple regressions, height was the most determinant factor of each lung function variable, as it has been found in previous studies[4,10,13,16,27]. Also, similar to these studies, the correlation coefficients (r2) were moderate between height and volumes and low for FEVt/FVC ratios and forced expiratory flows (table 4). Predictive formulas are thus proposed for preschool children, for average value, and lower limit value (5th Percentile), which are shown in table 4.

We consider weaknesses of the study not having achieved a higher number of spirometries in 3-year-olds. At this age, it is more difficult to obtain acceptable efforts, and on the other hand, it is more difficult to get volunteers since, in general at this age, they are not in school. Another weakness could be that the n of 202 would be not sufficient[33], explaining the moderate correlation coefficients and part of the differences with other theoretical values, although a larger sample size does not ensure better results.

Conclusions

Forced basal spirometry in preschool children living in Santiago can be performed adequately and successfully in a large percentage of cases. We have obtained normal values in a healthy population strictly following the current regulations published by the ATS/ERS 2007. We propose the use of these formulas for the interpretation of spirometries of patients between three years and five years and 11 months with respiratory diseases living in Chile. Failing this, GLI could also be used, since their differences are not significant. These latter formulas have the advantage of continuously covering the calculation of theoretical values from three to 95 years.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

Pediatric Pulmonology Chilean Society.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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Attached 1. Spirometric mean values by gender

Gender (n)	FVC (L)	FEV_1 (L)	FVC/FEV_1 (%)	$FEV_{0.5}$ (L)	$FEV_{0.5}/FVC$ (%)	$FEV_{0.75}$ (L)	FEF_{25-75} (L/s)	FEM (L/s)
Masculino (90)	1.26 ± 0.22*	1.18 ± 0.18	93 ± 5.3	0.92 ± 0.15	73.5 ± 7.46	1.09 ± 0.17	1.56 ± 0.35	2.67 ± 0.50
Femenino (112)	1.20 ± 0.21*	1.14 ± 0.17	93.6 ± 4.8	0.90 ± 0.14	75.9 ± 7.07	1.05 ± 0.16	1.59 ± 0.36	2.62 ± 0.47
Promedio grupo	1.22 ± 0.22	1.16 ± 0.18	93.3 ± 5.07	0.91 ± 0.15	74.9 ± 7.32	1.07 ± 0.17	1.58 ± 0.36	2.64 ± 0.48

*$p < 0.01$. FVC: Forced Vital Capacity. FEV: Forced Expiratory Volume. FEF: Forced Exiratory Flow. FEM: Peak Expiratory Flow.

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