

Spirometry with FEV_{0.75} Increases the Sensitivity for the Diagnosis of Obstructive Disorder in Children of Asthmatic Mothers

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Abstract

Objective: To evaluate and compare the sensitivity of spirometry in children of asthmatic mothers by the parameters FEV₁ and FEV_{0.75}.

Methods: An observational cross-sectional analytical study nested in a cohort of 4,757 pregnant women. Clinical evaluation was performed for the diagnosis of asthma, besides the realization of spirometry in the children of asthmatic mothers, evaluating the following parameters and relationships: FEV₁, FVC, FEV₁/FVC, FEV_{0.75} and FEV_{0.75}/FVC.

Results: A total of 86 children of asthmatic mothers were included in the study, with age mean of 79.8 ± 1.1 month old. Regarding the breathing pattern there was a predominance of normality. When using FEV₁, changes were observed in 26 children, representing 30.3% of the sample. Of these, 17 were classified as restrictive and nine as obstructive. Using the FEV_{0.75} instead of the FEV₁ (and its consequent FEV_{0.75}/FVC) 29 ventilatory tests found changed, representing 33.7%. Of these, 27 were classified as obstructive and only two were restrictive. Of the 16 children diagnosed with asthma, only five had presented obstructive pattern when FEV₁ customization spirometry was used. In contrast, when we used FEV_{0.75}, 12 of these patients were considered obstructive. The sensitivity was higher in the spirometric test that used FEV_{0.75}, with even greater negative predictive value. On the other hand the test set for the parameter FEV₁ showed greater specificity and higher positive predictive value.

Conclusions: Spirometry, though with recognized value in the complementary diagnosis of obstructive disturbance, classically presents limitations in the pediatric population, especially in younger children. We observed a significantly higher sensitivity and negative predictive value when we used FEV_{0.75} in substitution to the FEV₁. As a consequence, the parameter FEV_{0.75} is probably more effective for the diagnosis of obstructive disorder in patients with clinical history or family history of asthma.

Keywords: Asthma; Child; Spirometry

Introduction

Asthma is a recognized multifactorial disease, resulting from the interaction between genetics and environment. However, heredity does not follow the classic Mendelian patterns and genetics of this disease is especially complicate because of its polygenic nature. The heritage transmitted by the mother seems to be more significant than the one transmitted by the father [1-3].

Over the past 30 years, the world population has seen a major technological breakthrough, which led to profound changes in the pattern of lifestyle and eating habits. However, parallel to this, an improvement in sanitary conditions and reduction of infectious diseases was noted. Nevertheless, asthma continues to impact on morbimortality in various age groups and all social groups [4,5].

The pulmonary function tests are usually performed with computerized systems that analyze the data and provide immediate results. Spirometry is one of these tests and it is recommended to clarify the diagnosis in patients with chronic cough (>3 weeks). Chronic cough is often an isolated manifestation of asthma. In asthma should be made in the following situations: in patients with wheezing or chest tightness applicant, to confirm the diagnosis, during the initial evaluation and after treatment with stabilization of symptoms and peak expiratory flow (PEF) to document the level of pulmonary function (normal or not), in patients with severe persistent asthma, when changes in maintenance treatment were done and the results achieved [6-8].

In respiratory evaluation of children over six years old as well as in adults, spirometry has an important role because of its simplicity and its low cost, combined with good reproducibility. It also demonstrates the importance when the symptoms are not well characterized by the patients and their respective responsible, which may result in a ranking of asthma and thus inadequate treatment. Then we use spirometry as a resource to establish the most appropriate management of the patient. The spirometry is also used extensively in research, and the most common complementary outcome in studies of respiratory diseases [9,10].

Ideally, the interpretation of spirometry should be compared with reference values. There are dozens of reference equations in use today and many included in pulmonary function equipment. However,

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racial, socioeconomic, gender, equipment and application technique of spirometry affect the accuracy of interpretation, particularly when the results are compared with the predicted values of another ethnic group [9,11].

The “American Thoracic Society” suggests that in every place where tests of pulmonary function are performed their own reference values are produced from a random selection of individuals without lung disease [9,12].

One of the limiting factors that we can notice is the sudden interruption of expiration, which may interfere with the accuracy of spirometry. By submitting this expiratory maneuver usually shorter than that of an adult applying the criteria of acceptability of spirometry in adults is not indicated in children. This characteristic in children stimulated the formation of this study, which aims to compare the use of spirometry with FEV₁ and forced expiratory volume in time 75 hundredths of a second (FEV_{0.75}) [13,14].

Materials and Methods

The method used was an analytical cross-sectional observational study nested in a cohort. In the original cohort (started in 2005) was applied a questionnaire to 4,757 pregnant women, with informed consent. Through this survey we identified 135 who reported physician-diagnosed asthma before pregnancy. Patients included in the study were children above cohort participants whose mothers had asthma since agreed to participate in the study signed by their parent or legal represent, the Term of Free and Informed Consent Form (ICF).

After about six years and eight months of the original work, were located and evaluated 86 children within the group of 135 mothers with a previous diagnosis of asthma. This number conforms to the expected sample size calculation; we estimated at least 82 at *n*. The conditions adopted for this calculation were as follows: frequency obstructive respiratory pattern for the study group equal to 15% (with an interval of 7-23%), the level of significance equal to 0.05, the test power equal to 0.80, the statistical test was used for a binomial proportion, the two-tailed test, and it was considered a waste sampling of 10%. It is a non-random sample, having children was consecutively selected.

There were no losses exclusion criteria. These were previously defined as birth weight <2500 g, gestational age <37 weeks, presence of respiratory distress at birth, abdominal surgery, thoracic or ophthalmic recent airway infections or wheezing in the previous two weeks and underlying diseases that could come interfering in ventilatory function test (heart disease, sickle cell anemia, cystic fibrosis, collagen diseases, neuromuscular diseases).

The age was considered in full months, since all subjects included were born in the range of four months period of initial data collection of the original cohort. For a clinical evaluation, we used the criteria adopted in clinical severity (Global Initiative for Asthma-GINA, 2002), which includes research symptoms and their frequency, and the measurement of peak expiratory flow (PEF). Finally, we conducted the evaluation of lung function by spirometry based on all children participating in the study, the tests being performed by one of the study authors. For this study, we considered the following parameters and relationships: FEV₁, FVC, FEV₁/FVC, FEV_{0.75} and FEV_{0.75}/FVC. The results were used as the criteria considered ATS/ERS (“American Thoracic Society” and “European Respiratory Society”) and benchmarks modified by Pereira (1992) [7]. The same way, the criteria for the interpretation of values and FEV_{0.75} FEV_{0.75}/FVC were those recommended by the same societies and cited by Aurora et al. (2004) and Burity et al. (2011) [12,14].

To start the tests we detected the beginning of the rapid peak flow and retro-extrapolation (VRE) ≤ 80 ml or 12.5% of CVF. Tests were suspended after 5 failures or before if the child shows to be fatigued. All tests were done by the same investigator (Valadares MA) [15].

The spirometer was used MicroloopR and SpidaR software. Five tests were conducted with each child, with the advantage of better results. Not used post-bronchodilator testing not append data to preconceived goals of the research, as well as after bronchial provocation test, for similar reasons, and because it was done at home. During the tests the children were helped to conduct the test in the most appropriate (standing and nose occluded). In addition, all children received an explanation of how to position the nozzle mouth and how to perform a forced expiration.

The results were tabulated in a spreadsheet program SPSSR version 17.0. It included means and standard deviations to describe quantitative variables, while simple frequencies and percentages were used for categorical variables. For calculation of sensitivity and specificity, as well as the positive and negative predictive values (and their respective confidence intervals for 95%) was applied EPIDATR (Program for Epidemiological Analysis of Tabulated Data) version 3.1 (January 2006). For the confidence interval (CI) calculation we used bootstrap technic, where estimation is done after “n” aleatory resampling. Receiver Operating Characteristic (ROC) curve was constructed to evaluate the relation of FEV₁/FVC e FEV_{0.75}/FVC variables with clinical diagnosis of asthma.

The study was approved by the Ethics Committee for Human Research of the Federal University of Sergipe (UFS-CEP), with approval number CAAE (Certificate of Appreciation Presentation for Ethics) 0104.0.107.000-11. Parents of all children included in the study signed consent form authorizing their participation in the research.

Results

The gender distribution showed 55.8% of boys and 44.2% girls, constituting the sample of 86 children with a mean age of 79.8 ± 1.1 months.

Being questioned about the presence of physician-diagnosed asthma for the child’s study, 9.3% of mothers said yes (which represents eight patients). On the other hand, when responding to the minor symptoms, there was a percentage of 18.6% of asthma (16 patients). As intermittent asthma were classified eight patients. Of the other eight, six met criteria for persistent mild to moderate and two. No case of severe persistent found.

Spirometric parameters, described in their respective means and standard deviations, are shown in (Table 1).

Regarding the breathing pattern we obtained a distribution with a

Variable	Mean	Std deviation
FEV ₁ (absolute)	1.18	0.24
FEV ₁ (relative)	90.3	17.83
FEV _{0.75} (absolute)	1.06	0.25
FVC (absolute)	1.28	0.25
FVC (relative)	92.44	17.86
PEF	2.16	0.73
FEV ₁ /FVC (absolute)	92.18	9.38
FEV _{0.75} /FVC (absolute)	83.43	12.6

FEV₁ (absolute) and FVC (absolute): expressed in liters; relative values described in percentages PEF expressed in liters/second

Table 1: Values obtained in spirometry base.

	N	%	95% CI
Normal	60	69.7	59.3–79.1
Restrictive	17	19.8	11.6–29.1
Obstructive	9	10.5	4.7–17.4

n: frequency

95% CI: confidence interval of 95% (bootstrap; based on 1000 bootstrap samples)
Classification according to reference standards of Polgar and Promadhat modified by Pereira, 1992

Confidence interval obtained through simulation with a thousand samples

Table 2: Frequency children's according to the ventilatory pattern observed spirometry base using FEV₁.

	n	%	95% CI
Normal	57	66.3	57-76.7
Restrictive	2	2.3	0-5.8
Obstructive	27	31.4	22.1-40.7

n: frequency

95% CI: confidence interval of 95% (bootstrap; based on 1000 bootstrap samples)
Classification according to reference standards of Polgar and Promadhat modified by Pereira, 1992 Confidence interval obtained through simulation with a thousand samples

Table 3: Children's frequency according to the ventilatory pattern observed spirometry base using FEV_{0.75}.

Variable	T1	T2
Sensitivity	31.25 (5.41-57.09)	75 (50.66-99.34)
Specificity	94.29 (88.13-100)	78.57 (68.24-88.9)
Positive predictive value	55.56 (17.54-93.57)	44.44 (23.85-65.04)
Negative predictive value	85.71 (77.25-94.18)	93.22 (85.96-100)

T1: spirometry with FEV₁

T2: spirometry with FEV_{0.75}

Values expressed in % (95% CI)

Prevalence of asthma in the sample: 18.6%

Table 4: Comparison of spirometric tests using FEV₁ and FEV_{0.75}.

predominance of normality. When using FEV₁ changes were observed at a frequency of 26, representing 30.3% of the sample. Of these, 17 were classified as restrictive as obstructive while nine (Table 2).

TEF median was 1.4seg, with 25 and 75 percentiles of 0.9 and 2.6 seg. A total of 29 patients (33.7%) had TEF below 1 second. Of these, 23 (26.7%) presented this time superior to 0.75 seconds.

Using the FEV_{0.75} in the place of the FEV₁ (and its consequent relative to the FVC) 29 ventilatory tests found changed, representing 33.7%. Of these, 27 were classified as obstructive and restrictive as only two (Table 3).

Of the 27 patients who demonstrated obstructive lung disease using the FEV_{0.75} as observed spirometric parameter 23 as mild, two as moderate and two as severe. When using FEV₁, the nine appointed as having obstructive, seven were characterized as mild and two moderate, none severe was found.

Of the 16 children diagnosed with asthma, only five had presented obstructive pattern when used in FEV₁ customization spirometry. In contrast, when used FEV_{0.75}, 12 of these patients proved to have obstructive. This difference in sensitivity can be seen in the results shown in Table 4.

By analyzing the sensitivity and specificity of spirometric tests using either forced expiratory volume (FEV₁ and FEV_{0.75}) met the above in Table 4. The sensitivity was higher in the spirometric test that used FEV_{0.75}, with even greater negative predictive value. On the other

hand the test set for the parameter FEV₁ showed greater specificity and higher positive predictive value.

When we associated clinical diagnose of asthma to the FEV₁/FVC relation using ROC curve we found 0.632 ± 0.087 (95% CI: 0.461-0.804; p=0.10) under the curve (Figure 1). Inversely when clinical diagnosis of asthmas was associated to FEV_{0.75}/FVC relation, the area under the curve was 0.860 ± 0.440 (CI 95%: 0.775-0.948; p<0.0001) (Figure 2).

Discussion

The studied population had a previous diagnosis of asthma in the frequency of 9.3%. When subjected to critical evaluation, there was an increase that rate to 18.6%, which clearly indicates a possible under diagnosis of this disease in our country. Asthma is recognized as the most common chronic illness in children, affecting about 15% of the

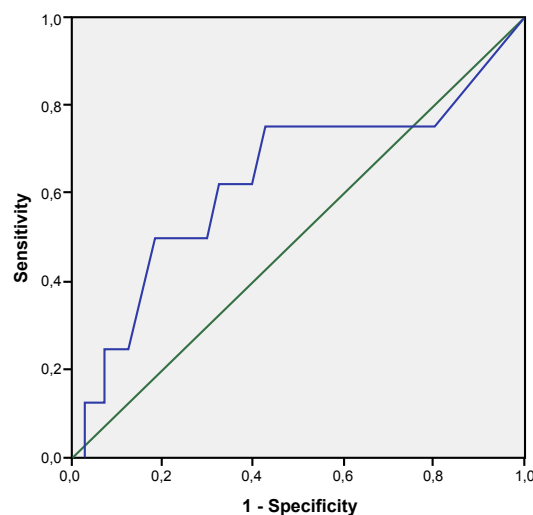


Figure 1: ROC Curve FEV₁/FVC. Area under the curve: 0.632 ± 0.087 (95% CI: 0.461-0.804).

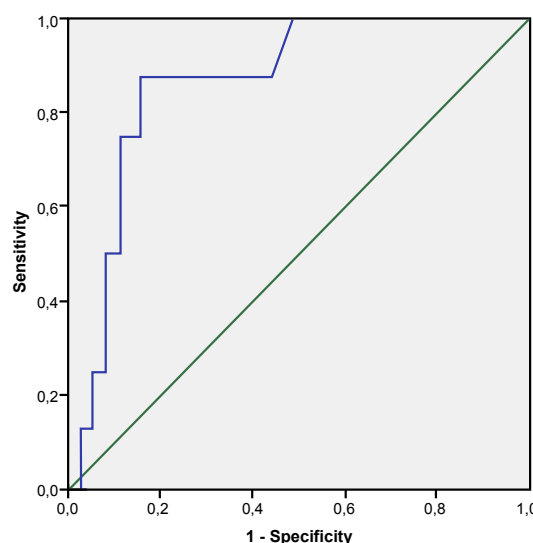


Figure 2: ROC Curve FEV_{0.75}/FVC. Area under the curve: 0.860 ± 0.440 (95% CI: 0.775-0.948).

pediatric population. However, it is estimated that the prevalence of symptoms associated with asthma is higher than 20% [13].

Spirometry, though with recognized value in the diagnosis of obstructive supplement, classically presents limitations in the pediatric population, especially in younger children. The obstructive pattern expected to be observed in a population with a clinical diagnosis of asthma may sometimes not be evidenced by the technical implementation of spirometry, which requires patient cooperation. The expiratory time limited, characterizing the so-called “short breath” is the largest of these limitations. This limitation was describe in the research of Veras and Pinto [16].

In the present study, we used the traditional FEV₁ and its correspondent relationship with FVC, met only nine children with obstructive pattern. That number rose to 27 when used FEV_{0.75} and their corresponding relationships. In 2007, as the studies of Piccioni et al., involving children younger than 6 years old proposed equations with parameter in 0.75 s FEV (FEV_{0.75}), this is perhaps the most appropriate parameter for this age group. This follows from the fact that children have smaller airways proportionally greater than their lung volumes, which enables them to perform forced expiration in less than 1 second, as cited Stanojevic et al. (2009) [15,17].

In our sample 33.7% of the patients could not execute TEF superior or equal to 1 second. This justifies the high inadequacy level when using VEF1. Restrictive disturbs moderate to severe full CVF can be expired within the first second and VEF1=CVF (relation VEF1/CVF%=100%). This can explain the high number of restrictive disturbs found when VEF1 and its relation to CVF was used. Although several VEF1 may be obtained, its value for young children is questioned, because of the airway size is bigger than pulmonary volume and this volume is expelled faster, showing VEF1/CVF relation >90%, which may underestimate obstructive pulmonary pathology [14].

By using FEV₁, struck by the large number of tests that accused restrictive disorder (27 in total) that number dropped to just two when used FEV_{0.75}, which leads invariably to think that many of those with restrictive pattern initially were by the technical limitation (short breath).

A limitation of this study is the absence of repeating the test after bronchodilator, which may explain the lower specificity of the test when using FEV_{0.75} and its corresponding lower positive predictive value. Other limitation is that, with the general agreement that asthma obstruction is a reversible condition, we can expect several patients with normal spirometric results in some moments. Consequently a single evaluation may underestimate diagnosis accuracy.

An important correspondence indicated by this study was the high sensitivity of the test using the FEV_{0.75} to diagnose obstructive pattern within the group of patients with asthma. Associated with this, we must reveal a high negative predictive value for this reference because of the reduced forced expiratory volume. Spirometry, though with recognized value in the diagnosis of obstructive supplement, classically presents limitations in the pediatric population, especially in younger

children. We observed a significantly higher sensitivity and negative predictive value when we used FEV_{0.75} in substitution to the FEV₁. As a consequence, the parameter FEV_{0.75} is probably more effective for the diagnosis of obstructive disorder in patients with clinical history or family history of asthma.

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