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Respiratory disease screening in school-aged children using portable spirometry

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Abstract

Objectives: To assess the prevalence of respiratory disease in school-aged children and to determine the value of field spirometry.

Methods: Data on 313 1st and 4th graders from four public schools in Lisbon were analyzed. A respiratory self-answered questionnaire and standard spirometry were performed. Descriptive and bivariate analysis was followed by multiple logistic regression.

Results: Thirty-five percent of the children presented at least one episode of wheezing (18% ≥ 2 episodes), and 4% had asthma. Wheezing was more frequent with family history of atopy (adjusted OR = 2.7; 95%CI 1.4-5.1), maternal smoking during pregnancy, lower respiratory tract infection (LRTI) (adjusted OR = 2.8; 95%CI 1.2-6.2), bronchiolitis (adjusted OR = 3.3; 95%CI 1.3-8.2), and allergy to aeroallergens (adjusted OR = 3.2; 95%CI 1.4-7.2). Asthma was more frequent with previous history of LRTI (adjusted OR = 14.6; 95%CI 1.7-122.9) and allergy to aeroallergens (adjusted OR = 8.2; 95%CI 2.0-34.2). Fifty-five percent of spirometry measurements met the acceptability criteria of the American Thoracic Society and of the European Respiratory Society. Wheezers presented mean lower z scores for forced expiratory volume in 1 second (FEV_1), ratio between FEV_1 and forced vital capacity (FVC) (FEV_1/FVC), and forced expiratory flow between 25 and 75% (FEF_{25-75}) ($p < 0.05$), as well as higher percentage of abnormal FEV_1, FEV_1/FVC and FEF_{25-75} (FEF_{25-75}, $p < 0.05$).

Conclusions: This pilot study showed a high prevalence of obstructive airway symptoms in school-aged children in Lisbon. Symptoms assessed by the questionnaire showed good correlation with spirometric values. The small prevalence of asthma leads us to speculate that asthma is under-diagnosed in this population.

J Pediatr (Rio J). 2011;87(2)123-130: Questionnaire, wheezing, asthma, portable spirometry.

Introduction

Asthma and other wheezing disorders are among the most frequent childhood diseases.[1] Asthma is the leading cause of childhood morbidity and the most common chronic disease in children[2]. Moreover, its prevalence has increased considerably worldwide in the last decades, especially in western countries.[2-5]

Chronic obstructive pulmonary disease (COPD) remains an important public health problem. It is a major cause of chronic morbidity and mortality throughout the world, which results in an increasing economic and social burden.[6] The World Health Organization estimates that COPD will be the third main cause of death worldwide in 2030.[6] Even though

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the benefits of community-based spirometric screening are still unclear,[6] it is considered that some of the factors implicated in adult COPD can and should be identified and prevented in childhood.[7]

Various longitudinal studies[8-10] have contributed to the identification of risk factors associated with recurrent wheezing and asthma, enlightening the natural history of obstructive respiratory diseases. Nevertheless, the relationship between lung function in childhood and asthma or adult COPD remains uncertain. The most relevant implicated factors are viral infections, secondhand tobacco smoke exposure, and atopy, all with impact on the children's lung function.[9-13]

Children with viral-induced recurrent wheezing seem to have an increased risk of chronic asthma in infancy.[9,14-17] Viral infections can be an important environmental stimulus for the damage and remodeling of airways, resulting in impaired lung function, and lastly, asthma.[15]

Pre and postnatal environmental tobacco smoke (ETS) exposure constitutes a determinant factor in respiratory morbidity and in early lung function reduction in children.[18-20] It has been shown that ETS exposure, either *in utero* or postnatal, influences the frequency of respiratory symptoms,[21,22] existing a dose-dependent relationship between the dose of ETS (one or two smoking parents), the respiratory symptoms, and the spirometric indices.[18,19,23] However, no level of exposure to secondhand smoke is safe.[24]

Finally, concerning the association between atopy and asthma, the data differ, depending on the region studied. Different studies have shown that atopy markers increase the risk of persistence of asthma in adults, while viral-induced wheeze rarely persists beyond 12 years of age.[8,10] Even in the absence of respiratory symptoms, children of atopic parents and those with personal atopy have impaired lung function in early life.[25]

In pediatrics, the most used epidemiological questionnaire for detection of respiratory disease in children derives from the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Nevertheless, questions from ISAAC questionnaire are essentially directed to asthma and allergic disease, leaving out other frequent respiratory symptoms like cough and phlegm. Regarding the evaluation of lung function, laboratory-based spirometry is the "gold standard" for the assessment of lung function in children, both in clinical and research protocols.[26] Various studies have shown that portable spirometers can provide measurements that are highly comparable to those obtained from laboratory spirometers, in several scenarios like offices[27] or schools.[28] In the setting of early detection of chronic pulmonary disease in childhood, we aim to assess the ability of a survey adapted from the American Thoracic Society (ATS) questionnaire[29] and of field spirometry to diagnose respiratory disease in children.

Our main goal was to evaluate if the methodology adopted for early screening of COPD in adults can be used in children, i.e., to analyze the prevalence and risk factors for respiratory disease in school-aged children, based on the application of a broad respiratory questionnaire and on spirometry, and, secondly, to determine the value of field spirometry.

Study design, population and methodology

An observational, cross-sectional study was done.

The population was selected from a group of children attending the first and forth school grades of four public basic schools located in the area of the Centro de Saúde do Lumiar. Parents gave written consent to the participation in the study, and the project was approved by the Ethics Committee of the Hospital de Santa Maria, Lisbon, and by the participating schools.

Clinical questionnaire

Parents answered a respiratory questionnaire in Portuguese adapted and translated from the ATS questionnaire.[29] The questionnaire includes socio-economic and cultural history (parental education and occupation), environmental history (ETS exposure), and history of respiratory symptoms since birth. Parental occupation was classified in nine categories, according to a national classification of professions[30], and further grouped into skilled jobs (categories 1-3) and less/unskilled jobs (categories 4-9). ETS exposure was defined as: smoking mother during pregnancy (ETS during pregnancy), smoking mother/father or ex-smokers after pregnancy (smoking mother/father), and living with smokers in the home (household smokers), including smokers in child's bedroom.

Respiratory disease was defined by the presence of the symptoms cough and wheeze. Pathological cough (symptom cough) was considered if it occurred without respiratory infections, after exercise, and while the child played or laughed; and wheezing (symptom wheeze) if it occurred with or without respiratory infections, after exercise, while the child played or laughed, and if bronchodilator therapy was used for symptom relief. Asthma was considered if an affirmative answer was given to the following questions: "Has any doctor diagnosed your child with asthma?" and "Has your son/daughter ever had asthma?"

Anthropometric determination and lung function indices

Weight and height were measured and a brief physical examination (respiratory rate, pulmonary auscultation, and assessment of pulse oximetry) was performed at the day of the study. For the obesity evaluation (body mass

index [BMI] > 95th percentile for age and sex[31]), we used the BMI growth charts built by the National Center for Health Statistics and by the Center for Disease and Control and Prevention in 2000.[32]

All children underwent standard spirometry according to the guidelines published by the ATS and by the European Respiratory Society, in the school setting, using an apparatus with a digital volume transducer (MicroLab Spiro V1.34, Micro Medical Ltd). Three to five measurements were obtained. The device records the best curve and registers the three best individual results according to standard procedures. The following parameters were registered: forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), ratio between FEV_1 and FVC (FEV_1/FVC), and forced expiratory flow between 25 and 75% of FVC (FEF_{25-75}). Procedures were explained and exemplified by a cardiopneumologist technician with specific training in pediatrics. Children breathed through a mouthpiece, in sitting position, and nose clips were worn by those who tolerated it. The indices were obtained in the absence of recent bronchodilator use (in the previous 6 hours), and after an upper or lower respiratory infection in the previous 2 weeks was ruled out.

When interpreting the results, the individual spirograms were considered satisfactory if they showed satisfactory exhalation and were free from artifacts (cough or glottis closure), early termination or cut-off, and leak and/or obstructed mouthpiece. The spirometer was calibrated every morning following the manufacturer's instructions. We visited the schools in June and September 2007. Afterwards, the spirograms were evaluated by two independent observers to determine acceptability according to published recommendations. For the acceptable curves, the absolute values were selected and a database was assembled in MS Excel® (Microsoft, USA). Using the reference values created at the Institute of Child Health at University College London,[33] the percentage predicted value and z scores of the spirometric indices were automatically calculated. Z scores of spirometric values between -2 and +2 were considered normal.

Statistical analysis

Quantitative variables were described by mean, median, standard deviation, minimum and maximum. Qualitative variables were summarized in frequency/contingency tables as counts (n) and percentages (%). In cases when the responses had missing values, we classified them as unknown. A descriptive analysis of all the variables relevant to the study was performed, namely socio-demographic characteristics, family history, environmental factors (ETS exposure), past medical history, occurrence of respiratory symptoms (cough and wheeze), asthma diagnosis, physical examination, and spirometric results.

A bivariate analysis was performed between some demographic data (gender, age, and ethnicity), school, family history, environmental factors, past medical history, and physical examination, and dependent variables, namely respiratory symptoms (cough and wheeze), asthma, and spirometric indices. Chi-square/exact Fisher tests (to assess the association between categorical variables) and *t*-Student/Mann-Whitney U tests (to compare a quantitative variable between two independent groups) were carried out. In this analysis, the spirometric results (z score for FEV_1, FEV_1/FVC, and FEF_{25-75}) were classified as "normal" if the values were within the normal range, and "abnormal" if outside that range, as described before.

A multiple regression analysis was then performed for the dependent variables related to respiratory symptoms (cough and wheeze) and to asthma, with the independent variables that showed clinically and/or statistically significant values in the bivariate analysis. The magnitude of the association with the dependent variables was quantified using odds ratios (OR) and 95% confidence intervals (95%CI). The multiple regression models were tested by the likelihood ratio, and the model goodness of fit was also evaluated using the Hosmer and Lemeshow test and area under the receiver operating characteristic (ROC) curve.

The association between respiratory symptoms (cough and wheeze), asthma, and spirometric indices was also analyzed. The spirometric results were considered as categorical and numerical (using the respective units of z score values).

All tests were two-sided, considering a significance level of 5%. The statistical analysis was done using Statistical Package for Social Sciences® (SPSS Inc., Chicago, USA) software, version 13.0 for Windows.

Results

Overall response rate to the questionnaires was 62% (313/509 children).

Demographic and social characteristics

Of the children enrolled in the study, 163 (52%) were male, 143 (46%) attended first grade (ages between 5 and 7 years), and the remainder attended fourth grade (n = 170, 54%) (ages between 8 and 13 years). In 85% of the cases (n = 262), the questionnaire was answered by the mother, and in 10% by the father (n = 30). The mother's and father's median age (range) was 37 (23 to 49) and 39 (24 to 58) years, respectively. On average, parents mentioned approximately 12 years of education (for 23 mothers and 50 fathers the answer was unknown), 57% of the mothers and 58% of the fathers had a skilled occupation (groups 1-3) (unknown: 93 and 94 respectively) (Table 1).

Family history

Allergy/atopy was present in at least one first-degree relative (mother, father, sibling or half-sibling) in 72 children (24%, unknown: 13), rhinitis in 82 (27%, unknown: 11), asthma in 64 (21%, unknown: 12), and eczema in 41 children (14%, unknown: 13).

ETS exposure

We found 101 children exposed to ETS at home (34%), and 36 children usually exposed to ETS outside the home (12%) (unknown: 13 and 15 respectively). Moreover, 98 children had a smoking mother (32%, unknown: 4), 112 had a smoking father (38%, unknown: 14), and 57 were exposed to ETS during pregnancy (18%, unknown: 2).

Symptoms and past history

Children had on average one sibling, and the vast majority attended day care during infancy (n = 263, 96%, unknown: 39). Only one third of the children had pets at home (n = 99, 32%), 49 of whom had a dog (16%), and 20 had a cat (7%) (unknown: 4). There was a high prevalence of upper (43%) and lower respiratory tract infections (LRTI) (32%) in the past medical history (unknown: 15 and 9 respectively). Regarding previous symptoms of allergy/atopy, 24 children had food allergy (8%, unknown: 6), 44 were allergic to aeroallergens (14%, unknown: 7), and 30 had eczema (10%, unknown: 13).

Cough during respiratory infections or rhinitis occurred in 222 children (72%, unknown: 6), cough without infections (pathologic cough) occurred in 64 children (21%), and wheezing in 104 children (35%) (53 children [18%] had ≥ 2 wheezing episodes). Asthma was considered in 11 children (4%), 5 of whom had had exacerbations in the past year, and 7 referred using regular treatment for their asthma (Table 1).

Lung function

Concerning the spirograms, 169 were considered acceptable (54%). Of these, 10 (6%) had lower than normal z score for FEV_1 (average: -0.08, range: -3.66 to 3.23),

Table 1 - Demographic and social characteristics, respiratory symptoms, and asthma diagnosis (n = 313)

	n (%)*	Unknown
Children		
Gender		
Female	150 (48)	
Male	163 (52)	
Age		
5-7 years	143 (45)	
8-13 years	170 (54)	
Children's mothers		
Median age, years (min-max)	37 (23-49)	–
Median education, years (min-max)	12 (2-21)	23
Occupation		93
Groups 1-3	126 (57.2)	
Groups 4-9	94 (42.7)	
Children's fathers		
Median age, years (min-max)	39 (24-58)	–
Median education, years (min-max)	12 (2-25)	50
Occupation		94
Groups 1-3	126 (57.5)	
Groups 4-9	93 (42.5)	
Respiratory symptoms/disease		
Cough	64 (21)	7
Wheezing	104 (35)	14
Asthma diagnosis	11 (4)	7

max = maximum; min = minimum.
* Data shown as absolute numbers and (percentages), unless otherwise specified.

7 (4%) had a low FVC z score (average: -0.06, range: -2.91 to 3.40), 1 (0.6%) had a low z score for FEV_1/FVC (average: -0.10, range: -2.22 to 1.44), and 7 (5% of 148 acceptable spirographic curves) presented low FEF_{25-75} z score (Table 2).

Table 2 - Spirometric results (n = 169)

Spirometric indices*	n (%)†	NA
Abnormal FEV_1	10 (6)	–
Abnormal FVC	7 (4)	–
Abnormal FEV_1/FVC	1 (0.6)	–
Abnormal FEF_{25-75}	7 (5)	21

FEF_{25-75} = forced expiratory flow between 25 and 75%; FEV_1 = forced expiratory volume in 1 second; FEV_1/FVC = ratio between forced expiratory volume in 1 second and forced vital capacity; FVC = forced vital capacity; NA = not acceptable.
* Abnormal is synonymous of reduced values (< -2 z scores).
† Data are shown as absolute numbers and (percentages).

Multivariable statistical analysis

The multiple regression analysis showed that: 1) children whose mothers smoked were 2.1 times more likely to have cough than children with non-smoking mothers; 2) children with a family history of allergy/atopy and past history of bronchiolitis were respectively 2.7 and 3.3 times more likely to have wheezing than children without family history of allergy/atopy or past history of bronchiolitis; 3) children with LRTI were 2.6 times more likely to have cough, 2.8 times more likely to have wheezing, and 14.6 times more likely to have an asthma diagnosis that children without LRTI in their past medical history; 4) children with a history of allergy to aeroallergens were 4.4 times more likely to have cough, 3.2 times more likely to have wheezing, and 8.2 times more likely to have asthma than children without allergy to aeroallergens (Table 3).

In the bivariate analysis between respiratory symptoms and spirometric indices, we found the following differences: 1) children with wheezing had lower average values of z score for FEV_1/FVC and FEF_{25-75} (-0.25 vs. 0, p = 0.028, and -0.55 vs. -0.17, p = 0.022, respectively); 2) the percentage of children with abnormal FEF_{25-75} z scores was higher in the group of children with wheezing (9 vs. 1%, p = 0.034); 3) children with asthma had lower average values of z score for FEV_1, FVC, FEV_1/FVC and FEF_{25-75} (-1.4 vs. -0.01, p = 0.001; -1.55 vs. 0, p = 0.004; -0.61 vs. -0.07, p = 0.046; and -1.47 vs. -0.26, p = 0.004, respectively); and 4) the percentage of children with abnormal FEV_1/FVC and FEF_{25-75} z scores was higher in the group of children with asthma (14 vs. 0%, p = 0.043, and 33 vs. 4%, p = 0.028, respectively) (Table 4).

The group of children with wheezing also presented on average lower values of FEV_1 and a higher percentage of abnormal values for FEV_1 and FEV_1/FVC, but the differences were not significant.

Discussion and conclusion

In this pilot epidemiological study, we demonstrated the applicability and usefulness of a respiratory questionnaire and of field spirometry in revealing the association between risk factors and the occurrence of respiratory symptoms and impairment of lung function in school-aged children.

Table 3 - Impact of the independent variables on the occurrence of respiratory symptoms (cough and wheeze) and on asthma diagnosis

	OR	95%CI OR	p
Cough			
Smoking mother	2.15	1.15-4.03	0.017
Lower respiratory tract infection	2.62	1.40-4.90	0.003
Allergy to aeroallergens	4.43	2.15-9.14	< 0.001
Wheezing			
Family history of allergy/atopy	2.68	1.40-5.14	0.003
Lower respiratory tract infection	2.78	1.24-6.20	0.012
Bronchiolitis	3.31	1.34-8.18	0.010
Allergy to aeroallergens	3.20	2.15-9.14	0.005
Asthma			
Lower respiratory tract infection	14.65	1.75-122.88	0.013
Allergy to aeroallergens	8.17	1.95-34.20	0.004

95%CI = 95% confidence interval; OR = odds ratio.

Table 4 - Bivariate analysis between wheezing, asthma diagnosis, and spirometric results (average z scores)

Spirometric indices	Wheezing/asthma		p
	Yes	No	
Wheezing			
FEV_1/FVC z score	-0.25	0.0	0.028
FEF_{25-75} z score	-0.55	-0.17	0.022
Children with reduced FEF_{25-75}	9%	1%	0.034
Asthma			
FEV_1 z score	-1.40	-0.01	0.001
FVC z score	-1.55	0.0	0.004
FEV_1/FVC z score	-0.61	-0.07	0.046
FEF_{25-75} z score	-1.47	-0.26	0.004
Children with reduced FEV_1/FVC	14%	0%	0.043
Children with reduced FEF_{25-75}	33%	4%	0.038

FEF_{25-75} = forced expiratory flow between 25 and 75%; FEV_1 = forced expiratory volume in 1 second; FEV_1/FVC = ratio between forced expiratory volume in 1 second and forced vital capacity; FVC = forced vital capacity.

Our response rate was similar to that reported by other studies using questionnaires published in the same area of research,[9,34,35] which strengthens the fact that questionnaires are valid and reproducible tools for the investigation of respiratory disease in the community.

This study revealed a high frequency of respiratory symptoms in schoolchildren in our city, since 21 and 35%, respectively, of the study population reported having had cough or wheeze at sometime, even though only 4% had a diagnosis of asthma. The risk factors associated with the occurrence of symptoms were similar to what has been described in the literature,[8-10,14-22] namely family history of allergy/atopy, ETS exposure, past history of LRTI, and allergy to aeroallergens. In our children, family history of allergy/atopy, past history of LRTI (and bronchiolitis), and allergy to aeroallergens were associated with an increased risk of having wheeze (OR between 2 and 3), and those with past history of LRTI and allergy to aeroallergens were 8 and 14 times more likely to have asthma, respectively.

Concerning lung function, although only slightly more than half the spirograms were considered acceptable, there was a good correlation between the questionnaire and the spirometry. Symptomatic children exhibited spirometric flows compatible with impaired lung function, and FEF_{25-75} was one of the most sensitive parameter. The earliest change associated with airflow obstruction in small airways is thought to be a slowing in the terminal portion of the spirogram, even when the initial part of the spirogram is barely affected.[36] Quantitatively, this slowing of expiratory flow is reflected in a proportionally greater reduction in $FEF_{75\%}$ or FEF_{25-75} than in FEV_1.[36] However, abnormalities in these mid-range flow measurements during a forced exhalation are not specific for small airway disease in individual patients[36] and should be interpreted with caution. The absence of statistical significance for the remainder parameters might be explained by the low number of available spirograms.

On the other hand, children with asthma diagnosis had, on average, lower values for all parameters of spirometric flows (FEV_1, FVC, FEV_1/FVC, and FEF_{25-75}). These lower levels of lung function, and the higher percentage of children with reduced FEV_1/FVC and FEF_{25-75}, support findings that have shown associations between the severity of asthma symptoms and the level of lung function that tracked over time.[8-10] We also speculate that asthma might be under-diagnosed in this group of children, since one third of the children experienced wheezing (about 20% had ≥ 2 episodes of wheezing), but only 4% had an asthma diagnosis, which is less than what has been reported in the literature[37]; furthermore, wheezing children had some impairment of lung function.

Studies of respiratory disease prevalence with objective measures of lung function are crucial for the comprehension of the epidemiology of these illnesses. This will allow the implementation of directed treatment programs, with consequent reduction in associated morbidity and in direct (medication and use of health services) and indirect costs (school and work absenteeism). The longitudinal study conducted in Tucson by Taussig et al.[10] allowed the

description of distinct wheezing phenotypes that occur during childhood. One of these phenotypes, the group of children with transient early wheezing, had diminished lung function both in infancy and at 6 years of age when compared to children who never wheezed. The lung function of these children improved with time (lung function tracking), but never matched that of children who never wheezed during their growing years. The group of children with persistent wheezing showed a decline in lung function from infancy to 6 years, suggesting that the loss of respiratory function happened after birth and persisted throughout life.[10]

Even though our study did not prospectively evaluate the respiratory health of children throughout time, in order to classify them into phenotypes, and it relied on parental recall and on report of respiratory events, it showed that the presence of known risk factors is associated with the occurrence of respiratory symptoms, and that their presence implicates some lung function disability. This screening tool can therefore potentially identify a cohort of children at increased risk of COPD, and consequently direct future interventions aiming at prevention of further damage.

Our study has also other limitations. First, response rate must always be maximized, in order to improve the design of an epidemiological study, to increase the sample size, the power and precision of the results, and decrease bias.[38] The amount of non-responders limits the extrapolation of the results, since this could bias our study towards the most symptomatic children. Different strategies have been suggested in order to improve response rates[39,40]; in our case, pre-notification of parents, *in loco* explanation to the directors and school teachers, and recall of non-respondents are some examples. Secondly, we had no measures of airway inflammation (like measurement of fractional exhaled nitric oxide concentration) or evidence of allergic sensitization in our children, and we did not stratify our symptomatic cases as to the occurrence of symptoms in a specific time window (the past year for instance). These measures would better stratify children with an active disease process, and perhaps determine a cohort requiring specific treatment. They would also better classify our asthmatic population as to their disease control.

In conclusion, our screening tools proved to be easily implemented in a non-clinical setting and were effective in identifying symptomatic schoolchildren with lung function deficits. We described risk factors for pulmonary disease, which have been documented in countries other than Portugal. If this screening strategy will be cost-effective in preventing further lung function damage and progression to COPD remains to be elucidated.

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