Variation in spirometry parameters in children with and without recurrent respiratory problems

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Abstract

Background: Children having recurrent episodes of respiratory symptoms account for a major source of hospitalization. These children have increased morbidities and if not identified in time can have impaired lung function as adults.

Objectives: The aim of our study was to compare the spirometry parameters and bronchodilator reversibility in children with and without recurrent respiratory problems.

Methods: This was a prospective observational study conducted in the Pediatric department of Manipal Teaching Hospital comparing 35 children with recurrent respiratory problems and 35 children with no history of recurrent respiratory problems. After thorough instructions, baseline spirometry was done in all children and recordings were noted. Thereafter they were given two puffs of salbutamol (100 μg) and repeat testing was done 20 minutes later. Bronchodilator reversibility was calculated according to standard formula. Various statistical tests were used to compare the findings between the two groups.

Results: The recurrent respiratory problem group had 31 (88%) cases of bronchial asthma, two (5.7%) bronchiolitis obliterans, one (2.8%) pulmonary eosinophilia, and one (2.8%) common variable immunodeficiency syndrome. The median values of FEV_1 (p=<0.001), FVC (p=0.007), FEV_1/FVC (p=0.005), PEF (p=0.042) and FEF_{25-75}(p=0.026) were lower in the group with recurrent respiratory problems. Post-bronchodilator reversibility of FEV_1 (p=0.001), FVC (p=<0.001) and FEF_{25-75} (p=0.026) was higher in the groups with recurrent respiratory problems

Conclusion: Lung function parameters in children with recurrent respiratory problems showed features of obstructive defect. The post-bronchodilator response was higher in the group with recurrent respiratory problems as compared to normal children.

Key words: Child; Recurrent; Respiratory problem; Spirometry.

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INTRODUCTION

Respiratory symptoms account for one of the most common causes of hospital visits in children <15 years of age. Recurrent respiratory symptoms in children can be manifested as repeated episodes of cough, audible wheezing, stridor, respiratory tract infections, etc. Among the many causes of recurrent respiratory symptoms are aspiration syndromes, bronchial asthma, immunodeficiency syndromes, congenital heart disease, foreign body aspiration, anomalies of the respiratory system, gastroesophageal reflux, etc[1-3]. Children with repeated episodes of respiratory symptoms have higher morbidities like failure to thrive, psychological distress due to repeated illness and the trauma that repeated hospitalization causes; not to mention the financial burden it poses to the family.

Spirometry is a tool that is used to measure lung volumes during forced breathing maneuvers. Lung function parameters are influenced by many factors like age, sex,

ethnicity, weight, height, environmental factors, method and patient effort, presence or absence of respiratory diseases,etc[4-6]. Reference ranges have been devised in several populations to define normality due to these various factors[7-11]. This test has traditionally been used to diagnose obstructive airway diseases like bronchial asthma, but it has been found to be abnormal in many other diseases as well[6,12-18]. Spirometry is not difficult to do but it is not a test that is widely used in children[19,20]. One of the reasons why it is not so much in use is because children are not able to perform the forced voluntary breathing that is required for this test. However, newer techniques introduced have made it possible to measure lung function in children as young as 24 months of age[21]. No studies were found which tried to analyze the difference in spirometry findings in children with and without recurrent respiratory problems in our part of the world. So the primary aim of our study was to find if differences exist in spirometry parameters in children with and without recurrent respiratory problems. The secondary aim was to find the postbronchodilator response between the two groups.

METHODS

This was a prospective, observational study conducted at Manipal Teaching Hospital over a duration of one year. Children between the ages of 6-13 years brought to the pediatric department for recurrent respiratory symptoms were recruited for the study. A modified American Thoracic Society and Division of Lung Diseases (ATS-DLD-78-C) questionnaire[22] was filled for all children to assess the presence of respiratory symptoms. To act as controls, children who were admitted for other illnesses and had no history of recurrent respiratory symptoms were enrolled. For the purpose of this study, recurrent respiratory symptom was defined as the presence of cough with shortness of breath or audible wheezing or fast breathing two or more times in a year or three or more episodes ever. Excluded were children less than six years of age with recurrent respiratory symptoms, children unable to follow instructions to perform the procedure, those on long-term inhaler therapy, the presence of obvious structural deformity of the chest, and patients who did not give consent. This study was approved by the institutional review committee (IRC) prior to patient enrolment. Informed consent was taken from the patient's guardian/parents. The sample size was calculated using the means and standard deviation from a previously conducted study[23]. Demographic details were noted in a predesigned proforma. Anthropometric details especially weight and height were noted and body mass index (BMI) calculated using standard

formula. In children with recurrent respiratory problems (RP) history, frequency, date of last attack, and diagnosis were noted. Diagnosis of children in the no-recurrent respiratory problems (nRP) group was also noted.

Before performing the pulmonary function test (spirometry), the procedure was properly explained to the subject. His/her understanding of the instruction was assessed by asking him to repeat the instructions. A technician trained in spirometry (breath-educator) explained and assisted the child to perform the test. We used Spirolab III ver 4.1 SN 311436 to perform the test. Spirometry was done in the sitting upright position with feet placed firmly on the ground. Three attempts were made and the highest of three readings was taken as the final value. The test was assessed for accuracy as well as repeatability and was considered successful if both the criteria were met based on the ATS-DLD criteria[24]. The child was asked to take a deep breath in followed by a forced exhalation on the mouth-piece. Then he was asked to take a deep breath in followed by an exhalation. The respiratory efforts were recorded on a graph paper which depicted flow-volume and volume-time curves. Various parameters recorded were forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), ratio of FEV_1/FVC, peak expiratory flow (PEF), forced expiratory flow between 25% to 75% of forced vital capacity (FEF_{25-75}). The predicted normal value was automatically calculated by the spirometer based on the standing height. After obtaining these readings salbutamol two puffs of 100 µg each were given from a metered-dose inhaler and the test was repeated 20 minutes later.

Bronchodilator reversibility was calculated by using the formula: Post-bronchodilator value- Prebronchodilator value/Pre-bronchodilator value x 100.

Statistical analysis was done by SPSS ver 20. The normality of data was checked by the Shapiro-Wilk test. Bivariate analysis was done using Chi-square tests to compare the two groups for categorical data which were presented as absolute number (%). Continuous data which were found to be non-normally distributed were expressed as median [interquartile range] while if normally distributed it was expressed as mean (SD). For analysis of continuous variables, the Mann-Whitney U test or independent sample t-test was used as necessary. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 70 children were enrolled in the study; of which 35 cases were in the recurrent RP group and 35

cases in the no-recurrent RP group. The median age of presentation in years in the two groups was 10 [6-13] and 12 [8-13] respectively. Male: female ratio in the recurrent RP group was 1.91:1 while in no recurrent RP group it was 1.18:1. The recurrent RP group comprised of 31 (88%) bronchial asthma, two (5.7%) bronchiolitis obliterans, one (2.8%) pulmonary eosinophilia, and one (2.8%) common variable immunodeficiency syndrome while the no-recurrent RP group consisted of cases who visited the department for other non-respiratory illnesses. The demographic characteristics of the two groups are as shown in Table 1.

The spirometric evaluation showed that the median values of FEV_1 were lower in the recurrent RP group as compared to the no-recurrent RP group. Similarly, FVC, FEV_1/FVC, PEF, and FEF_{25-75} were all lower in the group with recurrent RP than in the no-recurrent RP group. The mean value of FEV_1, FVC, FEV_1/FVC, PEF, and FEF_{25-75} in terms of percentage of predicted value was found to be lower in the recurrent RP group as compared to no-recurrent RP group (Table 2).

Bronchodilator reversibility in the various spirometric parameters assessed after nebulization with salbutamol shows that there was a difference between the two groups (Table 3). Reversibility of FEV_1, FVC, and FEF_{25-75} was significantly higher in the group with recurrent RP as compared to the no-recurrent RP group however there was no significant difference in the FEV_1/FVC.

Table 1: Characteristics of subjects with and without recurrent respiratory problems

Characteristic	Recurrent RP (n=35)	No-recurrent RP (n=35)
Age in years*	10 [6-13]	12 [8-13]
Male gender**	23 (65.7%)	19 (54.3%)
Resides near busy roads**	14 (40%)	5 (14.3%)
Family members*	4 [2-8]	4 [2-18]
Number of rooms*	3 [1-9]	3 [2-11]
Has in-house smoker in family**	3 (8.6%)	8 (22.9%)
Uses firewood for cooking**	1 (2.9%)	2 (5.7%)
Episodes of respiratory illness*	3 [2-12]	0.00 [0-1]
Weight in kgs*	30 [15-52]	31 [19-50]
Height in cm*	139 [108-169]	139 [116-165]
BMI in kg/sq. m*	15.3 [12.4-22]	16 [12-21]

*median [IQR]; ** n%

Table 2: Baseline spirometric parameters of children with and without recurrent respiratory problems

Parameter	Recurrent RP	No-recurrent RP	p-value
FEV_1*	1.5 [0.4-3.5]	1.8 [0.97-3.18]	<0.001
FVC*	1.6 [0.47-4]	2 [1-3.7]	0.007
FEV_1/FVC*	86.7 [64-100]	89 [81-100]	0.005
PEF*	2.4 [0.6-6.6]	2.8 [2-6.2]	0.042
FEF_{25-75}*	1.38 [0.54-4]	2.3 [1-4.3]	0.026
Measure of % predicted			
FEV_1**	75.7 (22.7)	102.5 (27.6)	<0.001
FVC **	79.5 (19.6)	101 (25)	<0.001
FEV_1/FVC **	91.4 (10)	98 (6)	0.001
PEF **	62.4 (23.5)	75.2 (20.8)	0.022
FEF_{25-75} **	62.7 (29)	92 (31.7)	<0.001

*median [IQR]; ** means (±SD)

Table 3: Reversibility in selected parameters after nebulization with salbutamol in the groups with and without recurrent respiratory problems

Parameter	Recurrent RP	N0-recurrent RP	p-value
FEV$_1$%-PB^{R*}	11 [-16,54]	5.5 [-35, 19]	0.001
FVC%-PBR*	7 [-16, 33]	4 [-21,24]	<0.001
FEV$_1$/FVC%-PBR*	-9 [-28,21]	0.00 [-20,11]	0.657
FEF$_{25-75}$%-PBR*	26 [-42,173]	14 [-54,71]	0.026

*median [IQR]

DISCUSSION

We conducted this study to compare the spirometry parameters in children with and without recurrent respiratory problems. To the best of our knowledge, this is the first study of its kind conducted in our part of the world. Spirometry has been used in the management of children with bronchial asthma for some time now[12,21,23,25,26]. Several studies have shown that derangements in lung function parameters can also be seen in bronchiolitis obliterans, bronchiectasis (cystic fibrosis-associated or otherwise), hemoglobin disorders like sickle cell disease, etc[14,15,18,27,28]. In our study maximum cases were of bronchial asthma while two were of bronchiolitis obliterans. Both these conditions are characterized by variable airflow obstruction. While in bronchial asthma the obstruction is said to be reversible; in bronchiolitis obliterans, it is said to be only partially reversible. Our study found that the baseline spirometry parameters (FEV$_1$, FVC, FEV$_1$/FVC, PEF, and FEF$_{25-75}$) were all significantly lower in the recurrent RP group as compared to the no-recurrent RP group. The mean values of percentage predicted of FEV$_1$, FVC, PEF, and FEF$_{25-75}$ were lower than the standard accepted level of 80% while the ratio of FEV$_1$/FVC was just above the acceptable level of 90% in the recurrent RP group as compared to the no-recurrent RP group where all the parameters were above the cutoff level. This indicates that there were varying degrees of obstruction in the group having recurrent respiratory problems as compared to the other group. According to a report by Global Initiative For Asthma (GINA 2018) FEV$_1$ and FEV$_1$/FVC are markers of expiratory airflow obstruction[29]. In a study conducted on 72 children with bronchiolitis obliterans, it was found that the baseline spirometric parameters were all below the reference parameters for all variables[30]. In our study since the FVC was also below 80%, it leads us to think that there was some degree of restrictive pathology involved. However, decreased FVC can be seen not only in restrictive disease but can also occur in severe obstructive disease and in case of suboptimal performance while undergoing the procedure in children[4,31].

PEF is a measure of patency of larger intrathoracic airways. PEF in both the groups was below the standard normal value of 80% and it was statistically lower in the group with recurrent RP. However, PEF is said to be subjective and effort-dependent and might not reflect the true degree of obstruction in children. FEF$_{25-75}$ on the other hand represents the mean forced expiratory flow between 25% to 75% of the forced vital capacity. It is considered as a marker of small airway patency and is less effort-dependent so it has useful value in the assessment of expiratory obstruction in children. In this study, the value of FEF$_{25-75}$ was significantly lower in the group with recurrent respiratory problems which indicates that there was the involvement of smaller airways leading to respiratory problems. This shows that children in the recurrent RP group had varying degrees of obstruction in the larger as well as smaller airways.

Bronchodilator reversibility testing in both the groups showed that there was significantly higher reversibility in FEV$_1$, FVC and FEF$_{25-75}$ after nebulization with salbutamol in the recurrent RP group as compared to the other group while there was no difference in FEV$_1$/FVC. Generally, bronchodilator reversibility is said to be present and suggestive of a reversible obstructive defect when there is a post-bronchodilator increase in FEV$_1$ by >12% in children (or >200 ml in adults) and >15-25% increment in FEF$_{25-72}$[4]. However several studies have found that a cutoff of FEV1>12% correlates poorly with reversibility in children and a lower cutoff would increase the sensitivity of diagnosing asthma in children[32,33]. In a study on post-infectious bronchiolitis obliterans in children and adolescents, it was found that the mean values of FEV$_1$, FVC, FEV$_1$/FVC and FEF$_{25-75}$ before nebulization with a bronchodilator were all below normal z-score value; there was some improvement post-nebulization but this change was not significant enough to reach normal levels[30]. Another study has shown that bronchodilator reversibility is seen in healthy children as well as those having obstructive lung disease but the reversibility is greater in asthmatics as compared to healthy children[34]. This finding was seen in our study also where there was

an improvement in all parameters after nebulization with bronchodilator in both the groups; however the degree of improvement was more in the recurrent RP group as compared to the normal group. In a study comparing the bronchodilator reversibility in healthy children against those with doctor-diagnosed asthma, cystic fibrosis, neonatal chronic lung disease, and current wheezers it was found that the reversibility was comparable between healthy and cystic fibrosis patients while those with neonatal chronic lung disease had higher reversibility as compared to healthy children. Those children who were current wheezers or had doctor-diagnosed asthma had a similar or slightly smaller reversibility than healthy controls. This was explained by the fact that these children were on inhaled corticosteroids which could have led to a decrease in reversibility nearing that of control subjects[35]. Other studies have found that FEF_{25-75} is a better marker to assess bronchodilator reversibility than FEV_1[36-38]. In our study, although the median value of FEF_{25-75} reversibility seems higher on gross comparison to FEV_1, a detailed comparison between the two was beyond the scope of this study.

The strength of our study is that this is the first study of its kind conducted on children in the context of Nepal. Limitations of our study are: a) Small sample size limited to a tertiary-level teaching medical college because of which the results cannot be extrapolated on a larger population, b) Most of the cases in the recurrent respiratory problem were cases of bronchial asthma; a greater mix of other pulmonary diseases might have produced a different result.

CONCLUSION

From our study, we conclude that children with recurrent respiratory problems tend to have features of obstruction involving the larger intrathoracic airways as well as the smaller airways. The baseline lung function parameters, as well as the percentage of predicted values, are lower than the standard predicted values and post-bronchodilator reversibility is higher in the children with recurrent RP as compared to healthy controls. Hence, spirometric study is recommended in all children who present with a history of recurrent respiratory problems so that the type of abnormalities can be identified and treated optimally in time before significant compromise in lung function occurs.

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