Mild respiratory symptoms in asthmatic patients might not be due to bronchoconstriction

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Abstract:
BACKGROUND: Although respiratory symptoms in asthmatic patients are likely to be caused by bronchoconstriction, this should be confirmed by spirometry. In this study, our aim was to determine the percentage of asthmatic patients who present with mild respiratory symptoms but fail to show any evidence of bronchoconstriction in spirometry.

MATERIALS AND METHODS: A total of 428 known asthmatic patients (57.5% females) participated in the study. Inclusion criteria were age ≥16 years, known asthmatics for at least 1 year, presenting with mild respiratory symptoms including cough, wheezes, shortness of breath, and chest tightness. Patients presenting with moderate or severe asthma exacerbations were excluded from the study. Spirometry measurements were performed according to the guidelines of the American Thoracic Society. SPSS was used for data analysis. The percentage of patients who did not show any evidence of airway obstruction was calculated. For spirometry variables, mean and standard deviation were calculated. For the categorical variables, Chi-square test was performed to determine statistical significance at alpha=0.05.

RESULTS: Typical obstructive pattern was found in 38 (or 9%) of all participants. Evidence of obstruction within small or middle airways was found in all those who showed an obstructive pattern and more than 90% of those who showed restrictive or mixed patterns. About 11% of the participants showed a normal spirometric pattern with no evidence of small airway obstruction. Statistical analysis showed an insignificant relation between patterns of spirometry and gender or body mass index of the participants.

CONCLUSION: About 11% of asthmatic patients with mild respiratory symptoms who attended the respiratory clinic have no evidence of bronchoconstriction. Spirometry is an essential step for evaluation of every asthmatic patient who presents with respiratory symptoms.

Keywords:
Airway obstruction, asthma, reversibility, spirometry

Introduction

Asthmatic patients who suffer from acute exacerbations of asthma present with a variety of symptoms including dyspnea, wheezes, chest tightness, and cough. On the other hand, many respiratory and cardiac diseases may present with asthma-like symptoms. Previous studies have shown that many medical problems could be misdiagnosed as acute exacerbations of asthma.¹⁻³ Besides, asthmatic patients may develop symptoms because of such comorbidities as acute viral infections or congestive heart failure. Such patients may receive unnecessary doses of anti-inflammatory drugs and bronchodilators that may exacerbate their suffering. In addition, the delay in the proper management can be fatal. Therefore, treating asthma without objective measurement of lung function and confirmation of the bronchoconstriction is utterly unacceptable. It is always recommended that spirometry should be used for the initial assessment of
every asthmatic patient who attends with respiratory symptoms. Spirometry is the most recommended tool for the detection of airway obstruction. The diagnosis of asthma depends on the demonstration of an obstructive pattern. However, in some patients, the only indicator of obstruction might be low values of the forced expiratory flows (FEFs) (FEF25, FEF50, FEF75, or FEF25–75), indicating obstruction within the middle and the small airways of the lungs. When there is no evidence of broncho-obstruction in spirometry, further investigations for an alternative diagnosis should be indicated. Unfortunately, there is general underutilization of spirometry at both primary and specialist health care levels of many countries worldwide. Few physicians use the spirometer to review their patients during their daily practice in spite of the equipment being available in their setting. Furthermore, there is a paucity of information about the percentage of symptomatic asthmatic patients who attend the outpatient clinic with alternative diagnoses and without evidence of airway obstruction. The aim of this study was to determine patterns of spirometry in symptomatic, already diagnosed, asthmatic patients who attend the respiratory clinic for consultation or follow-up and determine the percentage of those who present with a nonobstructive pattern.

Materials and Methods

A descriptive, cross-sectional study was conducted in Yastabshiron Hospital, a private hospital in Khartoum/Sudan. Participants were adult asthmatic patients who attended the respiratory clinic for consultation or follow-up. We took a stratified random sample of the attending patients over a period of 6 months. The physician in charge classified the selected patients into mild, moderate, or severe stage based on their symptoms and signs. Those who were included in our study fulfilled the following inclusion criteria: known asthmatics for at least 1 year, age ≥16 years, presenting with mild respiratory symptoms that included cough, wheezes, shortness of breath, and chest tightness. Exclusion criteria were age <16 years, not a known asthmatic or newly diagnosed (for <1 year), and presenting with moderate-severe asthma symptoms. A portable All-flow spirometer (Clement Clarke International, Harlow, UK) was used for the measurement of lung function of each participant. Measurements were carried out according to the guidelines of the American Thoracic Society. The measurements steps were as follows:

1. Air temperature and relative humidity of the room were measured and registered in a computer program that controls the spirometer
2. The spirometer was calibrated with a 3 L calibrating syringe
3. The age, sex, height, and weight of each participant were registered
4. Each participant was asked to sit down, take a deep breath, put a mouthpiece connected to the spirometer in his mouth with the lips tightly around it, and then blow air out as hard and as fast as possible for at least 6 s
5. The procedure was repeated until acceptable and reproducible results were obtained
6. Total measurement trials for each participant did not exceed five times to avoid exhaustion
7. Patients who failed to complete the spirometry measurements were excluded.

The research followed the ethical principles of medical research developed by the World Medical Association Declaration of Helsinki. Approval and permission letters were obtained from the Department of Physiology, Faculty of Medicine, University of Khartoum, Sudan. Acceptance was obtained from the respiratory physician who runs the respiratory clinic. The patients were asked to give their written consent before participation in the study. Data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 20. Results of the spirometry were expressed in the form of mean (standard deviation [SD]). For the categorical variables, Chi-square test was performed to determine statistical significance at alpha=0.05.

Results

A total of 428 patients were included in the study; 57.5% were females. Table 1 shows general characteristics and mean spirometric values of the participants. Their ages ranged from 16 to 86 years with a mean (SD) of 43.2 (16.1) years. Mean forced vital capacity (FVC), forced expiratory volume in the 1st s (FEV1), and peak expiratory flow rate were 2.6, 2.1, 4.2, respectively.

| Table 1: Characteristics of patients in the study group | Mean | SD |
|--------------------------------------------------------|------|----|
| Age (years)                                            | 43.2 | 16.1 |
| Height (cm)                                            | 165.0 | 9.6 |
| Weight (kg)                                            | 77.6 | 18.3 |
| BMI                                                    | 28.6 | 6.6 |
| FVC (l)                                                | 2.6  | 1.0 |
| FEV1 (l)                                               | 2.1  | 0.8 |
| Ratio (%)                                              | 78.6 | 13.3 |
| FEF25 (L/s)                                            | 3.7  | 1.7 |
| FEF50 (L/s)                                            | 2.5  | 1.3 |
| FEF75 (L/s)                                            | 1.1  | 0.7 |
| FEF25-75 (L/s)                                         | 2.1  | 1.2 |
| PEFR (L/s)                                             | 4.2  | 1.7 |

SD = Standard deviation, FEF = Forced expiratory flow, PEFR = Peak expiratory flow rate, FVC = Forced vital capacity, BMI = Body mass index, FEV1 = Forced expiratory volume in the 1st s
Patterns of spirometry in relation to the indicators of obstruction are summarized in Table 2. Typical obstructive pattern was found only in 9% of all participants. Evidence of obstruction within small or middle airways (as shown with low FEF values FEF25, FEF50, and FEF75) was found in 100% of those who showed an obstructive pattern and more than 90% of those who showed restrictive or mixed patterns. About half of those who showed normal patterns on spirometry had evidence of small airway obstruction. Eleven percent showed a normal spirometric pattern with no evidence of small airway obstruction.

The abnormal spirometric pattern was significantly higher among the older participants (>30 years) compared to the younger ones (<30 years); \( p = 0.017 \) [Table 3]. Statistical analysis showed that the spirometric pattern had no relation to gender or body mass index of the participants.

### Discussion

The results of this study confirmed the previous findings that asthma can present with nonobstructive patterns.\(^{[9,11,12]}\) The exclusion of those who presented with moderate and severe asthma symptoms caused a reduction in the percentage of those who showed typical obstructive patterns. The finding that 11% of the participants presented with a normal pattern, with no evidence of small airway obstruction, is important. In these patients, the diagnosis of asthma should be revised. Many previous studies found that some patients who had been managed as asthmatics for years were not asthmatics.\(^{[1,3,13]}\) On the other hand, it is worth noting that, even for the known asthmatic patients, respiratory symptoms could be related to other diseases such as heart failure or a respiratory tract infection rather than an acute exacerbation of asthma. For this reason, it is recommended that every asthmatic patient who presents with inadequate control of asthma symptoms should be reevaluated.\(^{[4]}\) This should include an objective measurement of lung function using spirometry to differentiate between difficult to treat asthma and alternative problems. The use of spirometry is strongly associated with a reduced risk of misdiagnosis.\(^{[13]}\) Unfortunately, in spite of the availability of spirometers, few physicians use them for the evaluation of asthmatic patients in the outpatient clinic.\(^{[4]}\)

In this study, more than half of the patients had nonobstructive patterns on spirometry and a considerable number had normal FEV1 and FVC, but fewer patients had normal FEF25, FEF50, and FEF75. The FEF indicators measure the airflow through the middle portion of the forced expiration, and they have the advantage of avoiding the effort-dependent part of the FEV1 that appears at the beginning of the forced expiration. For this reason, they could be more sensitive to the detection of airway obstruction.
obstruction within the middle and small airways of the lungs. The disadvantage is that their normal range is very wide, and the possibility of reproducibility is not high.

Because of the direct mechanical effect of their chest walls on their lungs, obese patients are likely to show restrictive patterns on spirometry. However, we found an insignificant relation between obesity and pattern of spirometry. The air trapping that is caused by the early closure of the small airways during expiration may cause a reduction in the vital capacity and could be a possible explanation for the restrictive pattern. Similar atypical presentations of asthmatic patients on spirometry were reported in previous studies. When a diagnosis of bronchial asthma is clinically suspected, measurement of the total lung capacity could be more useful than the FEFs and reversibility tests done for the confirmation of the diagnosis.

This study has the following limitations. First, with the random selection of the participants, sampling bias is inevitable. The second limitation is the lack of static lung volume measurement that would confirm lung restriction or air trapping. A third limitation is that investigations for alternative diagnoses were not considered.

Conclusion

Our findings suggest that mild respiratory symptoms in asthmatic patients might not be caused by bronchoconstriction. Lung function tests should be indicated before unnecessary bronchodilators are prescribed. Continuous educational programs are highly recommended to increase physicians’ awareness of the value of spirometry in the reevaluation of the symptomatic asthmatic patients.

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Conflicts of interest
There are no conflicts of interest.

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