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Characteristics of bronchial asthma with persistent airflow limitation

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Abstract:

BACKGROUND: Asthma is a chronic inflammatory disorder of airway characterized by variable symptoms and variable airflow limitation. There are many patients developed persistent airflow limitation in due course of disease due to many factors. The present study was conducted to characterize this phenotype and to identify the factors which are implicated in causing persistent airflow limitation.

MATERIALS AND METHODS: We recruited consecutive 164 patients aged <40 years (to exclude chronic obstructive pulmonary disease [COPD]), diagnosed, and treated as bronchial asthma in our asthma clinic for at least 6 months. We took all clinical, lung function detail and compared between asthma with or without persistent airflow limitation. The patients were assigned to the group with persistent airflow obstruction if they presented postbronchodilator forced expiratory volume in 1 s (FEV1) or FEV1/forced vital capacity values <70% predicted.

RESULTS: A total of 114 patients included in the study and 42 (36.84%) patients had persistent airflow limitation. The patients with persistent airflow limitation have a higher age and more proportion of patients were male. History of allergic rhinitis is an important risk factor found associated with asthma with persistent airflow limitation ($P \leq 0.001$). 26.19% of patients with persistent airflow limitation had a history of symptom since childhood and generally having a longer disease duration compared to patient without airflow limitation ($P < \text{nonsignificant}$). Reversibility criteria ($>12\%$ and >200 ml increase in FEV1) was fulfilled by only 26.7% of the study patients. The factors such as onset of disease after 18 years, history of atopy, serum IgE level, family history of asthma, and biomass fuel exposure did not differ between groups with or without airflow limitation.

CONCLUSIONS: Bronchial asthma is more having a COPD such as spirometry features if it has been started since childhood, longer disease duration, and history of allergic rhinitis. Reversibility in spirometry, which is specific for asthma diagnosis, is found only in one-fourth of the patients.

Keywords:

Asthma, chronic obstructive pulmonary disease, persistent airflow limitation, serum IgE

Introduction

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation.^[1] Heterogeneity means asthma have different phenotypes which

vary in their etiology (atopy/nonatopy), severity, inflammatory profile, age of onset, and response to treatment. Although airways' limitation is mostly reversible, persistent airflow limitation can develop in a subgroup of patients with asthma who have no significant history of smoking and optimal treatment.^[2]

The etiology of persistent airflow limitation in asthma is still unknown, although most investigators assume that such loss of lung function is causally related to inflammatory processes in the airway

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wall.^[3] The presence of persistent airflow obstruction may lead to wrong diagnosis of chronic obstructive pulmonary disease (COPD), especially in smokers with characteristics of asthma and/or atopic.^[4,5]

Persistent airway obstruction in asthma has been shown to be associated with more severe disease^[6,7] and has been reported to be a predictor of overall mortality in patients with asthma.^[8] However, data about the exact prevalence of and risk factors for persistent airflow limitation are limited.

The aim of the present study is to evaluate the differences in clinical, pathophysiologic characteristics and treatment between asthmatic patients with and without persistent airflow obstruction. We compare variables such as age at onset, smoking history, obesity, and atopic status as clinical characteristics, bronchodilator reversibility, total IgE, and eosinophil and neutrophil percentages in the peripheral blood markers of airway inflammation, and ICS responsiveness.

Aims and objectives of the study

1. Clinical characteristics of bronchial asthma with persistent airflow limitation
2. Pulmonary function characteristics of bronchial asthma with persistent airflow limitation.

Materials and Methods

Study population

We recruited consecutive 163 patients aged less than 40 years, diagnosed, and treated as bronchial asthma in the pulmonary medicine department of AIIMS, Patna. All the patients who have been followed up in an asthma clinic for at least 6 months included in the study. Demographic data, smoking status, body mass index, and type of treatment were recorded for all patients.

Diagnosis of asthma was based on the GINA guidelines.^[1] If patient has a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and intensity and/or variables expiratory airflow limitation (forced expiratory volume in 1 s [FEV1]/forced vital capacity (FVC) <75% of LLN, FEV1 <80%, FEV1 increases by >12% and 200 ml after 400 mcg of salbutamol). Early-onset asthma was defined as the onset of asthma symptoms before the age of 18 years. The study was approved by the Institute Ethical Committees of AIIMS, Patna.

Exclusion criteria

Patients with a diagnosis of other respiratory disease, concomitant malignancy, and severe heart, liver, renal, or collagen disease were excluded. Patients with a

respiratory tract infection or an asthma exacerbation in the past 8 weeks were also excluded.

Definition of persistent airflow limitation

Patients were assigned to the group with persistent airflow obstruction if they presented postbronchodilation FEV1 or FEV1/FVC values <70% predicted. We took cutoff of 70% instead of 75% (which was used by other study^[9]) because fixed airflow limitation or irreversible airflow limitation defined by a cutoff of 70% postbronchodilator similar to used in COPD diagnostic criteria.^[10] All other subjects were considered to be able to achieve a normal or near-normal FEV1 and were classified to the group without persistent airflow obstruction.

The sociodemographic and disease characteristics of the patients documented according to a detailed pro forma. The age at onset of asthma was judged as accurately as possible and used to calculate the duration of asthma. Pulmonary function tests were performed with reversibility testing. Reversibility performed with 400 mcg of salbutamol given by MDI with spacer. All lung function parameters were expressed as percentages of predicted values. Persistent airflow limitation was defined as a postbronchodilator FEV1 or FEV1/FVC <70% predicted. All patients underwent blood tests such as complete blood count and serum total IgE to know atopic status.

Statistical analysis

Categorical variables are presented as *n* (%), whereas numerical variables are presented as mean $\pm$ standard deviation or median (interquartile ranges) for normally distributed and skewed data, respectively. Comparisons between patients with fixed and nonfixed airway obstruction were performed using Chi-square tests for categorical data, as well as unpaired *t*-tests or Mann-Whitney U-tests for normally distributed or skewed numerical data, respectively.

Results

A total of 164 consecutive patients diagnosed as bronchial asthma and followed in our asthma clinic were included in the study. Fifty patients excluded as they did not have all data. Hence, a total of 114 patients included in study and 42 (36.84%) patients had persistent airflow limitation. Baseline characteristics which include demographic and clinical data are represented in Table 1. Patients with persistent airflow limitation have a higher age, and more proportion of the patients were male. History of allergic rhinitis is an important risk factor associated with asthma with persistent airflow limitation ($P = 0.001$). 26.19% of the patients with persistent airflow limitation had a history of symptom since childhood and generally having a longer disease duration as compared to patients

without airflow limitation ($P < \text{nonsignificant [NS]}$). Most of the study patients (92.98% – 92.08% with persistent airflow limitation and 93.05% of patients without airflow limitation) were nonsmoker. The factors such as onset of disease after 18 years, history of atopy, family history of asthma, and biomass fuel exposure did not differ between group with or without airflow limitation [Table 1].

Patients with persistent airflow obstruction had a significantly lower both pre- and post-bronchodilator FEV1 and FEV1/FVC ratio compared to patients without persistent airflow obstruction. There were significantly more proportion of the patients with persistent airflow limitation required Step 4 treatment for control of their symptoms as compared to without persistent airflow limitation. History oral corticosteroid use in the past 1 years and proportion of severe asthma did not differ in both group of patient with or without airflow limitation. More number of patients with persistent airflow limitation had wheeze on chest auscultation, decreased air entry, and hyperinflation in chest X-ray but statistically not significant. Only six patients have a normal IgE level (<150) in total study patients. The patients with persistent airflow limitation had lower IgE value than without persistent airflow limitation (868.43 ± 757.97 vs. 1182.51 ± 915.67) [Table 2].

Discussion

This study conducted to evaluate the clinical and pulmonary function characteristics of patients of bronchial asthma with or without persistent airflow limitation, which is also called sometimes as reversible and irreversible airflow obstruction. Asthma is mainly characterized by variable symptoms and variable airflow limitation. However, several asthma patients developed persistent airflow limitation in due course of disease, which makes some times challenging to differentiate from COPD. This challenge highlighted by the ATS statement in late back 1995^[11] is “it may be impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from persons with chronic bronchitis and emphysema with partially reversible airflow obstruction and bronchial hyperresponsiveness.” Hence we took asthma patients who have an age less than 40 years to exclude COPD and characterized clinically and on lung function parameters between reversible and irreversible airflow limitation. Our study shows that advancing age and male gender were found important risk factors for persistent airflow limitation. History of symptom since childhood and allergic rhinitis were the important factors leading to persistent airflow limitation. The factors such as onset of disease after 18 years, history of atopy, family history of asthma, and biomass fuel exposure did not differ

Table 1: Demographic and functional characteristics of the study patients according to the presence or absence of persistent airflow obstruction

Characteristics	Persistent airflow obstruction (n=42)	Without persistent airflow obstruction (n=72)	P
Age	29.1±11.09	25.04±8.24	0.0279
Sex (male:female)	25:17	36:36	0.3254
BMI	20.71±3.90	21.07±6.81	0.7544
TDI (years)	9.19±9.76	8.71±9.07	0.7915
Since childhood (years)	11 (26.19)	15 (20.83)	
<5	27 (64.28)	47 (65.27)	0.676*
>10	4 (9.52)	10 (13.88)	
Biomass exposure	12 (28.57)	15 (20.83)	0.3485
Current exposure	3 (7.10)	5 (6.94)	0.9681
Exsmoker	(-)	(-)	(-)
Nonsmoker	39 (92.8)	67 (93.05)	0.9681
Obesity (>30)	2 (4.76)	0 (0.0)	
Late onset of asthma	22 (52.38)	37 (51.38)	0.9186
Atopy	18 (42.85)	25 (34.72)	0.3873
Allergic rhinitis (%)	34 (85)	36 (50)	0.0011
Family history of asthma	12 (28.57)	24 (33.33)	0.5978

Number in parentheses is showing percentage out of total patients (n=42 and n=72). P value of t-test for difference of means and proportion between two groups. *P value of Chi-square test. BMI=Body mass index, TDI=Total duration of illness

between group with or without airflow limitation. History of smoking is an important risk factor for asthma which increases both morbidity and mortality. We could not find the difference statically significant as a number of smokers are very few in number. The current standard for asthma diagnosis is based on the typical clinical features in addition to the presence of airway dysfunction documented objectively with a significant change in (FEV1) after bronchodilator administration. There is overlap in bronchodilator reversibility and other measures of variation between health and disease.^[12] In our study, less than half of patients shown reversibility of >12% and this proportion of patient further reduced in patients with persistent airflow limitation (36.11%). If we put criteria of both >12% and >200 ml increase in FEV1, only 26.7% of the study patients show this finding. Our finding supported by many studies which show incomplete airflow reversibility in asthma.^[2,13] Reversibility also depends upon severity of bronchial asthma. Generally, patients of severe asthma have lesser reversibility and more of persistent airflow limitation spirometry as compared to mild-to-moderate asthma. There is a study^[14] which measures proportion of severely asthmatic patients with persistent airflow limitation and it was found as high as 49%. In another study,^[15,16] in moderate-to-severe asthma, 23% of the patients exhibited incomplete reversibility of airways obstruction. During chest auscultation, bilateral air entry got reduced more in patients who have persistent airflow limitation as

Table 2: Comparison of clinical and pulmonary function variable of asthma with or without fixed airway obstruction

Variables	Persistent airflow limitation (n=42)	Without persistent airflow obstruction (n=72)	P
Wheeze on auscultation	42 (100)	63 (87.5)	0.065
Bilateral decreased air entry on auscultation	12 (28.57)	14 (19.44)	0.262
Hyperinflation in CXR	5 (11.90)	7 (9.72)	0.7142
Bronchodilator reversibility (%) change in FEV1	17.51±19.08	18.29±18.82	
>12% reversibility	21 (50)	26 (36.11)	0.8322
>12%+>200 ml	11 (26.33)	22 (30.55)	
Prebronchodilator FEV1/FVC, % predicted	54.54±11.10	75.47±9.62	0.0001
Postbronchodilator FEV1, % predicted	42.65±17.69	64.69±20.96	0.0001
Postbronchodilator FEV1/FVC, % predicted	59.82±12.11	80.82±8.25	0.0001
Postbronchodilator FEV1, % predicted	49.89±18.80	66.59±17.89	0.0001
Total IgE	868.43±757.97	1182.51±915.67	0.063
OCS (>2 course/year)	13 (30.95)	21 (29.16)	0.840
Step 4 maintenance treatment	14 (33.33)	8 (11.11)	0.0037
Severe asthma	4 (9.52)	3 (4.16)	0.2504

Number in parentheses is showing percentage out of total patients. *P* value of *t*-test for difference of means and proportion between two groups. CXR=Chest X-ray, FEV1=Forced expiratory volume in 1 s, FVC=Forced vital capacity, OCS=Oral corticosteroids

compared to without but this difference was not statically significant. Our study shows very high level of IgE which could be due to viral infections, which is the commonest cause of exacerbation of symptoms in asthma or may simply represent a generalized upregulation of IgE production.^[17]

Persistent airflow obstruction represents a specific phenotype with severe disease requiring more intense treatment. However, we cannot exclude other factors that may contribute to the presence of persistent airflow obstruction. These factors may be related to the presence of persistent air-trapping,^[18] domestic exposure to molds, hospitalization during the last year, and frequent exacerbations. Almost 10% of asthma patients in this study have hyperinflated lung fields in chest X-ray which was found more with patients with persistent airflow limitation. This study also shows that patients with persistent airflow limitation have a more of severe asthma category than without (*P* < NS).

Our study has few limitations. The sample size is small in which difficult to assess association between variables and persistent airflow limitation. We could not identify other eosinophilic lung disease such as Allergic bronchopulmonary aspergillosis (ABPA) and tropical pulmonary eosinophilia. We have also not measured eosinophilia markers such as Fraction of Exhaled Nitric oxide (FENO) and sputum eosinophil which could help in characterized asthma patients with persistent airflow limitation.

Conclusions

Bronchial asthma is now recognized as a heterogeneous disease with number of phenotype. Many a times, it is

very difficult to differentiate from COPD because of poor reversibility in spirometry. We found that patients developed irreversible airflow limitation or COPD such as spirometry variables if it has been started since childhood, longer disease duration, and history of allergic rhinitis. The factors such as onset of disease after 18 years, history of atopy, family history of asthma, and biomass fuel exposure did not differ between group with or without airflow limitation.

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Conflicts of interest

There are no conflicts of interest.

References

1. Global Strategy for Asthma Management and Prevention; 2017. Available from: <http://www.ginasthma.org>. [Last accessed on 2019 May 26].
2. Brown PJ, Greville HW, Finucane KE. Asthma and irreversible airflow obstruction. *Thorax* 1984;39:131-6.
3. Homer RJ, Elias JA. Consequences of long-term inflammation. Airway remodeling. *Clin Chest Med* 2000;21:331-43, ix.
4. Lange P. Persistent airway obstruction in asthma. *Am J Respir Crit Care Med* 2013;187:1-2.
5. Perret JL, Dharmage SC, Matheson MC, Johns DP, Gurrin LC, Burgess JA, et al. The interplay between the effects of lifetime asthma, smoking, and atopy on fixed airflow obstruction in middle age. *Am J Respir Crit Care Med* 2013;187:42-8.
6. Akhter J, Gaspar MM, Newcomb RW. Persistent peripheral airway obstruction in children with severe asthma. *Ann Allergy* 1989;63:53-8.
7. Carr DH, Hibon S, Rubens M, Chung KF. Peripheral airways obstruction on high-resolution computed tomography in chronic severe asthma. *Respir Med* 1998;92:448-53.
8. Hansen EF, Phanareth K, Laursen LC, Kok-Jensen A, Dirksen A. Reversible and irreversible airflow obstruction as predictor of

- overall mortality in asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999;159:1267-71.
9. Konstantellou E, Papaioannou AI, Loukides S, Patentalakis G, Papaporfyriou A, Hillas G, *et al.* Persistent airflow obstruction in patients with asthma: Characteristics of a distinct clinical phenotype. *Respir Med* 2015;109:1404-9.
10. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of COPD; 2013.
11. Wenzel SE. Asthma phenotypes: The evolution from clinical to molecular approaches. *Nat Med* 2012;18:716-25.
12. Tan WC, Vollmer WM, Lamprecht B, Mannino DM, Jithoo A, Nizankowska-Mogilnicka E, *et al.* Worldwide patterns of bronchodilator responsiveness: Results from the burden of obstructive lung disease study. *Thorax* 2012;67:718-26.
13. Peat JK, Woolcock AJ, Cullen K. Rate of decline of lung function in subjects with asthma. *Eur J Respir Dis* 1987;70:171-9.
14. ten Brinke A, Zwinderman AH, Sterk PJ, Rabe KF, Bel EH. Factors associated with persistent airflow limitation in severe asthma. *Am J Respir Crit Care Med* 2001;164:744-8.
15. Ulrik CS, Backer V. Nonreversible airflow obstruction in life-long nonsmokers with moderate to severe asthma. *Eur Respir J* 1999;14:892-6.
16. Corne JM, Holgate ST. Mechanisms of virus induced exacerbations of asthma. *Thorax* 1997;52:380-9.
17. Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X, *et al.* Identification of asthma phenotypes using cluster analysis in the severe asthma research program. *Am J Respir Crit Care Med* 2010;181:315-23.
18. Newby C, Heaney LG, Menzies-Gow A, Niven RM, Mansur A, Bucknall C, *et al.* Statistical cluster analysis of the British Thoracic Society severe refractory asthma registry: Clinical outcomes and phenotype stability. *PLoS One* 2014;9:e102987.

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