Original Article

Atopy Is Associated with Age at Asthma Onset in Elderly Patients

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What is already known about this topic? There are conflicting findings about the prevalence of allergic asthma in elderly patients.

What does this article add to our knowledge? Atopy, especially mite allergy, was observed in most elderly asthmatic patients. There was a negative correlation between duration of asthma and forced expiratory volume in 1 second values, independent of the presence of atopy.

How does this study impact current management guidelines? Atopy should be investigated in elderly asthmatic patients, because there are specific management approaches that can be applied to atopic asthmatic patients.

BACKGROUND: Asthma in the elderly population (60 years of age and older) is frequently underdiagnosed, as well as atopy. Atopy, although more prevalent in younger patients, can be a major cause of asthma in the elderly. Chronic obstructive pulmonary disease (COPD) and cardiovascular disease are common differential diagnoses, especially in elderly smokers. OBJECTIVE: The objective of this study was to assess atopy and comorbidities in elderly patients with asthma.

METHODS: This was an observational and retrospective study involving elderly asthmatic patients followed up at a tertiary center. Patients were assessed for severity of asthma, frequency of atopy, and frequency of comorbidities concomitant with asthma. Then, they were classified according to their age at asthma onset and the groups compared with each other for atopy, spirometric parameters, and comorbidities.

RESULTS: This study included 243 elderly asthmatic patients, 71.8% of them presenting severe disease and 82.3% forced expiratory volume in 1 second (FEV₁) < 80%. Gastroesophageal reflux disease, obesity, and asthma-COPD overlap syndrome were observed, respectively, in 64%, 37%, and 13% of these patients. Atopy was observed in 63%, mainly in those with early onset disease, and its frequency decreased as the age of asthma

onset increased (P<.05). Total serum IgE was higher for allergic patients and FEV₁ values were lower for patients with long-term asthma. Aspirin-exacerbated respiratory disease was more frequent in patients with nonallergic asthma.

CONCLUSIONS: Most elderly asthmatic patients followed up in our tertiary center were atopic and higher values of total serum IgE suggest atopy. Atopy was inversely correlated with age of asthma onset. The diagnosis of allergic asthma in the elderly population is essential to treat patients more properly, improving their quality of life and decreasing asthma morbidity and mortality. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017; =: =-=)

Key words: Asthma; Allergic asthma; Elderly; Aeroallergens; Atopy; IgE; Asthma-COPD overlap syndrome (ACOS); Age of asthma onset

The forecast is that the number of elderly persons in the population will increase in the coming years throughout the world, and it will be around 20% by 2030 in Brazil. Similarly, the prevalence of asthma and allergic disease is growing in some parts of the world, and in Brazil, the prevalence of asthma patients is 13% of the population. Atopy affects individuals of all ages and its prevalence in elderly people is around 8% to 15%. At the prevalence in elderly people is around 8% to 15%.

Asthma is a heterogeneous disease characterized by chronic inflammation of the respiratory tract. It is defined by the history of respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough that vary over time and in intensity, associated with variable expiratory airflow limitation.^{5,6} The prevalence of asthma in the elderly population (≥65 years of age), although difficult to establish because of its clinical heterogeneity, has been reported to be around 5% to 12%, being more frequent in women.⁷ The burden of asthma is more significant in the elderly than in younger asthmatic patients, particularly with respect to mortality, hospitalization, medical costs, and quality of life.⁷

Various factors are involved in asthma pathogenesis in the elderly, such as allergic sensitization and immunological

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Abbreviations used

ACOS-Asthma-COPD overlap syndrome

AERD-Aspirin-exacerbated respiratory disease

BMI-Body mass index

COPD-Chronic obstructive pulmonary disease

CT- Computed tomography

FEV1-Forced expiratory volume in 1 second

FVC-Forced vital capacity

GERD-Gastroesophageal reflux disease

HDM-House dust mite

ICS-Inhaled corticosteroids

LABA-Long-acting β -agonist

LTRA-Leukotriene receptor antagonist

NSAID-Nonsteroidal anti-inflammatory drug

SD-Standard deviation

SPT-Skin prick tests

alterations of immunosenescence. The immunological and structural consequences of immunosenescence involved in asthma include impairment of the mucociliary clearance and impairment of high-affinity antibody production, leading to an increased risk of respiratory infections (these infections could exacerbate asthma or play a role in the pathogenesis of late onset asthma). 8,9

According to the data published in the literature, allergic sensitization in elderly asthmatic patients varies widely; 28% to 74% of them are sensitized to at least 1 allergen. The major aeroallergens related to allergic asthma in elderly patients are house dust mites (HDM) and cockcroaches. ^{10,11}

The investigation of allergic asthma in the elderly is a challenge to the clinician due to several reasons. Dyspnea is a common symptom of many respiratory diseases, and in the elderly, this symptom is often considered normal because of aging and deconditioning. Differential diagnoses or comorbidities, such as chronic obstructive pulmonary disease (COPD) and congestive heart failure, may mask the diagnosis of asthma in these population. ^{7,12} COPD is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways and the lungs to noxious particles or gases. ¹³

Asthma exacerbations and associated comorbidities contribute to the overall severity of the disease in elderly patients. 6 Moreover, distinguishing asthma from COPD can be problematic, particularly in smokers and older adults. The presence of asthma and COPD symptoms in the same patient has recently been named asthma-COPD overlap syndrome (ACOS). 14 There is no universally accepted definition of ACOS. 15,16 Therefore, ACOS is identified in clinical practice by the features that it shares with both asthma and COPD. A specific definition for ACOS cannot be developed until more evidence is available regarding its clinical phenotypes and underlying mechanisms. ¹⁴ Sin et al ¹⁶ proposed a definition for ACOS that incorporated features such as persistent airflow limitation in symptomatic patients 40 years of age and older, a well-documented history of asthma in childhood or early adulthood, and a significant history of exposure to cigarette or biomass smoke. Tobacco smoking is the most important and preventable risk factor for the development and progression of COPD. 17,1

Asthma may be classified according to the age at onset of symptoms: (1) early-onset asthma, whose onset occurred before 12 years of age, that is, a long-term, more symptomatic, and severe asthma, with high prevalence of atopy and lower forced expiratory volume in 1 second (FEV $_{\rm 1}$); (2) late-onset asthma, whose symptoms and FEV $_{\rm 1}$ are, initially, less severe than the early-onset asthma, and atopy is less common. 12,19,20 Forty-eight percent of elderly asthmatic patients presented asthma onset before 40 years of age, and around 30% had their disease onset before 20 years of age. 12,19,21,22 It is important to characterize elderly asthmatic patients for the presence of atopy and/or ACOS to provide other therapeutic options to control their disease.

The major objective of this study was to assess atopy and comorbidities in elderly patients with asthma. These patients were also classified according to age at disease onset, which was correlated to the occurrence of atopy, lung function parameters, and comorbidities.

METHODS

This was an observational, retrospective study involving elderly asthmatic patients who have been followed up at the Asthma Outpatient Clinic of the Clinical Immunology and Allergy Division, University of São Paulo, Brazil. Patients 60 years of age or older were considered elderly (according to the Brazilian Institute of Geography and Statistic's—IBGE's—definition for Brazil¹); the diagnosis of asthma was made according to Holgate et al,⁶ that is, a characteristic pattern of respiratory symptoms such as wheezing, dyspnea, chest tightness, or cough, besides the presence of reversibility and variability of these symptoms and reversibility and variability of these symptoms are reversibility and variability of these tymptoms are reversibility and variability of these tymptoms and reversibility and variability of expiratory airflow limitation. Patients were included sequentially in the study, in the order in which they were seen in the clinic, when they met the inclusion criteria.

Spirometry was performed using a Koko spirometer (PDS Instrumentation, Louisville, Colo), which provides flow-volume and volume-time curves. The techniques and interpretation of the results were those recommended by the 2005 American Thoracic Society consensus and the 2005 European Respiratory Society consensus. ^{23,24} The reference values used were those established for Brazilians. ²⁵ The tests were repeated 15 minutes after the inhalation of 400 mcg of salbutamol via a metered-dose inhaler with a spacer. The bronchodilator response was defined as an increase (over baseline) of at least 12% and 200 mL in FEV₁ and/or forced vital capacity (FVC).

To be considered asthmatic and included in the study, patients had to present a characteristic pattern of respiratory symptoms compatible with asthma and reversibility and variability of expiratory airflow limitation. Because many patients have been followed up in the clinic for a long time, only those who showed reversibility in at least 1 spirometry were included.

Cardiovascular disease is a common differential diagnosis or comorbidity in patients with asthma and/or COPD, particularly in elderly patients. In this study, asthma was diagnosed based on the presence of reversibility and variability of symptoms and lung function, during months or years of medical follow-up. Patients with uncontrolled cardiovascular disease were excluded.

Asthma severity was classified according to the treatment step prescribed, as suggested in GINA guidelines. ^{5,6} Briefly, patients prescribed step 2 treatments (low-dose inhaled corticosteroids[ICS], or leukotriene receptor antagonist [LTRA], or low-dose theophylline) were defined as mild asthma cases; step 3 therapies (low-dose ICS/LTRA, or medium/high-dose ICS) were classified as moderate;

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