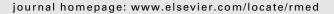


Available online at www.sciencedirect.com

ScienceDirect





Prevalence of asthma and its association with rhinitis in the elderly



H. Pite a,b,c,*, A.M. Pereira a,b,d,e,f, M. Morais-Almeida a,b,g, C. Nunes b,h, J. Bousquet J.A. Fonseca b,d,e,f,g

- ^a Hospital CUF-Descobertas and Hospital CUF-Infante Santo, Immunoallergy Department, Lisbon, Portugal
- ^b Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC), Portugal
- ^c CEDOC, Faculty of Medical Sciences, Pharmacology Department, Lisbon, Portugal
- ^d Hospital S. João EPE, Allergy and Clinical Immunology Department, Porto, Portugal
- ^e Faculdade de Medicina da Universidade do Porto, Health Information and Decision Sciences Department, Porto, Portugal
- ^f Instituto e Hospital CUF Porto, Allergy Unit, Porto, Portugal
- $^{
 m g}$ CINTESIS Center for Research in Health Technologies and Information Systems, Porto, Portugal
- ^h Centro de Imunoalergologia do Algarve, Portimão, Portugal

Received 11 February 2014; accepted 1 May 2014 Available online 14 May 2014

KEYWORDS

Asthma; Elderly; Epidemiology; Prevalence; Rhinitis; Rhinoconjunctivitis

Summarv

Background: Asthma and rhinitis are frequent respiratory diseases in children and adults. Despite the increase in the aging population, there are few epidemiologic data on both diseases in the elderly. So far, no population-based study has analyzed the association between asthma and rhinitis symptoms and severity in this age group. This study aimed to estimate the prevalence of physician-diagnosed asthma in the population aged \geq 65 years in mainland Portugal and to evaluate its association with the presence and classification of rhinitis according to ARIA recommendations, in this age group.

Methods: A cross-sectional, nationwide, population-based survey of individuals aged \geq 65 years, living in mainland Portugal was performed.

Results: Data were obtained from 3678 respondents. The prevalence of physician-diagnosed asthma was 10.9% (95% confidence interval (95%CI) 9.9–11.9). The frequency of asthma diagnosis increased with the number of nasal symptoms (p < 0.001). A strong association between asthma and rhinitis was found (odds ratio (OR) 13.86 (95%CI 10.66–18.02)). The strength of this association increased with the persistence and severity of rhinitis, being particularly high in elderly subjects with moderate-severe persistent rhinitis (OR 39.9 (95%CI 27.5–58.0)).

E-mail address: helenampite@gmail.com (H. Pite).

Department of Allergy and Respiratory Diseases, University Hospital and INSERM, Montpellier, France

^{*} Corresponding author. Dept. of Immunoallergy, Hospital CUF-Descobertas, Rua Mário Botas, 1998-018 Lisbon, Portugal. Tel.: +351962790162; fax: +351213582301.

Conclusions: Asthma is common in the elderly and strongly associated with rhinitis. The OR for asthma is especially high in persistent and severe ARIA classification rhinitis types. This study strengthens the need for an integrated assessment of asthma together with rhinitis in the elderly.

© 2014 Elsevier Ltd. All rights reserved.

Introduction

Asthma and rhinitis are common and they are often associated in children and adults [1-3]. Rhinitis is a risk factor for asthma, being associated with increased severity and health resource use in asthma. Therefore, international guidelines consensually recommend that asthma and rhinitis should be considered together [1,2].

In recent decades, a significant increase in the elderly population has occurred, both in Europe and the U.S. This increase in life expectancy joins a growing concern for healthy, active aging. Epidemiological studies at the population level have been critical to the assessment of population's needs with regard to chronic respiratory diseases [3]. However, elderly-targeted, population-based studies considering asthma and rhinitis are scarce [4–7], although the greatest burden of asthma deaths has occurred among elderly subjects [8,9].

We have recently estimated the prevalence of rhinitis in the elderly population in Portugal and, for the first time, rhinitis has been classified according to Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations in this age group [6]. This study showed that rhinitis was a highly prevalent but underdiagnosed and undertreated disease in the elderly population, despite that over 40% had moderate-severe disease. These data reinforced the need to further explore the association between asthma and rhinitis symptoms and severity in this age group, which, to our knowledge, has not been addressed before in any population-based study targeting the elderly.

Thus, we aimed to estimate the prevalence of physiciandiagnosed asthma (PDA) in the population aged \geq 65 years in mainland Portugal and to analyze its association with the presence and classification of rhinitis according to ARIA recommendations [2]. The secondary aim was to describe socio-demographic characteristics associated with asthma diagnosis and treatment, in this age group.

Methods

Study design and participants

Population-based, cross-sectional survey applied by face-to-face interview to individuals aged ≥ 65 years, living in mainland Portugal.

The study's methodology has been previously detailed [6]. Briefly, a stratified (by gender, age and region), multistep sampling strategy was used. The estimation of the number of needed participants was based on the data from the 2001 Portuguese Census on individuals aged \geq 65 years, considering all five regions of mainland Portugal [10].

The selection criteria of municipalities within each Portuguese region corresponded to the aging index, population density and purchasing power, indicators that summarize the main regional social disparities [10]. The final selection was done by random-route methodology, where households and nursing homes from the selected municipalities were included. This sampling strategy allowed for a representative sample of the mainland Portuguese population aged \geq 65 years, regarding the factors used for sample stratification [6].

Informed consent was obtained from all participants. This study's protocol was reviewed and approved by the Ethics Committee of CUF-Descobertas Hospital, Lisbon, Portugal.

Instruments and data collection

The instrument for data collection has been previously published [6]. The questions on PDA and physician-diagnosed asthma on current treatment (PDA/CT) were based on the European Community Respiratory Health Survey (ECRHS) [11].

Rhinitis severity was assessed using a 0-10 visual analogue scale (VAS), as previously suggested [12].

Questionnaires were applied by trained interviewers between May and July 2008. Inter-interviewer variability in the results was controlled by standardized training and interview framework, which application was monitored by a supervisor.

Definitions

Definitions used in this study are presented in Table 1. In individuals with rhinitis, it was further classified into intermittent/persistent and mild/moderate-severe, according to current ARIA guidelines [2] (Table 1).

Socio-demographic characteristics included gender ("male" or "female") and age (in years); municipality was considered as "urban" or "rural", according to living municipality typology [10], and residency was categorized as living in "own house" (i.e., home ownership), living "with relatives" (i.e., in family members' home ownership) or in "nursing home" (i.e., home for the elderly).

Sample size and statistical analysis

The primary endpoint of the study was rhinitis prevalence [6]. Considering that the prevalence of asthma in the elderly is estimated to be around 8% [13], the inclusion of 3500 subjects (computed based on rhinitis endpoints) allows the estimation of asthma prevalence with an error of 0.9% (precision) in 95% confidence interval (95%CI).

Variable	Source	Definition
Physician-diagnosed asthma (PDA)	Adapted from ECRHS [11]	Positive answer to the question "Has a doctor ever said you have asthma?".
Physician-diagnosed asthma on current treatment (PDA/CT)	Adapted from ECRHS [11]	Presence of physician-diagnosed asthma and a positive answer to the question "Do you take medication for asthma?".
Current rhinitis	Based on ECRHS and ARIA [2,11,43]	Presence, usually or in the last 12 months, of at least two of the following symptoms: "repeated sneezing and itchy nose"; "blocked nose for more than one whole hour" or "runny nose when not having a cold or flu".
Intermittent rhinitis	Built according to ARIA [2]	Current rhinitis with nasal symptoms lasting less than 4 days in a week or lasting more than 4 days/week but less than 4 consecutive weeks.
Persistent rhinitis	Built according to ARIA [2]	Current rhinitis with nasal symptoms lasting for at least 4 days in a week and for more than 4 consecutive weeks.
Mild rhinitis	Adapted from Bousquet et al. [12]	Current rhinitis that had a visual analogue scale severity score ranging between 0 and 5.
Moderate-severe rhinitis	Adapted from Bousquet et al. [12]	Current rhinitis that had a visual analogue scale severity score ranging between 6 and 10.
Rhinoconjunctivitis	Adapted from ECRHS [11]	Presence of rhinitis and a positive answer to the question "Do nasal symptoms usually occur along with red or itchy-watery eyes?".
Physician-diagnosed rhinitis	Additional question [43]	Positive answer to the question "Has a doctor ever said you have rhinitis?".
Current rhinitis treatment	Adapted from ECRHS [11]	Positive answer to the question "Have you had any medication for rhinitis (nasal topical drug or pill) in the last 12 months?".

Categorical variables were described using absolute and relative frequencies with 95%CI; comparisons were performed using the Pearson's chi-square test and linear by linear association. Continuous variables were described with mean and standard deviation (SD); comparisons were performed using an independent samples t-test, or Welch

test if equality of variances was not assumed. A significance level of 5% was considered.

Univariate logistic regression models for "PDA" and "PDA/CT" were developed using independent variables as risk/predictive factors. Gender, age group, municipality typology and residency were considered as possible risk

Table 2 Socio-demographic characteristics of the participants, including stratification by "physician-diagnosed asthma" status.

	Total (n = 3678) n (%)		Physician-diagnosed asthma					
			Yes (n = - n (%)	401)	No (n = 3274) n (%)			
Gender								
Female	2151	(58.5)	254	(63.3)	1896	(57.9)		
Age, years								
65-74	2128	(57.9)	232	(57.9)	1896	(57.9)		
75-84	1204	(32.7)	126	(31.4)	1077	(32.9)		
≥85	346	(9.4)	43	(10.7)	301	(9.2)		
Municipality								
Urban	2752	(76.5)	288	(71.8)	2461	(75.2)		
Rural	845	(23.5)	107	(26.7)	738	(22.5)		
Residency								
Own house	2657	(73.2)	254	(63.3)	2400	(73.3)		
With relatives	632	(17.4)	81	(20.2)	551	(16.8)		
Nursing home	343	(9.4)	64	(16.0)	279	(8.5)		

Table 3 Prevalence of physician-diagnosed asthma and physician-diagnosed asthma on current treatment and logistic regression models with crude and adjusted odds ratio (OR) with 95% confidence intervals (95%CI).

	Physician-diagnosed asthma					Physic	cian-diagnosec	l asthma o	n current treatm	ent	(95%CI) (0.64-1.08) (0.88-1.54) (1.23-2.26) (1.67-3.35)	
	Prevalence		Crude Adjusted		Prevalence		Crude		Adjusted			
	%	(95%CI)	OR	(95%CI)	OR	(95%CI)	%	(95%CI)	OR	(95%CI)	OR	(95%CI)
Whole sample	10.9	(9.9-11.9)					7.6	(6.7-8.4)				
Gender			0.037*		0.097*				0.046*		0.162*	
Female	11.8	(10.5-13.3)	1.00		1.00		8.3	(7.1 - 9.5)	1.00		1.00	
Male	9.6	(8.3-11.4)	0.80	(0.64-0.99)	0.83	(0.67-1.03)	6.6	(5.4-7.9)	0.77	(0.60-1.00)	0.83	(0.64-1.08)
Age, years			0.569*		NI				0.531*		NI	
65–74	10.9	(9.8-12.5)	1.00				7.6	(6.5 - 8.7)	1.00			
75—84	10.5	(8.7-12.3)	0.96	(0.76-1.20)			7.1	(5.7 - 8.6)	0.93	(0.71-1.23)		
≥85	12.4	(9.0-16.1)	1.17	(0.83 - 1.65)			9.0	(6.0-12.0)	1.19	(0.80-1.79)		
Municipality			0.076*		0.102*				0.214*		0.299*	
Urban	10.5	(9.4-11.7)	1.00		1.00		7.3	(6.3 - 8.3)	1.00		1.00	
Rural	12.7	(10.5–15.1)	1.24	(0.98-1.57)	1.22	(0.96 - 1.55)	8.6	(6.7-10.5)	1.19	(0.90-1.58)	1.16	(0.88-1.54)
Residency			<0.001*		<0.001*				<0.001*		<0.001*	
Own house	9.6	(8.5-10.8)	1.00		1.00		6.2	(5.3-7.1)	1.00		1.00	
With relatives	12.8	(10.2-15.5)	1.39	(1.06-1.81)	1.36	(1.04-1.78)	10.1	(7.6-12.5)	1.71	(1.27 - 2.32)	1.66	(1.23-2.26)
Nursing home	18.7	(14.2-22.6)	2.17	(1.60-2.93)	2.06	(1.51-2.79)	14.3	(10.6 - 18.0)	2.53	(1.80 - 3.56)	2.37	(1.67 - 3.35)
Current rhinitis			<0.001*		NI				<0.001*		NI	
No	2.9	(2.3-3.6)	1.00				2.1	(1.6-2.7)	1.00			
Yes	29.6	(27.0 - 32.4)	13.86	(10.66-18.02)			20.5	(18.1-22.9)	12.08	(8.88 - 16.41)		
Rhinoconjunctivitis			<0.001*		NI				<0.001*		NI	
No	4.3	(3.6-5.1)		1.00			2.7	(2.1-3.3)	1.00			
Yes	36.4	(32.9 - 39.8)	22.15	(17.53-27.98)			26.6	(23.4-29.8)	16.92	(12.36-23.18)		
Physician-diagnosed rhinitis			<0.001*		NI				<0.001*		NI	
No	7.4	(6.6 - 8.5)	1.00				5.3	(4.5-6.1)	1.00			
Yes	34.1	(30.1 - 38.7)	6.46	(5.13 - 8.13)			23.1	(19.3-26.9)	5.40	(4.15 - 7.03)		
Current rhinitis treatment		,	<0.001*	,	NI			,	<0.001*	,	NI	
No	7.6	(6.7 - 8.5)	1.00				5.5	(4.7-6.3)	1.00			
Yes	32.8	(28.6-37.0)	5.96	(4.74 - 7.51)	NI		21.5	(17.9–25.1)	4.75	(3.65-6.19)	NI	

^{*} p-value; OR, odds ratio; 95%CI, 95% confidence interval; NI, Not included.

factors; and current rhinitis, rhinoconjunctivitis, physician-diagnosed rhinitis, current rhinitis treatment and rhinitis classification categories as possible predictive factors (frequently associated pathologies that may share common risk factors). Multivariate logistic regression models were developed for "PDA" and "PDA/CT". Only possible risk factors were included in the multivariate logistic regression models; they were chosen according to the p-value of the univariate analysis, considering a cut-off of <0.250. The Hosmer—Lemeshow test was used to assess calibration of the multivariate models; a p>0.05 was deemed necessary to consider that the model was calibrated. Results of both univariate and multivariate logistic regression models were presented as odds ratio (OR) with 95%CI.

Data analyses were performed using SPSS® version 19.0 for Windows (IBM SPSS, Chicago, IL, USA).

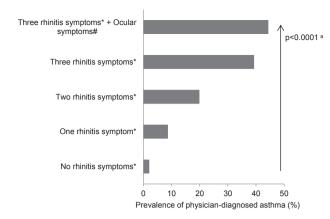
Results

Participants' characteristics

A total of 3699 out of 4000 invited subjects answered the questionnaire (response rate 92.5%). There was no evidence of different response rates according to age. From the answered questionnaires, 21 were excluded: 13 subjects were aged less than 65 years old and eight had insufficient information due to incomplete interviews. Data was obtained from 3678 responders. Participants' sociodemographic characteristics are summarized in Table 2.

Prevalence of physician-diagnosed asthma and physician-diagnosed asthma on current treatment

The prevalence of PDA was 10.9% (95%CI 9.9%—11.9%). Seventy per cent of the elder subjects with asthma



(* - Runny nose, Sneezing and itchy nose, Blocked nose; # - Red or itchy-watery eyes; a - p-value, linear-by-linear association)

Figure 1 Prevalence of physician-diagnosed asthma in relation to nasal and ocular symptoms.

reported to be under current asthma treatment. The prevalence of PDA/CT was 7.6% (95%CI 6.7%—8.4%).

The prevalence of PDA was lower in men compared to women (9.6% vs 11.8%, p=0.037). No statistically significant differences were found in the prevalence of asthma according to the age group or between urban and rural municipalities (Table 3). Adjusting for other independent variables, living with relatives and, especially, living in a nursing home, when compared with living in their own house, was significantly and positively associated with PDA and PDA/CT (Table 3). In the multivariate analysis, there was no significant effect of gender on both outcomes (Table 3). Table 4 shows the comparison of elderly subjects with PDA according to asthma treatment. Elderly subjects with PDA living in their own house had current asthma treatment less frequently (Table 4).

	Physician-diagnosed asthma [p-Value	
	On current treatment [n = 279] n (%)	No current treatment [n = 122] n (%)	
Gender			0.608
Female	179 (64.2)	75 (61.5)	
Age, years			0.887
65-74	162 (58.1)	70 (57.4)	
75–84	86 (30.8)	40 (32.8)	
≥85	31 (11.1)	12 (9.8)	
Municipality			0.881
Urban	202 (72.4)	86 (70.5)	
Rural	73 (26.2)	34 (27.9)	
Residency			0.020
Own house	164 (58.8)	90 (73.8)	
With relatives	64 (22.9)	17 (13.9)	
Nursing home	49 (17.6)	15 (12.3)	
Current rhinitis	225 (80.6)	100 (82.0)	0.756
Rhinoconjunctivitis	200 (71.7)	72 (59.0)	0.013
Physician-diagnosed rhinitis	111 (39.8)	53 (43.4)	0.493
Current rhinitis treatment	105 (37.6)	53 (43.4)	0.221

Table 5	Prevalence of physician-diagnosed asthma and physician-diagnosed asthma on current treatment according to ARIA
rhinitis cl	assification categories.

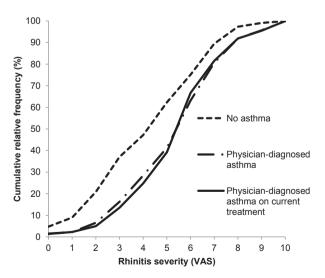
	Physician-diagnosed asthma		Physician-diagnosed asthma on current treatment		
	%	(95%CI)	%	(95%CI)	
Mild intermittent rhinitis	<0.0001*	_	<0.0001*		
No	9.2	(8.2-10.2)	6.6	(5.7–7.5)	
Yes	20.2	(16.8-23.6)	13.0	(10.1–15.9)	
Moderate-severe intermittent rhinitis	<0.0001*		<0.0001*		
No	9.1	(8.1-10.1)	6.2	(5.4–7.0)	
Yes	30.6	(25.4 - 35.8)	23.2	(18.4-28.0)	
Mild persistent rhinitis	<0.0001*		<0.0001*		
No	10.4	(9.4-11.4)	7.2	(6.4-8.0)	
Yes	33.3	(22.6-44.0)	24.0	(14.3-33.7)	
Moderate-severe persistent rhinitis	<0.0001*		<0.0001*		
No	8.6	(7.7 - 9.5)	6.0	(5.2-6.8)	
Yes	54.8	(47.5-62.1)	37.3	(30.2-44.4)	

p-value: 95%CI, 95% confidence interval.

Association between asthma and rhinitis

Of subjects with PDA, 81.1% had current rhinitis, 68.3% rhinoconjunctivitis and 40.9% reported to have physiciandiagnosed rhinitis. Current rhinitis was found in 80.7% of patients with PDA/CT, of whom 46.7% had physiciandiagnosed rhinitis and 43.6% were on current rhinitis treatment. On the other hand, PDA was reported by 29.6% subjects with current rhinitis, 36.4% with rhinoconjunctivitis and 34.1% with physician-diagnosed rhinitis. In univariate analysis, all three conditions were strongly associated with PDA and PDA/CT, particularly current rhinitis and rhinoconjunctivitis (Table 3). The frequency of rhinoconjunctivitis was higher in subjects with PDA/CT, compared to those without asthma treatment (Table 4).

The prevalence of PDA increased with the number of rhinitis symptoms, from 2.1% in no rhinitis symptoms to



(VAS - visual analogue scale, cm)

Figure 2 Cumulative relative frequency distribution of rhinitis severity visual analogue scale score in elderly subjects, according to the presence of physician-diagnosed asthma and physician-diagnosed asthma on current treatment.

39.3% in three nasal complaints and 44.4% in nasal symptoms combined with ocular symptoms; p < 0.0001 by linearby-linear association (Fig. 1).

Risk for asthma according to ARIA rhinitis classification

The prevalence of PDA and PDA/CT according to the ARIA classification of rhinitis is presented in Table 5. The

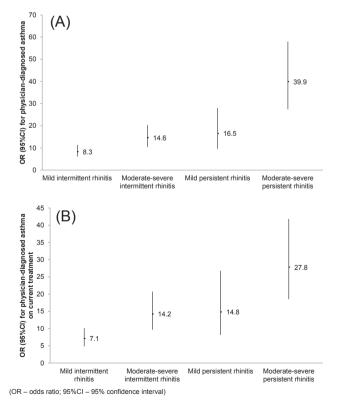


Figure 3 Odds ratio with 95% confidence interval for physician-diagnosed asthma (A) and physician-diagnosed asthma on current treatment (B) according to ARIA rhinitis classification categories.

association between PDA and current rhinitis was evident in all rhinitis classes.

Figure 2 shows the cumulative relative frequency distribution of rhinitis severity VAS score, according to the presence of PDA and PDA/CT. Rhinitis severity VAS scores were significantly higher in elderly subjects with PDA (5.7 cm SD 2.1 vs. 4.6 cm SD 2.3 in those without asthma, Welch test p < 0.001) and with PDA/CT (5.8 cm SD 2.0 vs. 4.6 cm SD 2.3 in those without asthma, Welch test p < 0.001).

The OR for asthma increased with increased frequency and severity of rhinitis symptoms, and was strongest in subjects with moderate-severe persistent rhinitis (Fig. 3A). Having current rhinitis was also significantly associated with PDA/CT; this relation was present in all rhinitis classes, especially in subjects with moderate-severe persistent rhinitis (Table 5; Fig. 3B).

Discussion

A high prevalence of self-reported PDA was found in the Portuguese population aged \geq 65 years (10.9%; IC95% 9.9–11.9). This study showed a strong association between rhinitis, rhinoconjunctivitis and asthma diagnosis in this age group. The strength of the association between asthma and rhinitis increased with longer persistence and higher severity of rhinitis symptoms, considering the ARIA rhinitis classification.

This study was the first nationwide population-based epidemiological study exclusively dedicated to the elderly that concurrently evaluated asthma and rhinitis symptoms and ARIA classification and that reported a relation between asthma and rhinitis severity/duration, in this age group. It included a large representative sample of elderly subjects, allowing the estimation of PDA prevalence in mainland Portugal and the characterization of its association with rhinitis according to ARIA recommendations.

The study's main limitations are due to its cross-sectional design, the absence of physician confirmation/evaluation, lung function parameters and *in vivo* and/or *in vitro* atopy markers, and the lack of information regarding environmental exposures (namely tobacco smoke), lower respiratory symptoms, asthma severity and control. Other factors, such as recall or information biases may have influenced the results. Nevertheless, the use of a short and simple questionnaire, applied by trained interviewers, facilitated the inclusion of the elderly subjects. It also minimized difficulties in reading or comprehending and the loss of compliance throughout the interview, allowing for very few missing data regarding all variables [6].

A recent study, the Portuguese National Asthma Survey, estimated that the prevalence of current asthma (i.e., with symptoms in the last 12 months) in Portugal was 6.8% (95%CI 6.0–7.7) [13]. In this study, the subgroup analysis by age groups showed no statistically significant difference in the prevalence of current asthma in individuals aged \geq 65 years. However, adjusting for possible confounding factors, the prevalence of asthma was lower in elderly subjects who reported no heart disease. Since heart disease is common in the elderly and may be a cause of respiratory symptoms, the authors pointed out the possibility of an overestimation

of current asthma in elderly subjects with cardiac disease. Asthma prevalence estimates did not change after adjusting for chronic bronchitis [13].

In the present study, in spite of the limitations due to PDA being only self-reported and the lack of information on environmental exposures including tobacco smoke, the fact that a doctor's diagnosis and current asthma treatment were considered may have helped to reduce bias and confounding factors related to respiratory symptoms caused by other conditions, such as heart disease, bronchitis or chronic obstructive pulmonary disease (COPD). Nonetheless, distinguishing asthma from COPD can be particularly difficult. COPD is often assumed to be an "aging-related disease", remaining an important comorbidity leading physicians to diagnose COPD rather than asthma in the elderly [14–16]. Conversely, other studies report asthma overdiagnosis in adults, including COPD misdiagnosis with asthma [17–19].

Considering the prevalence of PDA/CT as a proxy for "active asthma", we found that 7.6% (95%CI 6.7-8.4%) of the Portuguese elderly population had an active disease. Despite the lack of information on asthma control, this does not differ significantly from the estimated prevalence of current asthma in elderly in the study mentioned above (8.0% (95%CI 6.7-9.5)) [13], suggesting that this might be an accurate approximation of the real prevalence in the Portuguese population. In other epidemiological studies targeting elderly subjects from other countries, the prevalence of asthma varied between 3.6% and 7.6% [4,5,7,20-27]. However, the different selection criteria and definitions of asthma limit inter-studies comparisons. Asthma overdiagnosis or other stated biases may have concurred for the higher prevalence obtained in this study. A study including medical evaluation, information on tobacco and other environmental exposures, and lung function parameters would be of utmost importance to address this issue in the elderly.

In this study we noted that, as for rhinitis [6], after adjusting for independent variables, the diagnosis of asthma was associated with living with relatives and especially living in a nursing home. This may suggest that these elderly subjects, compared to those who reside in their own house, have greater frequency of asthma or better access to medical care. The fact that those individuals living in their own house had current asthma treatment less frequently may either reflect better asthma control in this group, or, on the contrary, support the assumption regarding worse access to medical care in elderly subjects living in their own house. Yet, it should also be considered that those elderly living in nursing homes often have greater deconditioning or multiple co-morbidities that may mimic asthma, which could contribute for misdiagnosis of this disease.

In accordance with the Portuguese National Asthma Survey [13], in multivariate analysis, asthma prevalence was similar in both genders and according to municipality typology. Unlike suggested by other studies [15,20], the prevalence of asthma in the elderly did not diminish with age. However, this could also reflect an increasing tendency for asthma misclassification with COPD or other mimicking conditions, with increasing age [17–19], which should be explored.

The present study, including only older adults, also showed a strong association between rhinitis, rhinoconjunctivitis and self-reported asthma diagnosis. About 80% of elderly subjects diagnosed with asthma had rhinitis: among elderly subjects with rhinitis, 30% had asthma diagnosed by a doctor. The prevalence of asthma diagnosis increased with the number of nasal symptoms, especially when they were associated with ocular symptoms. These results support an extensive nose-lung interaction also in the elderly, which has been observed by others [28-31]. Furthermore, considering the difficulties in distinguishing asthma from other relevant conditions in differential diagnosis, our data may more broadly indicate that there might also be a relationship between rhinitis and other diseases responsible for lower respiratory symptoms in the elderly, namely COPD. Other studies strengthen the fact that the "united airways" concept goes beyond the scope of asthma and also support an association between rhinitis and COPD [32-34].

The definition for current rhinitis used in this study, requiring the presence of at least two nasal symptoms, suggests the diagnosis of allergic rhinitis. This is reinforced in the elderly with concomitant complaints of red eye, eye pruritus or epiphora, suggesting allergic rhinoconjunctivitis. The fact that the association between rhinitis and asthma has been particularly notable in elderly patients with rhinoconjunctivitis may suggest an increased risk of asthma when there is greater likelihood of involvement of allergic mechanisms. Rhinoconjunctivitis was more frequent in elderly subjects with PDA/CT, compared to those without asthma treatment, which may suggest a possible relation with atopy. However, the definitions of allergic rhinitis and allergic rhinoconjunctivitis were not used because they require the assessment of the specific immunological mechanisms involved and that was not part of this study.

This report further emphasizes that rhinitis in the elderly is underdiagnosed and undertreated [6]. About 40% of elderly patients with PDA had complaints of current rhinitis but were not diagnosed or treated for rhinitis. This is reinforced in those on current treatment for asthma and concurrent current rhinitis, where more than half of these patients had no physician diagnosis of rhinitis. Considering that rhinitis symptoms and lack of control interfere with asthma [1,2], there should be a greater awareness for the assessment of nasal disease in patients with an asthma diagnosis.

The strong association found between asthma, asthma on current treatment and all ARIA classes of rhinitis further supports the importance of an accurate rhinitis diagnosis in the elderly, including in milder presentations. The ARIA classification of rhinitis provided important information with regard to the strength of the association with asthma, as it increased with increased persistency and severity of rhinitis. While contradicting some previous studies [35–37], moderate-severe persistent rhinitis had an especially strong association with asthma, as also reported by other authors, in different age groups [2,38–42].

Addressing respiratory diseases in the elderly, including asthma and rhinitis, is a recognized imperative need [1-3], especially when taking into account their impact and the trend for an increase in the elderly population in many countries worldwide. This study showed that asthma is prevalent in the elderly, being strongly associated with

rhinitis and rhinoconjunctivitis. The strength of this association increases very significantly with longer persistence and higher severity of rhinitis. This study highlights the need for a clinical integrated, global assessment of asthma together with rhinitis in this age group and may contribute to the designing of future studies addressing both diseases in the elderly.

Ethics statement

This study was conducted according to the principles of the Helsinki Declaration. Informed consent was obtained from all participants. This study's protocol was approved by the Ethical Review Board of the CUF-Descobertas Hospital, Lisbon, Portugal.

Author contributions

HP participated in data analysis and interpretation and wrote the manuscript draft, AMP participated in data interpretation and review, CN participated in the study conception, JB provided critical review during the project, JAF participated in data analysis and interpretation and provided critical review during the project, MMA coordinated the study participating in all stages and tasks. All authors have reviewed and approved the final manuscript.

Conflict of interest

Mário Morais-Almeida (MMA) reports lecture fees from Astrazeneca, GSK, OM Pharma, Sanofi and Siemens Diagnostics; lecture fees and honoraria for advisory board from FAES Farma; lecture fees and non-financial research project support from MSD; travel grant, lecture fees and honoraria for advisory board from Novartis; and honoraria for advisory board from Pfizer. Jean Bousquet (JB) received honoraria for scientific and advisory boards, lectures during meetings, press conferences from Stallergènes, Actelion, Almirall, AstraZeneca, Chiesi, GSK, Merck, MSD, Novartis, OM Pharma, Sanofi-Aventis, Schering Plough, Teva, Uriach. João Almeida Fonseca (JAF) reports lecture fees and non-financial research project support from MSD, lecture fees and honoraria for advisory board from Novartis and lecture and training fees from GSK. Helena Pité (HP), Ana Margarida Pereira (AMP), and Carlos Nunes (CN) have no conflicts of interest to declare.

Acknowledgments

Methodological support and field work was supplied by KeyPoint, Scientific Consultants.

This study was supported by a Schering-Plough Pharma grant attributed to Sociedade Portuguesa de Alergologia e Imunologia Clínica (SPAIC).

References

[1] From the Global Strategy for Asthma Management and Prevention. Global initiative for asthma (GINA). Available from: http://www.ginasthma.org/; 2012.

- [2] Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, Zuberbier T, Baena-Cagnani CE, Canonica GW, van Weel C, Agache I, Ait-Khaled N, Bachert C, Blaiss MS, Bonini S, Boulet LP, Bousquet PJ, Camargos P, Carlsen KH, Chen Y, Custovic A, Dahl R, Demoly P, Douagui H, Durham SR, van Wijk RG, Kalayci O, Kaliner MA, Kim YY, Kowalski ML, Kuna P, Le LT, Lemiere C, Li J, Lockey RF, Mavale-Manuel S, Meltzer EO, Mohammad Y, Mullol J, Naclerio R, O'Hehir RE, Ohta K, Ouedraogo S, Palkonen S, Papadopoulos N, Passalacqua G, Pawankar R, Popov TA, Rabe KF, Rosado-Pinto J, Scadding GK, Simons FE, Toskala E, Valovirta E, van Cauwenberge P, Wang DY, Wickman M, Yawn BP, Yorgancioglu A, Yusuf OM, Zar H, Annesi-Maesano I, Bateman ED, Ben Kheder A, Boakye DA, Bouchard J, Burney P, Busse WW, Chan-Yeung M, Chavannes NH, Chuchalin A, Dolen WK, Emuzyte R, Grouse L, Humbert M, Jackson C, Johnston SL, Keith PK, Kemp JP, Klossek JM, Larenas-Linnemann D, Lipworth B, Malo JL, Marshall GD, Naspitz C, Nekam K, Niggemann B, Nizankowska-Mogilnicka E. Okamoto Y, Orru MP, Potter P, Price D, Stoloff SW, Vandenplas O, Viegi G, Williams D. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008;63(Suppl. 86):8-160.
- [3] Bousquet J, Dahl R, Khaltaev N. Global alliance against chronic respiratory diseases. Allergy 2007;62:216—23.
- [4] Wuthrich B, Schmid-Grendelmeier P, Schindler C, Imboden M, Bircher A, Zemp E, Probst-Hensch N. Prevalence of atopy and respiratory allergic diseases in the elderly SAPALDIA population. Int Arch Allergy Immunol 2013;162:143—8.
- [5] Becerril Angeles M, Vazquez Merino CL, Angeles Garay U, Alvarado Moctezuma LE, Vilchis Guizar E. Prevalence of allergic diseases in the elderly. Rev Alerg Mex 2008;55:85—91.
- [6] Morais-Almeida M, Pite H, Pereira AM, Todo-Bom A, Nunes C, Bousquet J, Fonseca J. Prevalence and classification of rhinitis in the elderly: a nationwide survey in Portugal. Allergy 2013; 68:1150—7.
- [7] Bozek A, Jarzab J. Epidemiology of IgE-dependent allergic diseases in elderly patients in Poland. Am J Rhinol Allergy 2013;27:140-5.
- [8] Bugalho de Almeida A, Covas A, Prates L, Fragoso E. Asthma hospital admission and mortality in mainland Portugal 2000–2007. Rev Port Pneumol 2009;15:367–83.
- [9] Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, Liu X. Trends in asthma prevalence, health care use, and mortality in the United States, 2001–2010. NCHS Data Brief; 2012:1–8.
- [10] Instituto Nacional de Estatística. Censos 2001: Resultados definitivos. XIV Recenseamento geral da População. Lisbon: INE: 2002.
- [11] The European Community Respiratory Health Survey II Steering Committee. The European community respiratory health survey II. Eur Respir J 2002;20:1071–9.
- [12] Bousquet PJ, Combescure C, Neukirch F, Klossek JM, Mechin H, Daures JP, Bousquet J. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. Allergy 2007;62:367—72.
- [13] Sa-Sousa A, Morais-Almeida M, Azevedo LF, Carvalho R, Jacinto T, Todo-Bom A, Loureiro C, Bugalho-Almeida A, Bousquet J, Fonseca JA. Prevalence of asthma in Portugal the Portuguese National Asthma Survey. Clin Transl Allergy 2017:2:15.
- [14] Gibson PG, McDonald VM, Marks GB. Asthma in older adults. Lancet 2010;376:803—13.
- [15] de Marco R, Pesce G, Marcon A, Accordini S, Antonicelli L, Bugiani M, Casali L, Ferrari M, Nicolini G, Panico MG, Pirina P, Zanolin ME, Cerveri I, Verlato G. The coexistence of asthma and chronic obstructive pulmonary disease (COPD):

- prevalence and risk factors in young, middle-aged and elderly people from the general population. PLoS One 2013;8: e62985
- [16] Miravitlles M, Andreu I, Romero Y, Sitjar S, Altes A, Anton E. Difficulties in differential diagnosis of COPD and asthma in primary care. Br J Gen Pract 2012;62:e68—75.
- [17] Price D, Brusselle G. Challenges of COPD diagnosis. Expert Opin Med Diagn 2013;7:543—56.
- [18] Tinkelman DG, Price DB, Nordyke RJ, Halbert RJ. Misdiagnosis of COPD and asthma in primary care patients 40 years of age and over. J Asthma 2006;43:75—80.
- [19] Lucas AE, Smeenk FJ, Smeele IJ, van Schayck OP. Diagnostic accuracy of primary care asthma/COPD working hypotheses, a real life study. Respir Med 2012;106:1158–63.
- [20] Oraka E, Kim HJ, King ME, Callahan DB. Asthma prevalence among US elderly by age groups: age still matters. J Asthma 2012;49:593—9.
- [21] Song WJ, Kim SH, Lim S, Park YJ, Kim MH, Lee SM, Lee SB, Kim KW, Jang HC, Cho SH, Min KU, Chang YS. Association between obesity and asthma in the elderly population: potential roles of abdominal subcutaneous adiposity and sarcopenia. Ann Allergy Asthma Immunol 2012;109:243–8.
- [22] Wolkewitz M, Rothenbacher D, Low M, Stegmaier C, Ziegler H, Radulescu M, Brenner H, Diepgen TL. Lifetime prevalence of self-reported atopic diseases in a population-based sample of elderly subjects: results of the ESTHER study. Br J Dermatol 2007;156:693—7.
- [23] Ko FW, Lai CK, Woo J, Ho SC, Ho CW, Goggins W, Hui DS. 12-year change in prevalence of respiratory symptoms in elderly Chinese living in Hong Kong. Respir Med 2006;100:1598–607.
- [24] Choy DK, Hui DS, Li ST, Ko FW, Ho S, Woo J, Lai CK. Prevalence of wheeze, bronchial hyper-responsiveness and asthma in the elderly Chinese. Clin Exp Allergy 2002;32:702—7.
- [25] Nejjari C, Tessier JF, Letenneur L, Dartigues JF, Barberger-Gateau P, Salamon R. Prevalence of self-reported asthma symptoms in a French elderly sample. Respir Med 1996;90: 401–8.
- [26] Burr ML, Charles TJ, Roy K, Seaton A. Asthma in the elderly: an epidemiological survey. Br Med J 1979;1:1041-4.
- [27] Park J, Kim TB, Joo H, Lee JS, Lee SD, Oh YM. Diseases concomitant with asthma in middle-aged and elderly subjects in Korea: a population-based study. Allergy Asthma Immunol Res 2013;5:16–25.
- [28] Huss K, Naumann PL, Mason PJ, Nanda JP, Huss RW, Smith CM, Hamilton RG. Asthma severity, atopic status, allergen exposure and quality of life in elderly persons. Ann Allergy Asthma Immunol 2001;86:524—30.
- [29] Eriksson J, Bjerg A, Lotvall J, Wennergren G, Ronmark E, Toren K, Lundback B. Rhinitis phenotypes correlate with different symptom presentation and risk factor patterns of asthma. Respir Med 2011;105:1611—21.
- [30] Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, Wjst M, Cerveri I, Pin I, Bousquet J, Jarvis D, Burney PG, Neukirch F, Leynaert B. Rhinitis and onset of asthma: a longitudinal population-based study. Lancet 2008; 372:1049–57.
- [31] Passalacqua G, Ciprandi G, Canonica GW. The nose-lung interaction in allergic rhinitis and asthma: united airways disease. Curr Opin Allergy Clin Immunol 2001;1:7—13.
- [32] Hens G, Vanaudenaerde BM, Bullens DM, Piessens M, Decramer M, Dupont LJ, Ceuppens JL, Hellings PW. Sinonasal pathology in nonallergic asthma and COPD: 'united airway disease' beyond the scope of allergy. Allergy 2008;63:261—7.
- [33] Lindberg A, Larsson LG, Ronmark E, Lundback B. Co-morbidity in mild-to-moderate COPD: comparison to normal and restrictive lung function. COPD 2011;8:421–8.
- [34] Sichletidis L, Tsiotsios I, Gavriilidis A, Chloros D, Kottakis I, Daskalopoulou E, Konstantinidis T. Prevalence of chronic

obstructive pulmonary disease and rhinitis in northern Greece. Respiration 2005;72:270—7.

- [35] Antonicelli L, Micucci C, Voltolini S, Feliziani V, Senna GE, Di Blasi P, Visona G, De Marco R, Bonifazi F. Allergic rhinitis and asthma comorbidity: ARIA classification of rhinitis does not correlate with the prevalence of asthma. Clin Exp Allergy 2007;37:954—60.
- [36] Rolla G, Guida G, Heffler E, Badiu I, Bommarito L, De Stefani A, Usai A, Cosseddu D, Nebiolo F, Bucca C. Diagnostic classification of persistent rhinitis and its relationship to exhaled nitric oxide and asthma: a clinical study of a consecutive series of patients. Chest 2007;131:1345–52.
- [37] Bjerg A, Ekerljung L, Middelveld R, Dahlen SE, Forsberg B, Franklin K, Larsson K, Lotvall J, Olafsdottir IS, Toren K, Lundback B, Janson C. Increased prevalence of symptoms of rhinitis but not of asthma between 1990 and 2008 in Swedish adults: comparisons of the ECRHS and GA(2)LEN surveys. PLoS One 2011;6:e16082.
- [38] Price D. Asthma and allergic rhinitis: linked in treatment and outcomes. Ann Thorac Med 2010;5:63—4.

- [39] Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol 2002;109:419—25.
- [40] Bousquet J, Annesi-Maesano I, Carat F, Leger D, Rugina M, Pribil C, El Hasnaoui A, Chanal I. Characteristics of intermittent and persistent allergic rhinitis: DREAMS study group. Clin Exp Allergy 2005;35:728—32.
- [41] Navarro A, Valero A, Julia B, Quirce S. Coexistence of asthma and allergic rhinitis in adult patients attending allergy clinics: ONEAIR study. J Investig Allergol Clin Immunol 2008;18:233—8.
- [42] Bousquet J, Boushey HA, Busse WW, Canonica GW, Durham SR, Irvin CG, Karpel JP, Van Cauwenberge P, Chen R, Iezzoni DG, Harris AG. Characteristics of patients with seasonal allergic rhinitis and concomitant asthma. Clin Exp Allergy 2004;34: 897–903.
- [43] Todo-Bom A, Loureiro C, Almeida MM, Nunes C, Delgado L, Castel-Branco G, Bousquet J. Epidemiology of rhinitis in Portugal: evaluation of the intermittent and the persistent types. Allergy 2007;62:1038—43.