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Characteristics of allergic sensitization among adult asthmatics >55 years: Results from the National Health and Nutrition Examination Survey 2005–2006

Paula J. Busse, MD[*], **Richard D. Cohn, PhD**[**], **Paivi M. Salo, PhD**[***], and **Darryl C. Zeldin, MD**[***]

[*]Division of Clinical Immunology, Department of Medicine, Mount Sinai School of Medicine, New York, NY

[**]SRA International, Inc, Durham, NC

[***]NIH/National Institute of Environmental Health Sciences, Research Triangle Park, NC

INTRODUCTION

Asthma is relatively common among older adults. The prevalence of asthma in patients ≥ 60 years of age has been reported between 3.5–7.5%[1–4] however, the prevalence may be underestimated because asthma in older adults is often under-diagnosed.[3, 5–6] Furthermore, as the population over the age of 60 years grows, the number of older patients with asthma is expected to increase. It is well documented that rates of hospitalization and asthma mortality are high in older patients with asthma[7–9]. The reasons for these trends are not entirely clear, but are most likely multifactorial and include under-diagnosis and under-treatment of asthma in older patients, and medication non-compliance. Additionally, there is a limited understanding of the role of allergic sensitization in older patients with asthma.

The purpose of this study was to determine the difference in frequencies of IgE-mediated sensitization by serological evaluation between younger (20–40 years old) and older (≥55 years) groups of subjects with asthma and to determine the impact on measures of disease severity and control. A recent report on a workshop sponsored by the National Institutes of Aging on current understanding of asthma in the elderly has reported that there are small studies suggesting a higher level of positive allergy tests in older subjects with asthma, however, these studies have not been performed from a comprehensive national data base of subjects.[10] Prior studies of older asthmatics have focused on homogeneous populations, particularly white non-inner city populations, and reported sensitization rates between 23.9% and 36.6%.[4, 11] However, some studies have reported higher rates of sensitization; in a recent study of an inner-city population, the prevalence of sensitization was 41%, and in another study, nearly two thirds of older asthmatics were sensitized to at least one or more allergens. [12–13] The NHANES 2005–2006 data base offers a unique opportunity to compare the prevalence of allergen sensitization between a younger and older group of subjects from a nationally representative sample of the US population. The results of this study are the basis for this report.

METHODS

Data for this study were obtained from the NHANES 2005–2006 data-base, which is a Centers for Disease Control and Prevention, National Center for Health Statistics program, developed to assess the health and nutritional status of the civilian, non-institutionalized US population.[14–15] The NHANES 2005–2006 survey included a total of 10,348 subjects. Serum specific IgE was assessed in 80.6% of the participants. The NHANES 2005–2006 protocol was approved by the National Center for Health Statistics, Centers for Disease Control and Prevention, Institutional Review Board. Informed consent was obtained from all participants 18 years and older. Details of the survey design and implementation of NHANES 2005–2006 can be found online at http://www.cdc.gov/nchs/nhanes.htm.

Study Population

Our study population was restricted to data collection from participants ages 20–40 years of age and older than 55 years of age. These age groups were chosen based upon the few prior studies which have examined older and younger patients with asthma,[16–17] to look at distinct ages, and to include sufficient numbers of patients for evaluation. To best eliminate participants with COPD and not asthma, subjects were excluded if they had a history of any of the following: a) ≥ 10 pack years smoking, b) those who answered “yes” to bringing up phlegm on most days for 3 consecutive months or more during the year, or c) those answering “yes” to the question asking if a doctor or health care professional has told you that you have emphysema or chronic bronchitis. Based upon selection criteria, our initial population was a total of 2,573 subjects. Next, we selected subjects with asthma based upon a definition of doctor-diagnosed current asthma. This group included participants who responded affirmatively to both of the following questions: (1) Has a doctor or other health professional every told you that you have asthma? (2) Do you still have asthma? We identified 151 younger and older patients with current asthma.

Definition of atopy (i.e. Allergic sensitization, IgE-mediated sensitization)

We defined atopy using specific IgE measurements. Subjects with at least 1 positive allergen-specific IgE were considered atopic. A sample of peripheral blood was obtained on participants during the NHANES 2005–2006 data collection to measure IgE antibodies against 19 allergens, as previously described.[18] Specific IgE levels were determined with the Pharmacia Diagnositics Immuno-CAP 1000 System (Kalamazoo, MI). Specific IgE levels >0.35 kU_A/L were considered as indicative of sensitization. [19–22]

Asthma related outcomes

Individual measures of asthma control were defined as follows: a) use of health care resources (≥1 visit to ER/urgent care in the past 12 months or ≥1 visits to MD/ER for wheezing), b) use of medications for wheezing, c) symptoms and effect on activity of daily life including limitation of activities, ≥1 attacks of wheezing in past 12 months, sleep disturbance due to wheezing, chest sounding wheezy after exercise), ≥1 day missed because of work due wheezing.

Statistical Analysis

NHANES participants were selected using a complex, multistage, probability sampling design and all percentages, odds ratios and associated statistics were weighted to represent the civilian, non-institutionalized US population. NHANES is conducted to achieve a nationally representative sample in which sample weights are used to account for oversampling of selected subpopulations and for non-response. Sample weights were used in all analyses to obtain unbiased national estimates. Standard errors, CIs and p-values were

developed in accordance with the complex survey design by using Taylor series linearization methods. Distributional differences between age groups were assessed using chi-square tests. Logistic regression was used to construct adjusted odds ratios and 95% confidence intervals, to evaluate associations between asthma-related outcomes and allergic sensitization or exposures. Models were adjusted for gender, race/ethnicity, and education. It was verified that the observed associations were not greatly influenced by other potential confounders, including body mass index, serum cotinine, and total IgE. Interactions were examined to determine whether odds ratios differed across age groups and other factors of interest.

RESULTS

Prevalence of asthma

The initial study population was comprised of 1623 subjects between the ages of 20–40 years (females=51%) and 950 subjects 55 years and older (females=61.5%). Over 62% of both age groups were non-Hispanic whites, and approximately 80% had a high school education or above. Current asthma was reported by 6.65% of the population 20–40 years of age (n=108) and 4.53% of the population ≥55 years of age (n=43; Table 1). Among subjects with current asthma, the age groups were comparable with respect to gender, race/ethnicity and education. Although body mass index (BMI) varied across the age groups, the differences did not reach statistical significance.

Prevalence of allergic sensitization

The prevalence of allergic sensitization in the US population ages 20–40 years (n=1623; non-asthmatics + asthmatics), defined as detectable IgE to at least one specific allergen, was 51.1% (Table 2). The prevalence of allergic sensitization in subjects ≥55 years (n=950; non-asthmatics + asthmatics) was 38.8%. Those subjects ≥55 years old who were sensitized to at least one allergen, were more likely to be female and non-Hispanic white as compared to those 20–40 years old.

Association between asthma and allergic sensitization

The prevalence of allergic sensitization among subjects with current asthma was 75.4% in subjects between 20–40 years of age and 65.2% in subjects ≥55 years of age (Table 3). The adjusted OR of having a detectable IgE to at least one allergen, conditional to having asthma among subjects ≥55 years of age was 2.9 (95% CI, 1.7–4.9) and among subjects 20–40 years of age the OR was 3.5 (95% CI, 2.3–5.2). Differences in the allergic sensitization-asthma relationship were not statistically significant between the two age groups studied (P=0.914). The prevalence of allergic sensitization in those subjects ≥55 years of age who developed asthma prior to age 40 (n=12, 72% sensitized) also did not differ significantly from those subjects who developed asthma after the age of 40 years (n=31, 62.8% sensitized, p=0.7).

We examined other outcomes in addition to current asthma in the two age groups, and found largely consistent results. For example, for self-reported current hay fever, the prevalence of allergic sensitization was 83.7% in the 20–40 year old group and 76.4% in subjects ≥55. Corresponding ORs were both 7.4 and the sensitization-age group interaction nonsignificant (P=0.783). Similar results were found for current allergies (prevalences 64.6% among ages 20–40 and 46.5% among ages ≥55, ORs 2.5 and 1.9, respectively, and P=0.220).

Patterns of sensitization among subjects with asthma

The older asthmatics were most commonly sensitized to *D. pteronyssinus* (36.3%), followed by Rye grass (33.1%), D. *farinae* (27.9%), cat (26.9%), dog (24.4%) and German cockroach (10.5%; Table 4). In this age group of persons with asthma, 50.2% were sensitized to at least

one indoor allergen and 39.3% to at least one outdoor allergen. Among younger asthmatics (20–40 years of age), 60.2% were sensitized to at least one indoor allergen and 53.3% to at least one outdoor allergen. The most common environmental allergens to which the asthmatics 20–40 years of age were sensitized included dog (49.5%), *D. pteronyssinus* (44.8%), and *D. farinae* (41.4%). Although indoor and outdoor IgE sensitization levels were not significantly different across the age groups, asthma in subjects ≥55 years of age was more strongly associated with sensitization to indoor allergen levels alone, whereas asthma in subjects 20–40 years of age, was strongly associated with sensitization to both indoor and outdoor allergens.

Association of asthma control measures with allergic sensitization

The percent of asthmatic subjects reporting various markers of health care utilization and symptomatic markers of asthma control was determined, along with the percent allergic sensitization among them, to determine if there were age-related differences. Overall, the relationship between sensitization and health care utilization and asthma related symptoms did not appear to differ across the age groups (asthmatics ≥55 years of age vs. asthmatics 20–40 years of age; Table 5). 71.5% of the subjects between the ages of 20–40 years old and 100% of the subjects ≥55 years of age who had 1> ER/urgent care visits for asthma in the past 12 months were atopic. The adjusted OR for sensitization associated with several categories of health care utilization (i.e. >1 visit to ER/urgent care, >1 MD/ER visits for wheezing, medication used for wheezing) was 0.43 (95% CI, 0.18–1.0) and 0.60 (95% CI, 0.21–1.70) for the ≥55 year old and the 20–40 year old and groups, respectively.

DISCUSSION

Between 60–80%[23–24] of children and young adults with asthma are sensitized to at least one environmental allergen. However, the prevalence of allergic sensitization in older asthmatics has not been well characterized and is traditionally felt to be lower, as determined from studies of targeted populations. In this study, we demonstrated that the prevalence of sensitization in subjects with current asthma differed only moderately and not statistically significantly between subjects 20–40 years of age and those ≥55 years of age. These results suggest that allergic sensitization in older patients with asthma may be more common than previously reported.

Although asthma is frequently characterized as a disease of childhood and young adulthood, it is not uncommon in older patients. The literature suggests that asthma may be present in 3.5–7.5% of the population over the age of 60 years, [1–4] although a study reported that as high as 15% of a general population in Australia over the age of 55 years old had asthma.[25] We report that 4.5% of the US population in NHANES 2005–2006 over the age of 55 years had a physician-diagnosis of asthma. Asthma in the older age groups was more common in females with a greater BMI.

The prevalence of allergen-specific serum IgE levels in excess of a specific detectable threshold is reported to decrease with increasing age in general. These studies have included healthy subjects *with and without asthma and other atopic diseases,* and suggest that approximately 40–50% of subjects under the age of 50 years and approximately 35% of subjects older than 50 are IgE sensitized to at least one allergen.[26–28] (Of note, these studies have measured allergic sensitization to 6 or fewer antigens and used different methods to quantify IgE than in NHANES 2005–2006, therefore direct comparison of the same antigens and threshold would be difficult). In a group of 8,344 subjects between the ages 18–60 years, from the cross-sectional multicenter Swiss SAPALDIA study, serum allergen-specific IgE declined by 21.1% with every 10-year increase in age.[29] Our data from the 2,573 subjects (asthmatics and non-asthmatics) evaluated in NHANES 2005–2006, are consistent

with these previous studies; IgE-mediated sensitization to at least one allergen was present in 51.12% of our younger subjects and in 38.84% our of subjects ≥55 years.

For many years, asthma in older patients was characterized as non-atopic.[30] However, in the past two decades, data from large populations or from studies incorporating data from multiple sites of asthma care, demonstrate that *some* older patients with asthma are also atopic (demonstrated either by serum evaluation or skin prick testing). Multicenter studies from the Netherlands[31] and France[32] reported that approximately 35% of older patients with asthma were sensitized to at least one allergen. In the longitudinal US Tucson epidemiologic study of obstructive disease, 36.6% of the subjects with asthma over the age of 65 years were sensitized to allergen.[4] (IgE-mediated sensitization rates in younger patients were not reported in this study). Our study is similar to the Dutch and French studies in that it captures data from subjects seen at multiple sites of care. However, only the Dutch study compared sensitization rates across age groups and determined that prevalence of allergic sensitization decreases significantly with age in patients with asthma. Our study also allows comparison of sensitization rates among subjects in the general population (asthmatics and non-asthmatics) to those only with asthma. We demonstrated a higher allergic sensitization rate among asthmatics, at 62.5%, compared to 38.8% in the general population in subjects ≥55 years of age. We also noted that sensitization to indoor allergens was more strongly associated with asthma in subjects ≥55 years of age, whereas sensitization to both indoor and outdoor allergens was associated with asthma in subjects 20–40 years of age. Sensitization to indoor allergens alone, rather than indoor and outdoor allergens, has been suggested as potentially more important to asthma in older patients.[33]

Asthma in older patients is associated with high rates of morbidity and mortality. Older patients with asthma have one of the highest rates of hospitalizations from their disease.[8–9, 34] Additionally, greater than 50% of the deaths secondary to asthma were reported in patients over the age of 65 years.[35] The etiology of increased mortality and morbidity from asthma in older patients is most likely multifactorial and includes potential medication non-compliance, age-related change in response to medications, changes in the immune response with age and permanent changes of the airway parenchyma. In children and young adults, allergic sensitization and exposure to allergens increases asthma severity.[36–37] Whether the same relationship is seen in older patients has not been established. Rogers *et al* demonstrated in a study of 45 patients > 65 years of age recruited from an asthma clinic in New York City, that IgE-mediated sensitization to cockroach increased asthma severity.[38] We selected markers of asthma control including health care utilization for asthma and the presence of asthma symptoms and determined the percent of subjects with asthma who were sensitized to allergen(s) with the specific clinical outcome, for both the younger and older groups of subjects. We did not find strong evidence that the relationship between sensitization and the selected outcomes was different in these two age groups (subjects 20–40 years old vs. ≥55 years old).

Our study has several strengths and limitations that are worth acknowledging. One strength is that our study was based upon data collected from a nationally representative population with a wide range of ages. This allowed us to directly compare sensitization rates from asthmatic subjects of different ages. Second, atopy was confirmed by a standardized measurement of allergen-specific IgE. Third, we limited our subjects to those with a history of physician diagnosed disease and with active symptoms, and excluded patients with possible COPD. While, the numbers of asthmatics subjects in both the ≥55 year old and 20–40 year old groups were modest as compared to the entire NHANES population, our sample size was sufficient to to detect a 25.7% difference in sensitization rates between age groups with 80% power, which would have been comparable to that reported in other studies. A limitation of this study is the cross-sectional nature the NHANES population which

precludes temporality/causality conclusions from being drawn. We were unable to determine the natural history of asthma in the subjects 20–40 year old group as they age. Additionally, we could not determine the age at which subjects developed allergic sensitization. Although beyond the scope of this paper, future work should address the relationship between antigen exposure and asthma symptoms with increased age. Although it was a strength that we used strict diagnostic criteria for asthma in older patients, we may not have captured some subjects ≥55 years old with asthma who have not been diagnosed. Despite these potential limitations, we feel that our study is an initial first step in understanding allergic sensitization in older patients with asthma and should be addressed in future work.

In summary, our study of the NHANES 2005–2006 data base suggests that allergic sensitization in older patients with asthma is not uncommon and may differ only slightly from subjects ages 20–40. Physicians providing care for older patients with asthma should consider testing for allergic sensitization and counseling about environmental control practices particularly among those with poorly controlled asthma.

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Abbreviations used

BMI	Body mass index
COPD	Chronic obstructive lung disease
CI	Confidence interval
ER	Emergency room
MD	Medical doctor
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio

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Table 1

Distribution of the study population with respect to gender, race, education, and body mass index (BMI) for each age group, among participants with current asthma

	20–40 (N=108)		≥55 (N=43)		
	N	Percent	N	Percent	p-value[1]
Gender					
Male	37	43.21	17	42.67	0.963
Female	71	56.79	26	57.33	
Race/Ethnicity					
Non-Hispanic White	51	67.61	18	66.09	0.989
Non-Hispanic Black	34	16.98	12	16.68	
Mexican American	15	5.78	9	6.01	
Other	8	9.63	4	11.22	
Education					
Less than high school diploma	24	18.42	9	16.55	0.846
High school or above	79	81.58	34	83.45	
BMI					
Underweight (BMI < 18.5)	2	0.50	2	6.39	0.117
Normal (BMI >=18.5 – 25)	33	36.55	5	18.13	
Overweight (BMI >=25 – 30)	21	16.80	12	25.69	
Obese (BMI >=30)	51	46.15	22	49.80	

[1] p-value for test of differences between age groups with respect to subject characteristic distributions.

Table 2

Prevalence of atopy in the full population, and distribution with respect to gender, race, education, and body mass index (BMI) for each age group, among atopic participants

	20–40 (N=1623)		≥55 (N=950)		
	N Atopic	Percent[1]	N Atopic	Percent[1]	p-value[2]
Total	842	51.1	367	38.8	
Gender					
Male	412	55.5	181	45.9	0.024
Female	430	44.5	186	54.1	
Race/Ethnicity					
Non-Hispanic White	302	58.3	191	75.3	<0.001
Non-Hispanic Black	225	15.9	86	10.7	
Mexican American	228	13.0	68	4.3	
Other	87	12.8	22	9.7	
Education					
Less than high school diploma	216	18.1	103	17.9	0.963
High school or above	600	82.00	259	82.1	
BMI					
Underweight (BMI < 18.5)	16	2.1	5	1.3	0.256
Normal (BMI >=18.5 – 25)	257	36.2	87	28.5	
Overweight (BMI >=25 – 30)	280	31.4	130	36.9	
Obese (BMI >=30)	283	30.2	134	33.3	

[1] Total row indicates number and percent atopic among the overall population; subsequent rows indicate the distribution of each characteristic among atopics.

[2] p-value for test of differences between age groups with respect to subject characteristic distributions.

Table 3

Prevalence and odds ratios for atopy among U.S. adults with asthma, subjects aged 55 and older compared to younger adults aged 20–40 years

Outcome, Age Group	N	Percent (SE) atopic among those with outcome	Adjusted OR (95% CI)[1]	Interaction p-value[2]
Current asthma, ≥55	43	65.2 (6.5)	2.9 (1.7–4.9)	0.914
Current asthma, 20–40	108	75.4 (3.4)	3.5 (2.3–5.2)	

[1] OR and p-value adjusted for sex, race/ethnicity, and education.

[2] p-value for test of age group-by-atopy interaction in adjusted logistic model of current asthma.

Table 4

Prevalence of sensitization to indoor and outdoor allergens among U.S. adult asthmatics, subjects aged 55 and older compared to younger adults aged 20–40 years

Allergen-specific IgE	Percent (SE) sensitized ≥55 (N= 43)	Percent (SE) sensitized 20–40 (N= 108)	Adjusted OR (95% CI), ≥55[1]	Adjusted OR (95% CI), 20–40[1]	p-value[2]
Indoor					
D. pteronyssinus	36.3 (9.50)	44.8 (6.52)	4.09 (1.53–10.90)	2.73 (1.55–4.81)	0.301
D. farinae	27.9 (9.75)	41.4 (7.09)	2.35 (0.79–7.01)	2.60 (1.43–4.73)	0.796
Cat	26.9 (9.02)	40.5 (7.62)	3.33 (1.18–9.37)	5.81 (2.91–11.60)	0.261
Dog	24.4 (8.38)	49.5 (6.90)	4.46 (1.49–13.32)	8.49 (4.11–17.53)	0.457
German cockroach	10.5 (4.23)	18.3 (4.77)	1.14 (0.41–3.21)	1.89 (0.87–4.10)	0.734
Rat	0.0 (NA)	3.5 (2.38)	*3*	2.40 (0.40–14.59)	*3*
Mouse	0.0 (NA)	10.9 (4.19)	*3*	8.03 (2.72–23.72)	*3*
≥ 1 indoor	50.2 (6.84)	60.2 (5.73)	3.12 (1.60–6.10)	3.20 (1.88–5.45)	0.754
Outdoor					
Rye grass	33.1 (8.40)	42.1 (5.50)	2.51 (1.41–4.48)	2.51 (1.65–3.80)	0.765
Ragweed	10.7 (4.83)	31.9 (5.14)	0.86 (0.35–2.11)	1.98 (1.30–3.01)	0.159
Bermuda grass	15.9 (7.37)	29.4 (5.52)	1.47 (0.51–4.26)	1.93 (1.15–3.24)	0.851
Oak	9.0 (4.34)	24.0 (4.73)	0.98 (0.39–2.45)	2.11 (1.24–3.58)	0.186
Thistle	9.5 (4.35)	20.1 (4.37)	1.26 (0.46–3.44)	1.91 (1.06–3.44)	0.692
Birch	11.7 (5.72)	19.3 (4.75)	1.37 (0.40–4.62)	2.07 (1.06–4.04)	0.642
Alternaria alternata	10.0 (5.30)	27.7 (4.61)	2.44 (0.72–8.26)	3.63 (2.51–5.24)	0.618
Aspergillus fumigatus	6.4 (3.33)	17.1 (4.22)	1.98 (0.68–5.83)	2.71 (1.43–5.16)	0.877
≥ 1 outdoor	39.3 (8.07)	53.3 (5.63)	1.93 (1.02–3.66)	2.32 (1.54–3.49)	0.934

[1] OR and confidence interval adjusted for sex, race/ethnicity, and education.

[2] p-value for test of age group-by-sensitization interaction in adjusted logistic model of current asthma.

[3] OR and p-value not reported due to zero cell count.

Table 5

Prevalence of atopy by asthma control measures, and associated odds ratios for the relationship between the outcome measures and sensitization among U.S. adult asthmatics (aged 55 and older vs. 20–40 years old)

Outcome – Asthma control measures	Percent (SE) atopic among those with outcome, ≥55 (N=43)	Percent (SE) atopic among those with outcome, 20–40 (N=108)	Adjusted OR (95% CI), ≥55[1]	Adjusted OR (95% CI), 20–40[1]	Interaction p-value[2]
Health care utilization - in past 12 months					
1 or more ER/urgent care visits	100.0[3]	71.5 (12.6)	*3*	0.72 (0.10–4.98)	*3*
1 or more MD/ER visits for wheezing	58.7 (14.2)	72.8 (8.7)	0.68 (0.14–3.37)	0.59 (0.18–1.90)	0.909
Medication use for wheezing	49.5 (10.3)	75.2 (5.1)	0.27 (0.10–0.72)	1.08 (0.36–3.21)	0.108
Any utilization category above	55.3 (10.0)	72.1 (4.9)	0.43 (0.18–1.00)	0.60 (0.21–1.70)	0.568
Symptoms - in past 12 months					
Limited activities due to wheezing	50.3 (16.3)	78.0 (8.4)	0.35 (0.05–2.31)	0.85 (0.22–3.34)	0.301
1 or more wheezing attacks	66.0 (9.8)	71.3 (5.4)	0.95 (0.26–3.45)	0.32 (0.07–1.44)	0.353
Any sleep disturbance due to wheezing	64.2 (15.8)	78.2 (5.9)	0.81 (0.17–3.93)	1.06 (0.29–3.87)	0.610
Chest sounding wheezy after exercise	33.8 (18.1)	69.9 (6.7)	0.17 (0.03–1.00)	0.44 (0.08–2.39)	0.295

[1] OR and confidence interval adjusted for sex, race/ethnicity, and education

[2] p value is for age group-by-atopy interaction adjusted for sex, race/ethnicity, and education, age groups are 20–40 and ≥55

[3] SE, OR, and p-value not reported due to zero cell count