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Original Article

Increased blood eosinophils and airflow obstruction as new-onset asthma predictors in the elderly: The Nagahama study

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Abbreviations:
BMI, body mass index; CES-D, the Center for Epidemiological Studies-Depression; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; FSSG, frequency scale for the symptom of gastroesophageal reflux disease; FVC, forced vital capacity; GERD, gastroesophageal reflux disease; HDM, house dust mite; ODI, oxygen desaturation index; SDB, sleep-disordered breathing

ABSTRACT

Background: Asthma in the elderly needs more attention in an aging society. However, it is likely to remain underdiagnosed and undertreated. This study aimed to clarify clinical characteristics of new-onset asthma in the elderly, describing the prevalence, predictive factors, and comorbidities after asthma diagnosis of new-onset asthma in the elderly in the general population.
Methods: This community-based prospective cohort study enrolled 9804 generally healthy participants (30–74 years old) in Nagahama City, and conducted a follow-up assessment after 5 years. Elderly participants were those aged ≥65 years at baseline. Patients with new-onset asthma were defined as participants without asthma at baseline assessment and with asthma at the follow-up assessment.
Results: Among the 7948 participants analyzed in this study, 28 (1.4%) elderly and 130 (2.2%) non-elderly had new-onset asthma. Multiple logistic regression analysis revealed low forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) and high blood eosinophil counts at baseline as predicting factors for new-onset asthma in the elderly. Additionally, subsequent incidence of new-onset asthma was higher in elderly participants with both predictors (high blood eosinophil counts and low FEV_1/FVC at baseline) than those with none or one of the predictors before asthma diagnosis. Lastly, elderly patients with new-onset asthma had more frequent comorbidity of moderate to severe sleep disordered breathing than those non-elderly.
Conclusions: Eosinophilic inflammation and airflow obstruction may predict subsequent new-onset asthma after the age of 65 years. Revealing the characteristics of new-onset asthma in the elderly can aid in the prevention of underdiagnosed asthma.

Introduction

Growing attention to asthma in the elderly is desirable because of its increased prevalence in the elderly in many developed countries. Asthma in the elderly has distinct characteristics.[1] First,

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asthma in the elderly is likely underrecognized or underdiagnosed, especially when they have never been diagnosed with asthma.[2] Elderly patients with asthma tend to attribute their asthma symptoms to changes in aging and often delay their visits to a physician. Additionally, asthma in the elderly is easily confounded with other diseases such as heart failure and chronic obstructive pulmonary disease (COPD), because having multiple comorbidities and a smoking history is common in the elderly.[3–5] Furthermore, high mortality has been observed in elderly patients with asthma,[6] who remain underdiagnosed and undertreated. Therefore, the relevant characteristics of new-onset asthma in the elderly should be recognized.

Asthma is a heterogeneous disorder with various phenotypes. Age at asthma onset plays an important role in distinguishing these phenotypes. Early-onset asthma is characterized by the presence of atopy and symptoms concordant with airway inflammation and dysfunction.[7] Several phenotypes were identified in adult-onset asthma, including obese female predominant phenotype with a high symptom expression and active eosinophilic airway inflammation phenotype with few symptoms.[7–9] Conversely, information on the prevalence and clinical characteristics of new-onset asthma in the elderly is limited. Therefore, an approach to not only elderly patients who already have asthma but also new-onset asthma in the elderly is required. This study aimed to clarify the characteristics of new-onset asthma in the elderly.

Methods

Study design and participants

A community-based prospective cohort study, The Nagahama Prospective Genome Cohort for Comprehensive Human Bioscience (The Nagahama Study), recruited participants from generally healthy residents, aged 30–74 years, in Nagahama City, Shiga prefecture, Japan. A total of 9804 participants were enrolled from 2008 to 2010, i.e., the baseline assessment of the Nagahama Study. A follow-up assessment was conducted after 5 years from the baseline assessment from November 2013 to November 2015 on participants who had not waived their consent.[10] This study was approved by the Ethics Committee of Kyoto University Graduate School of Medicine and the Nagahama Municipal Review Board. All methods were performed following the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Questionnaire and measurements

Clinical measurements were composed of self-reported questionnaires, pulmonary function tests, and blood sampling. Frequency scale for the symptom of gastroesophageal reflux disease (FSSG) score, which consisted of questions related to acid-reflux symptoms and dyspeptic symptoms,[11] and the Center for Epidemiological Studies-Depression (CES-D) score with negative and positive domains[12] were also evaluated. Asthma-related symptoms were assessed by questionnaires at the follow-up assessment for difficulty in activities of daily living due to respiratory symptoms, increased coughing or breathlessness, modified Medical Research Council Dyspnea (mMRC) scores, wheezing, nighttime or early morning cough or chest tightness, nocturnal arousal due to cough, nocturnal arousal due to chest tightness, sputum production, and sputum production on waking (Supplementary Table 1). Pulmonary function was measured by a computed spirometer with automated quality checks (baseline; SP-350 COPD; Fukuda Denshi, Tokyo, Japan). A different type of spirometer (SP-370) was used with a large number of participants at the follow-up assessment.[13] Predicted normal values for FEV_1 were calculated according to the guidelines of the Japanese Respiratory Society.[14] Blood tests, including blood eosinophils, were conducted at both baseline and follow-up assessment, but serum total immunoglobulin E (IgE) and specific IgE for house dust mite (HDM), Japanese cedar pollen, grass pollen, weeds, mold, cat dander, and dog dander (ImmunoCAP® Specific IgE; Phadia, Tokyo, Japan) was measured at baseline assessment only. Perennial allergens were defined as HDM, weeds, molds, cat dander, or dog dander. Participants with specific IgE levels of 0.35 UA/ml or greater were considered to be sensitized to the allergen.[15] Pulse oximetry examination with actigraphy was also performed at the follow-up assessment.

Definition of terms and diseases

Elderly participants were defined as those who were aged ≥65 years. Asthma diagnosis was determined by using a self-reported questionnaire with the following question: “Have you ever experienced an asthmatic episode since becoming an adult?” Patients with new-onset asthma were defined as participants who answered “no” at baseline assessment and “yes” at follow-up assessment, as previously described.[16] New-onset asthma in the elderly is participants with new-onset asthma who were aged ≥65 years at baseline. Diagnosis of COPD, sinusitis, sleep apnea syndrome, hypertension, dyslipidemia, and diabetes mellitus was determined by a self-reported questionnaire at the baseline assessment. Participants were considered to have gastroesophageal reflux disease (GERD) if their total FSSG score was at least eight points at both baseline and follow-up assessments.[11] Allergic rhinitis was defined as having sensitization to some specific allergen in addition to rhinitis symptoms at baseline assessment. The presence of comorbidities was determined at follow-up assessment as hypertension, using antihypertensive agents or systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥90 mmHg; dyslipidemia, using antihyperlipidemic agents or serum low density lipoprotein of ≥140 mg/dL or serum high density lipoprotein of <40 mg/dL or serum triglyceride of ≥150 mg/dL; diabetes mellitus, using oral antihyperglycemic agents and/or insulin or hemoglobin A1c of ≥6.5%; depression, total CES-D score of ≥16 points.[12] Supplementary Table 2 shows the definition of the diseases.

Actigraphy-modified ODI3% (acti-ODI3%) was used as an indicator for sleep-disordered breathing (SDB) at follow-up assessment. A 3% oxygen desaturation index (ODI3%) was calculated based on a ≥3% decrease from baseline in oxygen saturation per hour. ODI3% was corrected by sleeping time determined by actigraphy. The SDB severity by acti-ODI3% levels was defined as follows: normal: <5 events/h; mild: 5–15 events/h; moderate: 15–30 events/h; and severe: ≥30 events/h. A detailed description of SDB assessment was shown in the previous article.[17]

Analyses and statistics

Statistical analyses were performed with JMP version Pro15 (SAS Institute, Tokyo, Japan). Logistic regression analyses were used to estimate the odds ratio of clinical indices for new-onset asthma in elderly and non-elderly participants. The chi-square test or Fisher's exact test for categorical variables and the Student *t*-test or Mann–Whitney *U* test for continuous variables were appropriately used to conduct comparisons between groups. Multivariable regression analyses for predictive factors of new-onset asthma were adjusted using a propensity score to control for each factor separately due to the relatively small number of new-onset asthma cases in the elderly. The propensity score was calculated for each factor and used as a covariate in a multivariable regression model.[18]

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Lastly, we examined differences in symptoms and comorbidities between elderly and non-elderly patients with new-onset asthma by univariate or multivariable analysis using follow-up data. False discovery rate estimation was used for multiple testing corrections. *P*-values <0.05 were regarded as statistically significant.

Results

Participants' characteristics

Among the 9804 initial participants, 9402 had no asthma at baseline assessment. Of the 7948 participants analyzed after excluding those participants who were lost to follow-up, 158 (2.0%) had new-onset asthma at follow-up assessment. A total of 130 (2.2%) had new-onset asthma among participants aged 30−64 years at baseline assessment (non-elderly, $n = 5904$). Meanwhile, 28 (1.4%) had new-onset asthma at follow-up assessment among participants aged ≥65 years at baseline (elderly, $n = 2044$), which was lower frequency than in the non-elderly participants ($P = 0.020$) (Fig. 1).

Predictive factors for new-onset asthma in the elderly

Table 1 shows the clinical characteristics of elderly and non-elderly participants with and without new-onset asthma at baseline assessment. Elderly patients with new-onset asthma had lower FEV_1 (% predicted) ($P = 0.005$) and FEV_1/FVC ($P = 0.0001$) and higher blood eosinophil counts ($P = 0.031$) at baseline than elderly participants without new-onset asthma. Multiple logistic regression analysis using the propensity score to control for covariates revealed low FEV_1/FVC and high blood eosinophil counts at baseline as predictive factors for new-onset asthma in the elderly (Table 2). The results of the significant predictive factors for new-onset asthma in the elderly remained after excluding patients with non-eosinophilic COPD (FEV_1/FVC of <70%, smoking history of ≥10 pack-year, and blood eosinophil counts of <300/μL at baseline assessment; $n = 164$) from the elderly participants (Supplementary Table 3). Body mass index (BMI) at baseline was not significantly associated with new-onset asthma in the elderly.

The incidence rates of new-onset asthma in the elderly with and without blood eosinophil counts of ≥300/μL or FEV_1/FVC of <70% at baseline are shown in Figure 2. The presence of either predictor, i.e., blood eosinophil counts of ≥300/μL or FEV_1/FVC of <70% at baseline, did not increase the odds of new-onset asthma in the elderly. On the other hand, elderly participants with both predictors had a significantly higher incidence of new-onset asthma (4/19, 21.1%) than those with one or none of the predictors, after adjustment for sex, and smoking status (Supplementary Table 4).

Predictive factors for new-onset asthma in the non-elderly

Univariate analysis revealed that childhood asthma and perennial allergen sensitization were predictive factors for new-onset asthma in the non-elderly. Only childhood asthma was a significant predictive factor in the multivariable analysis (Supplementary Table 5). Most patients (81.8%) had a relapse before 65 years old among patients with a history of asthma remission in childhood and newly diagnosed asthma in adulthood (Supplementary Fig. 1).

Comparison of symptoms and comorbidities between elderly and non-elderly patients with new-onset asthma after asthma diagnosis

Symptoms and comorbidities were compared between the elderly and the non-elderly patients with new-onset asthma to clarify their phenotypic differences. Elderly patients with new-onset asthma had a lower frequency of difficulty in activities of daily living, despite a higher frequency of dyspnea on exertion (mMRC scores), compared to non-elderly patients with new-onset asthma even after adjustment for sex, BMI, and smoking status. No significant differences were found in the frequencies of other symptoms, including sputum production or cough or chest tightness at nighttime or early morning, between elderly and non-elderly patients with new-onset asthma (Fig. 3).

The elderly had more comorbidities of hypertension and moderate to severe SDB and had less comorbidity of GERD than the non-elderly in univariate analysis among patients with new-onset asthma (Table 3). Multivariable analysis for differentiating new-onset asthma in the elderly from that in the non-elderly revealed significantly more comorbidity of moderate to severe SDB in patients with new-onset asthma in the elderly than those in the non-elderly after adjustment for sex, BMI and smoking status (Table 4).

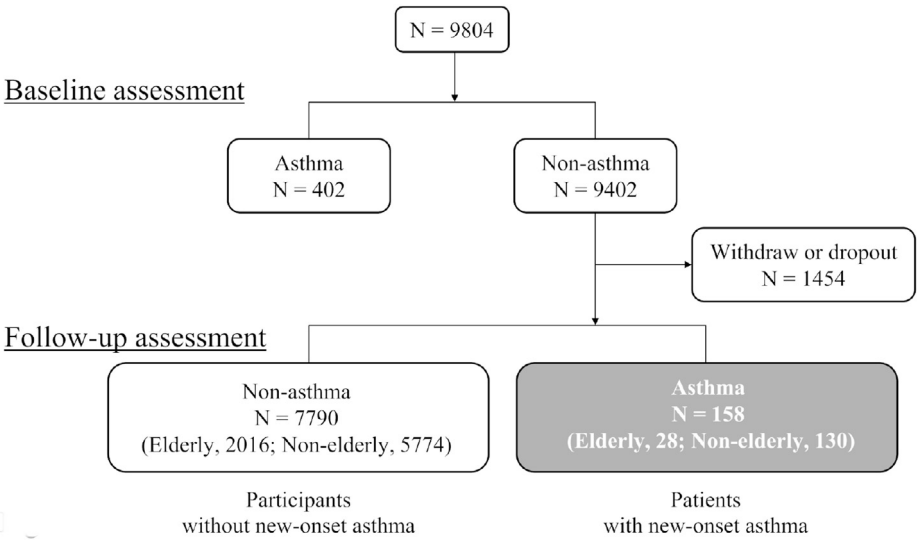

Fig. 1. Flow diagram of baseline and follow-up assessments. Among the 7948 participants analyzed in this study, 1.4% of the elderly and 2.2% of the non-elderly had new-onset asthma before follow-up assessment.

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Table 1
Participants' characteristics at baseline assessment.

	Elderly participants ($n = 2044$)		Non-elderly participants ($n = 5904$)	
	with new-onset asthma[§] ($n = 28$)	without new-onset asthma[§] ($n = 2016$)	with new-onset asthma[§] ($n = 130$)	without new-onset asthma[§] ($n = 5774$)
Age (years)[†]	67.0 (66.0–71.5)	69.0 (67.0–71.0)	45.5 (36.0–58.0)	51.0 (38.0–59.0)
Sex (female, %)	57.1	56.3	76.2	71.8
BMI (kg/m^2)[‡]	22.5 (2.9)	22.8 (2.9)	21.9 (3.4)	22.1 (3.3)
Smoking (current/ex/never, %)	3.6/32.1/64.3	8.9/26.3/64.8	15.4/22.3/62.3	14.9/17.8/67.3
Spirometry				
FEV_1 (% predicted)[‡]	92.0 (26.8)	101.0 (16.7)	99.7 (14.5)	103.6 (15.4)
FEV_1/FVC (%)[‡]	75.5 (10.2)	80.4 (6.6)	82.7 (6.3)	83.2 (6.1)
Blood tests				
Blood eosinophils (/μL)[†]	172.6 (92.1–293.3)	117.0 (70.2–182.0)	120.2 (69.0–214.5)	118.4 (69.7–198.0)
Blood neutrophils (/μL)[†]	3122.5 (2711.2–4099.1)	3200.0 (2599.0–3883.6)	3289.5 (2595.9–4176.8)	3192.8 (2540.5–3983.5)
Serum total IgE (IU/mL)[†]	75.9 (22.3–295.5)	59.0 (24.7–155.0)	81.0 (34.5–224.5)	64.1 (27.1–163.0)
High-sensitivity CRP (ng/mL)[†]	592.5 (144.8–1257.5)	396.0 (203.0–811.0)	266.5 (154.3–546.8)	266.0 (132.0–589.8)
Sensitization to perennial allergen (%)	21.4	21.3	47.7	37.6
Comorbidities (%)				
Allergic rhinitis	21.4	13.7	40.0	35.1
Sinusitis	14.3	10.1	13.8	9.9
COPD	3.6	1.4	6.9	0.5
Sleep apnea syndrome	7.1	7.1	6.2	4.6
Childhood asthma	3.6	1.0	7.7	2.2
Hypertension	46.4	37.3	13.1	13.9
Dyslipidemia	25.0	17.3	10.0	10.7
Diabetes mellitus	7.1	10.3	2.3	3.5
GERD	17.9	17.9	36.2	23.5

BMI, body mass index; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease.
[†] Median (interquartile range, IQR).
[‡] Mean (SD).
[§] Participants with new-onset asthma were determined regardless of whether they had childhood asthma or not.

Table 2
Factors associated with new-onset asthma[†] in elderly participants.

	Univariate analysis		Multivariable analysis	
	OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
FEV_1/FVC (<70%)	5.40 (2.25–12.95)	0.0002	5.63 (2.24–14.18)	0.0002
Blood eosinophil counts (≥300/μL)	3.67 (1.53–8.80)	0.004	3.19 (1.29–7.87)	0.012
Sensitization to perennial allergen (yes)	1.01 (0.41–2.50)	0.98	0.69 (0.26–1.83)	0.45
Allergic rhinitis (yes)	1.71 (0.69–4.26)	0.25	1.89 (0.73–4.93)	0.19
Childhood asthma (yes)	3.70 (0.48–28.54)	0.21	3.53 (0.46–27.30)	0.23
BMI (≥25 kg/m^2)	0.82 (0.31–2.17)	0.69	0.85 (0.32–2.26)	0.74

OR, odds ratio; CI, confidence interval; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; BMI, body mass index. Multivariable analysis was adjusted using a propensity score to control for each factor separately. Covariates for adjustment included sex, and smoking history (yes).
[†] Participants with new-onset asthma were determined regardless of whether they had childhood asthma or not.

Discussion

This large-scale epidemiological study revealed new-onset asthma in 1.4% of the elderly and 2.2% of the non-elderly participants during the study period. To our knowledge, this is the first study to demonstrate the predictors of new-onset asthma in the elderly, high blood eosinophil counts and airflow obstruction. In addition, both eosinophilia and airflow obstruction increased the odds of subsequent new-onset asthma in the elderly. Notably, the elderly had less difficulty in activities of daily living, despite a higher frequency of dyspnea on exertion (mMRC scores), than the non-elderly among patients with new-onset asthma. Lastly, elderly patients with new-onset asthma had a higher prevalence of moderate to severe SDB than non-elderly patients with new-onset asthma.

This study revealed that high blood eosinophil counts and airflow obstruction were predictive factors for new-onset asthma in the elderly, and that the combination of both increased the odds of new-onset asthma in the elderly. The importance of eosinophilic inflammation in the pathogenesis of asthma is well-recognized. This study suggested that elderly patients with new-onset asthma was also driven by eosinophilic inflammation. Previous studies noted the association between eosinophilic inflammation and asthmatic pathophysiology in the elderly. Busse PJ *et al.* reported that elderly patients with asthma treated with inhaled corticosteroids had higher sputum eosinophils along with neutrophils than younger patients.[19] The Normative Aging Study presented that airway hyperresponsiveness was associated with increased peripheral blood eosinophil counts in males with a mean age of 60 years and without an asthma diagnosis.[20] Next, airflow obstruction in patients with new-onset asthma in the elderly might reflect mucus plugs as well as airway wall remodeling due to untreated eosinophilic inflammation,[21–23] although these mechanisms were not examined in the present study. The elderly have decreased mucociliary clearance.[24] Increased eosinophilic inflammation and structural changes in the airway may have a role in the pathophysiology of asthma in the elderly.

While obesity has been reported to be associated with asthma onset,[25,26] in this study, BMI at baseline had no significant impact

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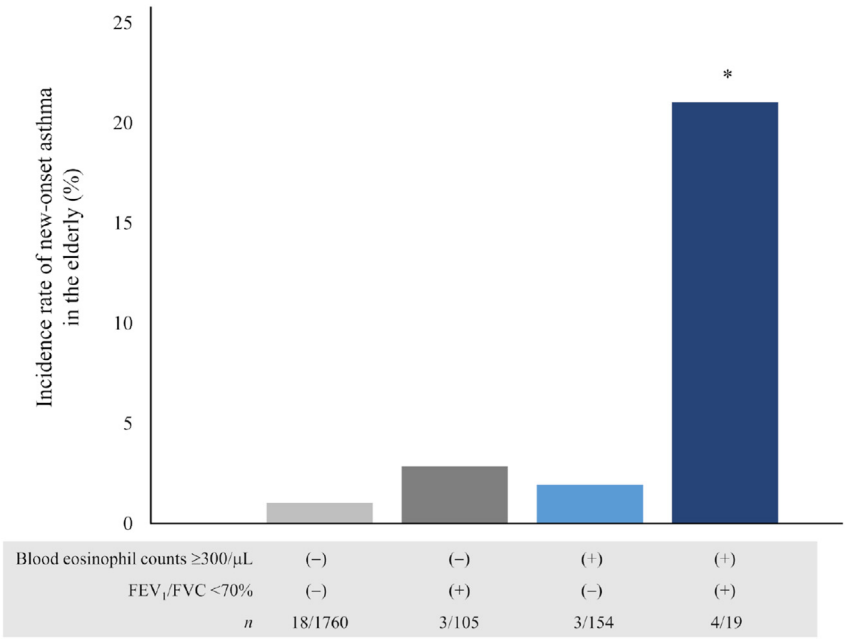

Fig. 2. Incidence rates of new-onset asthma in the elderly with and without blood eosinophil counts of ≥300/μL or FEV_1/FVC of <70% at baseline. *False discovery rate-adjusted *P* value < 0.05 versus all other groups. FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.

on new-onset asthma in the elderly. In our previous report using the Nagahama Study population,[27] a positive correlation was observed between blood eosinophil counts and BMI in the overall population, whereas a negative correlation was observed in the population with high eosinophil counts. Therefore, BMI may not have a significant impact on new-onset asthma in elderly patients who are likely to have high blood eosinophil counts.

Our findings indicated that the elderly had less difficulty in activities of daily living than the non-elderly, among patients with new-onset asthma, despite a higher frequency of dyspnea on exertion (mMRC scores). The mechanism of the discrepancy between these symptoms is unknown. However, elderly patients with new-onset asthma may limit their daily activities due to dyspnea on exertion, as is observed in patients with COPD.[28]

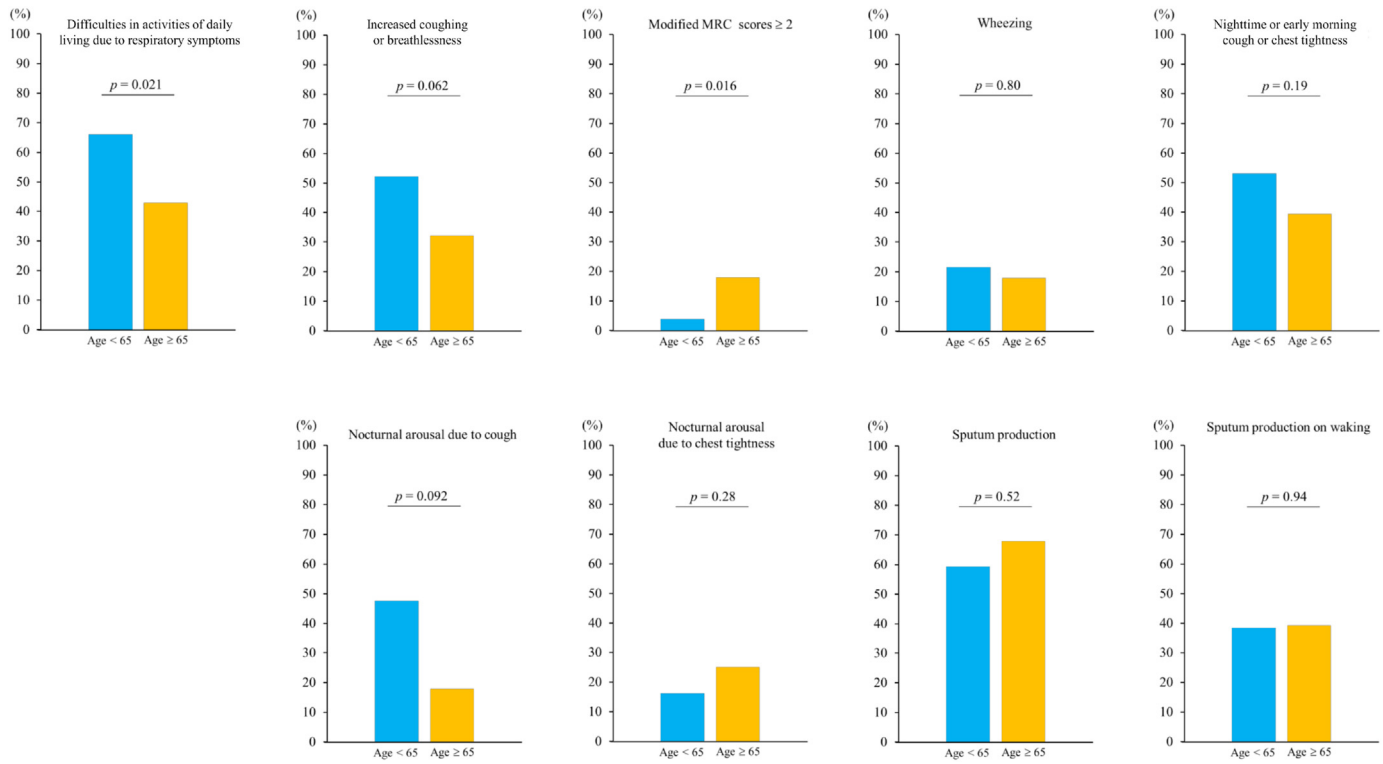

Fig. 3. Comparisons of asthma-related symptoms at follow-up assessment between elderly and non-elderly patients with new-onset asthma.

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Table 3
Comparison of comorbidities after asthma diagnosis between the elderly and the non-elderly, among patients with new-onset asthma.

	Patients with new-onset asthma ($n = 158$)		
	Non-elderly ($n = 130$)	Elderly ($n = 28$)	*P* value
Age (years)[†]	50.5 (41.0–63.0)	72.5 (71.0–76.5)	<0.0001
Sex (female, %)	76.2	57.1	0.040
BMI (kg/m^2)[‡]	22.2 (3.4)	22.3 (3.0)	0.89
Smoking (current/ex/never, %)	13.1/23.1/63.8	7.1/28.6/64.3	0.62
Sinusitis (%)	18.5	21.4	0.79
COPD (%)	6.9	17.9	0.076
Moderate to severe SDB (%)[§]	7.3	38.9	0.001
Hypertension (%)	28.5	67.9	0.0001
Dyslipidemia (%)	46.2	60.7	0.16
Diabetes mellitus (%)	3.9	7.1	0.61
Depression (%)	42.3	50.0	0.46
GERD (%)	36.9	10.7	0.007

Data at follow-up assessment.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; SDB, sleep-disordered breathing; GERD, gastroesophageal reflux disease.
[†] Median (interquartile range, IQR).
[‡] Mean (SD).
[§] Actigraphy-modified 3% oxygen desaturation index ≥15 events/hour.

Moreover, a higher prevalence of comorbidities, such as moderate to severe SDB, was found in the elderly than in the non-elderly among patients with new-onset asthma. SDB, mainly obstructive sleep apnea (OSA), is caused by upper airway obstruction. Old age is known to be one of the risk factors for OSA/SDB.[29,30] Mucosal swelling or produced mucus in association with elevated airway inflammation and subsequently increased upstream resistance may favor SDB development in elderly patients with asthma.[31] Attenuated ventilatory response[32] may also aggravate airway obstruction during sleep by hampering the expectoration of sputum in elderly patients with asthma. Moreover, OSA was associated with poor asthma control, reduced lung function, and severe asthma in the elderly among patients with asthma.[33] It is important to screen for SDB in elderly patients with new-onset asthma because SDB is common among elderly patients with new-onset asthma and is an aggravating factor of asthma.

Our findings demonstrated childhood asthma as a predicting factor for new-onset asthma in the non-elderly. Childhood asthma can go into remission, while not a few young aged patients relapse asthma.[34,35] Subclinical airway eosinophilic inflammation and airway hyperresponsiveness were reported to be present in adolescents with clinical remission of asthma,[36,37] which may lead to asthma relapse in young adults. Over 80% of a relapse of asthma was observed before the age of 65 years among adults with a history of remitted childhood asthma. Future studies of monitoring airway inflammation are required for the management of patients with asthma in remission.

Table 4
Multivariable analysis for differentiating new-onset asthma in the elderly from that in the non-elderly (data at follow-up assessment).

	New-onset asthma in the elderly/non-elderly		
	Adjusted OR	95% CI	*P* value[*]
Moderate to severe SDB[†]	5.82	1.52–22.25	0.030
GERD	0.27	0.05–1.33	0.16
Hypertension	2.43	0.78–7.56	0.12

OR, odds ratio; CI, confidence interval; SDB, sleep-disordered breathing; GERD, gastroesophageal reflux disease.
Multivariable analysis was adjusted by sex, body mass index (≥25 kg/m^2), and smoking history (yes).
[*] After multiple testing correction via false discovery rate estimation.
[†] Actigraphy-modified 3% oxygen desaturation index ≥15 events/hour.

This study has several limitations. First, asthma diagnosis was based on a self-reported questionnaire, rather than an objective test. A self-reported diagnosis can potentially overestimate the prevalence of asthma. In addition, the follow-up period of this study (5 years) may not be sufficient to detect new-onset asthma. However, the prevalence of new-onset asthma in this study (4.0 per 1000 person-years) is similar to that in previous population-based reports with a follow-up period of 9–10 years (4.4–4.5 per 1000 person-years).[38,39] Second, new-onset asthma in participants aged 75 years or older at baseline was not assessed. Further studies are required in this population. Lastly, differentiating asthma from COPD, particularly in the elderly, is difficult. As this study was based on a self-reported questionnaire, we could not completely exclude the possibility that patients with new-onset asthma overlapped with COPD. Patients with COPD exhibiting eosinophilic inflammation are treated similarly to those with asthma such as inhaled corticosteroids. Therefore, a sensitivity analysis, which excluded participants with non-eosinophilic COPD from the elderly, was conducted. This analysis did not change the findings of the predictive factors for new-onset asthma in the elderly. Conversely, this large community-based study had the strength of having little selection bias. Additionally, this longitudinal study with data before asthma diagnosis can provide insights that could lead to early disease detection and intervention.

In conclusion, this study revealed that individuals with characteristics of eosinophilic inflammation or airflow obstruction are at risk for new-onset asthma after the age of 65 years. The current study findings also revealed that airflow obstruction accompanied by high blood eosinophil levels might predict subsequent new-onset asthma in the elderly. Furthermore, the prevalence of comorbid SDB was higher in elderly patients with new-onset asthma than in non-elderly patients with new-onset asthma. The study findings characterize the specific phenotype of new-onset asthma related to inflammation, lung function, and comorbidities in the elderly.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.alit.2023.11.002.

Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

KN analyzed and interpreted the data and wrote the draft. TN analyzed and interpreted the data, wrote and edited the manuscript. HM conceived and designed the study, collected, analyzed and interpreted the data, and edited the manuscript. ST, NN, MK, and NT analyzed the data. TO, HS, KM, TM and SS collected the data and revised the work critically. TK, YT, FM contributed to the design of the Nagahama cohort study, recruited participants, acquired the funding, and critically revised the manuscript. KC and TH provided overall supervision and critically revised the manuscript.

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