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A 10-year comparative study of factors for allergic asthma and/or rhinitis in two cross-sectional surveys

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Abstract

Background: The allergenic relevance of the living environment changes over the last decades is largely unknown.

Objective: We aimed to compare the factors associated with asthma and/or rhinitis between 2008 and 2018.

Methods: We assessed two nationally representative cross-sectional datasets in 2008 and 2018. Within the rigorous protocol, questionnaire and serum IgE measurement were conducted in 2322 and 2353 patients with allergic asthma (A) and/or rhinitis (R) respectively. Multivariate logistic regression analysis was used to examine the effect of different factors on sensitization.

Results: The prevalence of sensitization increased in rhinitis alone (A-R+, 63% in 2008 vs. 67.7% in 2018, $P = 0.039$) and asthma with rhinitis (A+R+, 70.6% vs. 75.1%, $P = 0.014$). The common factors for sensitization were male sex, using mattress and air conditioner, family history of rhinitis, building age > 30 years, and meat consumption. Compared with 2008, secondhand smoke was an additional risk factor for A+R- (odds ratio [OR] 2.17, 95% confidence interval [CI] 1.18–7.01) and A+R+ (OR 1.72, 95%CI 1.03–3.14), and the odds of farmland or forest for pollen and mold sensitization were higher in 2018 (OR 3.61, 95%CI 2.79–4.66, and OR 1.86, 95%CI 1.34–2.58). Eating fish was inversely associated with A-R+ (OR 0.68, 95%CI 0.52–0.91, $P < 0.01$), while older age also showed an inverse relationship with sensitization. The OR of age 25–44 years was higher in 2018.

Conclusions: Repeated surveys showed variations in the factors affecting allergic asthma and/or rhinitis. The variable factors included age of 25–44 years, secondhand smoke, farmland, forest, and fish consumption.

Key words: Allergic sensitization, Asthma, rhinitis, risk factor, serum IgE, secondhand smoke

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Introduction

Allergy is the most frequent immune disorder, and its pathogenesis involves genetic susceptibility, environmental exposures, living style, social factors, and psychological factors.[1] Since tremendous transformations of living environment have taken place in urban areas, there has been a substantial increase in the prevalence of allergic disorders in developed countries and, more recently, in developing countries such as China.[2] Many different environmental and

other factors may contribute to the increased prevalence of allergic diseases. The China Alliance of Research on Respiratory Allergic Disease survey in 2008 (CARRAD-I) demonstrated that familial atopic history, male gender, using air conditioner, using a mattress, and frequent meat consumption were the predictors of allergy.[3] China has undergone massive population growth and a great-scale industrialization over the last decade, which dramatically upended all areas of life, leading to a profound change in priorities, both in the social-economic field and in human behaviors. In other countries, several studies have focused on the long-term trends and influences of climate on pollen allergenicity in public health.[4,5] However, the allergenic relevance of human behavior changes is largely unknown.

Few studies have reported the comparison of odds ratios (ORs) for sensitizations and allergen prevalence in one nation over more than 10 years using the same research methodology, and some studies focused on pediatric patients instead on all age groups.[6,7] China has vast territory and abundant resources, and there are discrepancies in people's living style and environment from north to south coast. Previous studies of factors for asthma and/or rhinitis were mainly conducted in industrialized countries and might not adequately reflect countries undergoing rapid transition, such as China.[8] Thus, we conducted the second study in 2018 (CARRAD-II) in multiple centers in China using the same questionnaire and the same study protocol as the CARRAD-I to compare the rate of IgE positivity and associated factor for sensitization.

Methods

Study design

The CARRAD-I was conducted from January 2008 to December 2008 in 17 cities with 24 participating hospitals, while the CARRAD-II was conducted from January 2018 to December 2018 in 26 cities with 36 participating hospitals from northern, eastern, central, and southern coastal regions. Finally, a total of 2322 and 2353 patients of attending outpatient clinics of pulmonology, ENT department and paediatrics form the above respective hospitals were enrolled in 2008 and 2018, respectively. The inclusion criteria were as follows: aged 5-65 years, patients who were diagnosed with allergic rhinitis and/or asthma based on their brief history, physical examination, lung function test and IgE level. While pregnant and lactating women, allergy immunotherapy using mite crude extracts in the past, taking terafidine, loratadine, fexofenadine, ebastine, cetirizine and leukotriene receptor antagonists within one week (asmizole within 3 months), and systemic corticosteroids (oral, intravenous, etc.) within four weeks, admitting to the emergency room or hospitalized for asthma exacerbation within 1 month, lack of cooperation or understanding and inability to complete the questionnaire, were excluded from the study. Uniform protocol, questionnaire, allergen testing set, and operating procedures were used among the centers. All questionnaire interviewers were trained before the study. Results of questionnaire were sent every month to Guangzhou, where the data were entered and analyzed. Quality control reports were then prepared for each center. Each completed questionnaire and blood test was verified by the center supervisor, and the results were double-checked by the principal investigator and fed back to each center. All data were coded and input into a programmed database by two persons independently and were checked for out-of-range values and logic mistakes. The protocol was approved by the First Affiliated Hospital of Guangzhou Medical University Ethics Board, and all patients provided written informed consent.

Questionnaire

The questionnaire used in the survey was adopted from the version of the standardized questionnaire[9] from the International Study of Asthma and sensitizations in Childhood phase II (ISAAC).[10] This version was the same as the one used in our study of CARRAD-I. Some modifications were made based on the real situation in China (**Appendix S1**). The questionnaire was administered by the physicians or research nurses face to face, and contained questions on baseline demographic characteristics; family history of atopy; nasal symptoms such as rhinorrhea, itching, sneezing, and blockage, and lung symptoms such as wheezing, coughing, and chest tightness; skin and eye symptoms such as eczema and burning or itchy eyes; smoking habits; environment exposure factors; pet ownership; and dietary habits. Questions about the impact of allergic symptoms on daily activities, work or school, nighttime sleep, and the use of medications for controlling the symptoms were also asked.

According to the guideline Allergic Rhinitis and its Impact on Asthma (ARIA), ever asthma was defined by a positive answer to either "Have you ever had attacks of breathlessness at rest with wheezing?" or "Have you ever had asthma attacks?" or being recruited as an asthma case. Asthma was defined as a history of recurrent dyspnea, wheezing, or cough episodes; positive airway reversibility testing (forced expiratory volume in the first second (FEV_1)) increasing ≥ 12% and 200 mL after inhalation of 400 mg salbutamol); or positive airway responsiveness testing (FEV_1 decreasing ≥ 20% when ≤ 7.8 μg cumulative dose of histamine is administered).[11] Allergic rhinitis ever was defined by a positive answer to "Have you ever had rhinitis?" or "Have you ever had hay fever?" or being recruited as a rhinitis case. Rhinitis was defined as having symptoms of sneezing, or a running, itchy, or blocked nose in the absence of a cold or flu.[12] Urticaria was defined as a condition characterized by the development of wheals (hives) and angioedema.[13] Inflammation of the conjunctiva was characterized by pruritus and watery, red eyes with positive results in skin tests with suspect allergens or serum specific IgE to whole allergens or their purified molecular components.[14]

Serum IgE measurement

All participants were also asked to sign a consent form to provide blood for measurement of serum IgE levels. A peripheral blood sample of 10 mL was taken from each subject; coagulated at room temperature, centrifuged, and stored at 4°C; and sent to the central laboratory at Guangzhou every month. The specific IgE (sIgE) levels against *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, cat dander, dog dander, timothy grass, *Populus nigra*, *Ambrosia artemisiifolia*, *Artemisia vulgaris*, and *Alternaria alternata* were measured on the ADVIA Centaur immunoassay system (Siemens AG, Erlangen, Germany). The analysis of sIgE was performed only in the patients in whom the SPT was done. The results were categorized into the following groups: grade 0 (< 0.35 IU/mL), grade 1 (0.35–0.70 IU/mL), grade 2 (0.70–3.50 IU/mL), grade 3 (3.5–17.5 IU/mL), grade 4 (17.5–50 IU/mL), grade 5 (50–100 IU/mL), and grade 6 (> 100 IU/mL). The sIgE cutoff value was set at 0.35 IU/mL, and the response was defined as positive if sIgE level was ≥ 0.35 IU/L.

Statistical analysis

The baseline characteristics and the differences in the allergen sensitization grades of the trend between two cohorts were compared by chi-square tests. The two-sample *t* test was used to analyze variables that were normally distributed, such as age. The Mann–Whitney U test was used to analyze variables that were not normally distributed, such as building age. Prevalence rates of aeroallergen sIgE positivity of the patients with asthma alone, rhinitis alone, and both rhinitis and asthma were compared by chi-square tests. Logistic regression analyses were performed to test for any association between explanatory variables and clinical outcomes (sIgE positivity and physical symptoms). Baseline variables that were considered clinically relevant or that showed a univariate relationship with outcomes (overall *P* value for the explanatory variable < 0.05) were introduced into a stepwise multivariate logistic regression model. All variables for inclusion were carefully chosen, given the number of events available, to ensure parsimony of the final model. The results are presented with adjusted ORs with 95% confidence intervals (95% CI). When 0 < OR < 1, an OR closer to 0 indicates stronger relationship than an OR closer to 1. When OR > 1, an OR higher than 1 indicates stronger relationship than OR closer to 1. A smaller OR indicates a marker of higher protection and a higher OR indicates a marker of higher risk. All data were analyzed using the Statistical Package for the Social Sciences for Windows Release 21.0 (SPSS, Inc., Chicago, IL). A two-tailed *P* value lower than 0.05 was considered statistically significant.

Results

Demographic characteristics

There were significant differences between the 2008 and 2018 cohorts in terms of atopic symptoms of seasonal (24.4% vs. 29.6%) and perennial (38.5% vs. 44.5%) character, including nose involvement (80% vs. 86.1%), lung involvement (50.1% vs. 57.1%), eye involvement (39.0% vs. 43.1%), and skin involvement (20.4% vs. 30.9%), never smoking (93.6% vs. 91.7%), secondhand smoking (49.8% vs. 56.7%), family history of food allergy (6.7% vs. 3.4%), atopic dermatitis (14.1% vs. 10.8%), allergic conjunctivitis (5.8% vs. 8.1%), raising dog (11.2% vs. 14.1%), pets in bedroom (11.5% vs. 9.1%), using air conditioner (70.9% vs. 87.6%), and sleeping on a mattress (83.5% vs. 90.8%). More subjects lived on the ninth floor or higher (31.6% vs. 20.3%) and below the third floor (15.0% vs. 7.3%) in 2018 than in 2008. Building age was also greater in 2018 than in 2008 (9.2 years vs. 5.9 years). Besides, eating habits showed that more subjects in 2008 favored fruits (52.0% vs. 40.6%), cooked vegetable (83.9% vs. 71.8%), and fruit juice (6.1% vs. 4.5%) than in 2018, while more subjects in 2018 favored meat (76.9% vs. 63.9%), fish (12.8% vs. 10.6%), raw vegetable (27.2% vs. 20.2%), and fizzy drink (9.2% vs. 4.0%) than in 2008 (**Table 1**).

Prevalence of sIgE sensitizations by diseases

In the patients with rhinitis alone, the 2018 findings showed higher sensitization rates to *Dermatophagoides pteronyssinus* (53.4%), dog (5.9%), timothy grass (4.0%), *Ambrosia artemisiifolia* (7.0%), and *Artemisia vulgaris* (14.3%) than in 2008. In the patients with asthma alone, there was no significant difference in the overall rate for three types of mite, but there were higher sensitization rates to dog (4.0%), timothy grass (3.0%), *Ambrosia artemisiifolia* (2.0%), and *Artemisia vulgaris* (7.9%) than in 2008. In the patients with both asthma and rhinitis, the sensitization rate to *Dermatophagoides pteronyssinus* was 56.9%; the sensitization rate to cat was higher in 2008 than in 2018 (10.7% vs. 7.3%), while the sensitization rate to *Ambrosia artemisiifolia* was higher in 2018 than in 2008 (5.9% vs. 1.9%). In 2018, the prevalence of sensitization significantly increased in rhinitis group and asthma with rhinitis group when compared to the first survey of 2008 (67.7% vs. 63% $P = 0.039$; 75.1% vs. 70.6%, $P = 0.014$). (**Table 2**).

Table 1. Demographic characteristics of the 2008 and 2018 cohorts.

	2008	2018	*P* value
Subjects	2322	2353	
Age (years)			
5–14	1110 (47.8)	1024 (43.5)	0.150
15–24	255 (11.0)	277 (11.8)	
25–34	325 (14.0)	344 (14.6)	
35–44	327 (14.1)	360 (15.3)	
45–54	202 (8.7)	226 (9.6)	
55–65	103 (4.4)	122 (5.2)	
Mean (SD)	22.8 (16.8)	23.4 (15.8)	0.132
Region			
North	813 (35.0)	842 (35.8)	0.241
East	436 (18.8)	421 (17.9)	
Central	511 (22.0)	584 (24.8)	
Southern coast	562 (24.2)	558 (23.7)	
Gender			
Male	1272 (54.8)	1273 (54.1)	0.641
Female	1050 (45.2)	1080 (45.9)	
Diagnosis			
Asthma	617 (26.6)	595 (25.3)	
Rhinitis	810 (34.9)	871 (37.0)	0.295
Asthma with rhinitis	895 (38.5)	887 (37.7)	
Physical symptoms			
Seasonal	567 (24.4)	696 (29.6)	< 0.001
Perennial	894 (38.5)	1047 (44.5)	< 0.001
Nasal symptoms	1857 (80.0)	2026 (86.1)	< 0.001
Lung symptoms	1163 (50.1)	1344 (57.1)	< 0.001
Eye symptoms	905 (39.0)	1014 (43.1)	0.004
Skin symptoms	474 (20.4)	727 (30.9)	< 0.001
Smoking history			
Never smoked	2173 (93.6)	2158 (91.7)	0.014
Present smoker	165 (7.1)	148 (6.3)	0.264
Secondhand smoker	1156 (49.8)	1334 (56.7)	< 0.001
Family history of allergic diseases			
Allergic rhinitis	703 (30.3)	671 (28.5)	0.187
Asthma	504 (21.7)	525 (22.3)	0.617
Food allergy	155 (6.7)	80 (3.4)	< 0.001
Atopic dermatitis	327 (14.1)	254 (10.8)	0.001
Allergic conjunctivitis	135 (5.8)	191 (8.1)	0.002
Paternal	1038 (44.7)	1071 (45.5)	0.576
Maternal	1114 (48.0)	1155 (49.1)	0.448
Parental	483 (20.8)	513 (21.8)	0.403
Resident conditions			
Raising cat	149 (6.4)	183 (7.8)	0.070
Raising dog	260 (11.2)	332 (14.1)	0.003
Raising other pets	111 (4.8)	122 (5.2)	0.525
Pets in bedroom	167 (11.5)	214 (9.1)	0.017
Pets in house	374 (16.1)	435 (18.5)	0.031
Sleep on a mattress	1939 (83.5)	2137 (90.8)	< 0.001
Using air conditioner	1646 (70.9)	2061 (87.6)	< 0.001
Resident level in the building			
the ninth floor or above	471 (20.3)	744 (31.6)	< 0.001
from the third to the ninth floor	1681 (72.4)	1257 (53.4)	< 0.001
below the third floor	169 (7.3)	353 (15.0)	< 0.001
Building age (years)*			
< 10	1244 (53.6)	1009 (42.9)	< 0.001
≥ 10 and < 30	845 (36.4)	1565 (66.5)	< 0.001
≥ 30	232 (10.0)	122 (5.2)	< 0.001
Mean (SD)	137 (5.9)	216 (9.2)	< 0.001
Eating habits (≥ three times/week)			
Meat	1484 (63.9)	1809 (76.9)	< 0.001
Fish	246 (10.6)	301 (12.8)	0.019
Fruits	1207 (52.0)	955 (40.6)	< 0.001
Raw vegetable	469 (20.2)	640 (27.2)	< 0.001
Cooked vegetable	1948 (83.9)	1689 (71.8)	< 0.001
Fruit juice	142 (6.1)	106 (4.5)	0.014
Fizzy drink	93 (4.0)	216 (9.2)	< 0.001

*It refers to the age of dwellings in which the people live.

Table 2. Prevalence of IgE sensitization for patients with asthma and/or rhinitis in the 2008 and 2018 cohorts.

Subjects	Rhinitis			Asthma			Asthma with rhinitis		
	2008	2018	*P* value	2008	2018	*P* value	2008	2018	*P* value
	n = 810	n = 871		n = 617	n = 595		n = 895	n = 887	
Dermatophagoides pteronyssinus[a]	308 (38.0)	465 (53.4)	< 0.001	305 (49.4)	300 (50.4)	0.731	479 (53.5)	505 (56.9)	0.147
Grade 0[b]	502 (62.0)	406 (46.6)	< 0.001	312 (50.6)	295 (49.6)	0.165	416 (46.5)	382 (43.1)	0.003
Grade 1	20 (2.5)	33 (3.8)		4 (0.6)	25 (4.2)		26 (2.9)	9 (1.0)	
Grade 2	45 (5.6)	58 (6.7)		31 (5.1)	37 (6.2)		62 (6.9)	40 (4.5)	
Grade 3	56 (6.9)	84 (9.6)		33 (5.3)	67 (11.2)		71 (7.9)	52 (5.9)	
Grades 4–6	187 (23.1)	290 (33.3)		235 (38.1)	170 (28.5)		319 (35.6)	403 (45.4)	
Dermatophagoides farinae	302 (37.3)	449 (51.6)	< 0.001	295 (47.8)	294 (49.4)	0.577	470 (52.5)	491 (55.4)	0.229
Grade 0	508 (62.7)	422 (48.4)	< 0.001	322 (52.2)	301 (50.6)	0.361	425 (47.5)	396 (44.6)	0.008
Grade 1	8 (1.0)	23 (2.6)		4 (0.6)	20 (3.3)		17 (1.9)	12 (1.4)	
Grade 2	49 (6.0)	57 (6.6)		26 (4.2)	40 (6.7)		80 (8.9)	32 (3.6)	
Grade 3	83 (10.2)	91 (10.4)		55 (8.9)	65 (10.9)		89 (9.9)	88 (9.9)	
Grades 4–6	163 (20.1)	279 (32.0)		210 (34.1)	167 (28.1)		283 (31.6)	356 (40.1)	
Blomia tropicalis	181 (22.3)	261 (30.0)	< 0.001	160 (25.9)	183 (30.7)	0.062	258 (28.8)	259 (29.2)	0.862
Grade 0	629 (77.7)	610 (70.0)	< 0.001	457 (74.1)	394 (69.3)	0.050	637 (71.2)	628 (70.8)	0.630
Grade 1	36 (4.4)	67 (7.7)		10 (1.6)	23 (3.9)		39 (4.4)	59 (6.7)	
Grade 2	76 (9.4)	98 (11.2)		76 (12.3)	73 (12.2)		107 (12.0)	103 (11.6)	
Grade 3	42 (5.2)	67 (7.7)		56 (9.0)	53 (8.9)		78 (8.7)	59 (6.7)	
Grades 4–6	27 (3.3)	36 (4.1)		19 (3.0)	34 (5.7)		30 (3.4)	34 (3.8)	
Cat dander	44 (5.4)	56 (6.4)	0.397	38 (6.2)	41 (6.9)	0.606	96 (10.7)	65 (7.3)	0.012
Grade 0	766 (94.6)	815 (93.6)	0.168	579 (93.8)	554 (93.1)	0.497	799 (89.3)	822 (92.7)	0.053
Grade 1	11 (1.4)	12 (1.4)		7 (1.1)	5 (0.9)		16 (1.8)	11 (1.2)	
Grade 2	21 (2.6)	25 (2.9)		19 (3.0)	17 (2.9)		44 (4.9)	25 (2.8)	
Grade 3	8 (1.0)	10 (1.1)		10 (1.6)	5 (0.9)		24 (2.7)	19 (2.1)	
Grades 4–6	3 (0.4)	9 (1.0)		3 (0.5)	11 (1.8)		12 (1.3)	11 (1.2)	
Dog dander	28 (3.4)	51 (5.9)	0.017	12 (2.0)	24 (4.0)	0.032	47 (5.3)	58 (6.5)	0.248
Grade 0	782 (96.6)	820 (94.1)	0.782	605 (98.0)	571 (96)	0.906	848 (94.7)	839 (93.5)	0.547
Grade 1	5 (0.6)	26 (3.0)		1 (0.1)	12 (2.0)		5 (0.6)	12 (1.4)	
Grade 2	7 (0.9)	16 (1.8)		2 (0.4)	12 (2.0)		10 (1.1)	9 (1.0)	
Grade 3	5 (0.6)	6 (0.7)		2 (0.4)	0 (0)		10 (1.1)	12 (1.4)	
Grades 4–6	11 (1.3)	3 (0.4)		7 (1.1)	0 (0)		22 (2.5)	24 (2.7)	
Timothy grass	10 (1.2)	35 (4.0)	< 0.001	6 (1.0)	18 (3.0)	0.010	28 (3.1)	34 (3.8)	0.417
Grade 0	800 (98.8)	836 (96.0)	0.001	611 (99.0)	577 (97.0)	0.048	867 (96.9)	853 (96.2)	0.717
Grade 1	2 (0.2)	7 (0.8)		2 (0.3)	6 (1.0)		4 (0.5)	6 (0.7)	
Grade 2	2 (0.2)	11 (1.3)		2 (0.3)	6 (1.0)		13 (1.4)	19 (2.1)	
Grade 3	3 (0.4)	10 (1.1)		1 (0.1)	0 (0)		6 (0.7)	6 (0.7)	
Grades 4–6	3 (0.4)	9 (1.0)		2 (0.3)	6 (1.0)		4 (0.5)	2 (0.2)	

Table 2. (Continued)

Subjects	Rhinitis			Asthma			Asthma with rhinitis		
	2008	2018	*P* value	2008	2018	*P* value	2008	2018	*P* value
	n = 810	n = 871		n = 617	n = 595		n = 895	n = 887	
Populus deltoides	21 (2.6)	36 (4.1)	0.078	14 (2.2)	18 (3.0)	0.412	36 (4.0)	40 (4.5)	0.611
Grade 0	789 (97.4)	835 (95.9)	0.276	603 (97.8)	577 (97.0)	0.295	859 (96.0)	847 (95.5)	0.949
Grade 1	3 (0.4)	5 (0.6)		2 (0.4)	12 (2.0)		4 (0.5)	11 (1.2)	
Grade 2	5 (0.6)	17 (1.9)		4 (0.6)	6 (1.0)		13 (1.4)	14 (1.6)	
Grade 3	4 (0.5)	6 (0.7)		4 (0.6)	0 (0)		8 (0.9)	11 (1.2)	
Grade 4–6	9 (1.1)	8 (0.9)		4 (0.6)	0 (0)		9 (1.0)	4 (0.5)	
Ambrosia artemisiifolia	33 (4.1)	61 (7.0)	0.008	2 (0.4)	12 (2.0)	0.006	17 (1.9)	52 (5.9)	< 0.001
Grade 0	777 (95.9)	810 (93.0)	0.028	615 (99.6)	583 (98.0)	< 0.001	878 (98.1)	835 (94.1)	< 0.001
Grade 1	0 (0)	4 (0.5)		2 (0.3)	0 (0)		1 (0.1)	16 (1.8)	
Grade 2	7 (0.9)	10 (1.2)		1 (0.1)	18 (2.0)		5 (0.6)	20 (2.2)	
Grade 3	6 (0.8)	12 (1.4)		0 (0)	0 (0)		5 (0.6)	11 (1.2)	
Grades 4–6	19 (2.4)	35 (4.0)		0 (0)	0 (0)		5 (0.6)	8 (0.9)	
Artemisia vulgaris	65 (8.0)	125 (14.3)	< 0.001	20 (3.2)	47 (7.9)	< 0.001	103 (11.5)	118 (13.3)	0.250
Grade 0	745 (92.0)	746 (85.7)	< 0.001	597 (96.8)	548 (92.1)	0.010	792 (88.5)	769 (86.7)	0.358
Grade 1	2 (0.2)	13 (1.5)		5 (0.8)	17 (2.9)		14 (1.6)	14 (1.6)	
Grade 2	17 (2.1)	24 (2.7)		6 (0.9)	11 (1.9)		17 (1.9)	30 (3.4)	
Grade 3	28 (3.4)	31 (3.6)		4 (0.7)	5 (0.9)		27 (3.0)	27 (3.1)	
Grade 4–6	24 (2.3)	57 (6.5)		5 (0.8)	11 (1.8)		45 (5.0)	48 (5.4)	
Alternaria alternata	38 (4.7)	52 (6.0)	0.233	39 (6.4)	41 (6.9)	0.690	65 (7.2)	75 (8.5)	0.349
Grade 0	772 (95.3)	819 (94.0)	0.307	578 (93.6)	554 (93.1)	0.632	831 (92.8)	812 (91.5)	0.615
Grade 1	5 (0.6)	4 (0.5)		6 (0.9)	6 (1.0)		13 (0.6)	5 (0.5)	
Grade 2	7 (0.9)	12 (1.4)		9 (1.4)	0 (0)		13 (1.0)	11 (0.8)	
Grade 3	9 (1.1)	21 (2.4)		15 (2.4)	29 (4.9)		32 (3.0)	30 (3.4)	
Grade 4–6	17 (2.1)	15 (1.7)		10 (1.7)	6 (1.0)		28 (2.6)	29 (3.3)	
≥1 positive specific IgE	510 (63.0)	590 (67.7)	0.039	381 (61.8)	354 (60.5)	0.483	632 (70.6)	672 (75.1)	0.014

[a]Test for difference
[b]Test for trend

Potential risk factors of sIgE positivity by diseases

In our multivariate logistic regression model, we found six common risk factors for sensitization in the two surveys, namely male gender, sleeping on a mattress, using air conditioner, family history of allergic rhinitis, resident building age (age of the building in which the subjects live) > 30 years, and meat consumption. In 2018, secondhand smoking was another risk factor for allergic asthma with or without rhinitis (OR 2.17, 95%CI 1.18–7.01, and OR 1.72, 95%CI 1.03–3.14, both $P < 0.05$), and eating fish emerged as a new protective factor against allergic rhinitis (OR 0.68, 95%CI 0.52–0.91, $P < 0.01$). The strongest inverse association with sIgE positivity was found in older age in both cohorts. Interestingly, we found that the ORs in age groups 25–34 and 35–44 years were both lower in 2008 than in 2018 (in rhinitis: age 25–34 years [OR 0.23, 95%CI 0.14–0.37, and OR 0.63, 95%CI 0.48–0.82, both $P < 0.05$] and age 35–44 years [OR 0.26, 95%CI 0.16–0.42, and OR 0.58, 95% CI 0.43–0.79, both $P < 0.05$]; in asthma with rhinitis: age 25–34 years [OR 0.20, 95%CI 0.12–0.33, and OR 0.56, 95%CI 0.36–0.87, both $P < 0.05$] and age 35–44 years [OR 0.17, 95%CI 0.10–0.28, and OR 0.56, 95%CI 0.34–0.91, both $P < 0.05$]) (**Table 3**).

Table 3. Univariate and multivariate logistic regression analysis with selected variables for specific IgE sensitizations in patients with rhinitis, asthma, and asthma with rhinitis.

Explanatory Variable	Specific IgE Positivity Odds Ratio (95% CI)[a]											
	Rhinitis				Asthma				Asthma with rhinitis			
	2008 (n = 810)		2018 (n = 871)		2008 (n = 617)		2018 (n = 595)		2008 (n = 895)		2018 (n = 887)	
	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
Age (yr)												
5-14	1	1	1	1	1	1	1	1	1	1	1	1
15-24	0.27 (0.13–0.52)[§]	0.53 (0.30–0.93)[§]	0.80 (0.63–1.02)	NS	0.12 (0.07–0.44)	NS	0.79 (0.14–4.50)	NS	0.16 (0.08–0.32)[§]	0.37 (0.20–0.68)[ψ]	0.76 (0.46–1.25)	0.64 (0.40–0.98)[ψ]
25-34	0.16 (0.08–0.27)[§]	0.23 (0.14–0.37)[ψ]	0.61 (0.50–0.74)[ψ]	0.63 (0.48–0.82)[ψ]	0.09 (0.04–0.22)[§]	0.33 (0.15–0.71)[ψ]	0.17 (0.04–0.69)[§]	0.43 (0.14–0.91)[§]	0.08 (0.04–0.14)[§]	0.20 (0.12–0.33)[ψ]	0.49 (0.33–0.75)[ψ]	0.56 (0.36–0.87)[§]
35-44	0.17 (0.09–0.30)[§]	0.26 (0.16–0.42)[ψ]	0.62 (0.50–0.76)[ψ]	0.58 (0.43–0.79)[ψ]	0.06 (0.03–0.13)[§]	0.21 (0.12–0.39)[ψ]	0.39 (0.15–0.87)[§]	0.37 (0.13–0.86)[§]	0.07 (0.04–0.13)[§]	0.17 (0.10–0.28)[ψ]	0.51 (0.32–0.81)[ψ]	0.56 (0.34–0.91)[§]
45-54	0.10 (0.05–0.19)[§]	0.21 (0.12–0.38)[ψ]	0.42 (0.32–0.56)[ψ]	0.43 (0.29–0.64)[ψ]	0.06 (0.03–0.12)[§]	0.21 (0.11–0.42)[ψ]	0.45 (0.16–0.94)[§]	0.19 (0.07–0.72)[§]	0.06 (0.03–0.11)[§]	0.17 (0.10–0.29)[ψ]	0.37 (0.21–0.64)[ψ]	0.41 (0.22–0.74)[ψ]
55-65	0.12 (0.05–0.33)[§]	0.11 (0.04–0.26)[ψ]	0.51 (0.35–0.75)[ψ]	0.38 (0.22–0.56)[ψ]	0.06 (0.02–0.16)[§]	0.22 (0.09–0.54)[ψ]	0.21 (0.08–0.76)[§]	0.16 (0.05–0.68)[§]	0.07 (0.03–0.15)[§]	0.14 (0.07–0.29)[ψ]	0.32 (0.16–0.65)[ψ]	0.32 (0.15–0.65)[ψ]
Gender												
Female	1	1	1	1	1	1	1	1	1	1	1	1
Male	1.24 (1.06–1.78)[ψ]	1.35 (1.10–1.67)[ψ]	1.54 (1.26–1.87)[ψ]	1.48 (1.05–2.07)[§]	1.96 (1.56–2.63)[ψ]	1.61 (1.16–2.38)[§]	1.50 (1.07–3.01)[§]	1.60 (1.10–3.71)[§]	1.69 (1.60–2.13)[§]	1.34 (1.03–1.90)[§]	1.98 (1.45–2.66)[ψ]	1.79 (1.29–2.49)[ψ]
Smoking history												
Never smoked	1	NA	1	NA	1	NA	1	1	1	NA	1	NA
Present smoker	0.72 (0.38–1.36)	NA	0.64 (0.43–0.96)[§]	NA	1.19 (0.40–3.51)	NA	1.31 (0.43–4.01)	NS	0.71 (0.31–1.60)	NA	0.69 (0.35–1.39)	NA
Second-hand smoker	0.99 (0.68–1.42)	NA	1.01 (0.82–1.25)	NA	1.07 (0.61–1.68)	NA	3.12 (1.27–8.84)[ψ]	2.17 (1.18–7.01)[ψ]	1.38 (0.96–1.99)	NA	1.53 (0.87–2.59)	1.72 (1.03–3.14)[§]

Table 3. (Continued)

Specific IgE Positivity Odds Ratio (95% CI)[a]												
Explanatory Variable	Rhinitis				Asthma				Asthma with rhinitis			
	2008 (n = 810)		2018 (n = 871)		2008 (n = 617)		2018 (n = 595)		2008 (n = 895)		2018 (n = 887)	
	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
Family history of												
Allergic rhinitis	1.92 (1.07–3.83)[§]	1.88 (1.05–3.65)[§]	2.18 (1.22–5.10)[§]	2.10 (1.17–4.96)[§]	1.80 (1.23–2.61)[§]	1.77 (1.15–2.53)[§]	1.89 (1.16–2.81)[§]	1.76 (1.12–2.64)[§]	1.85 (1.29–2.66)[§]	1.76 (1.22–2.54)[§]	2.06 (1.76–2.48)[ψ]	1.51 (1.09–2.25)[§]
Asthma	1.20 (0.72–2.10)	NA	0.95 (0.77–1.18)	NA	1.34 (0.80–2.23)	NA	1.22 (0.33–4.54)	NA	1.32 (0.90–1.93)	NA	1.21 (0.71–2.07)	NA
Food allergy	1.13 (0.54–2.33)	NA	1.24 (1.14–1.42)	NA	0.80 (0.35–1.85)	NA	1.02 (0.41–2.50)	NA	1.48 (0.77–2.85)	NA	1.12 (0.76–1.65)	NA
Allergic conjunctivitis	1.38 (1.20–1.81)	NA	1.02 (1.01–1.07)	NA	1.32 (1.11–1.93)	NA	0.89 (0.31–2.53)	NA	2.04 (1.12–3.72)[§]	NS	1.17 (0.51–2.69)	NA
Allergic dermatitis	1.04 (0.63–1.73)	NA	1.25 (1.18–1.34)	NA	1.46 (0.92–2.32)	NA	1.37 (0.51–3.66)	NA	1.81 (0.49–3.77)	NS	1.63 (0.40–3.99)	NS
Housing condition												
Raising cat	0.77 (0.36–1.66)	NA	1.12 (0.64–1.93)	NA	0.74 (0.39–1.43)	NA	0.52 (0.20–1.35)	NA	1.01 (0.53–1.95)	NA	0.58 (0.26–1.29)	NA
Raising dog	0.76 (0.45–1.26)	NA	1.29 (0.89–1.87)	NA	0.40 (0.23–0.72)[§]	NS	1.56 (0.45–5.38)	NA	0.66 (0.42–1.06)	NA	0.91 (0.52–1.60)	NA
Pets in bedroom	0.87 (0.50–1.51)	NA	1.14 (0.88–1.48)	NA	0.74 (0.40–1.37)	NA	2.32 (1.10–8.02)[ψ]	NS	1.55 (1.35–1.88)[§]	NS	1.60 (1.03–2.27)[§]	NS
Pets in house	1.23 (0.82–1.84)	NA	1.03 (0.82–1.31)	NA	1.12 (0.74–1.70)	NA	0.95 (0.37–2.43)	NA	0.88 (0.61–1.29)	NA	1.27 (0.88–1.84)	NA
Sleep with mattress	1.96 (1.17–4.03)[ψ]	1.53 (1.06–2.38)[§]	1.91 (1.59–2.42)[ψ]	1.54 (1.02–2.51)[§]	1.53 (1.05–1.89)[§]	1.50 (1.04–1.82)[§]	1.84 (1.52–2.35)[ψ]	1.67 (1.08–2.73)[ψ]	1.90 (1.06–3.05)[ψ]	1.59 (1.03–1.82)[ψ]	2.62 (2.45–3.87)[ψ]	1.61 (1.05–1.84)[ψ]
Using air conditioner	1.54 (1.03–2.55)[ψ]	1.57 (1.11–2.23)[§]	1.69 (1.43–2.10)[ψ]	1.94 (1.58–2.53)[ψ]	1.85 (1.28–2.64)[§]	1.74 (1.11–2.73)[§]	1.39 (1.06–4.18)[§]	2.10 (1.60–3.01)[ψ]	1.57 (1.08–2.30)[ψ]	1.90 (1.29–2.78)[ψ]	2.88 (1.12–9.03)[ψ]	3.47 (1.19–11.07)[ψ]

Table 3. (Continued)

Explanatory Variable	Specific IgE Positivity Odds Ratio (95% CI)[a]											
	Rhinitis				Asthma				Asthma with rhinitis			
	2008 (n = 810)		2018 (n = 871)		2008 (n = 617)		2018 (n = 595)		2008 (n = 895)		2018 (n = 887)	
	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
Resident level												
≥ 9 floor	1	NA	1	NA	1	NA	1	NA	1	1	1	NA
≥ 3 and < 9 floor	0.88 (0.54–1.42)	NA	1.01 (0.81–1.25)	NA	1.04 (0.53–2.03)	NA	0.63 (0.28–1.42)	NA	1.16 (0.70–1.91)	NS	0.93 (0.66–1.31)	NA
< 3 floor	0.99 (0.40–2.47)	NA	0.95 (0.69–1.33)	NA	1.16 (0.84–2.89)	NA	0.76 (0.29–2.03)	NA	1.95 (1.28–4.51)[§]	NS	0.73 (0.48–1.10)	NA
Resident building (yr)												
< 10	1	1	1	NA	1	NA	1	1	1	1		1
≥ 10 and < 30	0.74 (0.55–1.18)	NS	1.02 (0.80–1.30)	NA	1.18 (0.54–2.57)	NA	1.82 (0.77–4.31)	NS	1.18 (0.54–2.57)	NS	1.10 (0.77–1.59)	NS
≥ 30	1.86 (1.21–4.91)[ψ]	1.79 (1.19–4.86)[ψ]	1.85 (1.14–3.46)[ψ]	1.82 (1.12–3.28)[ψ]	1.83 (1.09–3.84)[ψ]	1.81 (1.05–3.70)[ψ]	1.97 (1.07–4.95)	1.92 (1.06–4.79)[ψ]	2.05 (1.19–4.84)[ψ]	1.98 (1.60–4.41)[ψ]	2.08 (1.59–5.25)[ψ]	2.03 (1.12–5.20)[ψ]
Eating habits (≥ three times/wk)												
Meat	1.07 (0.74–1.55)	NA	1.09 (0.47–1.73)[ψ]	1.72 (1.56–1.92)[ψ]	1.53 (1.01–2.35)[ψ]	NS	1.03 (0.40–2.67)	NA	1.33 (1.19–2.22)[ψ]	1.35 (1.18–2.28)[ψ]	1.55 (1.39–1.77)[ψ]	1.56 (1.38–1.81)[ψ]
Fish	1.08 (0.63–1.86)	NA	0.61 (0.46–0.79)[ψ]	0.68 (0.52–0.91)[ψ]	1.35 (1.03–2.99)[§]	NS	0.73 (0.34–1.56)	NA	0.82 (0.45–1.52)	NA	0.60 (0.37–0.98)[§]	NS
Fruits	0.94 (0.65–1.01)	NA	0.88 (0.71– 1.08)	NA	1.10 (0.84–1.34)	NA	0.71 (0.33–1.49)	NA	0.65 (0.35–0.74)[§]	NS	0.98 (0.71–1.34)	NA
Raw vegetable	0.72 (0.47–1.09)	NA	0.96 (0.79–1.17)	NA	0.77 (0.41–0.94)[ψ]	NS	1.38 (0.68–2.80)	NA	0.62 (0.33–0.86)[§]	NS	1.20 (0.89–1.62)	NA
Cooked vegetable	0.71 (0.40–1.26)	NA	0.97 (0.77–1.23)	NA	0.50 (0.20–1.23)	NA	1.22 (0.51–2.94)	NA	0.98 (0.52–1.83)	NA	1.16 (0.80–1.68)	NA
Fruit juice	2.10 (0.91–4.88)	NA	0.92 (0.66–1.28)	NA	0.81 (0.23–2.87)	NA	0.71 (0.13–3.79)	NA	1.67 (0.74–3.80)	NA	0.83 (0.46–1.49)	NA
Fizzy drink	1.47 (0.45–4.79)	NA	0.92 (0.62–1.34)	NA	1.84 (0.30–2.22)	NA	2.26 (1.70–6.65)[ψ]	NS	0.51 (0.20–1.29)	NA	0.80 (0.42–1.50)	NA

[a] Odds ratio adjusted for diagnosis, region, gender, and age group in a logistic regression model. NA = not available; ;NS = not significant
[ψ]$P < 0.01$; [§]$P < 0.05$

Table 4. Association between different allergen sensitizations and clinical symptoms.

	Nasal symptom OR (95%CI)[a]				Eye symptom OR (95%CI)[b]				Lung symptom OR (95%CI)[c]				Skin symptom OR (95%CI)[d]			
	Model 1		Model 2		Model 1		Model 2		Model 1		Model 2		Model 1		Model 2	
Study year	2008	2018	2008	2018	2008	2018	2008	2018	2008	2018	2008	2018	2008	2018	2008	2018
Any allergen	1.62 (1.50–1.78)[ψ]	1.68 (1.48–1.97)[$]	1.58 (1.46–1.87)[ψ]	1.63 (1.44–1.89)[$]	1.60 (1.50–1.73)[ψ]	1.69 (1.54–1.82)[ψ]	1.52 (1.43–1.63)[$]	1.59 (1.44–1.69)[ψ]	1.69 (1.57–1.83)[ψ]	2.05 (1.42–2.95)[ψ]	1.66 (1.54–1.79)[ψ]	1.74 (1.62–1.88)[ψ]	NS	NS	NS	NS
Any mite	1.76 (1.29–3.10)[ψ]	1.83 (1.42–3.09)[ψ]	1.78 (1.31–3.14)[ψ]	1.79 (1.39–2.98)[ψ]	1.82 (1.71–1.96)[ψ]	NS	NS	1.67 (1.55–1.76)[ψ]	1.82 (1.38–2.07)[ψ]	1.92 (1.73–2.16)[ψ]	1.75 (1.34–1.89)[ψ]	1.81 (1.54–2.02)[ψ]	NS	1.24 (1.08–3.13)[$]	NS	1.20 (1.05–2.97)[$]
Any pollen	1.69 (1.57–1.84)[ψ]	1.72 (1.07–2.69)[$]	1.61 (1.01–2.58)[$]	1.67 (1.56–1.82)[ψ]	1.61 (1.55–1.69)[ψ]	1.49 (1.38–1.63)[ψ]	NS	1.55 (1.43–1.71)[ψ]	NS	1.22 (1.12–1.34)[ψ]	NS	1.26 (1.15–1.38)[ψ]	NS	NS	NS	NS
Any animal	NS	NS	1.45 (1.12–1.97)[ψ]	1.42 (1.14–1.89)[ψ]	NS	NS	NS	NS	NS	NS	1.48 (1.23–1.87)[ψ]	1.50 (1.31–2.07)[ψ]	NS	NS	NS	NS
Any mould	NS	NS	NS	NS	NS	NS	NS	NS	NS	1.65 (1.13–2.98)[$]	NS	1.43 (1.08–2.77)[$]	NS	NS	NS	NS

Model 1: adjusted for gender, age and region.
Model 2: adjusted for smoking history, family history, resident level, resident building year.
[a]Nasal symptom was defined as any of congestion, rhinorrhea, sneezing, and nasal itching in the past 12 months.
[b]Eye symptom was defined as any of itching, redness, and swelling in the past 12 months.
[c]Lung symptom was defined as any of cough, wheezing, chest tightness in the past 12 months.
[d]Skin symptom was defined as any of itch-scratch and erythema in the past 12 months.
[ψ]$P < 0.01$; [$]$P < 0.05$; ;NS=not significant

Table 5. Association between allergen sensitizations and the environment where symptoms occured.

	Adjusted specific IgE positivity OR(95% CI)[a]							
	Mite		Pollen		Animal dander		Mould	
The place where physical symptoms occured	2008	2018	2008	2018	2008	2018	2008	2018
Living room	1.26 (1.09-2.02)[$]	1.38 (1.11-1.77)[ψ]	0.73 (0.48-0.91)[ψ]	0.71 (0.56-0.92)[ψ]	1.16 (1.02-1.94)[$]	1.31 (1.04-2.18)[ψ]	1.21 (0.93-2.03)	1.13 (0.70-1.83)
On the bed	2.17 (1.99-3.37)[ψ]	2. 29 (1.81-2.98)[ψ]	0.71 (0.55-0.91)[ψ]	0.84 (0.59-1.37)	1.33 (1.19-2.07)[ψ]	0.88 (0.58-1.06)	0.96 (0.71-1.59)	1.01 (0.71-1.43)
Supermarket	1.12 (0.81-1.54)	1.31 (1.06-1.61)[$]	1.07 (0.84-1.37)	0.93 (0.71-1.22)	0.99 (0.71-1.38)	0.83 (0.57-1.20)	1.10 (0.85-1.97)	0.88 (0.60-1.29)
Library	1.64 (1.18-1.89)[ψ]	1.50 (1.12-1.95)[ψ]	0.86 (0.60-1.17)	1.15 (0.91-1.45)	0.95 (0.78-1.17)	0.64 (0.46-0.89)[ψ]	1.02 (0.74-1.61)	0.95 (0.70-1.38)
Garden or park	0.72 (0.47-0.99)[ψ]	0.73 (0.62-0.85)[ψ]	2.21 (1.87-2.96)[ψ]	2.40 (1.89-3.05)[ψ]	1.07 (0.96-1.38)	1.14 (0.83-1.65)	1.05 (0.93-1.76)	1.31 (0.86-1.99)
Farmland or forest	0.76 (0.60-0.97)[ψ]	0.59 (0.29-0.88)[ψ]	1.33 (1.14-1.80)[ψ]	3.61 (2.79-4.66)[ψ]	0.84 (0.58-1.49)	0.66 (0.45-0.90)[ψ]	1.29 (0.96-2.11)	1.86 (1.34-2.58)[ψ]

[a]Odds ratio adjusted for diagnosis, region, gender, and age group in a logistic regression model.
[ψ]$P < 0.01$; [$]$P < 0.05$

Association between different allergen sensitizations and physical symptoms

After adjusting for confounders, both in model 1 and model 2, any allergen sensitization was associated with nasal, ocular, and lung symptoms. In 2018, mite allergen was associated with nasal, ocular, lung, and skin symptoms, while it was only related to three groups of symptoms in 2008. Similarly, pollen sensitization was associated with nasal, ocular, and lung symptoms in 2018, while in 2008 it was related to only two groups of symptoms. Animal dander was associated with nasal and pulmonary symptoms in both of the surveys. Furthermore, mold sensitization was associated with pulmonary symptoms in the 2018 cohort (**Table 4**).

Association between allergen sensitizations and the outdoor or indoor place

In both cohorts, mite sensitization symptoms usually occurred in indoor places. The OR was the highest in the bedroom (OR 2.17, CI 1.99–3.37 in 2008, and OR 2.29, CI 1.81–2.98 in 2018, both $P < 0.01$), while the garden and farmland rather protected from these symptoms. In contrast, lingering in the outdoor places such as garden, park, or farmland was a risk factor for pollen sensitization, but the OR of farmland or forest was higher in 2018 than in 2008 (OR 3.61, 95%CI 2.79–4.66 vs. OR 1.33, 95%CI 1.14–1.80, both $P < 0.01$). With respect to allergic symptoms to animals, living room was a common risk factor for both cohorts, whereas staying in library or farmland was less likely to sensitize to animals in the 2018 cohort. In addition, allergic symptoms to mold were likely to be seen in farmland or forest in the 2018 cohort (OR 1.86, 95% CI 1.34–2.58, $P < 0.01$) (**Table 5**).

Discussion

This is the first comparative study showing the changes of the rate and factors of sensitization of asthma and/or rhinitis over the last decade in China. Our findings revealed that the common factors were male gender, sleeping on a mattress, using air conditioner, family history of allergic rhinitis, building age > 30 years, and meat consumption. Secondhand smoke was an additional risk factor for allergic asthma in 2018. Older age remained a protective factor, but the OR in age group 25–44 years was higher in 2018 than in 2008. The ORs of farmland or forest for pollen and mold sensitization were also higher in 2018 than in 2008. More organs were involved in sensitization in 2018.

The study showed that the most prevalent allergen was *Dermatophagoides pteronyssinus*, which is in concordance with some studies in Asia,[15,16] while *Blomia* tropicalis still did not show a dominant position from 2008 to 2018. The explanation may be that warmer and more humid climate in China in the last decade facilitated house dust mite growth,[17] while urbanization made tropical mites lose their habitat (e.g., hay or agricultural land).[18] Another finding was that cat sensitization decreased in asthma and rhinitis. Our questionnaire showed that people tended to keep pets from the bedroom, which was a preventive behavior against cat allergies. *Artemisia vulgaris* was also an important risk allergen related to rhinitis in our survey, which is consistent with previous studies, especially in plateau grassland region of northwestern China and northern Beijing.[19,20] It might be related to expanded planting of *A. desertorum* to stop the sandstorm.[21]

Aging-related immune tolerance induced by long-term exposure to allergens could protect from allergen sensitization,[22,23] but we found that this protective effect drastically lower in the patients with rhinitis alone and those with asthma and rhinitis aged 25–44 years in 2018. On the one hand, there have been increasing installations of air conditioners in working places with the sedentary lifestyle, and this behavior is particularly popular in young adults. On the other hand, when people favor living in the yards all around trees, spores of phytopathogenic fungi are easily transferred into house through ventilation.[24] Our questionnaire revealed an increased use of sleeping mattresses in "modern" homes, which is an easier mite hiding place than the floor.[25]

Although pet-keeping rate had risen up, we did not find the association between raising pets and the risk of sensitization. Notably, raising pets in rural setting could protect against allergy.[26] Individuals with allergic disease likely removed the furred animals after diagnosis, and it took some time until IgE levels significantly decreased, but the responder might have chosen "yes" when asked the question about ever raising pets.

Secondhand smoke was an emerging risk factor for allergic asthma in the 2018 cohort. There has been convincing evidence suggesting a causal relationship between secondhand smoke exposure and allergic sensitization in children.[27,28] One of the mechanisms is that cigarette smoke can induce oxidative stress, which increases TSLP and IL-33 expression in the airway epithelium and shifts towards Th2 immunity.[29] Tobacco control policies would have a capacity to improve the well-being of children with allergic asthma in China.

We also detected the relationship between building type and sensitization. According to the previous literature, older dwellings have more dirt containing bioaerosols, where dampness, mold, and mites are more common.[30] A higher rate of living on the ninth floor or higher was observed in 2018. In recent years, buildings have become better constructed, and these are characterized by reduced outdoor fresh air and increased exposure to indoor chemicals, both of which are great risk for sensitization.[31,32] At present, Chinese diet habits have changed to westernized patterns, such as intake of excessive red meat, raw vegetables, and fizzy drinks. Glycosylation products from meat are the major allergen causing delayed anaphylaxis,[33] which could explain the higher odds of sensitization when eating meat. Fish could protect from allergy,[34] but this was not shown in 2008. The reason might be that eating different fish would have varying effects on allergy in the two cohorts, which could be related to the different fatty-acid components from fish.[35]

In 2018, more organs were involved in allergen sensitization, suggesting that the severity of allergic diseases was higher than before. In general, indoor allergens were linked more strongly to the development of asthma than outdoor allergens, which is concordant with a previous study.[36] We found that most allergens could elicit both nasal and lung symptoms, meaning that in patients diagnosed with allergic disease the involvement of the upper and lower airways should always be considered. Inhalation of the fungus *Alternaria alternata* is associated with an increased risk of allergic asthma exacerbations via protease-activated receptor-2 expression.[37] As could be seen in our results, the OR of farmland or forest for fungal sensitization increased in 2018. This might be explained as follows: *Alternaria alternata* spores disseminated primarily from outdoors sources with warm dry air, which induced lung symptoms.

Our dataset has certain limitations, so our results should be interpreted with these limitations in mind. The accuracy of questionnaire assignment was likely dependent on physician judgment and may not necessarily reflect the most accurate diagnosis. We did not have longitudinal information regarding date of initial diagnosis, making it impossible to confirm whether sensitization occurred before or after the onset of disease, or where sensitization could contribute to the pathogenesis of allergic disease. Finally, our study was an uncontrolled, retrospective, and cross-sectional study, and the conclusions are not necessarily representative of the general population in China. Our results should be confirmed by prospective, controlled studies to more rigorously address the factor discrepancy suggested by the current research.

In conclusion, our study suggests that since 2008, the changes in internal and external environmental factors have been associated with increased prevalence and odds of sensitization for asthma and/or rhinitis. The above evidence confirms the allergenic relevance of the environmental changes and facilitates decisions on preventive intervention of allergic disease in China.

Submission declaration

We confirm that the paper is an original work and that it has not been published, in whole or in any part, in any other journal.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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Author contributions

- Jing Li, Jianhong Wang, Yan Jiang, Xiaoli Han, Guolin Tan, Jianjun Chen, Qianhui Qiu, Huabin Li had the idea for and designed the study.
- Jing Li supervised the study and did the writing review.
- Wanjun Wang did the data curation and wrote the original draft.
- All authors contributed to acquisition, analysis or interpretation of data.
- All authors revised the report and approved the final version before submission
- All authors contributed equally to the work

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Supplementary Materials

Appendix S1. Screening Questionnaire.

Screening Questionnaire

We are seeking your collaboration for a "Multicenter Clinical Questionnaire on Allergens in the Chinese Population". This questionnaire is outlined as below. Please be assured that the data will be exclusively utilized for scientific analysis, and your personal information will be maintained with the utmost confidentiality. We sincerely appreciate your support and cooperation!

1. Name:*
_____

Clinic number:
_____

Contact phone number:
_____

2. Date of birth:*
_____

3. Gender: [Single-choice question]*
❍ Male ❍ Female

4. Ethnicity [Optional]*
❍ Han Chinese ❍ Uyghur ❍ Tibetan ❍ Hui
❍ Others _____

5. Place of residence [Optional]*
❍ Native ❍ Immigrant, Years of Residence _____

6. Are you a smoker [Multiple-choice question]*
❍ Currently still smoking ❍ Never smoked
❍ Quit smoking, how many years quit _____

7. How many cigarettes, if any, do you smoke per day? [Single-choice question]*
❍ Less than 10 ❍ 10 to 20 ❍ More than 20

8. At what age did you start smoking? [Fill in the blank]*
_____

9. How many people smoke in your household? [Fill in the blank]*
_____

10. Does anyone in your family suffer from allergic diseases? (If not, please skip to Question 17)*
❍ Yes ❍ No

11. Has your father ever suffered from any of the following? [Multiple-choice question]*
❍ Allergic rhinitis ❍ Bronchial asthma
❍ Eye allergies ❍ Food allergies
❍ Allergic dermatitis ❍ No
❍ Other, please specify _____

12. Has your mother ever suffered from any of the following? [Multiple-choice question]*
❍ Allergic rhinitis ❍ Bronchial asthma
❍ Eye allergies ❍ Food allergies
❍ Allergic dermatitis ❍ No
❍ Other, please specify _____

13. Do you have an older or younger brother? (If not, please skip to Question 15)*
❍ Yes ❍ No

14. If yes, has the elder or younger brother ever suffered from any of the following diseases? [Multiple-choice question]*
❍ Allergic rhinitis ❍ Bronchial asthma
❍ Eye allergies ❍ Food allergies
❍ Allergic dermatitis ❍ No
❍ Other, please specify _____

15. Do you have an older or younger sister? (If not, please skip to Question 17) [Single-choice question]*
❍ Yes ❍ No

16. If yes, has the elder or younger sister ever suffered from any of the following diseases? [Multiple-choice question]*
❍ Allergic rhinitis ❍ Bronchial asthma
❍ Eye allergies ❍ Food allergies
❍ Allergic dermatitis ❍ No
❍ Other, please specify _____

17. Have any of your other relatives ever suffered from any of the following diseases? [Multiple-choice question]*
❍ Allergic rhinitis ❍ Bronchial asthma
❍ Eye allergies ❍ Food allergies
❍ Allergic dermatitis ❍ No
❍ Other, please specify _____

18. Do you have or have you ever had nose allergies (including chilblain fever)? [Single-choice question]*
❍ Yes ❍ No

19. Over the past 12 months, have you ever had a sneeze, runny nose, or stuffy nose when you did not catch a cold or flu? [Multiple-choice question]*
❍ Yes ❍ No

20. Overall the past 12 months, have you had any contact with grass, trees or flowers? (If no, please skip to Question 22) [Single-choice question]*
❍ Yes ❍ No

21. If yes, have you experienced symptoms of itching, nasal congestion or sneezing? [Multiple-choice question]*
❍ Yes ❍ No

22. Over the past 12 months, have you had any contact with animals, such as horses, dogs, cats or voles with fur? (If no, please skip to Question 24) [Single-choice question]*
❍ Yes ❍ No

23. If yes, have you felt an itchy or stuffy nose or have you sneezed? [Single-choice question]*
❍ Yes ❍ No

24. In which months did you have the above nasal symptoms (sneezing, runny nose, itchy nose or stuffy nose)? [Multiple-choice question]*
❍ January ❍ February ❍ March
❍ April ❍ May ❍ June
❍ July ❍ August ❍ September
❍ October ❍ November ❍ December
❍ None

25. Do you have or have you ever had seasonal nasal allergies (chilblain fever)? [Single-choice question]*
❍ Yes ❍ No

26. Do you have or have you ever had allergic rhinitis? [Multiple-choice question]*
❍ Yes ❍ No

27. Over the past 12 months, how has the above nasal discomfort affected your daily life? [Multiple-choice question]*
❍ No impact ❍ Slight impact
❍ Moderate impact ❍ Serious impact

28. What are the episodes of nasal discomfort described above: [Single-choice question]*
❍ Seasonal ❍ Annual ❍ Irregular

29. Do you have or have you ever had eye allergies (itchy, watery or red eyes)? (If no, please skip to Question 31) [Single-choice question]*
❍ Yes ❍ No

30. If yes, do your eye symptoms coincide with symptoms of nasal discomfort? [Multiple-choice question]*
❍ Yes ❍ No

31. Over the past 12 months, did you have a gritty feeling, redness, watering or itching in your eyes when you did not have a cold? [Single-choice question]*
❍ Yes ❍ No

32. Over the past 12 months, have you had any contact with animals with fur (e.g., cats, dogs, horses, rats, etc.)? (If no, please skip to Question 34) [Single-choice question]*
❍ Yes ❍ No

33. If yes, do your eyes have a gritty feeling, redness, watering or itching? [Single-choice question]*
❍ Yes ❍ No

34. Over the past 12 months, have you had any contact with grass, trees or flowers? (If no, please skip to Question 36) [Single-choice question]*
❍ Yes ❍ No

35. If yes, do you have a gritty feeling, redness, tearing or itching in your eyes? [Single-choice question]*
❍ Yes ❍ No

36. In which month did the above symptoms occur in your eyes? [Multiple-choice question]*
❍ January ❍ February ❍ March
❍ April ❍ May ❍ June
❍ July ❍ August ❍ September
❍ October ❍ November ❍ December
❍ None

37. Over the past 12 months, have you had symptoms of wheezing or croup? [Multiple-choice question]*
❍ Yes ❍ No

38. Over the past 12 months, have you ever woken up at night from the tightness in your chest or the tightness of breath? [Single-choice question]*
❍ Yes ❍ No

39. Over the past 12 months, have you ever woken up at night with a cough? [Single-choice question]*
❍ Yes ❍ No

40. Have you had any asthma attacks over the past 12 months? [Multiple-choice question]*
❍ Yes ❍ No

41. Over the past 12 months, have you used nebulized inhalation medications to facilitate your breath? [Single-choice question]*
❍ Yes ❍ No

42. Are you currently experiencing any medications (including inhaled or oral medications) for the treatment of your asthma? [Multiple-choice question]*
❍ Yes ❍ No

43. Over the past 12 months, have you touched grass, trees or flowers? (If no, please skip to Question 45) [Single-choice question]*
❍ Yes ❍ No

44. If yes, have you experienced any symptoms of breathlessness or wheezing? [Multiple-choice question]*
❍ Yes ❍ No

45. Over the past 12 months, have you had any contact with animals such as horses, dogs, cats or voles? (If no, please skip to Question 47) [Single-choice question]*
❍ Yes ❍ No

46. If yes, do you experience any symptoms of breathlessness or wheezing? [Multiple-choice question]*
❍ Yes ❍ No

47. In the past 12 months, have you experienced symptoms of breathlessness or wheezing when you exercise or after exercising? [Multiple-choice question]*
❍ Yes ❍ No

48. Have you ever suffered from hives or other skin allergies? (If no, please skip to Question 50) [Single-choice question]*
❍ Yes ❍ No

49. Have you suffered from a recurring itchy rash over the past 6 months? [Single-choice question]*
❍ Yes ❍ No

50. Does anyone in your family or any of your relatives suffer from allergies? (If no, please skip to Question 53) [Single-choice question]*
❍ Yes ❍ No

51. What about the allergies run in your family [Multiple-choice question]*
❍ Parent ❍ Sibling ❍ Child

52. What is the type of allergy? [Fill in the blank]*
_____

53. How old was your mother when you were born? [Fill in the blank]*
_____

54. How many years of education do you have? [Fill in the blank]*
_____

55. How many brothers and sisters do you have? [Fill in the blank]*
_____

56. How many brothers and sisters do you have? [Fill in the blank]*
_____

57. How often do you eat meat on average? [Single-choice question]*
❍ No
❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

58. How often do you eat fish on average? [Multiple-choice question]*
❍ No ❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

59. How often do you eat fruit on average? [Single-choice question]*
❍ No ❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

60. How often do you eat raw green vegetables on average? [Single-choice question]*
❍ No ❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

61. How often do you eat cooked green vegetables on average? [Single-choice question]*
❍ No ❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

62. How often do you drink fruit juice on average? [Single-choice question]*
❍ No ❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

63. How often do you drink soda on average? [Multiple-choice question]*
❍ No ❍ Less than once a week
❍ Monthly to twice a week
❍ Wednesday to six times a week
❍ More than once a day

64. Do you consume processed cooking oils (e.g., peanut, canola or soybean oil) in your household [Single-choice question]*
❍ Yes ❍ No

65. When was the house you are living in built? [Fill in the blank]*
_____

66. What does the house you are living in look like? [Single-choice question]*
❍ Multi-story (less than nine stories)
❍ High-rise (more than nine stories)
❍ Bungalows
❍ One floor? (less than two households, two to four households, more than five households)
❍ Other _____

67. Where do you live? [Single-choice question]*
❍ Cities ❍ Rural areas
❍ Towns ❍ Suburbs

68. How many people live in your house? [Fill in the blank]*
_____

69. How many rooms are there in your house?
(Excluding kitchen, bathroom, toilet and laundry)
[Fill in the blank]*
_____

70. Do you have air conditioning in your home?
(If not, please skip to question 72) [Single-choice question]*
❍ Yes ❍ No

71. In which house is the air conditioner installed?
[Multiple-choice question]*
❍ Living room ❍ Your bedroom ❍ Both

72. What is the living room floor in your home?
[Multiple-choice question]*
❍ Tile or concrete ❍ Wooden flooring
❍ Laminate flooring ❍ Plastic flooring
❍ Carpeting

73. What is your bedroom floor? [Multiple-choice question]*
❍ Tile or concrete ❍ Wooden flooring
❍ Laminate flooring ❍ Plastic flooring
❍ Carpeting

74. What kind of pillow are you using?
[Multiple-choice question]*
❍ Cotton ❍ Sponge ❍ Synthetic material
❍ Feather ❍ Plant-based (herbal)

75. Are you using a mattress? [Single-choice question]*
❍ Yes ❍ No

76. What kind of quilt are you using?
[Multiple-choice question]*
❍ Quilt ❍ Synthetic material
❍ Feather ❍ Blanket
❍ Other _____

77. Which of the following devices are you using to heat your home? [Multiple-choice question]*
❍ Piped gas, bottled LPG ❍ Air conditioner
❍ Other _____

78. Which of the following devices are you using to boil hot water? [Multiple-choice question]*
❍ Electric water heater ❍ Gas water heater
❍ Electric kettle ❍ Gas kettle
❍ Kerosene kettle
❍ Other _____

79. Which of the following devices are you using for cooking?
[Multiple-choice question]*
❍ Electricity ❍ Gas or LPG
❍ Coal or firewood ❍ Kerosene
❍ Other _____

80. Do you own a cat? (If not, please skip to Question 82)
[Single-choice question]*
❍ Yes ❍ No

81. If yes, for how many years have you kept the cat?
[Fill in the blank]*
_____

82. Do you own a dog? (If not, please skip to Question 84)
[Single-choice question]*
❍ Yes ❍ No

83. If yes, for how many years have you kept the dog?
[Fill in the blank]*
_____

84. Do you own birds? (If not, please skip to Question 86)
[Single-choice question]*
❍ Yes ❍ No

85. If yes, for how many years have you kept the birds?
[Fill in the blank]*
_____

86. Do you have any other pets?
(If not, please skip to Question 88) [Single-choice question]*
❍ Yes ❍ No

87. If yes, for how many years have you kept the pets?
[Fill in the blank]*
_____

88. Do you allow pets in your house?
[Multiple-choice question]*
❍ Yes ❍ No

89. Do you allow pets in your bedroom?
[Multiple-choice question]*
❍ Yes ❍ No

90. Have you ever owned a pet before?
[Single-choice question]*
❍ Yes ❍ No

91. How old were you when you kept a pet?
[Single-choice question]*
❍ How long did you raise when you were 1 year old?
❍ How long did you raise when you were 1 to 4 years old?
❍ How long did you raise when you were 5 to 15 years old?