

Prevalence of allergen sensitization among 15,534 patients with suspected allergic diseases in Henan Province, China

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Abstract

Background: The prevalence of allergen sensitization varies in different geographic areas and population subsets. This study investigated the prevalence and distribution of inhaled and food allergens among allergic patients in Henan Province, China.

Method: The prevalence and distribution of 19 inhaled and food allergens among 15,534 patients with suspected allergic diseases were retrospectively analyzed in Henan Province, China between December 2012 and August 2016. Reactivity of their serum-specific immunoglobulin E (sIgE) to allergens was tested using the AllergyScreen test, sIgE \geq 0.35 IU/mL was considered positive.

Results: Of the 15,534 patients tested, the sIgE of 6520 (41.97%) was tested positive for at least one of the 19 tested allergens. *Dermatophagoides pteronyssinus* (3540, 22.79%), cockroach (1398, 9.00%), and mold mix (1301, 8.38%) were the most frequently tested positive inhaled allergens, while cashew nut (1320, 8.50%), mango (768, 4.94%) and cow's milk (748, 4.82%) were the most frequently tested positive food allergens. The overall sIgE positive rate was higher in males than that in females ($p < 0.05$). Moreover, the sIgE positive rates to the most of the inhaled and food allergens were statistically different between age groups ($p < 0.05$). The sIgE positive rates of the main inhaled allergens increased with age. However, the sIgE positive rates for the primary food allergens were higher in the younger groups and lower in the older groups.

Conclusions: The characteristics of allergen sensitization revealed in this study in Henan Province would facilitate the prevention, diagnosis, and management of allergic diseases in this region.

Key words: Allergen; Prevalence; specific IgE; Henan, China

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Background

Allergic diseases are chronic, immune-mediated diseases including allergic rhinitis, allergic asthma, atopic dermatitis, and food allergy. The clinical manifestations of allergic diseases include runny nose, red or itchy eyes, skin rash, hives, eczema, sneezing, shortness of breath which can seriously affect quality of life. Over the past few decades, the prevalence and incidence of allergic diseases have increased at different rates,¹⁻³ and they are associated with substantial medical and economic burdens to these patients.^{4,5}

Previous studies have demonstrated that both genetic and environmental factors play critical roles in the genesis and

development of allergic diseases^{6,7} Therefore, the prevalence of allergen sensitization may vary between different geographic areas, local climates, lifestyles, and population subsets. Data regarding local epidemiology of allergens are vital to support evidence-based prevention and management strategies. However, there was no local epidemiological data on the prevalence of sensitization to allergens among patients with allergic diseases in Henan Province, the central region of China over the past ten years.

Several techniques have been investigated in recent years to identify specific allergens for allergic diseases. Apart from skin

prick test, the serum-specific IgE test would be an attractive alternative method to identify specific allergens test,^{8,9} which is rapid, easy to perform and user friendly. In this study, we retrospectively analyzed the allergen sensitivity status of 15,534 patients with suspected allergies who underwent the Allergy Screen test for sIgE between December 2012 and August 2016 in Henan Province, China, to facilitate the prevention, diagnosis, and management of allergic diseases in this region.

Methods

Patients

In this retrospective study, the medical records of 15,534 consecutive patients with suspected allergy who sought medical care at the First Affiliated Hospital of Zhengzhou University, Henan Province, China, between December 2012 and August 2016 were analyzed. These patients were clinically evaluated by their attending physicians. All patients had suspected symptoms of allergies including runny nose, red or itchy eyes, skin rash, hives, eczema, sneezing, shortness of breath. Patients with other diseases had been excluded in this study.

The AllergyScreen test

The AllergyScreen test (Mediwiss Analytic GmbH, Moers, Germany), an immunoblot assay, was used to semi-quantitatively detect circulating allergen-specific immunoglobulin E (IgE) in human serum.

Allergens tested using this system include 10 inhaled allergens (*Dermatophagoides pteronyssinus*, house dust, mulberry, dog hair, cat dander, cockroach, amaranth, mold mix, grass mix, and tree pollen mix) and 9 food allergens (egg, cow's milk, shrimp, beef, cowry, crab, mango, cashew nut, and pineapple).

AllergyScreen tests were performed as below. Special allergens are bound to the surface of nitrocellulose membranes lying in a reaction trough. when the patient's serum is pipetted into the reaction trough and incubated, the allergen-specific IgE-antibody react with the allergens, after washing an anti-human IgE antibody coupled with biotin is added and incubated. Non-bound detector antibodies are removed by washing. Next a streptavidin is added which is conjugated with alkaline phosphatase to bind the biotin from the second incubation. Non-bound streptavidin conjugate is removed by washing. After adding the substrate and incubated, a specific enzymatic color reaction of the alkaline phosphatase takes place which results in the formation of precipitates on the strips. The coloration is directly proportional to the specific antibody content of the serum sample. Evaluation is carried out after complete drying of the test strip with the Rapidreader, which take a photo of the membrane and a software programme evaluates the colouration of the allergen lines.

The results of the AllergyScreen test were semi-quantified and categorized into the following groups: class 0 (< 0.35 IU/mL), class 1 (0.35–0.70 IU/mL), class 2 (0.70–3.50 IU/mL), class 3 (3.5–17.5 IU/mL), class 4 (17.5–50 IU/mL), class 5 (50–100 IU/mL), class 6 (> 100 IU/mL). The cut-off value was set as 0.35IU/mL, sIgE ≥ 0.35 IU/mL was considered positive.

Statistical Analysis

All data were analyzed using the Statistical Package for Social Sciences version 13.0 (SPSS Inc., Chicago, IL, USA). The chi-squared test or Fisher's exact probability method was used to evaluate differences between groups of categorical variables. $P < 0.05$ was considered statistically significant.

Results

Characteristics of the study population

The study population consisted of 7388 males (47.56%) and 8146 females (52.44%), including 5257 children (33.84%) and 10277 adults (66.16%). The patient age ranged from 1–95 years, the average age was 30.56 ± 20.98 (mean \pm SD) years. 44.6% of the patients come from towns and 55.4% of the patients come from rural areas.

Overall allergen sensitization to inhaled and food allergens

Of the 15,534 patients, 6520 (41.97%) tested positive for sIgE to at least one of the 19 allergens. *D. pteronyssinus* (3540, 22.79%), cockroach (1398, 9.00%) and mold mix (1301, 8.38%) were the top three inhaled allergens, while cashew nuts (1320, 8.50%), mango (768, 4.94%) and cow's milk (748, 4.82%) were the most frequently tested food allergens (Table 1).

Allergen sensitization in different gender groups

The allergen sensitization in this study were significantly different between male and female groups ($\chi^2 = 48.57$, $P < 0.01$). As shown in Table 2, the overall sIgE positive rate was higher among males than females (44.87% vs. 39.34%). All allergens, except cowry and mold mix, elicited a higher sIgE positive rate among males than that among females (Figure 1).

Allergen sensitization in different age groups

Individuals were divided into 10 groups based on age (0–3, 4–6, 7–9, 10–12, 13–15, 16–18, 19–24, 25–40, 41–59, and 60 years and above). As shown in Table 3, The sensitization to any allergen were significantly different among groups ($p < 0.01$). The sIgE positive rates to several inhaled allergens were low in the younger groups, increased with age, peaked, then declined. The rates of positive sIgE response to *D. pteronyssinus*, house dust, and cockroach peaked in the 19–24 age group (positive rates 34.91%, 5.93%, and 14.40%, respectively). But the sIgE positive rates for mulberry, amaranth, grass mix, and tree mix peaked in the 25–40 age group (6.88%, 9.80%, 9.15%, and 10.54%, respectively). However, the sIgE positive rates declined with age thereafter, but remained at a relatively high level. Unlike these inhaled allergens, the sIgE positive rates for cat dander and dog hair were higher in the 0–3 age group than all the other age groups (7.19% and 13.58% respectively). These rates then declined with age. The sIgE positive rate for mold mix increased with age, reaching 17.82% in those aged 60 and above (Figure 2).

With respect to food allergens, the rates of sIgE positivity to egg and cow's milk were highest in the 0–3 age group (6.92% and 23.83%, respectively). The rates of sIgE positivity to beef peaked at 1.90% in those aged 4–6 age years, and then declined with age. The sIgE positive rates to shrimp, crab, mango, cashew nut, and pineapple presented a similar trend as for

Table 1. Overall allergen sensitization to inhaled and food allergens.

Allergens	Patients (N)	% (cut-off = 0.35 IU/mL)	Patients (N)	% (cut-off = 0.35 IU/mL)
Inhaled				
<i>D. pteronyssinus</i>	3540	22.79	1608	10.35
Cockroach	1398	9.00	396	2.55
Mold mix	1301	8.38	368	2.37
Tree pollen mix	1273	8.19	538	3.46
Amaranth	1170	7.53	476	3.06
Grass mix	1029	6.62	425	2.74
Dog hair	902	5.81	103	0.66
Mulberry	806	5.19	257	1.65
House dust	560	3.60	37	0.24
Cat dander	275	1.77	89	0.57
Food				
Cashew nut	1320	8.5	409	2.63
Mango	768	4.94	220	1.42
Cow's milk	748	4.82	182	1.17
Shrimp	618	3.98	161	1.04
Crab	507	3.26	154	0.99
Pineapple	255	1.64	37	0.24
Egg	214	1.38	38	0.24
Beef	114	0.73	7	0.05
Cowry	52	0.33	5	0.03

Table 2. Allergen sensitization in male and female participants

Allergens	Male (N)	%	Female (N)	%	Chi square test (χ^2)	P value
<i>D. pteronyssinus</i>	1788	24.20	1752	21.51	15.979	< 0.01
House dust	290	3.93	270	3.31	4.159	0.041
Mulberry	463	6.27	343	4.21	33.299	< 0.01
Cat dander	173	2.34	102	1.25	26.445	< 0.01
Dog hair	509	6.89	393	4.82	30.208	< 0.01
Cockroach	792	10.72	606	7.44	50.921	< 0.01
Amaranth	658	8.91	512	6.29	38.216	< 0.01
Mold mix	575	7.78	726	8.91	6.441	0.011
Grass mix	592	8.01	437	5.36	43.933	< 0.01
Tree pollen mix	702	9.50	571	7.01	31.988	< 0.01
Egg	122	1.65	92	1.13	7.768	< 0.01
Cow's milk	463	6.27	285	3.50	64.777	< 0.01
Shrimp	322	4.36	296	3.63	5.327	0.021
Beef	67	0.91	47	0.58	5.788	0.016
Cowry	25	0.34	27	0.33	0.006	0.940
Crab	266	3.60	241	2.96	5.056	0.025
Mango	431	5.83	337	4.14	23.735	< 0.01
Cashew nut	759	10.27	561	6.89	57.147	< 0.01
Pineapple	150	2.03	105	1.29	13.187	< 0.01

Table 3. Allergen sensitization in different age groups

Allergens	Number of sIgE positive patients (%)											Chi Square (χ^2)	P value
	0-3 years	4-6 years	7-9 years	10-12 years	13-15 years	16-18 years	19-24 years	25-40 years	41-59 years	≥ 60 year			
Number of patients	751	1265	1197	957	591	496	1097	3663	3890	1627			
<i>D. pteromyssinus</i>	30 (3.99)	189 (14.94)	237 (19.80)	204 (21.32)	141 (23.86)	148 (29.84)	383 (34.91)	1020 (27.85)	836 (21.49)	352 (21.63)	366.54	< 0.01	
House dust	17 (2.26)	42 (3.32)	65 (5.43)	42 (4.39)	22 (3.72)	28 (5.65)	65 (5.93)	121 (3.30)	110 (2.83)	48 (2.95)	50.04	< 0.01	
Mulberry	3 (0.40)	15 (1.19)	31 (2.59)	50 (5.22)	24 (4.06)	17 (3.43)	70 (6.38)	252 (6.88)	247 (6.35)	97 (5.96)	134.40	< 0.01	
Cat dander	54 (7.19)	47 (3.72)	31 (2.59)	31 (3.24)	15 (2.54)	8 (1.61)	14 (1.28)	31 (0.85)	34 (0.87)	10 (0.61)	222.96	< 0.01	
Dog hair	102 (13.58)	128 (10.12)	93 (7.77)	74 (7.73)	43 (7.28)	36 (7.26)	90 (8.20)	169 (4.61)	113 (2.90)	54 (3.32)	244.53	< 0.01	
Cockroach	3 (0.40)	25 (1.98)	73 (6.10)	87 (9.09)	58 (9.81)	70 (14.11)	158 (14.40)	432 (11.79)	352 (9.05)	140 (8.60)	246.98	< 0.01	
Amaranth	10 (1.33)	19 (1.50)	37 (3.09)	62 (6.48)	36 (6.09)	28 (5.65)	99 (9.02)	359 (9.80)	365 (9.38)	155 (9.53)	206.23	< 0.01	
Mold mix	30 (3.99)	93 (7.35)	89 (7.44)	66 (6.90)	41 (6.94)	30 (6.05)	63 (5.74)	247 (6.74)	352 (9.05)	290 (17.82)	243.92	< 0.01	
Grass mix	7 (0.93)	17 (1.34)	40 (3.34)	57 (5.96)	35 (5.92)	23 (4.64)	86 (7.84)	335 (9.15)	322 (8.28)	107 (6.58)	179.01	< 0.01	
Tree mix	12 (1.60)	42 (3.32)	45 (3.76)	80 (8.36)	45 (7.61)	36 (7.26)	107 (9.75)	386 (10.54)	361 (9.28)	159 (9.77)	157.32	< 0.01	
Egg	52 (6.92)	60 (4.74)	28 (2.34)	13 (1.36)	7 (1.18)	2 (0.40)	7 (0.64)	20 (0.55)	19 (0.49)	6 (0.37)	345.17	< 0.01	
Cow's milk	179 (23.83)	171 (13.52)	92 (7.69)	78 (8.15)	29 (4.91)	16 (3.23)	45 (4.10)	71 (1.94)	44 (1.13)	23 (1.41)	1072.88	< 0.01	
Shrimp	6 (0.80)	18 (1.42)	32 (2.67)	30 (3.13)	22 (3.72)	32 (6.45)	98 (8.93)	201 (5.49)	135 (3.47)	44 (2.70)	158.54	< 0.01	
Beef	12 (1.60)	24 (1.90)	15 (1.25)	9 (0.94)	8 (1.35)	5 (1.01)	7 (0.64)	15 (0.41)	12 (0.31)	7 (0.43)	56.97	< 0.01	
Cowry	0 (0.00)	1 (0.08)	1 (0.08)	2 (0.21)	0 (0.00)	2 (0.40)	0 (0.00)	12 (0.33)	25 (0.64)	9 (0.55)	26.85	< 0.01	
Crab	5 (0.67)	15 (1.19)	25 (2.09)	15 (1.57)	12 (2.03)	22 (4.44)	59 (5.38)	167 (4.56)	139 (3.57)	48 (2.95)	89.01	< 0.01	
Mango	6 (0.80)	15 (1.19)	27 (2.26)	48 (5.02)	33 (5.58)	20 (4.03)	70 (6.38)	225 (6.14)	243 (6.25)	81 (4.98)	115.36	< 0.01	
Cashew nut	28 (3.73)	43 (3.40)	58 (4.85)	76 (7.94)	36 (6.09)	34 (6.85)	111 (10.12)	396 (10.81)	370 (9.51)	168 (10.33)	132.35	< 0.01	
Pineapple	1 (0.13)	4 (0.32)	12 (1.00)	24 (2.51)	12 (2.03)	3 (0.60)	23 (2.10)	81 (2.21)	67 (1.72)	28 (1.72)	38.36	< 0.01	

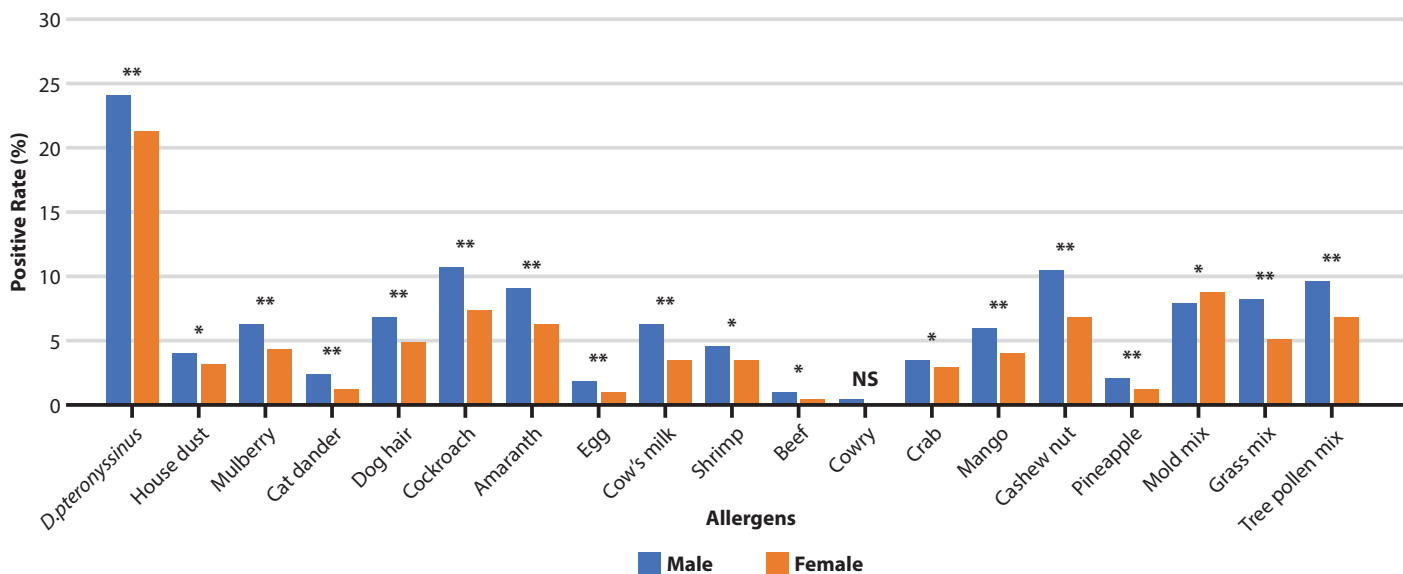


Figure 1. Allergen sensitization in different gender groups. * $p < 0,05$, ** $p < 0,01$, NS: no statistically significant difference.

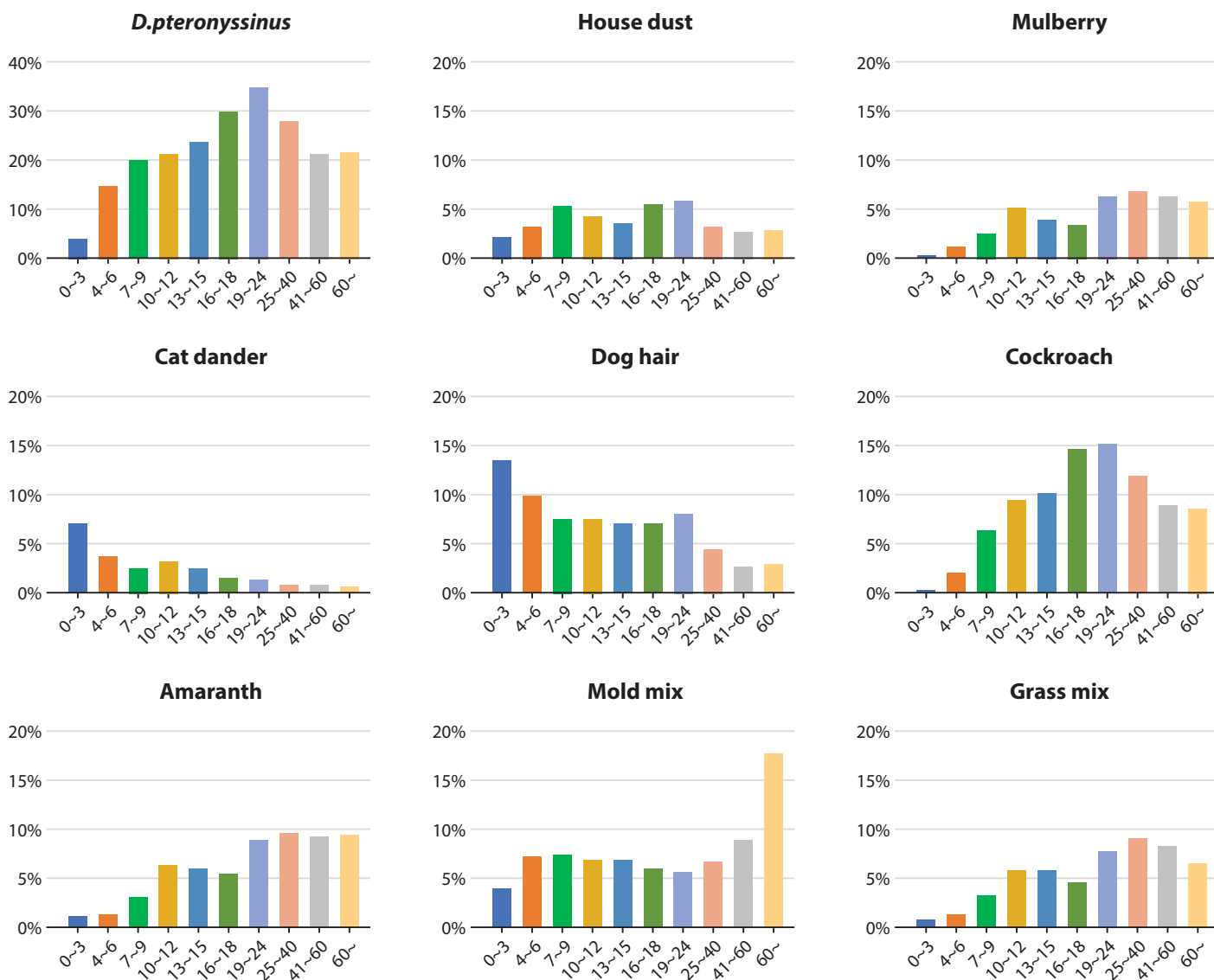


Figure 2. Sensitization to inhaled allergens in individuals of different age groups. The total number of cases in each age group: 0–3 years (n = 751), 4–6 years (n = 1265), 7–9 years (n = 1197), 10–12 years (n = 957), 13–15 years (n = 591), 16–18 years (n = 496), 19–24 years (n = 1097), 25–40 years (n = 3663), 41–59 years (n = 3890), and 60 years and above (n = 1627).

Tree pollen mix

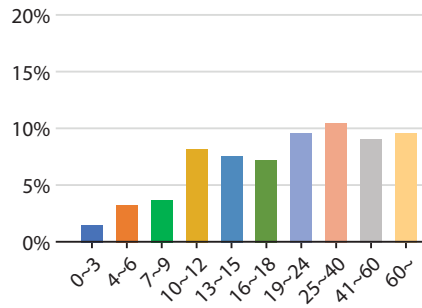
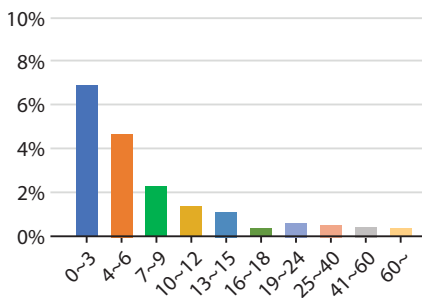
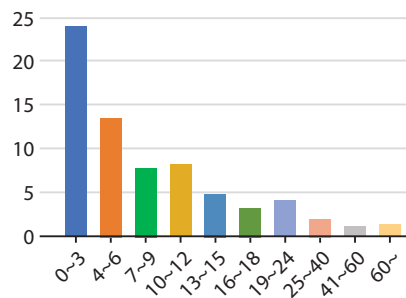


Figure 2. (Continued)

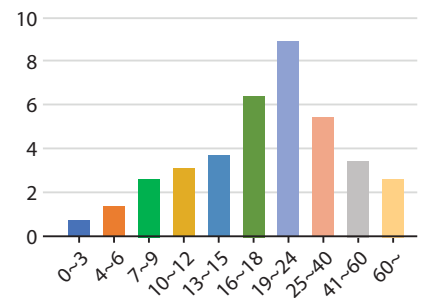
Egg



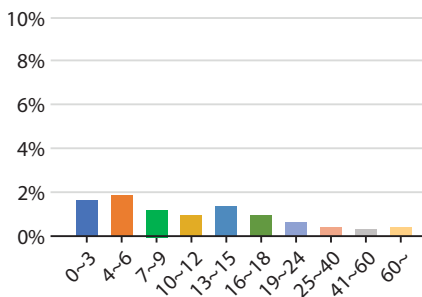
Cow's milk



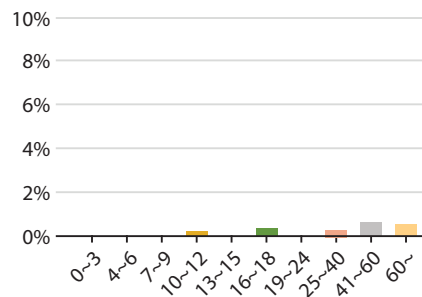
Shrimp



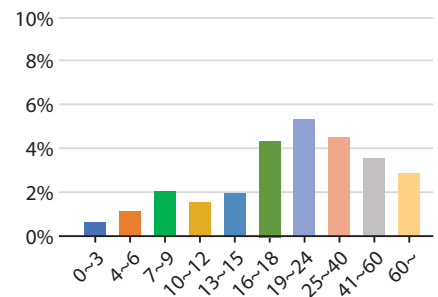
Beef



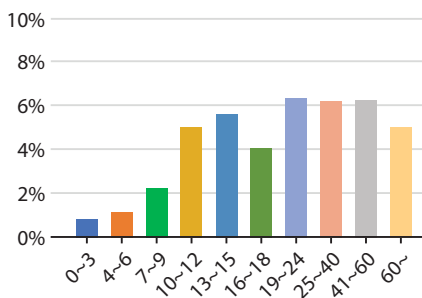
Cowry



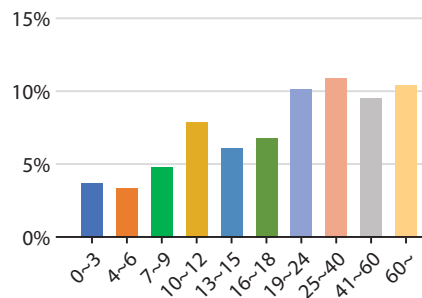
Crab



Mango



Cashew nut



Pineapple

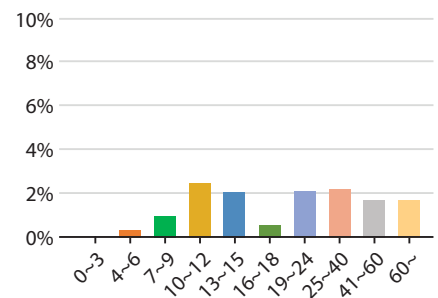


Figure 3. Sensitization to food allergens in individuals of different age groups. The total number of cases in each age group: 0-3 years (n = 751), 4-6 years (n = 1265), 7-9 years (n = 1197), 10-12 years (n = 957), 13-15 years (n = 591), 16-18 years (n = 496), 19-24 years (n = 1097), 25-40 years (n = 3663), 41-59 years (n = 3890), and 60 years and above (n = 1627).

D. pteronyssinus, and were lower in the younger age groups, increasing with age, and peaking at 19–24 or 25–40 years (8.93%, 5.38%, 6.38%, 10.81%, and 2.21%, respectively) (**Figure 3**).

Discussion

Due to the remarkable increase in the prevalence and incidence of allergic diseases in recent decades, effective prevention and treatment of allergies has become a public health priority.¹⁰ Identifying the specific allergens prevalent in a particular region can facilitate early diagnosis and inform development of strategies to prevent allergic diseases.^{11–13} Henan located at longitude 110°21′–116°39′E and latitude 31°23′–36°22′N with an area of 160,000 m², has a population of more than 107 million, 48.5% of which were urban population. Zhengzhou is the capital of Henan Province which has a population of more than 9.5 million, 60.8% of which were urban population. However, the prevalence and distribution of allergen sensitization in this region is unknown until now. To our knowledge, this is the first study to investigate the prevalence of allergen sensitization in recent years in Henan Province, a central region of China.

Our results indicated that 41.97% (6520) of the subjects were sIgE positive to at least one of the 19 tested allergens. The prevalence of reactivity to inhaled allergens ranged from 1.77–22.79%, while that to food allergens ranged from 0.33–8.50% in this region. The overall allergen sensitization was reported 33.1% in a north region of China and 69.1% in a south region of China.^{14,15} It seems that the overall allergen sensitization is higher in Henan province than that in north China but lower than that in south China. But the tested allergens sources were not so identical among these studies, we should not compare the difference directly.

Among the 19 tested allergens, individuals reacted more often to the inhaled allergen *D. pteronyssinus*, cockroach and mold mix (**Table 1**), which is consistent with the report of the previous study.¹⁶ However, cashew nut and mango were found to be the most frequently tested food allergens in this region which is inconsistent with other studies which reported that egg and cow's milk were the most frequently tested food allergens in China.^{14,15} This results might be due to the difference in study population subsets, this study included more adults than children (66.16% vs 33.84%). Food allergic diseases occur more frequently in younger individuals, especially in children under 6 years of age.¹⁷ Our study also indicated that the most frequently tested food allergens among children below 6 years of age were cow's milk (15.97%) and eggs (5.00%), respectively (**Table 3**). Sensitization to cashew nuts in this study seems unexpectedly high especially in adults. In general, babies and young children are prevented from eating nuts to avoid asphyxia. Less contact may lead less allergic diseases occurrence in children, less contact in children may also lead failure of tolerance induction in older age. This may be one of the reasons, the exact reason remains need further studies. Although seafood is consumed more frequently, certain seafood such as cowry are not common in Henan Province. This might be why the sIgE positive rate for cowry in this region was as low as 0.33% (**Table 1**).

There were studies reported that allergic diseases appear to be more frequently diagnosed in females than in males.^{18–20} But in this study, the results indicated that in this region male patients were more likely to be sensitive to allergens, and the sIgE positive rates of all individual allergens except cowry and mold mix were higher in males than females (**Figure 1**). This result was consistent with the findings in two previous studies.^{21,22} However, further studies should be conducted to explain the gender-related difference in allergen sensitization.

At least, three factors are required for the development of allergic disease: allergens, a sensitized host and close contact between them.²³ Age group analysis in this study revealed that the most frequently tested inhaled allergens in the 0–3, 4–6 groups were cat dander and dog hair, in the 7–9, 10–12, 13–15, 16–18, 19–24, 25–40 groups were *D. pteronyssinus* and dog hair, in the 41–60 group were *D. pteronyssinus* and cockroach, and in the over 60 age group was *D. pteronyssinus* and mold mix (**Figure 2**). Babies have limited contact with allergens, but encounter more allergens with age. Therefore, the rates of sIgE reactivity to inhaled allergens such as *D. pteronyssinus* and house dust increased from the younger groups to older groups, peaking in the 19–24 or 25–40 age groups. With the acquisition of immune tolerance, they had a descending tendency (**Figure 2**). The sIgE positive rates for cat dander and dog hair were high in the younger age groups, perhaps because children are more likely to be in close contact with pets as they like to play with them.

Cow's milk and eggs have been reported to be the primary food allergens in children worldwide, including in China.^{24,25} In this study, Cow's milk and eggs were also found the most frequently tested food allergens in the early age groups. As cow's milk is the earliest food given to babies, followed by eggs, and these are both commonly consumed foods in daily life. Therefore, sensitization to egg and cow's milk primarily occurs in infants and young children.

Several previous studies have investigated the incidence of allergen sensitization for allergic disease in Chinese populations.^{14,20,26} However, this is the first large-scale study to report the prevalence of allergen sensitization among patients with suspected allergic diseases in Henan Province, a central region of China. The finding in this study may also be applicable in other provinces in the central region of China which have similar climates, lifestyles to Henan, but further studies are needed to provide evidence. However, the present study has several limitations. First, sampling error may exist in the study as all the patients enrolled in this study were not clinically diagnosed cases but had symptoms typical of allergies, and were suspected to have allergies, the overall positivity reactivity 41.97% we got may be lower than the real positivity reactivity in patients with allergic diseases in this region. Second, many allergens present in the environment, reactivity to only 19 allergens was tested.²⁷ Meanwhile the difference in tested allergen sources would also limit the capability to compare with other studies. Furthermore, there may be bias due to the retrospective nature of this study. Further prospective studies should be conducted on a larger scale to determine the incidence and prevalence of allergen sensitization in China.

In conclusion, the prevalence and distribution of allergens differed in gender and age groups in Henan Province, a central region of China. The characteristics of allergen sensitization revealed in this study would facilitate the prevention, diagnosis, and management of allergic diseases in this region.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (No.81501715) and the Key Project on Science and Technology Research provided by Henan Province, China (No.152102410067).

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