

Seasonal distribution of inhaled allergens in allergic asthma patients with or without allergic rhinitis

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To the Editor: Allergic asthma and allergic rhinitis (AR) are common diseases that often occur concomitantly. Approximately 80% of allergic asthmas suffer from AR symptoms, as the two diseases share common immunopathological mechanisms. Sensitization and exposure to allergens are the risk factors that induce and aggravate allergic airway diseases such as allergic asthma and AR. With climate change, the distribution of allergens during different seasons has become very heterogeneous. Therefore, the identification of specific allergens prevalent during different seasons and in various population subsets would be useful for formulating strategies that would help to prevent and treat respiratory allergic diseases, including allergic asthma and AR. The main purpose of this study was to investigate that whether the distribution of inhaled allergens among allergic asthma patients with or without AR who visited the hospital for the first time in different seasons had seasonal specificity.

A total of 404 allergic asthma patients (208 males and 196 females) who visited the Department of Allergy, Yantai Yuhuangding Hospital, during 2018 were included in the study. Among the 404 patients, 130 had asthma without AR and 274 had asthma with AR. Allergic asthma was defined as meeting asthma guidelines and in the presence of sensitization to environmental allergens.^[1] The diagnosis of AR was consistent with the Chinese Society of Allergy Guidelines for Diagnosis and Treatment of Allergic Rhinitis.^[2] The protocol for this retrospective study was approved by the Institutional Ethics Review Board of Yantai Yuhuangding Hospital (No. 2017-209) and all patients signed an informed consent form. The

fluoroenzyme immunoassay (UniCAP[®] 100, Pharmacia, Uppsala, Sweden) was used to detect the levels of total immunoglobulin E (tIgE) and specific IgE (sIgE) in the serum from asthma patients. A positive test for sIgE was defined as ≥ 0.35 kU/L for at least one of the tested allergens. The degree of allergen sensitization was evaluated using seven levels (classes 0–6) according to the sIgE level.^[3] A total of nine types of common inhaled allergens in the region were tested, including dermatophagoides farinae (d1), dermatophagoides pteronyssinus (d2), tree pollen mix (tx5 include *alnus incana*, *corylus avellana*, *ulmus Americana*, *salix caprea*, and *populus deltoides*), molds and yeasts mix (mx2 include *penicillium chrysogenum*, *cladosporium herbarum*, *aspergillus fumigatus*, *candida albicans*, *alter-naria alternata*, and *setomelanomma rostrata*), weed pollen mix (wx5 include *ambrosia artemisiifolia*, *artemisia vulgaris*, *chrysanthemum leucanthemum*, *taraxacum vulgare*, and *solidago virgaurea*), wormwood (w6), *Artemisia vulgaris* (m3), cat, and dog. All data were analyzed using SPSS 25.0 software (IBM Corp, Armonk, NY, USA). Categorical data were reported as a percentage showing the proportion of positive results; the proportions in different groups were compared using the chi-squared test or Fisher exact test. $P < 0.05$ was considered to be statistically significant.

We found that d1 and d2 were the main inhaled allergens among the 404 allergic asthma patients. The rates of sensitization to wx5, tx5, and w6 in the fall were significantly higher than those in the spring ($P = 0.070$, 0.031, 0.003, respectively), summer ($P < 0.001$, = 0.002,

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<0.001, respectively), and winter ($P = 0.006, 0.008, 0.032$, respectively). The rate of sensitization to mx2 in the patients visiting the hospital in the summer was significantly higher than that in the spring ($P < 0.001$), fall ($P < 0.001$), and winter ($P = 0.011$) [Supplementary Table 1, <http://links.lww.com/CM9/A853>]. Allergic degree of wx5 in allergic asthma patients visiting the hospital in the fall was significantly higher than those in the other three seasons ($P = 0.007, 0.004, 0.006$, respectively), and the allergic degree of other allergens did not show the difference among the allergic asthma patients visiting the hospital in different seasons [Supplementary Table 2, <http://links.lww.com/CM9/A853>].

The levels of tIgE in the allergic asthma with AR group were significantly higher than those in the allergic asthma without AR group ($P < 0.001$). Similarly, the percentage of eosinophils (EOS) in the allergic asthma with AR group was significantly higher than that in the allergic asthma without AR group ($P < 0.001$) [Supplementary Table 3, <http://links.lww.com/CM9/A853>]. There was no statistically significant difference in the sensitization rates of inhaled allergens between allergic asthma with AR group and allergic asthma without AR group during the spring months (all P values > 0.05). The rates of sensitization to mx2 in the allergic asthma with AR group were higher than those in the allergic asthma without AR group during the summer ($P = 0.026$). In the fall, the rates of sensitization to tx5, wx5, and w6 in the allergic asthma with AR group were significantly higher than those in the allergic asthma without AR group ($P = 0.022, 0.028, 0.025$, respectively). In addition, the rates of sensitization to wx5 in the allergic asthma with AR group were significantly higher when compared to those in the allergic asthma without AR group during the winter ($P = 0.026$) [Table 1].

We further compared the degree of sensitization to inhaled allergens between the two groups of patients who visited the hospital in different seasons and found that the degree of sensitization to d1 and mx5 showed higher in the allergic asthma with AR group during the spring ($P = 0.036$ and 0.019 , respectively). In the summer, the allergic degree of

d2, mx2, and wx5 in the allergic asthma with AR group were higher than those in the allergic asthma without AR group ($P = 0.021, 0.039, 0.040$, respectively). In the fall, the allergic degree of d1, d2, and wx5 in the allergic asthma with AR group were significantly higher than in the allergic asthma without AR group ($P = 0.046, 0.033, 0.021$, respectively). In addition, the patients visiting the hospital in the winter from asthma with AR group showed a higher allergic degree of d1 and d2 when compared to those from allergic asthma without AR group ($P = 0.001$ and 0.017 , respectively) [Supplementary Table 4, <http://links.lww.com/CM9/A853>].

As a region with four distinct seasons, a change of seasons will inevitably lead to environmental changes that affect the distribution of various allergens in the environment.^[4] We found that the rate of sensitization to each inhaled allergen was different in the patients visiting the hospital for the first time in different seasons. However, the rates of sensitization to d1 and d2 were always dominant in the patients from different seasons. A multi-center investigation in China found that dust mites were the main allergens of asthma and AR, which was basically consistent with our results. We also found that the positive rates of allergic detection to wx5, tx5, and w6 during fall were higher than in other seasons, and there were more patients with AR in the fall, while mold had the highest positive rate in summer. Therefore, we should strengthen the management of patients with allergic asthma who visited the hospital in the summer and in the fall. These results can provide more detailed guidance to local medical institutions on ways to prevent and control seasonal allergens, and thereby reduce the risk for asthma exacerbations.

Our results showed that the tIgE levels and EOS percentages in asthma patients with AR were higher than those in patients with asthma without AR, which means the inflammation that occurs in asthma with AR patients is more severe than that in patients with asthma without AR.^[5] Further comparisons found that the positive rates of allergic detection to certain allergens in patients with asthma plus AR were higher than those in patients with

Table 1: Distribution characteristics of inhaled allergens in allergic asthma patients visiting hospital in different seasons from allergic asthma with AR group and allergic asthma alone group.

Allergens	Spring		Summer		Fall		Winter	
	Asthma with AR	Asthma alone	Asthma with AR	Asthma alone	Asthma with AR	Asthma alone	Asthma with AR	Asthma alone
d1	25 (67.57)	25 (71.42)	42 (67.74)	21 (60.00)	103 (76.87)	24 (68.57)	26 (63.41)	13 (52.00)
d2	27 (72.97)	24 (68.57)	40 (64.52)	22 (62.86)	100 (74.63)	27 (77.14)	30 (73.17)	13 (52.00)
mx2	13 (35.14)	11 (31.43)	51 (82.26)*	15 (42.86)	39 (29.10)	15 (42.86)	18 (43.90)	13 (52.00)
wx5	8 (21.62)	9 (25.71)	10 (16.13)	5 (14.29)	62 (46.27)*	9 (25.71)	13 (31.71)*	2 (8.00)
tx5	6 (16.22)	4 (11.43)	8 (12.90)	2 (5.71)	41 (30.60)*	4 (11.43)	4 (9.76)	3 (12.00)
w6	3 (8.11)	0	2 (3.23)	1 (2.86)	30 (22.39)*	2 (5.71)	4 (9.76)	1 (4.00)
m3	0	0	0	1 (2.86)	0	0	1 (2.44)	1 (4.00)
Cat	0	0	1 (1.61)	1 (2.86)	1 (0.74)	1 (2.86)	1 (2.44)	0
Dog	0	1 (2.86)	2 (3.23)	0	2 (1.49)	0	2 (4.88)	0

Values are expressed as n (%). * $P < 0.05$ vs. the asthma alone group in the same season. AR: Allergic rhinitis; d1: Dermatophagoides farinae; d2: Dermatophagoides pteronyssinus; m3: Aspergillus fumigatus; mx2: Molds and yeasts mix; tx5: Tree pollen mix; w6: Wormwood; wx5: Weed pollen mix.

asthma without AR during the different seasons. This high positive rate indicates that patients are more likely to produce specific inflammatory responses to their surrounding allergens. It was found that the allergic degrees of certain allergens in patients with AR were higher than those in patients without AR during all four seasons. These findings suggest that the positive rates of allergic detection and allergic degree of patients with asthma complicated with AR were higher than those of patients with asthma without AR. Furthermore, pharmacotherapeutic studies have already shown that treatments for AR can improve asthma and vice versa. Thus, we can understand the theory of controlling asthma by treating AR from a new perspective, and enhance clinicians' awareness of treating AR to improve asthma.

In conclusion, our study found that the distribution of positive allergens in asthma patients who visited hospitals in different seasons had seasonal specificity in Yantai, China. Moreover, there are differences in allergic status between allergic asthma with AR and allergic asthma without AR in different seasons. In the next step, we need to expand the sample size and carry out a multi-center investigation to provide more comprehensive guidance for the prevention and treatment of asthma.

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Conflicts of interest

None.

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