Li et al. World Allergy Organization Journal (2022) 15:100624
http://doi.org/10.1016/j.waojou.2021.100624

WORLD ALLERGY ORGANIZATION JOURNAL

Open Access

Serum IgE profiles in Chinese pollinosis patients with grass pollen sensitisation

Jun-Da Li, MM[a,b,c,#], Jian-Qing Gu, MD[a,b,c,#], Ying-Yang Xu, MD[a,b,c], Le Cui, MD[a,b,c], Li-Sha Li, MD[a,b,c], Zi-Xi Wang, MD[a,b,c], Jia Yin, MD[a,b,c]** and Kai Guan, MD[a,b,c]*

ABSTRACT

Purpose: Pollen from trees, grasses, and weeds is a common allergen source. The characteristics of pollen allergy in China are obviously different from Europe. Most studies have focused on tree and weed pollen, but there is a paucity of data on grass pollen sensitisation in China. Therefore, we used component-resolved diagnostics to investigate the serum-specific immunoglobulin E (sIgE) to grass pollen in Chinese patients with pollinosis.

Methods: We retrospectively analysed 547 patients with pollen allegy from an outpatient Allergy Department in Beijing, China. All the patients answered questionnaires about their clinical allergy histories. Total immunoglobulin E (IgE) and sIgE levels to grass pollen (Bermuda, Timothy grass) were quantified by ImmunoCAP using 0.35 kUA/L as a threshold for positivity.

Results: Of the 547 pollinosis patients, 389 (71.1%) showed a positive sIgE reaction to either grass pollen, or both. The prevalence of food allergy was significantly lower in patients with grass pollen sensitisation. Among the 389 patients with grass pollen sensitisation, the prevalence of sIgE to allergen extracts of bermuda, mugwort, ragweed, plane, hop, ash, birch, and timothy grass was 97%, 96%, 94%, 88%, 88%, 84%, 78%, and 78%, respectively. However, only 134/389 (34%) were positive for Cyn d 1, 29/389 (7%) for Phl p 1, and 8/389 (2%) for Phl p 5b. For pollinosis patients, 62/547 (11%) were sIgE-positive for cross-reactive carbohydrate determinants (CCDs), and their grass pollen-sIgE was also positive.

Conclusions: The prevalence of *in vitro* IgE sensitisation to grass pollen extract is high in Chinese patients with pollinosis. But mostly spurious and characterized by IgE sensitisation to profilins and CCD, induced by other pollen. Component-resolved diagnostics is an extremely useful tool precise diagnostics of pollen allergy in China.

Keywords: Pollinosis, sIgE, Pollen and food allergens, Cross-reactivity, Multi-sensitisation

[a]Department of Allergy, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, China
*Corresponding author. Department of Allergy, Peking Union Medical College Hospital, #1 Shuaifuyuan, Wangfujing, Beijing, 100730, China. E-mail: dr_guankai@126.com
**Corresponding author. Department of Allergy, Peking Union Medical College Hospital, #1 Shuaifuyuan, Wangfujing, Beijing, 100730, China. Email: doctoryinjia@163.com
[#] Jun-Da Li and Jian-Qing Gu contributed equally to this study

Full list of author information is available at the end of the article.

http://doi.org/10.1016/j.waojou.2021.100624
Received 30 June 2021; Received in revised from 16 December 2021; Accepted 20 December 2021
Online publication date xxx

INTRODUCTION

The prevalence of allergic diseases has increased significantly over the last few decades and has resulted in a high socioeconomic burden worldwide.[1,2] Pollen from trees, grasses, and weeds is the most clinically important and abundant allergen source, which can induce allergic rhinitis, allergic conjunctivitis, and bronchial asthma.[3] Due to the cross-reactivity of pollen and food allergens, patients with a pollen allergy often display food allergy after consuming fresh fruits, vegetables, or nuts, with clinical symptoms like the oral allergy syndrome, urticaria, angioedema, and anaphylaxis.[4]

Grass is ubiquitous throughout the world, with 3 common allergenic, pollen-producing grass subfamilies: the temperate Pooideae (eg, timothy grass and ryegrass), subtropical Chloridoideae (eg, bermuda grass) and Panicoideae (eg, bahia grass) subfamilies.[5] According to a systematic review, unlike for tree and weed pollen, high grass pollen levels were a necessary factor for thunderstorm asthma events[6] and mugwort was also considered a contributing factor in thunderstorm asthma attacks.[7]

In China, a study of seasonal and geographical dispersal regularity of airborne pollens showed that most regions only have 2 seasonal peaks of airborne pollen: tree pollen in spring and weed pollen in autumn.[8] This finding has been substantiated by other studies on pollen allergens that have shown a high prevalence of tree pollen and weed pollen.[9-11] There was only 1 study that focused on grass allergens in Guangdong, the largest province of southern China; however, the study showed a relatively low prevalence of allergy to grass pollen.[12] Nonetheless, there is a known cross-reactivity of pollen allergens and many pollinosis patients often experience a multi-sensitisation to diverse pollen allergens. In this study, we aimed to investigate the serum-specific immunoglobulin E (sIgE) of the grass pollen extracts and its components in Chinese patients with pollen allergy.

MATERIAL AND METHODS

Study population

This was a retrospective study of pollinosis patients from the outpatient Allergy Department of the Peking Union Medical College Hospital between January 2011 and August 2012. They were diagnosed by an experienced allergist and enrolled in the study. All the patients had convincing clinical histories of allergic rhinitis, allergic conjunctivitis, or bronchial asthma during the pollen season in China and positive IgE tests for at least one pollen allergen. A survey questionnaire on self-reported food allergy was completed by patients or their parents/caregivers. In total, 547 pollinosis patients signed written informed consent forms before study enrolment. This study was reviewed and approved by the Ethical Committee of Peking Union Medical College Hospital (No.PUMCH1103).

Blood sampling and storage

A 5 ml peripheral venous blood sample was obtained from each participant, incubated at 18–25 °C for 15 min, and centrifuged for 10 min at 4000 *g*. The serum supernatant was divided into 1.5 ml tubes and stored at −80 °C until further analysis to reduce the number of freeze/thaw cycles.

Total IgE and specific IgE testing

The total serum IgE and allergen-specific IgE antibody levels were measured using the ImmunoCAP system (Thermo Fisher Scientific, Uppsala, Sweden). The allergen-specific IgE tests included tests for tree pollens (birch [t3], juniper [t6], plane [t11], ash [t15]), weed pollens (ragweed [w1], mugwort [w6], kochia [w17], and hop [w22]), grass pollens (bermuda [g2] and timothy grass [g6]).Common pollen components, such as pathogenesis-related protein group 10 [PR-10], [Bet v 1], profilin [Bet v 2], polcalcin [Bet v 4], and pectate lyase [Amb 1], defensin-like protein [Art v 1], non-specific lipid transfer proteins [nsLTP], [Art v 3], beta-expansins ([Phl p 1] and [Cyn d 1]), the grass group 5 [Phl p 5b], and cross-reactive carbohydrate determinants (CCDs) MUXF3 were also tested. Specific IgE values above the threshold of 0.35 kUA/L were considered positive.

Statistical analysis

SPSS 22.0 (IBM Corp., Armonk, NY, USA) and Prism 8.0 (GraphPad, California, USA) was used to analyse the data. Pearson's Chi-square test was used to compare the frequencies of the

categorical variables. The Wilcoxon rank-sum test was used to compare the specific IgE levels between the groups. Correlation analyses for parametric data were performed using Pearson's Chi-square tests, with the correlation coefficients expressed as "*r*." *P*-values <0.05 were statistically significant.

RESULTS

Clinical characteristics of pollinosis patients

Five hundred and forty-seven pollinosis patients were enrolled in this study (Table 1). Of these, 389 (71.1%) patients showed positive sIgE reactions to grass pollen with 97% being bermuda sIgE-positive and 78% being timothy grass sIgE-positive. We found no differences in the demographic data of pollinosis patients with and without grass pollen sensitisation. The majority of pollinosis patients (55.8%) had asthma and 14.1% had drug allergies. Moreover, 270 of 547 (49.4%) participants reported having had allergic reactions to plant food and 54 (20%) had experienced food-induced anaphylaxis at least once. A significant higher proportion of patients without grass pollen sensitisation experienced plant food allergy compared to patients with grass pollen sensitisation, but the incidences of anaphylaxis were not different between the 2 groups. In addition, the total IgE levels of patients with grass pollen sensitisation (median 332 kU/L; range 23.3–5000 kU/L) were significantly higher than that of patients without grass pollen sensitisation (median 209 kU/L; range 27.3–2472 kU/L) (see Table 1).

Specific IgE profiles to natural pollen allergens and components

The serological analysis of specific IgE to natural pollen allergens identified mugwort (468, 86%), ragweed (425, 78%), ash (406, 74%), hop (400, 73%), birch (385, 70%), and plane (382, 70%) pollen as major sources of pollen allergy in Chinese pollinosis patients. All of the grass pollen sensitized patients were also sensitized to other pollen species. The percentage of patients with a positive sIgE to 8 common pollens in China were significantly higher in patients with a grass pollen sensitisation than in those without (Fig. 1A). The dominant cosensitizer, mugwort (96%), followed by ragweed (94%), plane (88%), hop (88%), ash (84), birch (78%) sIgE-positive.

Among the 389 patients with grass pollen sensitisation, the prevalence of IgE antibodies specific to Cyn d 1, Phl p 1, and Phl p 5b was only 34%, 7%, and 2%, respectively (Fig. 1B). The prevalence of other pollen components-sIgE was higher in patients sensitized to grass pollen extract compared with those without grass pollen sensitisation. One hundred twenty-five patients with grass pollen positive and Phl p 1/Cyn d 1 negative were CCD positive and/or Bet 2/4 positive. In 302 birch sIgE-positive patients with grass pollen sensitisation, only 125 (41%) patients had sIgE to Bet v 1. However, 72 of 83 (87%) birch sIgE-positive patients without grass pollen sensitisation had sIgE to Bet v 1, and only 8% had sIgE to Bet v 2.

About patients with plant food allergy, Bet v 1 was more prevalent among patients without grass

	Non-Grass	Grass	*P*-value
Female, n (%)	89 (56.3%)	197 (50.6%)	0.257
Age, mean ± SD	29.4 ± 14.9	28.4 ± 14.3	0.477
Asthma, n (%)	83 (52.5%)	222 (57.1%)	0.334
Drug allergy, n (%)	20 (12.7%)	57 (14.7%)	0.590
Plant food allergy, n (%)	93 (58.7%)	177 (45.5%)	0.005
OAS, n (%)	77 (82.8%)	139 (78.5%)	0.429
SR, n (%)	16 (17.2%)	38 (21.5%)	0.429
Total IgE in kU/L, median (range)	209 (27.3–2472)	332 (23.3–5000)	<0.001

Table 1. Clinical and demographic characteristics of pollinosis patient. *OAS, oral allergy syndrome; SR, systemic reaction; kU/L, kilo unit per litre*

	Bermuda		Timothy			Bermuda		Timothy			Cyn d 1		Phl p 1		Phl p 5b	
	SEN (%)	SPE (%)	SEN (%)	SPE (%)		SEN (%)	SPE (%)	SEN (%)	SPE (%)		SEN (%)	SPE (%)	SEN (%)	SPE (%)	SEN (%)	SPE (%)
Bermuda	100	100	82.8	93.9	Cyn d 1	61.4	87.6	67.3	86.1	Cyn d 1	100	100	70.0	86.5	62.5	77.0
Timothy	85.7	90.5	100	100	Phl p 1	64.3	67.5	70.0	64.8	Phl p 1	65.4	81.0	100	100	62.5	96.8
Birch	86.5	47.3	91.4	43.9	Phl p 5b	65.9	68.6	72.6	66,4	Phl p 5b	66.2	82.7	43.3	89.6	100	100
Sabina	84.4	62.13	88.8	66.4	Bet v 1	81.2	37.9	64.4	49.2	Bet v 1	80.1	48.9	36.7	61.7	75.0	49.2
Plane	80.4	88.8	80.5′	80.7	Bet v 2	65.1	82.8	69.6	73.8	Bet v 2	69.9	56.2	56.7	57.6	75.0	68.5
Ash	70.4	74.6	63.7	86.1	Bet v 4	37.6	87.6	55.8	74.2	Bet v 4	74.3	68.1	20.0	91.7	37.5	96.8
Ragweed	92.6	68.6	79.9	79.5	Amb a 1	70.4	69.8	67.3	75.0	Amb a 1	72.8	75.4	43.3	74.7	50.0	63.6
Mugwort	69.0	71.0	89.1	40.6	Art v 1	46.0	84.0	47.2	75.8	Art v 1	47.1	79.6	30.0	93.8	87.5	36.0
Kochia	88.6	75.1	79.2	74.2	Art v 3	78.6	52.7	84.2	36.1	Art v 3	75.0	44.0	23.3	91.9	75.0	61.0
hop	80.4	75.7	85.5	70.9	CCDs	55.8	78.1	46.5	88.5	CCDs	70.6	88.3	40.0	74.5	75.5	35.3

Table 2. Sensitivity and specificity between pollens and allergen components. *SEN: sensitivity; SPE: specificity*

pollen sensitisation than with grass pollen sensitisation (60% vs 33%, p < 0.001). On the other hand, the Bet v 1-sIgE levels was significantly higher in patients without grass pollen sensitisation, Bet v 2, Art v 1 and Art v 3-sIgE levels was significantly lower in patients with grass pollen sensitisation.

The relationship between grass pollen and other pollen species

A correlation analysis on sIgE levels to common pollen and grass pollen in patients with grass pollen sensitisation, was conducted (Table 3). Of the bermuda sIgE-positive patients (n = 378), there was a strong correlation with timothy grass ($r = 0.945$, $P < 0.001$), plane ($r = 0.817$, $P < 0.001$), ash ($r = 0.826$, $P < 0.001$), and ragweed-sIgE levels ($r = 0.837$, $P < 0.001$). Among the timothy grass sIgE-positive patients (n = 303), there was a strong correlation with bermuda ($r = 0.942$, $P < 0.001$), ash (r = 0.763, $P < 0.001$), ragweed ($r = 0.768$, $P < 0.001$), and plane-sIgE levels (r = 0.811, $P < 0.001$). However, the correlation for the specific IgE between mugwort and grass pollen (bermuda, $r = 0.237$, $P < 0.001$; timothy, $r = 0.207$, $P < 0.001$, respectively) was low.

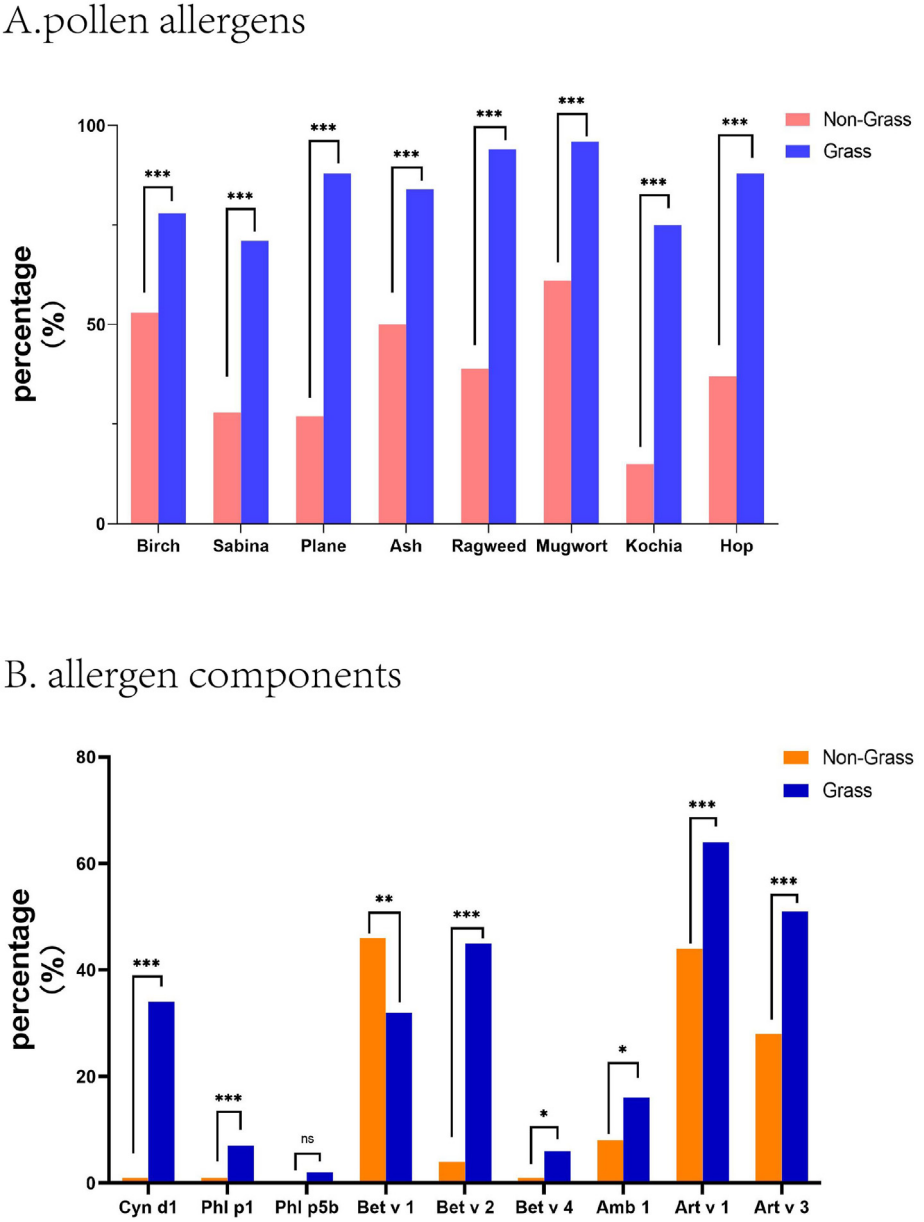

Fig. 1 Frequencies of specific pollen allergens and components by different groups. Specific IgE >0.35 kUA/L were considered positive. ***, significantly different at $P < 0.001$; Non-grass, pollinosis patients without grass sensitisation; Grass, pollinosis patients with grass sensitisation

	Bermuda (n = 378)	*P*-value	Timothy (n = 303)	*P*-value	CCDs (n = 62)	*P*-value
bermuda	1	<0.001	0.942	<0.001	0.005	0.971
timothy	0.945	<0.001	1	<0.001	0.180	0.160
birch	0.540	<0.001	0.483	<0.001	−0.107	0.410
sabina	0.120	0.019	0.127	0.027	0.6060	<0.001
plane	0.817	<0.001	0.811	<0.001	0.24	0.854
ash	0.826	<0.001	0.763	<0.001	−0.1	0.937
ragweed	0.837	<0.001	0.768	<0.001	−0.21	0.869
mugwort	0.237	<0.001	0.207	<0.001	−0.026	0.839
kochia	0.598	<0.001	0.653	<0.001	0.231	0.07
hop	0.387	<0.001	0.401	<0.001	0.278	0.029

Table 3. Correlations between sensitisation to grass pollen, cross-reactive carbohydrate determinants and other pollen types

We also used correlation analysis to evaluate the pollen components-sIgE levels (Table 4). We identified only a strong correlation between Bet v 2 and grass (bermuda, $r = 0.842$, $P < 0.001$; timothy, $r = 0.738$, $P < 0.001$). All the Bet v 2 sensitive patients were sensitized to bermuda while 87% were sensitized to timothy grass. There was a weak correlation between grass pollen allergen components and the grass pollen-sIgE levels. However, of the 29 Phl p 1-sIgE-positive patients with grass pollen sensitisation, there was a strong correlation between the timothy grass and Phl p 1-sIgE levels ($r = 0.830$, $P < 0.001$) and the bermuda and Cyn d 1-sIgE levels ($r = 0.904$, $P < 0.001$) (Fig. 2).

The characteristics of CCDs-specific IgE

In our study, the CCDs marker the MUXF3-specific IgE in pollinosis patients was analysed

	Bermuda (n = 378)	*P*-value	Timothy (n = 303)	*P*-value	CCDs (n = 62)	*P*-value
Cyn d1	0.369	<0.001	0.327	<0.001	0.945	<0.001
Phl p1	0.324	<0.001	0.315	<0.001	0.112	0.385
Phl p 5b	0.008	0.881	0.084	0.143	0.040	0.756
Bet v 1	0.097	0.061	0.039	0.496	−0.086	0.505
Bet v 2	0.842	<0.001	0.738	<0.001	−0.115	0.371
Bet v 4	0.351	<0.001	0.491	<0.001	−0.047	0.718
Amb a 1	0.112	0.03	0.1	0.081	0.148	0.253
Art v 1	0.149	0.004	0.143	0.012	−0.055	0.669
Art v 3	0.119	0.02	0.087	0.13	−0.011	0.935
CCDs	0.088	0.086	0.156	0.007	1	<0.001

Table 4. Correlations between sensitisation to grass pollen, cross-reactive carbohydrate determinants and other allergen component types

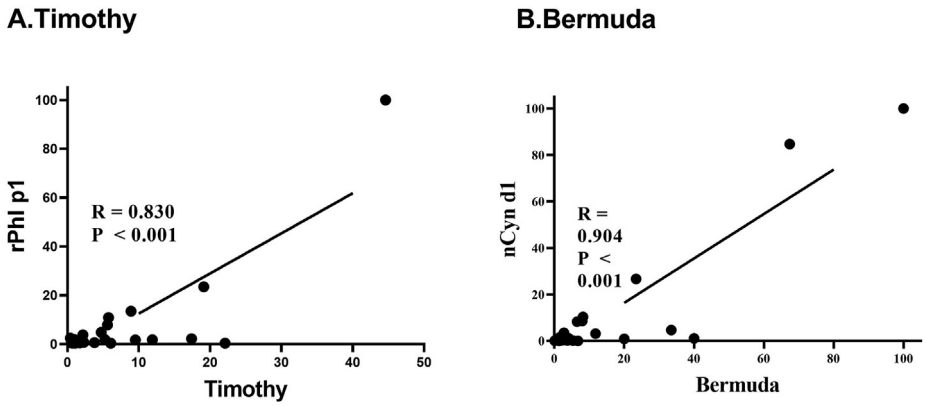

Fig. 2 Results of the correlation analysis between grass pollen (timothy and bermuda) and their components (rPhl p 1 and nCyn d 1) in Phl p 1-sIgE-positive patients

(Table 2). None of the patients without grass pollen sensitisation were sIgE-positive for CCDs. Among the patients with grass pollen sensitisation, 16% (62/389) were sIgE-positive for CCDs. The sIgE levels of pollen allergens were significantly higher than CCDs-sIgE levels (median, 0.69 kUA/L; range, 0.35–17.5 kUA/L) (Fig. 3). The Spearman's rank correlation analysis showed a strong correlation between the CCDs and Cyn d 1-sIgE levels ($r = 0.945$, $P < 0.001$), and a moderate correlation between CCDs and Sabina-sIgE levels ($r = 0.606$, $P < 0.001$).

DISCUSSION

In the present study, we analysed the serum IgE profiles of pollinosis patients with grass pollen sensitisation in China. Of the 547 patients with pollinosis visiting our outpatient allergy department, 71.1% of patients with pollinosis showed a positive sIgE reaction to grass pollen, virtually all the grass pollen sensitized patients are also sensitized to other pollen species. This was a high prevalence of sensitisation to grass pollen. There were no differences between the patients with grass pollen sensitisation and patients without grass pollen sensitisation with regard to demographic data, the rate of asthma, or drug allergy. When we analysed the serum-specific IgE profiles of natural pollen allergens, grass pollen sensitized pollinosis patients were more often multi-sensitized to diverse pollen sources compared to patients without grass pollen sensitisation. The multi-sensitized patients were more prone to higher IgE levels as previous shown.[13]

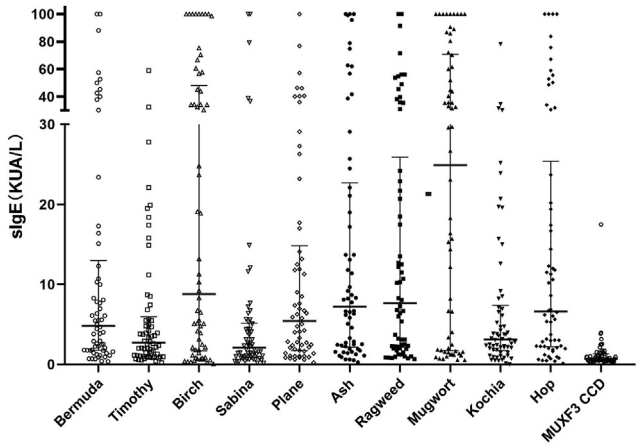

Fig. 3 Specific IgE levels of pollen allergens in CCDs-sIgE-positive patients. CCDs, cross-reactive carbohydrate determinant; sIgE, specific immunoglobulin E; kUA/L, kilo unit of allergen per litre

While our study showed that patients with grass pollen sensitisation had a lower prevalence of plant food allergy compared to patients without grass pollen sensitisation, a previous study suggested that pollen pan-allergen sensitized patients were more likely to show pollen-related food allergy.[14] From the allergen component testing, we found that the percentage of specific IgE to Bet v 2 in patients with grass pollen sensitisation was significantly higher than the percentage in patients without pollen sensitisation; however, the Bet v 1 was significantly lower, suggesting that the high frequency of sensitisation to Bet v 1 was correlated with pollen-related food allergies. These results were supported by a previous study in China.[15]

Phl p 1 belongs to the grass pollen group 1 antigen, and is a marker of a true sensitisation to grass pollen.[16] In our study population only a small

minority (7.5% (29/389)) of patients with grass pollen sensitisation were positive for Phl p 1 and even less (2.1% (8/389)) were positive to Phl p 5. This is notably different from the data from the findings of studies conducted in Europe,[17–19] and slightly lower than the findings of a study in the north of China.[10] Phl p 1 and Cyn d 1 each had stronger correlations with timothy grass and bermuda grass in Phl p 1-sIgE-positive patients. This indicated that Phl p 1 is a major marker of grass pollen allergy in China. Cyn d 1 also belongs to the grass pollen group 1 antigen, and has a high homology in amino acid sequence compared with Phl p 1.[20] In our study, population only 134/378 (35.4%) of patients showing bermuda pollen sIgE positivity were really sensitized to Cyn d 1, which was significantly lower than that in the study in Guangdong. BY contrast, in Europe,[21] it sensitized 76–100% of patients allergised to bermuda grass areCyn d 1 positive.

The clinical relevance for pollen allergy diagnostics in China is obvious. Our results suggest that CRD must be performed in China to discriminate genuine from spurious IgE sensitisation to grass pollen extract. The high prevalence of patients with IgE to grass pollen extract but no IgE to Phl p 1 or Phl p 5 is mostly explained by the high sensitisation to mugwort and Art v 1. Our data suggest that mugwort pollen induces a genuine IgE response in mugwort allergic patients which involves also Art v 5 and/or Art v 4 and/or CCD. Then the mugwort allergic patients develop a spurious atopic reactivity also to Phl p 12 and/or Phl p 7 and, with that, to grass pollen extract. This phenomenon is mirroring the situation in Europe, where genuine grass pollen allergy is dominant and IgE reactivity to extracts of weeds (mugwort, ragweed) is often spurious.[22,23]

CCDs, which can cause cross-reactivity between extensive allergen sources, such as plants, latex, and insects, was shown to cause non-specific false-positive results with *in vitro* serum-specific IgE tests.[24] This was because most patients with IgE against CCDs did not seem to have any clinically relevant allergy symptoms.[25] In our study, 16% of bermuda grass positive patients, were also CCDs-sIgE-positive. However, this was significantly lower than in the patients in the study in Guangdong (41.4%). There was a strong correlation between CCDs and Cyn d 1-sIgE levels and no correlation between CCDs and Phl p 1, This can be explained considering that Cyn d 1 is in native form in the ImmunoCAP system, while Phl p 1 is in a recombinant, and hence CCD-free, formulation. Furthermore, the CCDs-sIgE levels were extremely low in pollinosis patients. This indicated that CCDs was cross-reactive between grass pollen, but not as a consequence of the high prevalence of grass pollen sensitisation in China.

Several limitations of our study should be acknowledged. First, we diagnosed food allergy based on clinical histories using a questionnaire and allergen-specific IgE testing, instead of using a double-blinded placebo-controlled food challenge. Therefore, there may have been some recollection bias. Second, because patients were enrolled in this study from our outpatient department, there was an inherent selection bias. Furthermore, most patients came from northern China, so the generalization of our results to the whole population of China is questionable. In addition, due to the lack of inhibition assays, the cross-reactivity between allergen components, could not be explained completely.

CONCLUSION

In conclusion, there was a high prevalence of grass pollen sensitisation in China, but most of grass pollen *in vitro* sensitisation was spurious, the main reason was CCDs and other cross-reactivity molecules, such as profilins, which simulate *in vitro* IgE sensitisation to grass and other cross-reactivity molecules containing pollens. We used component-resolved diagnosis to find that some patients have true allergies to grass pollen in China. Therefore, we recommend that further studies focus on grass pollen allergy in China and that component-resolved diagnostics is used in the routine diagnostic procedures of Chinese grass pollen allergic patients.

Abbreviations

sIgE: specific immunoglobulin E; CCDs: cross-reactive carbohydrate determinants; nsLTP: non-specific lipid transfer proteins; ROC: receiver operating characteristics.

Ethics approval and consent to participate

All the patients have signed a written informed consent form before they were recruited. This study was approved by the ethics committee of Peking Union Medical College Hospital.

Authors contributions
Jun-Da Li analysed and interpreted the data and drafted the article. Jian-Qing Gu made substantial contributions to acquisition of the cases. Ying-Yang Xu made substantial contributions to acquisition of the cases. Li-Sha Li made substantial contributions to acquisition of the cases. Le Cui made substantial contributions to acquisition of the datas. Zi-Xi Wang made substantial contributions to acquisition of the datas. Jia Yin made substantial contributions to acquisition of the datas. Kai Guan made substantial contributions to conception and design and gave final approval of the version to be published.

Funding
Supported by Beijing Natural Science Foundation (No.7212074).

All authors' consent for publication
All the authors listed have approved the manuscript.

Availability of data and materials
This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. All study participants provided informed consent, and the study design was approved by the appropriate ethics review board.

Declaration of competing interest
All of authors report no competing interests or financial disclosure.

Acknowledgements
We are appreciated all the patients and investigators who participated in this study.

Author details
[a]Department of Allergy, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, China. [b]Beijing Key Laboratory of Precision Medicine for Diagnosis and Treatment on Allergic Diseases, China. [c]National Clinical Research for Dermatologic and Immunologic Diseases, China.

REFERENCES

1. Schou Nielsen J, Meteran H, Ulrik CS, Porsbjerg C, Backer V. Natural history of skin prick test reactivity: a 20-year prospective study of a random population sample of children and adolescents. *Ann Allergy Asthma Immunol*. 2017;119:184–188 e181.
2. Zuberbier T, Lotvall J, Simoens S, Subramanian SV, Church MK. Economic burden of inadequate management of allergic diseases in the European Union: a GA(2) LEN review. *Allergy*. 2014;69:1275–1279.
3. Verdino P, Barderas R, Villalba M, et al. Three-dimensional structure of the cross-reactive pollen allergen Che a 3: visualizing cross-reactivity on the molecular surfaces of weed, grass, and tree pollen allergens. *J Immunol*. 2008;180:2313–2321.
4. Steering Committee A, Review Panel M. A WAO - ARIA - GA(2) LEN consensus document on molecular-based allergy diagnosis (PAMD@): update 2020. *World Allergy Organ J*. 2020;13:100091.
5. Davies JM. Grass pollen allergens globally: the contribution of subtropical grasses to burden of allergic respiratory diseases. *Clin Exp Allergy*. 2014;44:790–801.
6. Idrose NS, Dharmage SC, Lowe AJ, et al. A systematic review of the role of grass pollen and fungi in thunderstorm asthma. *Environ Res*. 2020;181:108911.
7. Xu YY, Xue T, Li HR, Guan K. Retrospective analysis of epidemic thunderstorm asthma in children in Yulin, northwest China. *Pediatr Res*. 2020;89(4):958–961.
8. Qing-yu LQ-sJS-xLX-zZx-mW. Seasonal and geographical dispersal regularity of airborne pollens in China. *Med J Chin Peoples Lib Army*. 2017;42:951–955.
9. Ma T, Wang X, Zhuang Y, et al. Prevalence and risk factors for allergic rhinitis in adults and children living in different grassland regions of Inner Mongolia. *Allergy*. 2020;75:234–239.
10. Hao GD, Zheng YW, Gjesing B, et al. Prevalence of sensitization to weed pollens of Humulus scandens, Artemisia vulgaris, and Ambrosia artemisiifolia in northern China. *J Zhejiang Univ - Sci B*. 2013;14:240–246.
11. Tang R, Sun JL, Yin J, Li Z. Artemisia allergy research in China. *BioMed Res Int*. 2015:179426, 2015.
12. Luo W, Huang H, Zheng P, et al. Major grass pollen allergens and components detected in a southern Chinese cohort of patients with allergic rhinitis and/or asthma. *Mol Immunol*. 2016;78:105–112.
13. Ghunaim N, Gronlund H, Kronqvist M, et al. Antibody profiles and self-reported symptoms to pollen-related food allergens in grass pollen-allergic patients from northern Europe. *Allergy*. 2005;60:185–191.
14. Bircher AJ, Van Melle G, Haller E, Curty B, Frei PC. IgE to food allergens are highly prevalent in patients allergic to pollens, with and without symptoms of food allergy. *Clin Exp Allergy*. 1994;24:367–374.
15. Li JD, Du ZR, Liu J, Xu YY, Wang RQ, Yin J. Characteristics of pollen-related food allergy based on individual pollen allergy profiles in the Chinese population. *World Allergy Organ J*. 2020;13:100120.
16. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, et al. EAACI molecular allergology user's guide. *Pediatr Allergy Immunol*. 2016;27(Suppl 23):1–250.
17. Sekerkova A, Polackova M, Striz I. Detection of Phl p 1, Phl p 5, Phl p 7 and Phl p 12 specific IgE antibodies in the sera of children and adult patients allergic to Phleum pollen. *Allergol Int*. 2012;61:339–346.
18. Niederberger V, Laffer S, Froschl R, et al. IgE antibodies to recombinant pollen allergens (Phl p 1, Phl p 2, Phl p 5, and Bet v 2) account for a high percentage of grass pollen-specific IgE. *J Allergy Clin Immunol*. 1998;101:258–264.
19. Almeida E, Caeiro E, Todo-Bom A, Duarte A, Gazarini L. Sensitization to grass allergens: Phl p1, Phl p5 and Phl p7 Phl p12 in adult and children patients in Beja (Southern Portugal). *Allergol Immunopathol*. 2019;47:579–584.

20. Duffort O, Quintana J, Ipsen H, Barber D, Polo F. Antigenic similarity among group 1 allergens from grasses and quantitation ELISA using monoclonal antibodies to Phl p 1. *Int Arch Allergy Immunol*. 2008;145:283–290.

21. Frenguelli G, Passalacqua G, Bonini S, et al. Bridging allergologic and botanical knowledge in seasonal allergy: a role for phenology. *Ann Allergy Asthma Immunol*. 2010;105: 223–227.

22. Tripodi S, Frediani T, Lucarelli S, et al. Molecular profiles of IgE to Phleum pratense in children with grass pollen allergy: implications for specific immunotherapy. *J Allergy Clin Immunol*. 2012;129:834–839 e838.

23. Ciprandi G, Scala E, Ariano R, Allergy ASGoP, Laboratory Study Group on Pollen S. Phleum pratense molecular pattern across Italy. *Eur Ann Allergy Clin Immunol*. 2017;49: 176–180.

24. Homann A, Schramm G, Jappe U. Glycans and glycan-specific IgE in clinical and molecular allergology: sensitization, diagnostics, and clinical symptoms. *J Allergy Clin Immunol*. 2017;140:356–368.

25. Mari A, Ooievaar-de Heer P, Scala E, et al. Evaluation by double-blind placebo-controlled oral challenge of the clinical relevance of IgE antibodies against plant glycans. *Allergy*. 2008;63:891–896.