

Peanut Component Ara h 1 and 2 Sensitization in Patients with Food Allergy in Kuwait

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Keywords

Food allergy · IgE-mediated allergy · ImmunoCAP · Peanut allergy · Recombinant allergens

Abstract

Introduction: There is limited knowledge on the sensitization patterns to peanut proteins and food allergy in the Middle East. The objective of this study is to analyze the relationship between sensitization patterns to peanut proteins and clinical symptoms in a group of patients with physician-diagnosed peanut allergy (PA) in Kuwait. **Methods:** PA patients were evaluated by the skin prick test (SPT), serum total IgE, peanut-specific IgE (sIgE), and sIgE against Ara h 1–3, 8, and 9, and clinical data were collected. **Results:** Sixty-nine patients were included. A positive correlation between peanut SPT and sIgE was detected for all 3 storage proteins (Ara h 1–3) in patients <6 years old and for Ara h 1 and 2 in older patients. ROC analysis of positive correlations showed that oral food challenge should be considered for definite diagnosis of PA only if the level of Ara h 2 is <22.25 KUA/L, with level of Ara h 2 ≥15.4 allowing the detection of systemic reactions with a sensitivity of 55.56%. Patients presenting with systemic reactions more frequently had positive Ara h 1 (88.9%) and Ara h 2 (83.3%), compared with 44.1% and 52.9%

in those with local reaction ($p = 0.0046$ and $p = 0.0378$). The levels of Ara h 1 and 2 were also significantly higher in patients with systemic reactions compared to those with a local reaction, with those differences being especially relevant for Ara h 2 (15.9 vs. 0.4) ($p = 0.0005$). **Conclusions:** The pattern of sensitization to peanut proteins in the Middle East is similar to that of the Western world. Measurement of sIgE antibodies to Ara h 1, 2, and 3 is useful in the diagnosis of PA and in the investigation of reactions to raw and roasted peanuts.

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Introduction

Peanut allergy (PA) prevalence in the USA is increasing over time [1]. Although lower prevalence has been reported in Asia [2], the adoption of a Westernized life style in Asian countries influences the reported increasing trend [3, 4].

An accurate diagnosis is essential to provide appropriate, potentially lifesaving, advice on how to prevent and manage allergic reactions and to prevent unnecessary di-

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etary restrictions in peanut-tolerant subjects [5, 6]. Introduction of testing individual peanut allergenic molecules [7] with component resolved diagnostic (CRD) is potentially capable of differentiating between sensitization and clinical reactivity avoiding the need of oral food challenge (OFC) [8, 9] especially in patients without a clear clinical history of PA [8, 10]. Ara h 2 (2S albumin)-sIgE is an immunodominant peanut allergen [7] which shows the best diagnostic accuracy [11, 12]. On the other hand, sensitization to nonspecific lipid-transfer protein in peanuts (nsLTP-Ara 9, 16, and 17), birch pollen Bet v 1 homologs (Ara h 8), and profilins (Ara h 5) is caused by cross-reactions [13–15].

The pattern of allergenic component recognition varies in peanut-sensitized patients from different geographical areas [16]. For instance, in the USA 56.7–90.0% of people were allergic to peanut storage proteins and frequently experience severe symptoms; in South Europe, patients are often sensitized to Ara h 9, and PA follows other plant-derived food allergies [16]; and Swedish patients have relatively high IgE-positive responses to Ara h 8, Bet v 1 homolog [17]. Measurement of IgE antibodies to rAra h 1, 2, and 3 has been proven useful in Asian countries like Japan [18], Singapore [19], Taiwan [19], and China [20].

Although in the Middle East consumption of roasted peanuts is common, the knowledge regarding PA is limited [21]. In the present study, we analyzed the relationship between sensitization patterns to peanut proteins and clinical manifestation in a group of patients with physician-diagnosed PA.

Materials and Methods

This is a cross-sectional study of children and adults with physician-diagnosed PA who were referred to the allergy clinic at the Allergy Centre, Kuwait, from April 2018 to January 2019. These patients had a clear history of an acute allergic reaction immediately after ingestion of a food in which peanut protein was the only possible allergen. All patients with physician-diagnosed PA underwent an allergic evaluation by completing a questionnaire and performing further tests. All patients completed a questionnaire, part of a clinical practice protocol, which included the following: patient's age at first occurrence of clinical manifestation, clinical symptoms, type of reaction, presence of other food allergy, and presence of other atopic diseases. The following tests were measured for all participants: peanut skin prick test (pSPT) (Diater, Leganés, Spain), serum total IgE, peanut-specific IgE (psIgE), sIgE to local pollens, and specific IgE directed against peanut protein components (Ara h 1–3, 8, and 9) by the ImmunoCap system (Phadia, Uppsala, Sweden).

At least 7 days before SPT, all patients refrained from antihistamine drugs. SPT was performed by single head prick lancets on

the volar aspect of the forearm, 2–3 cm from the wrist and the antecubital fossae. Histamine (10 mg/mL) and saline were used as positive and negative controls, respectively. Results were read 15–20 min following allergen extract application. A positive SPT to peanut allergen or inhalants was considered if the mean wheal diameter of SPT is ≥ 3 mm.

Serum total IgE, psIgE, and sIgE to local pollens were done on the same day of performing SPT. A cutoff level of psIgE and sIgE to local pollens ≥ 0.35 KUA/L was considered positive. A specific IgE directed against peanut protein components (Ara h 1–3, 8, and 9: with a lower limit of 0.35 KUA/L and an upper detection limit of 100 KUA/L) according to the manufacturer's proposed instructions was done in all patients.

Patients were divided into 2 groups, according to the age of the first known occurrence of clinical reaction after apparent peanut consumption: ≤ 6 years old (younger group) or > 6 years including adults (older group). The frequency of positivity and the level of peanut protein components in relation to clinical manifestation were analyzed, as well as cutoffs for the most common peanut proteins which can predict PA and severity of the reaction. Clinical symptoms were categorized as a local reaction if symptoms affected 1 organ only: skin (urticaria with/without angioedema/pruritis), oral allergy syndrome, and gastrointestinal or respiratory symptoms (bronchial-obstruction/dyspnea). Involvement of 2 or more organs, with or without cardiovascular compromise, which rapidly occurred after exposure to peanuts, was defined as a systemic reaction [6, 22].

Statistic

Nonparametric and parametric methods were used to calculate statistical significance. The distribution value was determined by D'Agostino and Pearson omnibus test normality. Student's *t* test, Mann-Whitney test, Fisher's test, and χ^2 test were used for calculating the difference between the groups. The ANOVA test was used to calculate the relative difference distribution variance between variables. The statistical hypotheses were tested at the level of $\alpha = 0.05$, and the difference between the groups in the sample was considered significant when $p < 0.05$. Statistical significance was depicted as $p < 0.05$, $p < 0.01$, and $p < 0.001$. All data were analyzed using GraphPadPrism version 7 (San Diego, CA, USA).

Results

From a total of 69 patients, the majority (75.4%) reported initial occurrence of PA in early childhood (≤ 6 years), while 24.6% of them reported it later. The median age of allergy onset was 2 years (1, 43). Patients who experienced the first clinical symptoms in early childhood exhibited a significantly bigger pSPT wheal size (6.0 vs. 4.0, $p = 0.0004$) and higher levels of total IgE (653 vs. 340, $p = 0.014$) and psIgE (2.8 vs. 0.5, $p = 0.0349$). They also showed both a positive result and a higher level for Ara h 1 (0.5 vs. 0.2, $p = 0.0271$), Ara h 2 (1 vs. 0, $p = 0.0002$), and Ara h 3 (0.2 vs. 0, $p = 0.0002$) and systemic allergic reactions, compared to patients from the other group (Table 1).

Table 1. Characteristics of patients regarding age of onset of symptoms

	≤6 years	>6 years	<i>p</i> value
Patients, <i>n</i> (%)	52 (75.4)	17 (24.6)	–
Females, <i>n</i> (%)	16 (30.8)	8 (47.1)	0.3519
Mean age, years	11.3±7.5	23.6±11.8	<0.0001*
Local allergic reaction, <i>n</i> (%)	34 (65.4)	17 (100)	0.0034*
Systemic allergic reaction, <i>n</i> (%)	18 (34.6)	0 (0.0)	
Total IgE, KUA/L	653.0 (0.0, 2,000)	340.0 (46.0, 1,220.0)	0.0149*
pSPT, mm	6.0 (0.0, 10.0)	4.0 (0.0, 6.0)	0.0004*
psIgE, KUA/L	2.8 (0.0, 100)	0.5 (0.0, 12.5)	0.0349*
Ara h positivity, <i>n</i> (%)			
Ara h 1	31 (59.6)	6 (35.3)	0.0404*
Ara h 2	33 (63.5)	1 (5.9)	0.0001*
Ara h 3	23 (44.2)	2 (11.8)	0.0334*
Ara h 8	9 (17.3)	1 (5.9)	0.4443
Ara h 9	25 (48.1)	10 (58.8)	0.5781
Ara h 1	0.5 (0.0, 100)	0.2 (0.0, 32.1)	0.0271*
Ara h 2	1.0 (0.0, 100)	0.0 (0.0, 1.3)	0.0002*
Ara h 3	0.2 (0.0, 91.9)	0.0 (0.0, 35.0)	0.02*
Ara h 8	0.0 (0.0, 91.7)	0.0 (0.0, 3.8)	0.681
Ara h 9	0.2 (0.0, 20.4)	0.1 (0.0, 49.1)	0.4191

Values for Ara h 1–3, 8, and 9 are expressed in KUA/L. * *p* value was significant.

Table 2. Total Pearson coefficient of correlation, 95% confidence interval, and *p* values for correlation of age and Ara h 1, Ara h 2, Ara h 3, Ara h 8, and Ara h 9

	Total Pearson coefficient	95% CI	<i>p</i> value
pSPT, mm			
≤6 years			
Ara h 1	–0.03153	–0.3045 to 0.2463	0.8261
Ara h 2	–0.05400	–0.3248 to 0.2250	0.7066
Ara h 3	–0.1527	–0.4110 to 0.1284	0.2848
Ara h 8	–0.02797	–0.3013 to 0.2496	0.8455
Ara h 9	–0.2298	–0.4754 to 0.04891	0.1047
>6 years			
Ara h 1	–0.2476	–0.6509 to 0.2647	0.338
Ara h 2	–0.2816	–0.6714 to 0.2303	0.2735
Ara h 3	–0.2785	–0.6696 to 0.2335	0.279
Ara h 8	0.3372	–0.1713 to 0.7039	0.1856
Ara h 9	0.2954	–0.2160 to 0.6796	0.2496
psIgE, KUA/L			
≤6 years			
Ara h 1	0.7231	0.5609–0.8319	<0.0001*
Ara h 2	0.7263	0.5655–0.8340	<0.0001*
Ara h 3	0.4451	0.1959–0.6402	0.0009*
Ara h 8	0.1594	–0.1188 to 0.4143	0.2591
Ara h 9	–0.1253	–0.3851 to 0.1529	0.3759
>6 years			
Ara h 1	0.8339	0.5895–0.9384	<0.0001*
Ara h 2	0.8340	0.5896–0.9385	<0.0001*
Ara h 3	–0.04425	–0.5141 to 0.4460	0.8661
Ara h 8	–0.03653	–0.5083 to 0.4522	0.8893
Ara h 9	–0.03999	–0.5109 to 0.4494	0.8789

Values for Ara h 1–3, 8, and 9 are expressed in KUA/L. * *p* value was significant.

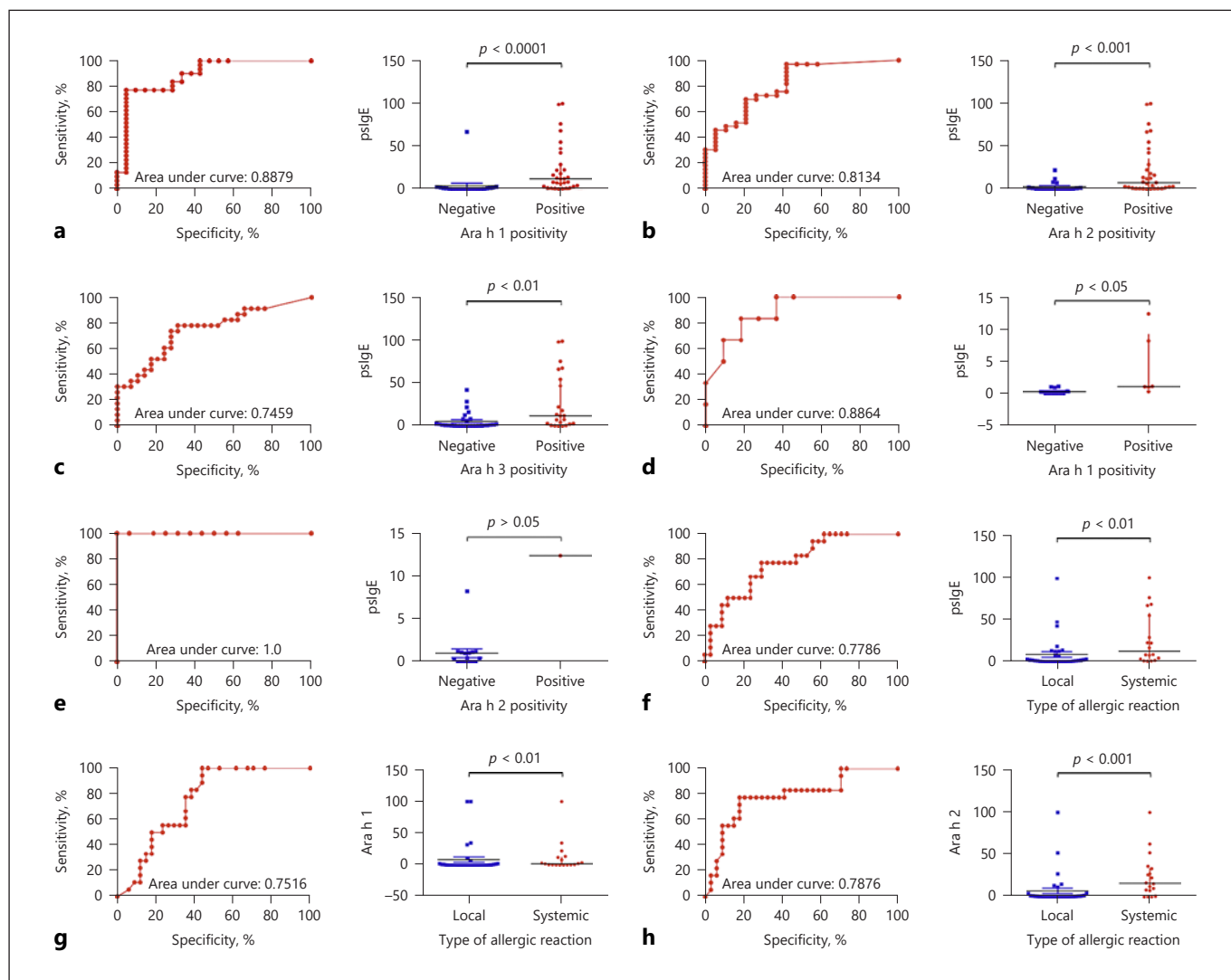


Fig. 1. **a–e** ROC analysis regarding levels of psIgE in predicting the positivity of Ara h 1 (**a**), Ara h 2 (**b**), and Ara h 3 (**c**) in patients with onset of allergic symptoms in the age of ≤ 6 years and of Ara h 1 (**d**) and Ara h 2 (**e**) in patients with onset of allergic symptoms in the age of > 6 years. **f–h** ROC analysis to detect the cutoff value of psIgE and Ara h 1–3 in predicting the systemic allergic reaction among patients with onset of allergic symptoms in the age of ≤ 6 years.

To detect diagnostic importance of pSPT and psIgE, their Pearson correlation was done with all the measured peanut allergen components (Ara h 1–3, 8, and 9). A positive correlation was detected between all 3 storage proteins (Ara h 1–3) in the younger group, while in the other group, a correlation was detected between Ara h 1 and 2 only. No significant correlation was observed between psIgE and Ara h 8 and 9 in either group, as well as no significant correlation between pSPT and any measured peanut allergen component (Table 1).

Systemic and local allergic reactions were compared in patients with onset of allergic symptoms in the younger group (Table 2). To detect the cutoff values of pSPT and psIgE, which could predict the positivity of Ara h mono-components, ROC analysis was done and applied only to a positive Pearson correlation. In other words, ROC analysis was done for psIgE and Ara h 1 and 2 for both groups, but also for psIgE and Ara h 3 in the patients with the onset of allergic symptoms in early childhood. ROC analysis regarding levels of psIgE in predicting the positivity of Ara h 1, Ara h 2, and Ara h 3 in patients with an allergic

Table 3. Cutoff value of psIgE, sensitivity, specificity, area under the curve, standard error, 95% confidence interval, and *p* values of ROC analysis in predicting positivity of Ara h 1, Ara h 2, and Ara h 3 in different groups

Age of onset of symptoms	Ara h	Cutoff of psIgE	Sensitivity, %	Specificity, %	Area under curve	SE	95% CI	<i>p</i> value
≤6 years	1	>2.77	77.42	90.48	0.89	0.05	0.79–0.98	<0.0001
	2	>22.25	30.3	100	0.81	0.06	0.69–0.93	<0.001
	3	>7.05	60.87	75.86	0.75	0.07	0.61–0.88	<0.01
>6 years	1	>4.74	33.3	100	0.89	0.08	0.73–1.04	<0.05

reaction in early childhood and of Ara h 1 and Ara h 2 in patients who had a first known occurrence of allergic reaction in the other group was done. Figure 1 shows the cutoff value of psIgE, sensitivity, specificity, area under the curve, standard error (SE), 95% confidence interval (CI), and *p* values of ROC analysis in predicting positivity of Ara h 1, Ara h 2, and Ara h 3 in the younger group. Moreover, ROC was also done to detect the cutoff value of psIgE, directed to storage proteins, in predicting the systemic allergic reaction. Cutoff value of psIgE, Ara h 1, 2, and 3, sensitivity, specificity, area under the curve, SE, 95% CI, and *p* values of ROC were analyzed in predicting the presence of systemic allergic reaction in patients with onset of allergic symptoms in early childhood. Results are shown in Table 3 and Figure 1.

By applying ROC analysis, we detected cutoff values of those peanut allergen components which showed a positive Pearson correlation. The calculation observed that for onset of allergic symptoms in the younger group, cutoff for Ara h 2 >22.25 KUA/L has 100% specificity, while cutoffs for Ara h 1 and 3 (>2.77 and >7.05, respectively), although statistically significant, showed less value of both sensitivity and specificity (90.48% and 75.86%; *p* = 0.001 and 0.01, respectively).

Furthermore, the results of the ROC analysis were used to detect the cutoff value of psIgE and Ara h 1–3, to predict systemic allergic reaction. We observed that psIgE to Ara h 2 ≥15.4 enabled the detection of possible systemic reaction, with sensitivity 55.56% and specificity 91.18%, area under the curve 0.79, SE 0.07, 95% CI: 0.65–0.92; *p* < 0.001 (Fig. 1). The calculation observed that for onset of allergic symptoms in the older group, cutoff for Ara h 1 >4.74 KUA/L has 100% specificity.

Discussion

Consumption of raw or roasted peanuts is common in Kuwait and introduced early on in children's diets. The knowledge regarding PA including cross-reactivity with

tree nuts or other pollen allergens is limited, and OFC is rarely performed [16]. A recent study conducted on 3,738 young Kuwaiti students estimated the self-reported prevalence of PA of 1.3% [21], similar to the rate reported in the Western world, probably due to adoption of a Westernized lifestyle. Previous studies have calculated 95% positive predictive value (PPV) for SPT if using SPT wheal ≥8 mm and psIgE with cutoff values ≥14 KUA/L. However, Codreanu et al. [23] conferred a cutoff point of psIgE of 0.23 KUA/L, 96.0% sensitivity, and 93.0% specificity investigating 237 French children, while Dang et al. [24] reported a cutoff point of 1.19 KUA/L yielded 60% sensitivity and 98% specificity for psIgE in 200 Australian infants. In the present study, although a median of psIgE showed lower level than 14 KUA/L, it was higher in the group of patients with onset of allergic symptoms in the younger group: 2.8 (0.0, 100) versus 0.5 (0.0, 12.5); *p* = 0.0349. Similar observations were documented with pSPT wheal size: 6.0 mm (0.0, 10.0) versus 4.0 (0.0, 6.0); *p* = 0.0004 (Table 1). Several studies showed that measurements of IgE to major peanut allergen Ara h 2 are more useful in predicting clinical PA than the currently used skin or blood tests based on the whole extract [13, 16, 25]. The obtained results from the current study also observed significantly higher numbers of positive sIgE to all 3 peanut storage proteins, the highest being Ara h 2 (63.5%), followed by Ara h 1 (59.6%). However, in a smaller number of patients, Ara h 3 was positive in patients with onset of allergic symptoms in the younger group (44.2%) (Table 1). Furthermore, the obtained results documented a positive correlation between psIgE and Ara h 1–3 in the same group. On the other hand, no correlation was found between psIgE and Ara h 8 and 9 in either group. Lack of correlation between psIgE and Ara h 8 and 9, especially in group 2, suggested further investigation of cross-reactivity with other food and potential misdiagnosis of primary PA. Although Ara h 9, nsLTP, in peanuts is a widespread pan-allergen and might be responsible for allergic reactions in particular geographical areas, sensitization to Ara h 9 in all our patients was insignificant, with the me-

dian level being below a lower limit (Table 1). This is in contrast to the results documented in the studies from South Europe [26, 27] and some Asian countries [20] where Ara h 9, as a single component, might be a primary sensitizer agent in peanut-sensitized patients [27] with more than half of the PA patients being sensitized to peach LTP pru p3 in a South Europe study [28]. In addition, Ara h 8, an important peanut allergen in North Europe, was undetectable in both groups of patients (0.0 [0.0, 91.7] vs. 0.0 [0.0, 3.8], $p = 0.681$) (Table 1). Likely because birch pollen is not present in the Middle East where allergic rhinitis is linked to the abundant local weeds especially *Salsola kali*, possible cross-reactivity between peanuts and *Salsola kali* has been investigated. However, no cross-reactivity was found in patients with allergic rhinitis and positive skin test to *Salsola kali* [29]. Our results confirmed a poor PPV of pSPT, frequently noticed with other food allergen extracts. Similarly, Klemans et al. [10] reviewed 21 studies in pediatric cohorts and confirmed that sIgE to Ara h 2 had the highest odds ratio (OR) in predicting PA, compared to SPT (in any geographical location), and as a result, the authors suggested the replacement of previous tests with Ara h 2 in daily clinical practice. Our results supported the importance of both Ara h 1 and 2 as the main elicitors of allergic reactions in children and their severity. This was similarly observed by others [18] (Table 2).

The results from ROC analysis suggest that the OFC should be considered for definite diagnosis of PA only if the level of Ara h 2 is <22.25 KUA/L and suggest that physician-diagnosed PA, based on pSPT and pIgE of the whole peanut extract, often offers an overestimated diagnosis of PA in our patients. This can be compared with studies from northern Europe reporting Ara h 2 cutoff level with 100% PPV for a positive provocation test ≥ 1.75 KUA/L [30] or >5.17 KUA/L [10].

One of the limitations of this study included age heterogeneity. To avoid this bias, all patients were divided according to their age at the first known clinical reaction. Due to the high cutoff point of Ara h 2, we considered that

cross-reactivity should be further investigated in forthcoming studies in the region.

In conclusion, the pattern of sensitization to peanut proteins in the Middle East was similar to that of the Western world. The obtained results support the diagnostic accuracy of Ara h 2 across different geographical regions, even in predicting systemic reactions in patients who develop PA in early childhood. Measurement of IgE antibodies to Ara h 1–3 is useful in the diagnosis of PA and in the investigation of reactions to raw and roasted peanuts. Using CRD offers a wider sensitization profile for patients and might reduce the number of OFC (once the cutoffs of PPV are found).

Statement of Ethics

All patients were informed about the risk and outcomes of the procedure and provided informed consent. This study protocol was reviewed and approved by the Kuwait Ministry of Health, Approval No. 2017/517.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors have contributed equally.

Data Availability Statement

All data generated or analyzed during this study are included in this article or its online supplementary material files (for all online suppl. material, see www.karger.com/doi/10.1159/000519297). Further enquiries can be directed to the corresponding author.

References

- 1 Sicherer SH, Muñoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol*. 2010 Jun; 125(6):1322–6.
- 2 Suratannon N, Ngamphaiboon J, Wongpiyabovorn J, Puripokai P, Chatchatee P. Component-resolved diagnostics for the evaluation of peanut allergy in a low-prevalence area. *Pediatr Allergy Immunol*. 2013 Nov; 24(7):665–70.
- 3 Liew WK, Chiang WC, Goh AE, Lim HH, Chay OM, Chang S, et al. Paediatric anaphylaxis in a Singaporean children cohort: changing food allergy triggers over time. *Asia Pac Allergy*. 2013 Jan; 3(1):29–34.
- 4 Loh W, Tang MLK. The Epidemiology of food allergy in the global context. *Int J Environ Res Public Health*. 2018 Sep 18; 15(9):2043.
- 5 Custovic A, Nicolaou N. Peanut allergy: overestimated in epidemiology or underdiagnosed in primary care? *J Allergy Clin Immunol*. 2011 Mar; 127(3):631–2.

- 6 Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, Bindslev-Jensen C, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy*. 2014 Aug;69(8):1008–25.
- 7 Koppelman SJ, Wensing M, Ertmann M, Knulst AC, Knol EF. Relevance of Ara h1, Ara h2 and Ara h3 in peanut-allergic patients, as determined by immunoglobulin E Western blotting, basophil-histamine release and intracutaneous testing: Ara h2 is the most important peanut allergen. *Clin Exp Allergy*. 2004 Apr;34(4):583–90.
- 8 Nicolaou N, Custovic A. Molecular diagnosis of peanut and legume allergy. *Curr Opin Allergy Clin Immunol*. 2011 Jun;11(3):222–8.
- 9 Schussler E, Kattan J. Allergen component testing in the diagnosis of food allergy. *Curr Allergy Asthma Rep*. 2015 Sep;15(9):55.
- 10 Klemans RJ, Otte D, Knol M, Knol EF, Meijer Y, Gmelig-Meyling FH, et al. The diagnostic value of specific IgE to Ara h 2 to predict peanut allergy in children is comparable to a validated and updated diagnostic prediction model. *J Allergy Clin Immunol*. 2013 Jan;131(1):157–63.
- 11 Klemans RJ, van Os-Medendorp H, Blankestijn M, Bruijnzeel-Koomen CA, Knol EF, Knulst AC. Diagnostic accuracy of specific IgE to components in diagnosing peanut allergy: a systematic review. *Clin Exp Allergy*. 2015 Apr;45(4):720–30.
- 12 Flores Kim J, McCleary N, Nwaru BI, Stoddart A, Sheikh A. Diagnostic accuracy, risk assessment, and cost-effectiveness of component-resolved diagnostics for food allergy: a systematic review. *Allergy*. 2018 Aug;73(8):1609–21.
- 13 Nicolaou N, Poorafshar M, Murray C, Simpson A, Winell H, Kerry G, et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. *J Allergy Clin Immunol*. 2010 Jan;125(1):191–7.e1–13.
- 14 Hoffmann-Sommergruber K, Pfeifer S, Bublin M. Applications of molecular diagnostic testing in food allergy. *Curr Allergy Asthma Rep*. 2015 Sep;15(9):56.
- 15 Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, et al. EAACI molecular allergology user's guide. *Pediatr Allergy Immunol*. 2016 May;27 Suppl 23:1–250.
- 16 Vereda A, van Hage M, Ahlstedt S, Ibanez MD, Cuesta-Herranz J, van Odijk J, et al. Peanut allergy: clinical and immunologic differences among patients from 3 different geographic regions. *J Allergy Clin Immunol*. 2011 Mar;127(3):603–7.
- 17 Martinet J, Couderc L, Renosi F, Bobée V, Marguet C, Boyer O. Diagnostic value of antigen-specific immunoglobulin E immunoassays against Ara h 2 and Ara h 8 peanut components in child food allergy. *Int Arch Allergy Immunol*. 2016;169(4):216–22.
- 18 Ebisawa M, Movérare R, Sato S, Maruyama N, Borres MP, Komata T. Measurement of Ara h 1-, 2-, and 3-specific IgE antibodies is useful in diagnosis of peanut allergy in Japanese children. *Pediatr Allergy Immunol*. 2012 Sep;23(6):573–81.
- 19 Chiang WC, Pons L, Kidon MI, Liew WK, Goh A, Wesley Burks A. Serological and clinical characteristics of children with peanut sensitization in an Asian community. *Pediatr Allergy Immunol*. 2010 Mar;21(2 Pt 2):e429–38.
- 20 Ma S, Nie L, Li H, Wang R, Yin J. Component-resolved diagnosis of peanut allergy and its possible origins of sensitization in China. *Int Arch Allergy Immunol*. 2016;169(4):241–8.
- 21 Ziyab AH. Prevalence of food allergy among schoolchildren in Kuwait and its association with the coexistence and severity of asthma, rhinitis, and eczema: a cross-sectional study. *World Allergy Organ J*. 2019;12(4):100024.
- 22 Cianferoni A, Muraro A. Food-induced anaphylaxis. *Immunol Allergy Clin North Am*. 2012 Feb;32(1):165–95.
- 23 Codreanu F, Collignon O, Roitel O, Thouvenot B, Sauvage C, Vilain AC, et al. A novel immunoassay using recombinant allergens simplifies peanut allergy diagnosis. *Int Arch Allergy Immunol*. 2011;154(3):216–26.
- 24 Dang TD, Tang M, Choo S, Licciardi PV, Koplín JJ, Martin PE, et al. Increasing the accuracy of peanut allergy diagnosis by using Ara h 2. *J Allergy Clin Immunol*. 2012 Apr;129(4):1056–63.
- 25 Keet C, Plesa M, Szegal D, Shreffler W, Wood R, Dunlop J, et al. Ara h 2-specific IgE is superior to whole peanut extract-based serology or skin prick test for diagnosis of peanut allergy in infancy. *J Allergy Clin Immunol*. 2021 Mar;147(3):977–83 e2.
- 26 Pascal M, Munoz-Cano R, Reina Z, Palacin A, Vilella R, Picado C, et al. Lipid transfer protein syndrome: clinical pattern, cofactor effect and profile of molecular sensitization to plant-foods and pollens. *Clin Exp Allergy*. 2012 Oct;42(10):1529–39.
- 27 Asero R, Piantanida M, Pinter E, Pravettoni V. The clinical relevance of lipid transfer protein. *Clin Exp Allergy*. 2018 Jan;48(1):6–12.
- 28 Zambrano Ibarra G, Fuentes Aparicio V, Infante Herrero S, Blanca M, Zapatero Remon L. Peanut allergy in Spanish children: comparative profile of peanut allergy versus tolerance. *Int Arch Allergy Immunol*. 2019;178(4):370–6.
- 29 Al-Ahmad M, Rodriguez-Bouza T, Fakim N, Pineda F. Extensive cross-reactivity between salsola kali and salsola imbricata. *J Investig Allergol Clin Immunol*. 2018;28(1):29–36.
- 30 Kansen HM, van Erp FC, Knulst AC, Ehlers AM, Lyons SA, Knol EF, et al. Accurate prediction of peanut allergy in one-third of adults using a validated Ara h 2 cutoff. *J Allergy Clin Immunol Pract*. 2021 Apr;9(4):1667–74 e3.