International Archives of Allergy and Immunology

Clinical Allergy – Brief Report

Int Arch Allergy Immunol 2021;182:153–157
DOI: 10.1159/000510314

Received: June 30, 2020
Accepted: July 20, 2020
Published online: September 14, 2020

Sensitization to Local Seafood Allergens in Adult Patients with Atopic Dermatitis in Malaysia

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Keywords
Atopic dermatitis · Shellfish · Crustaceans · Fish · Mollusk · Seafood sensitization

Abstract
Background: Seafood is an important source of nutrition in Asia. However, it was believed to cause or aggravate atopic dermatitis (AD). ***Objectives:*** We aim to determine relevant seafood sensitization among adults with AD and investigate cross-sensitization to aeroallergens. ***Methods:*** One hundred thirty-two adults with AD who were subjected to skin prick test (SPT) with 7 common local seafood allergens (anchovy, tuna, mackerel, squid, giant freshwater prawn, shrimp, and crab), house dust mites (HDMs), and cockroach were analyzed retrospectively. ***Results:*** The median age of the study subjects was 32 years (range 17–77 years) with a male to female ratio of 1:3. The mean duration of AD was 16 years. Eighty-two patients (62.2%) had other atopic conditions. Using SCORAD, 44.7% had mild, 42.4% moderate, and 12.9% severe disease. Eighty-six patients (65.2%) self-reported to have seafood allergy, with the main symptoms of transient pruritus and erythema within 2 h of ingestion. SPT revealed 51.5% of the patients were sensitized to at least 1 of the 7 seafood allergens. The relevant sensitization rate was 45.1%. Interestingly, 46% of those without a history of seafood allergy developed at least 1 positive reaction in the SPT. Prawn, shrimp, and crab were the 3 most frequently sensitized allergens. Nearly all patients (98.3%) who were sensitized to crustaceans were also sensitized to HDMs and/or cockroach. There was no significant correlation between a positive SPT to seafood with age, age of onset of AD, duration, and severity of AD, and the presence of other atopic diatheses. ***Conclusion:*** The relevant sensitization rate of local seafood among adults with AD was 45.1%.

Introduction

Food is believed by many to be the cause and aggravating factor of atopic dermatitis (AD) [1, 2]. Avoidance of seafood, in particular, has been documented in up to 64% of AD in various countries, including the UK, Switzerland, Korea, Hong Kong, and Malaysia [2–8]. Interestingly, seafood allergy has not been studied extensively in adults with AD. Here, we aimed to determine the relevant

Edited by: H.-U. Simon, Bern.

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Table 1. Demographic data of 132 subjects with AD

Median age (range), years	32 (17–77)
Male:Female ratio	1:3
Median age of onset of AD (range), years	13 (infancy – 66)
Mean duration of disease (range), years	16 (4 months – 54)
Types of other atopic diatheses, *n* (%)	
Allergic rhinitis	60 (45.5)
Bronchial asthma	31 (23.5)
Allergic conjunctivitis	22 (16.7)
Urticaria	26 (19.7)
Presence of family history of atopy, *n* (%)	116 (87.9)
Present predominant cutaneous presentation, *n* (%)	
Eczema at flexures	53 (40.2)
Papular eczema	43 (32.6)
Lichen simplex chronicus	12 (9.1)
Hand and feet eczema	12 (9.1)
Discoid eczema	7 (5.3)
Generalized xerosis	4 (3.0)
Erythroderma	1 (0.8)
Disease activity using SCORAD	
Mean score (range)	29.3 (0–73)
Mild (0–24.9), *n* (%)	59 (44.7)
Moderate (25–49.9), *n* (%)	56 (42.4)
Severe (50–103), *n* (%)	17 (12.9)

AD, atopic dermatitis.

Table 2. SPT results of 132 adults with AD and the sensitization rate (positive reaction) of allergens tested

Category of history	
Positive history of "seafood allergy" (*n* = 82)	
Negative SPT	37 (45.1)
Positive SPT, clinically related seafood	37 (45.1)
Positive SPT, clinically unrelated	8 (9.8)
Negative history of "allergy" to 7 seafood tested (*n* = 50)	
Positive SPT	23 (46.0)
Negative SPT	27 (54.0)
Allergens	
Local seafood allergens	
Macrobrachium rosenbergii (giant freshwater prawn)	51 (38.6)
Parapenaeopsis hardwickii (shrimp)	48 (36.4)
Portunus pelagicus (blue crab)	43 (32.6)
Loligo edulis (squid)	17 (12.9)
Scomberomorus commerson (mackerel)	16 (12.1)
Thunnus tonggol (tuna)	15 (11.4)
Stolephorus commersonnii (anchovy)	12 (9.1)
Inhalant allergens	
Dermatophagoides mix	96 (72.7)
Blomia tropicalis	93 (70.5)
Blattella germanica	45 (34.1)

Values are given as n (%). AD, atopic dermatitis; SPT, skin prick test.

seafood sensitization among adults with AD and to investigate the cross-sensitization between seafood and aeroallergens.

Materials and Methods

We retrospectively reviewed the skin prick test (SPT) results of 132 patients with AD aged 17 years and above for seafood sensitization and aeroallergen (house dust mites (HDMs) and cockroach) cross-sensitization, performed at the Dermatology Clinic, Kuala Lumpur Hospital from September 2014 to June 2015. The extent and severity of AD was assessed by using SCORAD (0–103) [9]. The anamnestic history after seafood intake was also retrieved. The seven most consumed seafood were tested using locally produced allergens, as previously described (see online suppl. file; see www.karger.com/doi/10.1159/000510314 for all online suppl. material) [10, 11]. These included anchovy (*Stolephorus commersonnii*), mackerel (*Scomberomorus commerson*), tuna (*Thunnus tonggol*), squid (*Loligo edulis*), shrimp (*Parapenaeopsis hardwickii*), giant freshwater prawn (*Macrobrachium rosenbergii*), and blue crab (*Portunus pelagicus*). HDMs (*Dermatophagoides mix* and *Blomia tropicalis*) and cockroach (*Blattella germanica*) (ALK Abello, Madrid, Spain) were also tested. Descriptive statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS 19.0, IBM, Armonk, NY, USA). Normally distributed continuous variables were summarized as mean, while non-normally distributed variables were expressed as median. For categorical variables, frequencies and percentages (%) were tabulated. The significance level was set at $p < 0.05$.

Results

The demographic characteristics are shown in Table 1. Nearly two-thirds of the patients (62.2%) had other concomitant atopic diatheses, with allergic rhinitis being the most common. Out of 132 patients, 86 (65.2%) claimed to have seafood allergy in the past. About 84.8% of the allergies were caused by shellfish and 15.2% were due to fish, with a ratio of 5.6:1 (online suppl. Table 1). The total number of self-reported reactions experienced was 855, with most of the subjects having had mild skin reactions within 2 h of ingestion of the seafood (online suppl. Table 2). Of these, 5.5% of the patients claimed to have worsening of existing eczema following seafood ingestion. SPT revealed that 68 patients (51.5%) were sensitized to at least 1 of the 7 seafood allergens (Table 2). The relevant sensitization rate was 45.1%. Interestingly, 46% of those without a history of seafood allergy developed at least 1 positive reaction to seafood allergens in the SPT. Giant freshwater prawn, shrimp, and crab were the 3 most frequently sensitized allergens, with the sensitization rate of between 32 and 39% (Table 2). There were 60 patients (45.5%) with a positive SPT to crus-

Table 3. Seafood sensitization in allergic rhinitis, bronchial asthma, chronic urticaria, and AD

Special group	Author, year	Country	*n*	Age, years	% Sensitized (SPT)												
					giant freshwater prawn	shrimp	crab	squid	mackerel	anchovy	hilsa fish	Rohu fish	fish mix	shell fish mix	shrimp and fish	tiger prawn	sea crab
Allergic rhinitis	Gendeh et al. [28], 2000	Malaysia	148	Adult	–	48.0	–	–	–	–	–	–	–	–	–	–	–
	Gendeh et al. [29], 2004	Malaysia	141	<12	–	24.8	24.1	10.6	2.8	1.4	–	–	–	–	–	–	–
	Zahedi et al. [30], 2011	Malaysia	580	5–12	–	18.0	18.5	8.7	2.7	1.9	–	–	–	–	–	–	–
	Lin et al. [31], 2015	China	2,841	3–12	–	36.3	–	–	–	–	–	–	–	–	–	–	1.51
Respiratory allergy (bronchial asthma±allergic rhinitis)	Mandal et al. [32], 2009	India	800	5–60	–	53.5	–	–	–	–	4.3	11.8	–	–	–	–	–
Chronic urticaria	Litu et al. [33], 1998	Finland	91	13–80	–	–	–	–	–	–	–	–	–	–	8.8	–	–
	Kulthanan et al. [34], 2008	Thailand	88	18–65	5.7	9.1	12.5	–	3.4	–	–	–	–	–	–	12.5	9.1
AD	Hon et al. [35], 2008	Hong Kong	90	<18	–	–	–	–	–	–	–	–	36	22	–	–	–
	Hon et al. [36], 2012	Hong Kong	816	<18	–	–	–	–	–	–	–	–	15.3	46.2	–	–	–
	Current study, 2016	Malaysia	132	>17	38.6	36.4	32.6	13.4	12.6	9.4	–	–	–	–	–	–	–

AD, atopic dermatitis; SPT, skin prick test.

taceans (giant freshwater prawn, shrimp, and/or crab). From these, 98.3% (59 out of 60 patients) were also sensitized to inhalant allergens (*D. mix*, *B. tropicalis*, and/or *Blattella germanica*). There were 98 patients who tested positive to at least 1 inhalant allergen. Of these, 60.2% (59 out of 98) were sensitized to crustaceans. Thirteen out of 17 subjects (76.5%) with severe AD (SCORAD of 50–103) were sensitized to at least 1 of the seafood allergens. It was higher than that in those with mild (SCORAD of 0–24.9) and moderate (SCORAD of 25–49.9) AD (50.8 and 42.9%, respectively). However, the difference was not statistically significant ($p = 0.052$). In addition, there was no significant correlation between seafood sensitization and age ($p = 0.20$), age of onset of AD ($p = 0.86$), duration of AD ($p = 0.21$), and the presence of other atopic diatheses ($p = 0.24$).

Discussion

More studies have reported that a significant proportion of subjects with AD (especially children) experienced worsening of eczema with certain food in addition to the immediate symptoms. In contrast to the popular belief that seafood is highly sensitizing, higher fish consumption is associated with lower risk of eczema [12]. Nevertheless, eczema developed after 2 years of age was observed to be associated with shellfish allergy in a Canadian study [13].

It has been well studied that the most common allergen causing shellfish allergy is tropomyosin, followed by arginine kinase [14]. On the other hand, parvalbumin is the most common allergen in fish [14]. Tropomyosin shares significant homology to the allergen found in arthropods, which include the HDMs and cockroaches [14]. Strikingly, nearly all of the patients who were sensitized to crustacean(s) in the current study were sensitized to HDM(s). This finding is consistent with various study findings of a high rate of cross-reactivity between seafood allergen and this aeroallergen [15, 16]. The complex interrelationship between HDM and shrimp allergens has been extensively studied in the attempt to determine the primary sensitizer. Interestingly, sublingual HDM immunotherapy has been shown to improve shrimp tolerance in a shrimp-allergic patient [17].

Seafood sensitization pattern in patients with atopic diathesis [18–26], which studied individually or collectively patients with allergic rhinitis and asthma, tends to have a higher incidence of shellfish sensitization, as shown in studies done in Malaysia [18–20] and India [22]. The seafood sensitization among patients with chronic urticaria was found to be lower, between 5 and 12% [23, 24]. SPTs done on children (<18 years) with AD in Hong Kong showed a sensitization rate of 46.2% to shellfish and 15.3% to fish [25, 26]. There is no similar study done on adults with AD. This present study showed a fairly high shellfish sensitization in AD, which was nearly 40%. Interestingly, the sensitization rates to fish (mackerel, anchovy, and tuna) in the current cohort were much higher than that in other reports, at around 10% (Table 3).

As shown in this study, the reported seafood allergy was 65% by history and the relevant sensitization rate was 45%. This revealed that history alone is not reliable to ascertain sensitization. A few conditions such as Scombroid poisoning, marine algal toxin poisoning, paralytic shellfish toxin poisoning, diarrhetic shellfish poisoning, ciguatera poisoning, bacterial and viral contamination, intolerance to histamine in the seafood, and anisakiasis should be considered [14]. These conditions are not IgE mediated, but the symptoms are type 1 hypersensitivity-like reactions. We had 8 patients in the cohort who presented with a positive SPT to at least 1 of the 7 seafood tested, which did not correlate historically. Here, we probably need to bear in mind the issue of cross contamination of seafood products during food preparation.

Complete seafood avoidance is practically difficult in this region as it is one of the major food components and source of protein in the diet. This is because cross contamination of seafood products with other types of food resulting from undiscriminated food handling is known to be quite common. Immuno-tolerance to seafood may have occurred among subjects who continue to take seafood despite having mild reactions which are regarded as primary skin lesions of AD. This probably explained why 46% of the current cohort who claimed to have no history of seafood allergy demonstrated a positive SPT to seafood. Allergen-specific immunotherapy for shellfish allergy using novel immunotherapeutic strategies, such as shrimp extract, hypoallergens, high hydrostatic pressure processing, chemical modification, polypeptide fragmentation, epitope manipulation, immunoregulatory peptides, and DNA vaccine, is still in experimental stages [27]. Hence, treating seafood allergies without avoiding seafood per se may not be impossible.

Our data contribute important yet long unrevealed facts about the local seafood sensitization rate among adults with AD in this region of Asia. It serves as supplementary data for further research, such as oral challenge and oral immunotherapy with seafood in patients with atopic diathesis who are sensitized to seafood. The comprehensiveness of our data is limited by the retrospective nature of the study, and it was not followed by confirmatory, double-blind, placebo-controlled seafood challenge tests. Apart from that, we recruited only a small number of patients with severe AD. The current data showed that more than 75% of patients with severe atopic eczema were sensitized to seafood. However, it was not statistically significant.

In conclusion, two-thirds of adults with AD self-reported to have seafood allergy. The most commonly reported reactions were transient pruritus and erythema. The relevant sensitization rate of local seafood was 45.1%. Crustacean was the most sensitizing seafood. Its sensitization rate was 3 times higher than that of mollusks and fish. The sensitization rate of seafood did not correlate with the age of patients, duration of atopic eczema, severity of skin disease, and the presence of other atopic conditions. There was also high cross-sensitizations between shellfish and HDMs.

Acknowledgements

The authors would like to thank the Director General of Health, Malaysia, for permission to publish this study.

Statement of Ethics

This study has been undertaken on secondary data retrieved from the Department of Dermatology, Hospital Kuala Lumpur. The Malaysian Research and Ethics Committee (MREC) allows the use of secondary data, provided that they have been anonymized for analysis.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors did not receive any funding.

Author Contributions

M.M. Tang, F. Bakthiar, and A. Johar conceived and planned the study design; H.L. Lee, M.M. Tang, and Z.H. Mohamad Yadzir performed the study and were involved in acquisition of data; H.L. Lee, M.M. Tang, and F. Bakthiar analyzed and interpreted the data; H.L. Lee, M.M. Tang, and F. Bakthiar drafted the manuscript; and all of the authors read and approved the final version of this work.

References

1 Webber SA, Graham-Brown RA, Hutchinson PE, Burns DA. Dietary manipulation in childhood atopic dermatitis. Br J Dermatol. 1989;121(1):91–8.
2 Jensen P. Use of alternative medicine by patients with atopic dermatitis and psoriasis. Acta Derm Venereol. 1990;70(5):421–4.
3 Barth GA, Weigl L, Boeing H, Disch R, Borelli S. Food intake of patients with atopic dermatitis. Eur J Dermatol. 2001;11(3):199–202.

4 Lim H, Song K, Kim R, Sim J, Park E, Ahn K, et al. Nutrient intake and food restriction in children with atopic dermatitis. Clin Nutr Res. 2013;2(1):52–8.
5 Johnston GA, Bilbao RM, Graham-Brown RA. The use of dietary manipulation by parents of children with atopic dermatitis. Br J Dermatol. 2004;150(6):1186–9.
6 Hon KL, Leung TF, Kam WY, Lam MC, Fok TF, Ng PC. Dietary restriction and supplementation in children with atopic eczema. Clin Exp Dermatol. 2006;31(2):187–91.
7 Leung TF, Wang SS, Kwok FY, Leung LW, Chow CM, Hon KL. Assessment of dietary food and nutrient intake and bone density in children with eczema. Hong Kong Med J. 2017;23(5):470–9.
8 Low DW, Jamil A, Md Nor N, Kader Ibrahim SB, Poh BK. Food restriction, nutrition status, and growth in toddlers with atopic dermatitis. Pediatr Dermatol. 2020;37(1):69–77.
9 Severity scoring of atopic dermatitis: the SCORAD index. Consensus report of the European task force on atopic dermatitis. Dermatology. 1993;186(1):23–31.
10 Yadzir ZH, Misnan R, Abdullah N, Bakhtiar F, Arip M, Murad S. Identification of the major allergen of Macrobrachium rosenbergii (giant freshwater prawn). Asian Pac J Trop Biomed. 2012;2(1):50–4.
11 Misnan R, Murad S, Jones M, Taylor G, Rahman D, Arip M, et al. Identification of the major allergens of Indian scad (Decapterus russelli). Asian Pac J Allergy Immunol. 2008; 26(4):191–8.
12 Zhang GQ, Liu B, Li J, Luo CQ, Zhang Q, Chen JL, et al. Fish intake during pregnancy or infancy and allergic outcomes in children: a systematic review and meta-analysis. Pediatr Allergy Immunol. 2017;28(2):152–61.
13 Becker S, Gröger M, Canis M, Pfrogner E, Kramer MF. Tropomyosin sensitization in house dust mite allergic patients. Eur Arch Otorhinolaryngol. 2012;269(4):1291–6.
14 Ruethers T, Taki AC, Johnston EB, Nugraha R, Le TTK, Kalic T, et al. Seafood allergy: a comprehensive review of fish and shellfish allergens. Mol Immunol. 2018;100:28–57.
15 Wong L, Huang CH, Lee BW. Shellfish and house dust mite allergies: is the link tropomyosin? Allergy Asthma Immunol Res. 2016; 8(2):101–6.
16 Asero R, Pravettoni V, Scala E, Villalta D. House dust mite-shrimp allergen interrelationships. Curr Allergy Asthma Rep. 2020; 20(4):9.
17 Cortellini G, Spadolini I, Santucci A, Cova V, Conti C, Corvetta A, et al. Improvement of shrimp allergy after sublingual immunotherapy for house dust mites: a case report. Eur Ann Allergy Clin Immunol. 2011;43(5):162–4.
18 Gendeh BS, Murad S, Razi AM, Abdullah N, Mohamed AS, Kadir KA. Skin prick test reactivity to foods in adult Malaysians with rhinitis. Otolaryngol Head Neck Surg. 2000; 122(5):758–62.
19 Gendeh BS, Mujahid SH, Murad S, Rizal M. Atopic sensitization of children with rhinitis in Malaysia. Med J Malaysia. 2004;59(4):522–99.
20 Zahedi FD, Gendeh BS, Husain S. Sensitisation to common allergens in children with allergic rhinitis. Brunei Int Med J. 2011;7(4): 200–6.
21 Lin H, Lin R, Li N. Sensitization rates for various allergens in children with allergic rhinitis in Qingdao, China. Int J Environ Res Public Health. 2015;12(9):10984–94.
22 Mandal J, Das M, Roy I, Chatterjee S, Barui NC, Gupta-Bhattacharya S. Immediate hypersensitivity to common food allergens: an investigation on food sensitization in respiratory allergic patients of Calcutta, India. World Allergy Organ J. 2009;2(1):9–12.
23 Liutu M, Kalimo K, Uksila J, Kalimo H. Etiologic aspects of chronic urticaria. Int J Dermatol. 1998;37(7):515–9.
24 Kulthanan K, Jiamton S, Rutnin NO, Insawang M, Pinkaew S. Prevalence and relevance of the positivity of skin prick testing in patients with chronic urticaria. J Dermatol. 2008; 35(6):330–5.
25 Hon KL, Leung TF, Ching G, Chow CM, Luk V, Ko WS, et al. Patterns of food and aeroallergen sensitization in childhood eczema. Acta Paediatr. 2008;97(12):1734–7.
26 Hon KL, Wang SS, Wong WL, Poon WK, Mak KY, Leung TF. Skin prick testing in atopic eczema: atopic to what and at what age? World J Pediatr. 2012;8(2):164–8.
27 Wai CYY, Leung NYH, Chu KH, Leung PSC, Leung ASY, Wong GWK, et al. Overcoming shellfish allergy: how far have we come? Int J Mol Sci. 2020;21(6):2234.