

Low resolution rates of seafood allergy



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Clinical Implications

- This is the first cohort study to assess resolution rates in seafood allergy. Our findings indicate a low resolution rate for seafood allergy.

TO THE EDITOR:

Seafood allergy includes allergy to either fish or shellfish although the main allergenic proteins differ between these groups.¹ Worldwide prevalence of allergy to fish is reported to be as high as 1.5% for adults and 7% for children, whereas shellfish allergy is reported to affect up to 2% of adults and 5.5% of children.² The prevalence estimates are influenced by geographic location, race/ethnicity, age, and the diagnostic criteria.² Furthermore, food poisoning (scombroid and ciguatera fish poisoning), or an immune-mediated reaction to parasites infesting fish may be misinterpreted as an allergic reaction and hence contribute to an overestimate of an IgE-mediated seafood allergy. In a nationwide Canadian telephone survey, 0.6% of adults and 1.0% of children self-reported fish allergy and shellfish allergy was reported by 1.4% of adults and 1.9% of children.³ Similarly, in a telephone survey conducted by Sicherer in the United States, 0.5% of adults and 0.2% of children self-reported fish allergy and shellfish allergy was reported in 2.5% versus 0.5%, respectively.⁴ Seafood is therefore a relatively prevalent group of allergens and together with peanut and tree nut accounts for the most severe cases of food-induced anaphylaxis. Despite this, seafood allergy has attracted much less research attention than other food allergies, such as peanut. Furthermore, there is only 1 study assessing change in specific IgE levels to shrimp over time, indicating no significant temporal changes in levels,⁵ and there are no studies assessing the rate of clinical seafood allergy resolution. The purpose of our study was to estimate the seafood allergy resolution rate in Canadians diagnosed with seafood allergy.

Patients meeting criteria for fish/shellfish allergy were recruited through the allergy clinics at the Montreal and British Columbia Children's Hospitals and from Food Allergy Canada, an allergy advocacy organization, between 2011 and 2016. Patients were approached by our research team member at participating centers. Consenting patients/legal guardians completed a questionnaire at study enrolment, and medical charts were reviewed to collect data regarding their initial and most severe reaction to fish/shellfish, including details on the food ingested, signs, and symptoms, time duration between seafood contact and reaction, and initial skin prick test (SPT) wheal size and/or specific IgE levels if available. Recruitment from Food Allergy Canada differed: patients were informed of our research in advocacy newsletters and at annual meetings. Interested individuals were asked to contact our research team via telephone or e-mail and provide their contact information. They were then mailed a consent form, questionnaire, and request for release of medical information. All participants had to complete a resolution questionnaire. Information was also collected on demographic characteristics and personal history of atopy.

Participants were considered allergic to fish/shellfish if they met at least 1 of the following criteria³: (1) Convincing history and positive SPT result. (2) Specific IgE levels for fish of at least 20 kU/L (in the absence of exposure/convincing history).⁶ (3) Positive oral challenge.

A convincing clinical history referred to at least 2 mild signs and/or symptoms or 1 moderate or severe sign and/or symptom that was likely IgE-mediated and occurred within 120 minutes of seafood ingestion, skin contact, or inhalation. Mild signs/symptoms included pruritus, urticaria, flushing, itchy throat, or rhinoconjunctivitis; moderate signs/symptoms included angioedema, stridor, coughing, abdominal pain, difficulty breathing (other than wheezing), voice changes, nausea, vomiting, or diarrhea; severe symptoms included wheezing, cyanosis, and circulatory collapse.

Patients were contacted between March and August 2017 and queried on whether the allergy had resolved. The patient was considered to have resolved seafood allergy if they self-reported that they were able to tolerate seafood at least once a week or self-reported that a physician had diagnosed the allergy as resolved.

The study was approved by the Research Ethics Boards of the McGill University Health Centre, University of Calgary, and British Columbia Children's Hospital.

TABLE I. Characteristics of responders and nonresponders

Characteristic	All patients	Nonresponders	Responders	95% CI of the difference between nonresponders and responders
Total number of subjects	N = 95	N = 32	N = 63	
Sex: Female, n (%)	40 (42.1)	13 (40.6)	27 (42.9)	−0.023 (−0.232 to 0.186)
White, n (%)	59 (62.1)	14 (43.8)	45 (71.4)	−0.276 (−0.481 to −0.071)*
Allergen, n (%)				
Fish	58 (61.1)	21 (65.6)	37 (58.7)	0.069 (−0.136 to 0.274)
Shellfish	34 (35.8)	9 (28.1)	25 (39.7)	−0.116 (−0.313 to 0.081)
Both	3 (3.2)	2 (6.3)	1 (1.6)	0.047 (−0.043 to 0.137)

*Indicates a significant difference between the groups compared.

TABLE II. Characteristics of responders with fish and shellfish allergy

Characteristic	Responders with fish allergy (n = 38)	Responders with shellfish allergy (n = 26)
Sex: female, n (%)	16 (42.1)	12 (46.2)
White, n (%)	26 (68.4)	20 (76.9)
Adult (>18 y), n (%)	8 (21.1)	7 (26.9)
Age at diagnosis (y), median (IQR)	1.9 (1.0-3.3)	4.3 (2.9-8.6)
Median (IQR) age at the time the resolution questionnaire was filled in	13.8 (8.3-17.0)	13.3 (10.2-18.7)
Comorbidities (self-reported), n (%)		
Asthma	13 (34.2)	12 (46.2)
Eczema	26 (68.4)	13 (50)
Hay fever	13 (34.2)	11 (42.3)
Anaphylaxis	18 (47.4)	7 (26.9)
Other food allergies	25 (65.8)	13 (50.0)
Initial size of SPT wheal (mm)	3.0-43.0	3.0-14.0
Types of allergens reported by patients, n (%)		
Fish	37 (97.4)	1 (3.9)
Shellfish	1 (2.6)	22 (84.6)
Seafood/unspecified	1 (2.6)	4 (15.4)
Subtypes of fish, n (%)*		
Cod	1 (2.6)	0 (0)
Sole	2 (5.3)	0 (0)
Tilapia	1 (2.6)	0 (0)
Halibut	1 (2.6)	0 (0)
Whitefish, unspecified	3 (7.9)	0 (0)
Salmon	7 (18.4)	0 (0)
Tuna	2 (5.3)	0 (0)
Trout	3 (7.9)	0 (0)
Fish, unspecified	26 (68.4)	1 (3.9)
Subtypes of shellfish, n (%)*		
Lobster	0 (0)	4 (15.4)
Crab	0 (0)	4 (15.4)
Shrimp	0 (0)	13 (50.0)
Crustaceans, unspecified	0 (0)	3 (11.5)
Scallops	0 (0)	1 (3.9)
Squid	0 (0)	1 (3.9)
Mollusks	1 (2.6)	2 (7.7)
Shellfish, unspecified	0 (0)	5 (19.2)
Other food allergies (Y/N), other than seafood, n (%)	25 (65.8)	13 (50.0)
Route of exposure, n (%)†		
Ingestion	34 (89.5)	24 (92.3)
Contact	4 (10.5)	2 (7.7)

(continued)

TABLE II. (Continued)

Characteristic	Responders with fish allergy (n = 38)	Responders with shellfish allergy (n = 26)
Inhalation	1 (2.6)	0 (0)
Severity of most severe reaction, n (%)		
Mild	4 (10.5)	2 (7.7)
Moderate	25 (65.8)	20 (76.9)
Severe	9 (23.7)	4 (15.4)
Median time from study entry to resolution questionnaire follow-up (y) (IQR)	5.42 (3.75-5.87)	5.14 (4.09-5.67)
Median follow-up time from study entry to study end (y),‡ (IQR)	5.42 (3.67-5.87)	5.14 (4.09-5.65)
Median time from study entry to first follow-up (y) (IQR)	2.22 (1.78-2.41) (n = 15)	2.05 (1.69-2.11) (n = 10)
Average time from study entry to resolution (y)	2.0 (n = 1)	5.5 (n = 1)
Average time from diagnosis to resolution (y)	2.9 (n = 1)	9.5 (n = 1)
% Confirmed resolution	1 (2.6)	1 (3.9)
Follow-up Time - Person Years	173.8563	124.6845

IQR, Interquartile range.

*Subtypes for fish/shellfish add up to more than 100%, as respondents could report more than one type of fish/shellfish.

†Route of exposure for fish/shellfish add up to more than 100%, as respondents could report more than 1 route of exposure.

‡Study end defined as resolution questionnaire follow-up date or date of resolution, whichever comes first.

Descriptive statistics and assessment of resolution were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

We recruited 95 participants with seafood allergy and 63 responded to the follow-up questionnaire (We were unable to contact 32 participants through the contact information provided at study entry.): 37 had fish allergy, 25 had shellfish allergy, and 1 individual had both. There were 49 children and 14 adults. The sociodemographic and clinical characteristics were similar between responders and nonresponders except for ethnicity (responders, 71.4% white; nonresponders, 43.8% white) (Table I). Among the fish and shellfish cohorts, there were 42.1% and 46.2% females, with a mean age at diagnosis of 3.4 and 6.8 years, respectively (Table II). Asthma and eczema were reported in 34.2% and 68.4% of cases with fish allergy and 46.2% and 50% of cases with shellfish allergy. The most common culprits were salmon (18.4%) and shrimp (50%). There was 1 case of confirmed fish allergy resolution and 1 case of confirmed shellfish resolution followed over 173.9 and 124.7 person-years, respectively. The resolution rate was 0.6% (95% CI, 0.02%-3.2%) per person-year for fish and 0.8% (95% CI, 0.02%-4.5%) per person-year for shellfish.

Given the relatively low resolution rate, we were unable to identify factors associated with resolution of seafood allergy. In the medical literature, there are little data on factors associated with seafood resolution, particularly on SPTs or IgE levels. There is a single case report describing clinical resolution of allergy to several fish species in a 14-year-old child who continued to have a positive SPT result for fish and low levels of fish-specific IgE (0.17–0.99 kU/L) to several species of fish.⁷

Our study is limited by a small sample size. Nevertheless, this is the first cohort study to describe resolution rates in seafood allergy and we have demonstrated that resolution is rare. Furthermore, similar to other studies reporting resolution,⁸ this is not an interventional study and depends on treating allergist decision to challenge patients in order to establish tolerance. However, we believe that given that all patients were reassessed by an allergist and given that skin test results and specific IgE levels were positive on follow-up in all patients with reported history of an IgE-mediated reaction, it would not be part of routine clinical practice to challenge these patients. It is possible that choosing a cutoff level of 20 kU/L would exclude patients who are more likely to outgrow fish allergy. However, given that inclusion criteria included convincing history and positive SPT result and given that all patients had a skin test, we do not believe that choosing a cutoff level of 20 has affected our estimates.

In conclusion, we observed a low rate of resolution of seafood allergy. Although there are a few case reports on resolution of fish allergies in children⁷ and adults,⁹ our study is the first cohort study to assess resolution of seafood allergy. Larger studies are needed to confirm these findings and to identify factors potentially associated with resolution.

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