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ORIGINAL RESEARCH

Risk Factors for Severe Seafood Allergy Among Adults in an Urban City in Vietnam

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Purpose: Increasing seafood consumption is associated with more frequent reports of food allergy. Little is known about seafood allergy (SFA) among adults in Vietnam. We investigated the characteristics of individuals with SFA and the risk factors for severe SFA.

Patients and methods: A cross-sectional, web-based survey was conducted among individuals aged ≥ 18 years from universities in Ho Chi Minh City (Vietnam) between December 2021 and July 2022. The survey was based on a structured, validated questionnaire related to FA. Strict definitions of "convincing allergy" were used. Multivariate analysis was used to estimate the risk factors for severe SFA after adjusting for covariates. Data were analyzed using JASP (v.0.16.3) and SPSS (v.22.0).

Results: Totally, 1038 out of 2137 (48.57%) individuals completed the questionnaire, of whom 285 (27.46%) had reported SFA. Convincing SFA accounted for 20.13% (209/1038) of the cases, with convincing shellfish allergy being more common than fish allergy. Participants with comorbid shellfish and fish allergy had higher prevalence of atopic dermatitis, peanut/nut allergy, other food allergy, and cutaneous and upper airway symptoms compared to participants with shellfish allergy ($p < 0.05$). The spectrum of reactive seafood was diverse and characterized by local species. The age of symptom onset was most commonly during late childhood and adolescence, with most reactions persisting into adulthood. A history of anaphylaxis, comorbid peanut, and tree nut allergy, and ≥3 allergens were associated with severe SFA.

Conclusion: Features of causative, coexisting seafood allergy, and risk factors for severe SFA were demonstrated, which can provide a reference for future studies.

Keywords: seafood allergy, shellfish allergy, fish allergy, Vietnam

Introduction

Over the past three decades, the prevalence of food allergy (FA) has been increasing in the urbanized world.[1–3] In the UK, the frequency of hospital admissions due to food-induced anaphylaxis was 1.2 per 10^5 individuals in 1998 which doubled to 2.4 per 10^5 individuals over 14 years.[2] In the USA, a recent population-based study showed that 40–48% of children and adults with FA had an allergy to multiple foods.[4] In Europe, the point prevalence of self-reported FA was 13.1% and higher than previous estimates.[3] Similar trends were seen in the New Zealand, and Australia.[2]

In Asia, the prevalence of FA is 1.11–7.65%, along with unique food allergy patterns,[5] but it has been gradually increasing, with a two-fold increase over the years.[6] However, its prevalence among adults has not been adequately explored. The Australian Health Survey found that 1.3% of individuals (in that country) aged 20–45 years have an FA, with peanut (0.4%) and prawn (0.9%) being the most common allergens.[2] In Vietnam, a population-based survey of students aged 16–50 years demonstrated a high prevalence of doctor-diagnosed FA (5.7%), with seafood accounting for a significant proportion (2.6%).[7] Indeed, seafood allergy (SFA) is more common in Asia than in other countries, which is attributable to the variation in the consumption of triggering foods, dietary habits, cooking patterns, and food sources

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across regions. Asians consume two-thirds of the world's seafood production, including species that are not commonly consumed in other countries.[8,9]

Despite its widespread occurrence, diagnosing and managing SFA remain challenging.[10] The consumption of various crustaceans, mollusks, and fish species complicates the identification of the causative food.[11,12] Seafood consumption can trigger both IgE-mediated and non-IgE-mediated reactions. A range of adverse reactions can occur following seafood consumption, which can be misdiagnosed as SFA, including scombroid poisoning, toxins, and *anisakis* infection.[11,13] Each seafood species contains multiple isoforms of allergens or cross-reactive allergens. Furthermore, the commercial extracts of seafood used in daily practice for allergic testing contain variable levels of allergens, which may result in overdiagnosis or underdiagnosis Thus, a standard diagnostic approach for SFA is not suitable for all patients. Efforts have been made to elucidate the important seafood allergens, providing a framework for implementing a component-resolved diagnostic strategy.[12] In Vietnam, although SFA is common in children aged 2–6 years and in adults, there is a paucity of information related to seafood allergens.[7,14,15] Thus, we investigated the prevalence of shellfish and fish allergy, evaluated the characteristics of SFA, and identified the risk factors for severe SFA among university students in an urban city of Vietnam. We selected Ho Chi Minh City (HCMC) because it is the largest and most highly populated city in the country, with a large number of migrants from the surrounding provinces.

Methods

Study Design

A cross-sectional, web-based survey was conducted among students aged ≥ 18 years old in HCMC, Vietnam, between December 2021 and July 2022. Based on convenience sampling, three universities were selected, including the University of Medicine and Pharmacy at HCMC, Pham Ngoc Thach University of Medicine, and Tan Tao University. An invitation letter with detailed information about the study was distributed among undergraduate and graduate students of the selected universities regardless of the presence or absence of SFA, and only patients reported SFA would be analyzed. After reading the study description, participants provided consent and agreed to join the study by clicking on the link to the survey. To have participants more likely to consume seafood species in HCMC, we selected the students who have continuously stayed in HCMC for more than one week. This study complies with the Declaration of Helsinki and the study protocol was approved by the Ethics Committee Review Board of the University of Medicine and Pharmacy at HCMC (No: 251/HĐĐĐ-ĐHYD).

Sample Size

The sample size was calculated using the following formula:

$$n = \frac{Z^2_{1-\frac{\alpha}{2}}(1-p)p}{d^2}$$

where n is the sample size, Z is the statistic corresponding to the level of confidence (95%), p is expected prevalence, and d is the allowable margin of error (0.05).[16] As the prevalence of shellfish and fish allergy among individuals with SFA in Vietnam is unknown, we selected a p value of 19% based on a study conducted in the US.[17] The minimum sample size was 237. Furthermore, we performed a pilot study to validate the survey among 30 participants.

Survey

The survey involved the administration of a structured questionnaire, which was validated in previous studies among the US and Asian populations.[18–20] The first part of the survey included questions related to demographic information (age, sex, household income, educational level), physicians' diagnosis of allergic disorders (asthma, eczema, and allergic rhinitis), and allergy to peanuts, tree nuts, crustacean shellfish, mollusk, and fish. All participants completed the first part of the survey, whereas only those with a history of allergic reactions to crustaceans, mollusks, or fish completed the second part. In the second part, participants answered specific questions pertaining to shellfish and fish allergy based on the original questionnaire.[18–20] The survey and questionnaire were translated from English into Vietnamese. To validate the survey, four independent translators performed forward and backward translations. An expert committee, including allergy specialists, reviewed the translated questionnaires. The seafood species included species originating

from Vietnam and approved by the expert committee. The web-based questionnaire was transformed into a hierarchical, web-based survey using Typeform™. Next, the pilot study was conducted on 30 participants to evaluate the survey before the study. Survey responses were collected anonymously and exported to Microsoft Excel for further analysis. Data were collected anonymously, kept confidential and only accessed by the lead investigator.

Definitions of SFA and Severe SFA

"Convincing SFA" and "probable SFA" were defined according to physician diagnosis and corresponding symptoms and history, as described by Sicherer et al.[19] Reactions considered convincing were urticaria/rash, angioedema, dyspnea, itchy mouth, throat tightness, and dizziness/cough with at least one gastrointestinal symptom (vomiting, abdominal pain, diarrhea, and nausea) within 2 h of food intake. The presence of other symptoms was defined as probable SFA. Although allergic testing results were also considered when classifying SFA, most participants had not undergone skin prick testing or food challenge; thus, SFA was defined based on the standardized questionnaire. The participants who did not meet the criteria for convincing or probable SFA were classified as having "self-reported SFA" and excluded from further analysis. SFA severity was defined according to the presence of choking, wheezing/dyspnea, or loss of consciousness, as reported previously.[20]

Statistical Analysis

We conducted a descriptive study using a survey data. The normality test was checked by Kolmogorov–Smirnov test. The continuous variables were expressed as mean ± SD. The categorical data were displayed as %. Comparison between groups was performed by Student's *t*-test or one-way ANOVA for the continuous data or by Pearson's chi-square or Fisher's exact test for the categorical variables. The risk factors of severe SFA compared with nonsevere SFA were analyzed by a multivariate logistic regression, calculating the odds ratios (ORs) and 95% confidence interval (CIs). Based on previous studies,[14,17] clinical experience, and significant association with the outcome variable, potential covariates were included, such as age, gender, history of asthma, history of anaphylaxis, comorbid peanut/nut allergy, and allergy to ≥ 3 seafood species. The cross-reactivity between species was calculated by Pearson correlation coefficient A P value < 0.05 was considered as statistical significance. All analysis was performed using JASP (v0.16.3), except for multivariate logistic regression was performed by IBM®SPSS® 22.0.

Results

Participation Rate and Demographic Characteristics of Participants

The number of individuals surveyed and their demographic characteristics were summarized in Table 1 and Supplementary Figure 1. The survey was administered to 2137 individuals, of whom 1038 agreed to participate (response rate of 48.57%). Among them, 285 had a history of SFA. Supplementary Table 1 presents data collected from 209 participants with convincing SFA (20.13%), 23 with probable SFA (2.22%), and 53 with self-reported SFA (5.11%). Shellfish allergy (18.98%) was more common than fish allergy (3.56%) and comorbid shellfish and fish allergy (2.41%) (Supplementary Table 1).

The median age of participants with convincing allergy was 21 years and the male:female ratio was 1:1.90 (Table 1). Most participants had income 2.2–5.0 million VND per month, and half lived in rental housing. There were no significant differences between only shellfish allergy, only fish allergy, and comorbid shellfish and fish allergy groups.

Causative Seafood and Coexisting Allergy Across Seafood Species

We analyzed the cross-reactions following seafood consumption among individuals with convincing allergy. The causative species included various crustaceans (tiger prawns, crabs, tiny shrimps, and lobsters), mollusks (squids, clams, oysters, and snails), and fishes (tuna, mackerel, pompano, and red tilapia) (Supplementary Table 2). Some participants (2.70–5.74%) were unaware of the species that caused allergic symptoms.

Most participants experienced allergic reactions following the consumption of multiple species within the same group of shellfish or fish or between shellfish and fish (Figure 1). Notably, cross-reactivity occurred among the the same group

Table 1 Demographic Characteristics of the Study Subjects

		Convincing SFA (N=209)	Shellfish allergy$^{\delta}$ (N = 197)	Fish Allergy$^{\delta\delta}$ (N = 37)	Only Shellfish Allergy$^{\delta\delta\delta}$ (N=173) (1)	Only Fish Allergy$^{\delta\delta\delta\delta}$ (N=11) (2)	Both shellfish and Fish Allergy$^{\delta\delta\delta\delta\delta}$ (N=23) (3)	*P* values between Groups	*P* values between (1) and (2)	*P* values between (1) and (3)
Age (years-old)*		21 ± 2.91	21 ± 2.83	22 ± 3.72	21 ± 2.77	21 ± 3.00	22 ± 3.65	0.309	0.19	0.46
Gender (N, %)	Male Female	72 (34.45%) 137 (65.55%)	95 (48.22%) 102 (51.78%)	11 (29.73%) 23 (62.16%)	87 (50.29%) 86 (49.71%)	3 (27.27%) 8 (72.73%)	15 (65.22%) 15 (65.22%)	0.15	0.21	0.19
Income (millions VND/ months) (N, %)	< 0.9 0.9 – < 1.3 1.3 – < 2.2 2.2 – < 5.0 ≥ 5.0	49 (23.44%) 0 32 (15.31%) 71 (33.97%) 57 (27.27%)	47 (23.86%) 0 (0%) 28 (14.21%) 63 (31.98%) 59 (29.95%)	9 (24.32%) 0 (0%) 6 (16.22%) 11 (29.73%) 8 (21.62%)	41 (23.7%) 0 (0%) 25 (14.45%) 56 (32.37%) 52 (30.06%)	4 (36.36%) 0 (0%) 3 (27.27%) 4 (36.36%) 0 (0%)	6 (26.09%) 0 (0%) 3 (13.04%) 7 (30.43%) 8 (34.78%)	0.481	0.16	0.98
Housing (N, %)	House Apartment Rental housing	72 (34.45%) 32 (15.31%) 105 (50.24%)	66 (33.5%) 33 (16.75%) 98 (49.75%)	10 (27.03%) 3 (8.11%) 22 (59.46%)	60 (34.68%) 30 (17.34%) 83 (47.98%)	3 (27.27%) 1 (9.09%) 7 (63.64%)	6 (26.09%) 2 (8.7%) 15 (65.22%)	0.49	0.58	0.28

Notes: Data are presented as N (%). *P* values were calculated by Pearson's chi square or Fisher's exact test.* *P* values were presented as median ± SD, and were calculated by Mann–Whitney *U*-test. Values in bold indicate significant *P* values. $^{\delta}$ Shellfish allergy: the respondents who had reported reactions to any shellfish species regardless of any reactions to fish among the convincing allergy group. $^{\delta\delta}$Fish allergy: the respondents who had reported reactions to any fish species regardless of any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta}$ Only shellfish allergy: the respondents who had reported reactions to any shellfish species but without any reactions to fish among the convincing allergy group. $^{\delta\delta\delta\delta}$ Only fish allergy: the respondents who had reported reactions to any fish species but without any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta\delta\delta}$ Both shellfish and fish allergy: the respondents who had reported reactions to both shellfish and fish among the convincing allergy group.

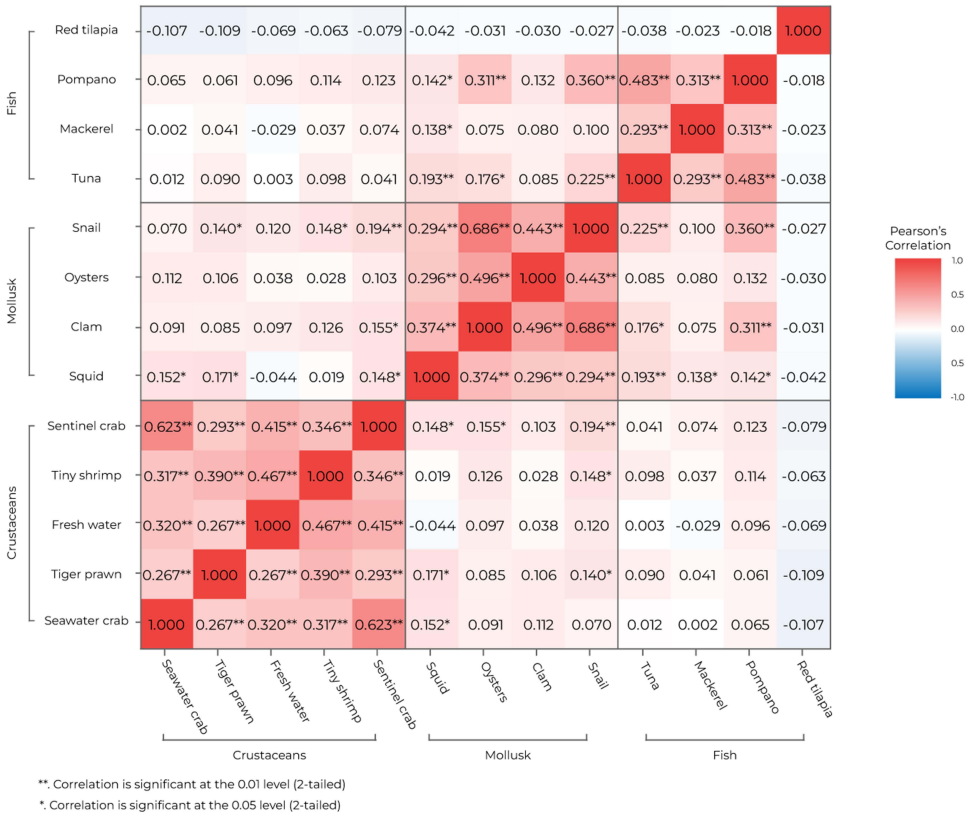

Figure 1 Coexisting allergy between seafood species among participants with convincing allergy. In each cell, the correlation of subjects who were allergic to each column had comorbid allergy to each row, and in reverse. Correlation was calculated by Pearson correlation coefficient. *P<0.05, **P<0.01.

(crustaceans/mollusk/fish) more frequently than between crustaceans and mollusks or fish, with the correlation of cross-reactivity being highest within the same group (all P<0.05).

History of Comorbid Allergic Diseases Among Participants with Convincing Allergy

As shown in Table 2, rash/urticaria was the most common comorbid disorder, followed by allergic rhinitis. Individuals with comorbid shellfish and fish allergy had a significantly higher prevalence of atopic dermatitis, peanut/nut allergy, and other food allergy than individuals with only shellfish allergy (P=0.044, P=0.018, P<0.001, respectively). Almost 10% of participants had a history of anaphylaxis (Table 2).

Age of Onset, Age at First introduction, and Reactions to Seafood Consumption

Most participants with SFA developed their first reactions after 6 years of age, with the highest frequency of reactions reported at ages 11–16 years and 6–10 years among participants with shellfish and fish allergy, respectively (Figure 2). A small number of participants developed SFA at age < 1 year or during adulthood. Furthermore, the ages at first consumption of shellfish and fish were 6–10 years and 11–16 years among participants with shellfish and fish allergy, respectively. Moreover, 6.30–20.30% of participants developed reactions to fish and shellfish during adulthood, respectively. The age of onset positively correlated with the age at first introduction of both shellfish (r=0.715, P<0.001) and fish (r=0.757, P<0.001). In most participants, SFA persisted until adulthood, with 69.19–84% of participants experiencing reactions sometimes or always following shellfish consumption and 33.33–68.00% experiencing reactions following fish consumption. Participants with comorbid shellfish and fish allergy (68.00%) had a higher prevalence of reactions than those with only fish allergy (33.33%) (p < 0.05).

Table 2 History of Comorbid Allergic Diseases Among Subjects with Convincing Allergy

	Convincing Allergy (N=209)	Shellfish Allergy$^{\delta}$ (N = 197)	Fish Allergy$^{\delta\delta}$ (N = 37)	Only Shellfish Allergy$^{\delta\delta\delta}$ (N=173) (1)	Only Fish Allergy$^{\delta\delta\delta\delta}$ (N=11) (2)	Both Shellfish and Fish Allergy$^{\delta\delta\delta\delta\delta}$ (N=23) (3)	*P* values between Groups	*P* values between and (2)	*P* values between (1) and (3)
Asthma (N, %)	20 (9.57%)	18 (9.14%)	3 (8.11%)	19 (10.98%)	2 (18.18%)	1 (4.35%)	0.42	0.36	0.48
Atopic dermatitis (N, %)	52 (24.88%)	49 (24.87%)	13 (35.14%)	40 (23.12%)	2 (18.18%)	10 (43.48%)	0.10	1	**0.044**
Allergic rhinitis (N, %)	84 (40.19%)	81 (41.12%)	13 (35.14%)	72 (41.62%)	2 (18.18%)	10 (43.48%)	0.40	0.21	1
Rash/urticaria (N, %)	97 (46.41%)	89 (45.18%)	33 (89.19%)	76 (43.93%)	8 (72.73%)	14 (60.87%)	0.06	0.07	0.18
Anaphylaxis (N, %)	21 (10.05%)	21 (10.66%)	3 (8.11%)	19 (10.98%)	0 (0%)	4 (17.39%)	0.34	0.61	0.49
Peanut/nuts allergy (N, %)	8 (3.83%)	8 (4.06%)	0	5 (2.89%)	0 (0%)	4 (17.39%)	0.06	0.74	**0.018**
Other food allergy (N, %)	26 (12.44%)	25 (12.69%)	10 (27.03%)	14 (8.09%)	1 (9.09%)	9 (39.13%)	**0.001**	0.97	**<0.001**

Notes: Data were presented as N (%). *P* values were calculated by $\chi 2$ Pearson or Fisher's exact test. Values in bold indicate significant *P* values. $^{\delta}$ Shellfish allergy: the respondents who had reported reactions to any shellfish species regardless of any reactions to fish among the convincing allergy group. $^{\delta\delta}$Fish allergy: the respondents who had reported reactions to any fish species regardless of any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta}$ Only shellfish allergy: the respondents who had reported reactions to any shellfish species but without any reactions to fish among the convincing allergy group. $^{\delta\delta\delta\delta}$ Only fish allergy: the respondents who had reported reactions to any fish species but without any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta\delta\delta}$ Both shellfish and fish allergy: the respondents who had reported reactions to both shellfish and fish among the convincing allergy group.

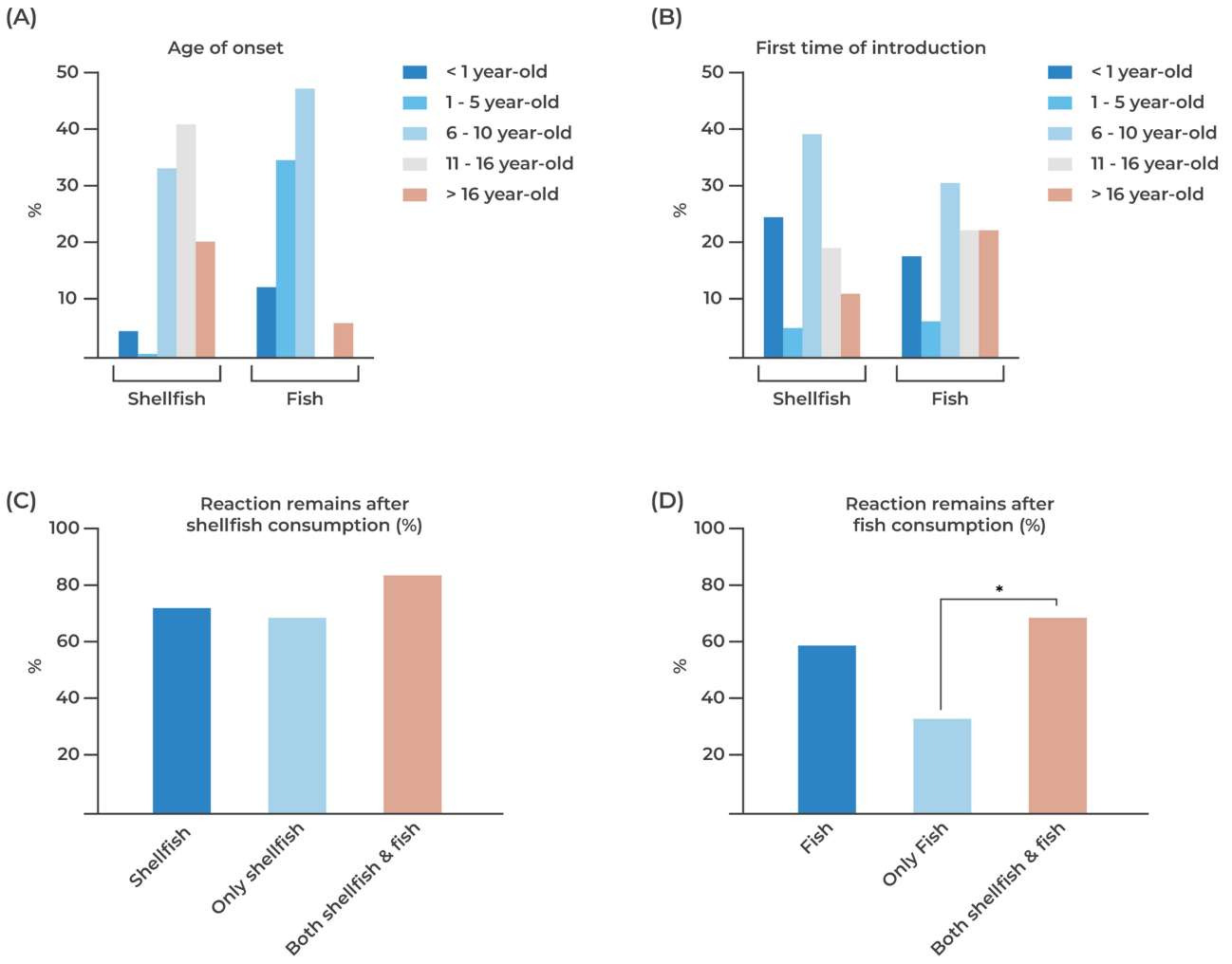

Figure 2 (**A**) Age of onset of SFA symptoms and (**B**) age of first introduction of shellfish/fish among convincing allergy subjects. The percentage of subjects who had persistent reactions after (**C**) shellfish or (**D**) fish consumption. *P <0.05. P values were calculated by Pearson's chi-square.

Symptoms Following Seafood Consumption Among Participants with Convincing Allergy

The participants experienced variable symptoms following the consumption of shellfish and fish (Table 3), with mild to moderate symptoms (rash/urticaria, cough, lip/face swelling, itchy throat/mouth, and flush) being the most common. Participants with comorbid shellfish and fish allergy developed cutaneous symptoms (urticaria/rash, lip/face swelling, and eye/eyelid swelling) and upper respiratory tract symptoms (cough, nasal congestion, and runny nose) more frequently than those with shellfish allergy (all $p < 0.05$). No significant differences were observed between the groups in terms of life-threatening symptoms (choking, wheezing, or shortness of breath, faint, or dizziness, and loss of consciousness).

Behavioral Characteristics of Participants

The participants were asked how they cope with fish and shellfish allergic reactions (Table 4). Almost half of the participants did not seek treatment, whereas a minority of participants underwent allergy testing and visited a physician. Participants with allergy to multiple species of shellfish and fish visited doctors and received steroids and asthmatic medications more commonly than those with shellfish allergy, although the difference was not statistically significant. Only 6.09% subjects with shellfish allergy and 2.70% subjects with fish allergy underwent allergy testing, and none of the participants received prophylactic or injectable epinephrine (data not shown).

Table 3 Prevalence of Symptoms Among the Convincing Allergy Group

	Convincing Allergy (N = 209)	Shellfish Allergy$^{\delta}$ (N = 197)	Fish Allergy$^{\delta\delta}$ (N = 37)	Only Shellfish Allergy$^{\delta\delta\delta}$ (N=173) (1)	Only Fish Allergy$^{\delta\delta\delta\delta}$ (N=11) (2)	Both Shellfish and Fish Allergy$^{\delta\delta\delta\delta\delta}$ (N=23) (3)	*P* values between Groups	*P* values between (1) and (2)	*P* values between (1) and (3)
Rash/urticaria	158 (75.60%)	146 (74.11%)	32 (86.49%)	124 (71.68%)	9 (81.82%)	22 (95.65%)	**0.035**	0.73	**0.01**
Cough	145 (69.38%)	137 (69.54%)	19 (51.35%)	118 (68.21%)	5 (45.45%)	21 (91.3%)	**0.027**	0.30	**0.026**
Lips/Face swelling	89 (42.58%)	87 (44.16%)	9 (24.32%)	71 (41.04%)	2 (18.18%)	15 (65.22%)	0.022	0.21	**0.042**
Itchy throat/mouth	92 (44.02%)	85 (43.15%)	13 (35.14%)	74 (42.77%)	2 (18.18%)	14 (60.87%)	0.11	0.19	0.19
Flush	66 (31.58%)	60 (30.46%)	9 (24.32%)	54 (31.21%)	3 (27.27%)	10 (43.48%)	0.47	1	0.25
Eye/eyelids swelling	53 (25.36%)	49 (24.87%)	9 (24.32%)	36 (20.81%)	3 (27.27%)	13 (56.52%)	**0.002**	0.70	**0.002**
Abdominal pain	50 (23.92%)	44 (22.34%)	10 (27.03%)	41 (23.7%)	4 (36.36%)	5 (21.74%)	0.59	0.47	1
Diarrhea	40 (19.14%)	35 (17.77%)	4/37 (10.81%)	35 (20.23%)	2 (18.18%)	5 (21.74%)	0.98	1	1
Vomit	27 (12.92%)	27 (13.71%)	1/37 (2.70%)	25 (14.45%)	0 (0%)	2 (8.7%)	0.32	0.37	0.75
Nasal congestion/runny nose	24 (11.48%)	24 (12.18%)	2/37 (5.41%)	16 (9.25%)	0 (0%)	8 (34.78%)	**0.001**	0.60	**0.002**
Throat choking	41 (19.62%)	38 (19.29%)	5 (13.51%)	33 (19.08%)	2 (18.18%)	5 (21.74%)	0.95	1	0.78
Wheezing/shortness of breath	30 (14.35%)	23 (11.68%)	3 (8.11%)	20 (11.56%)	2 (18.18%)	4 (17.39%)	0.66	0.62	0.50
Faint/dizziness	16 (7.66%)	10 (5.08%)	0 (0%)	10 (5.78%)	0 (0%)	1 (4.35%)	0.69	1	1
Loss of consciousness	5 (2.39%)	4 (2.03%)	0 (0%)	4 (2.31%)	0 (0%)	0 (0%)	0.67	1	1

Notes: Data were presented as N (%). *P* values were calculated by Pearson's chi square or Fisher's exact test. Values in bold indicate significant *P* values. $^{\delta}$ Shellfish allergy: the respondents who had reported reactions to any shellfish species regardless of any reactions to fish among the convincing allergy group. $^{\delta\delta}$Fish allergy: the respondents who had reported reactions to any fish species regardless of any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta}$ Only shellfish allergy: the respondents who had reported reactions to any shellfish species but without any reactions to fish among the convincing allergy group. $^{\delta\delta\delta\delta}$ Only fish allergy: the respondents who had reported reactions to any fish species but without any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta\delta\delta}$ Both shellfish and fish allergy: the respondents who had reported reactions to both shellfish and fish among the convincing allergy group.

Table 4 Characteristics of Behavior Towards Seafood Allergy

	Convincing Allergy (1)	Shellfish Allergy$^{\delta}$ (N = 197)	Fish Allergy$^{\delta\delta}$ (N = 37)	Only Shellfish Allergy$^{\delta\delta\delta}$ (N=173) (1)	Only Fish Allergy$^{\delta\delta\delta\delta}$ (N=11) (2)	Both Shellfish and Fish Allergy$^{\delta\delta\delta\delta\delta}$ (N=23) (3)	*P* values between Groups	*P* values between (1) and (2)	*P* values between (1) and (3)
No treatment	115 (55.02%)	102 (51.78%)	17 (45.95%)	97 (56.07%)	5 (45.45%)	13 (56.52%)	0.79	0.54	1
Antihistamine	84 (40.19%)	79 (40.10%)	16 (43.24%)	68 (39.31%)	4 (36.36%)	12 (52.17%)	0.49	1	0.06
Emergency/ Hospitalization	18 (8.61%)	18 (9.14%)	1 (2.70%)	15 (8.67%)	0 (0%)	2 (8.7%)	0.56	0.60	1
Steroid	19 (9.09%)	18 (9.14%)	5 (13.51%)	14 (8.09%)	1 (9.09%)	5 (21.74%)	0.14	1	0.06
Epinephrine	7 (3.35%)	6 (3.05%)	1 (2.70%)	6 (3.47%)	1 (9.09%)	0 (0%)	0.39	0.36	1
Asthmatic medications	5 (2.39%)	4 (2.03%)	2 (5.41%)	4 (2.31%)	1 (9.09%)	1 (4.35%)	0.39	0.27	0.48

Notes: Data were presented as N (%). *P* values were calculated by Pearson's chi square or Fisher's exact test. $^{\delta}$Shellfish allergy: the respondents who had reported reactions to any shellfish species regardless of any reactions to fish among the convincing allergy group. $^{\delta\delta}$Fish allergy: the respondents who had reported reactions to any fish species regardless of any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta}$ Only shellfish allergy: the respondents who had reported reactions to any shellfish species but without any reactions to fish among the convincing allergy group. $^{\delta\delta\delta\delta}$ Only fish allergy: the respondents who had reported reactions to any fish species but without any reactions to shellfish among the convincing allergy group. $^{\delta\delta\delta\delta\delta}$ Both shellfish and fish allergy: the respondents who had reported reactions to both shellfish and fish among the convincing allergy group.

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Table 5 Multivariate Logistic Regression Analysis of Severe Allergy to Shellfish or Any Seafood

	Any Seafood Allergy (N=209)		Shellfish[d] (N=197)	
	aOR (95% CI) (*)	*P* value	aOR (95% CI) (*)	*P* value
Age	0.99 (0.85–1.16)	0.94	0.99 (0.85–1.16)	0.89
Male	0.29 (0.12–0.69)	**0.006**	0.37 (0.16–0.89)	0.026
History of asthma	4.16 (1.31–13.27)	**0.016**	2.54 (0.79–8.19)	0.12
History of anaphylaxis	6.28 (2.08–19.03)	**0.001**	5.87 (1.96–17.64)	**0.002**
History of comorbid peanut/nut allergy	7.72 (1.58–37.74)	**0.012**	8.37 (1.69–41.20)	**0.009**
Allergy to ≥ 3 seafood species	4.49 (1.76–11.48)	**0.002**	5.86 (2.12–16.15)	**0.001**

Notes: (*) aOR, adjusted odd ratios for age and gender. Values in bold indicate significant *P* value.

Risk Factors of Severe Allergy to Shellfish, Fish, or Other Seafood

Multivariate logistic regression was used to analyze the risk factors of severe SFA. History of asthma, anaphylaxis, comorbid peanut and nut allergy, and allergic reactions to ≥3 seafood allergens were associated with an increased adjusted odds ratio of severe SFA (Table 5) (aOR=4.16, *P*=0.016; aOR=6.28, *P*=0.001; aOR=7.72, *P*=0.012; aOR=3.18, *P*=0.002). Furthermore, anaphylaxis, comorbid peanut and nut allergy and allergic reactions to ≥3 seafood allergens were predictors of shellfish allergy (aOR=5.87, *P*=0.002; aOR=8.37, *P*=0.009; aOR= 5.86, *P*=0.001). Males were less likely to have severe reactions to seafood than females, although there was no effect of sex on the prevalence of severe shellfish allergy.

Discussion

This study is the first to evaluate the prevalence of shellfish and fish allergy, as well as the risk factors of severe reactions, in the Vietnamese adult population. Our results confirm that shellfish allergy is more common than fish allergy. The study was conducted in HCMC, one of the largest municipal cities in Vietnam, with a high population density and diverse species transported from the southern provinces of Vietnam. The use of a strict definition used for convincing SFA provided precise estimates of the numbers, demographic information, and clinical manifestations among the adult population. Our findings demonstrate the diverse spectrum of causative seafood and the cross-reactivity between participants with SFA; these provide a useful basis for further studies on molecular seafood allergens. A small proportion of participants developed reactions to both shellfish and fish. More than half of the participants did not seek healthcare, despite persistent reactions to seafood. Moreover, a history of asthma, anaphylaxis, comorbid peanut and nut allergy, and multiple seafood allergy were risk factors for severe symptoms following seafood consumption.

SFA is the most common FA in many Asian countries, and has an increasing prevalence in the US.[7,15,21–23] In Europe, the pooled estimates for self-reported lifetime prevalence for fish and shellfish allergy were 1.4% and 0.4%, respectively.[24] While in Asia, the prevalence ranged from 0–7.23% for shellfish allergy, and 0–4.59% for fish allergy.[9] Our results demonstrate that shellfish allergy (18.98%) was more common than fish allergy (3.56%) among participants with SFA. Notably, a subgroup of patients developed reactions following fish and shellfish consumption (2.41%). In a previous study among Vietnamese adults, the prevalence of self-reported allergy to crustaceans, fish, and mollusk were 6.88%, 3.71%, and 3.09%. We found a similar prevalence of fish allergy and slightly higher prevalence of SFA and shellfish allergy.[15] We focused on describing the characteristics of participants with reactions to seafood. Crustacean allergy was more common than mollusk allergy, which is in line with previous studies and can be explained by the higher consumption of crustaceans than mollusks.[15,25,26] In Vietnam, the average seafood consumption has been increasing over the years. Although there was no information on the average consumption by species, crustaceans (shrimps, crabs, and sentinel crabs) account for a higher proportion among exported seafood than mollusks.[27] Interestingly, the causative seafood species were region-specific and differed from previous reports. For example, a study from Singapore found a high prevalence of reactions to threadfin, salmon, and cod,[28] whereas reactions to tuna, mackerel, and pompano were more common in our study. These discrepancies can be explained by the diversity of seafood species and their consumption, as well as differences in the food delicacies between countries.

Increasing evidence suggests the existence of cross-reactivity between seafood species.[10,29,30] Therefore, physicians should evaluate the coexistence of other seafood species among patients with suspected SFA. We found a high prevalence of cross-reactivity between seafood species, with most participants having allergy to multiple species and only a minority having isolated SFA. Prawns were the most common crustaceans causing SFA, in line with previous studies.[31,32] Participants with crustacean allergy developed reactions to mollusks (<50%) and fish (0–20%). Furthermore, 15–30% of participants had comorbid reactions to other foods. In a study in the US, 66.2% of adults with SFA had no comorbid allergy,[33] whereas another study reported that young adults with shrimp sensitivity developed reactions to multiple shellfish species.[30] These findings can be explained by frequent seafood consumption and homologous proteins between foods. Multiple allergenic epitopes of foods can lead to cross-reactivity.[34] Shared cross-reactive allergens, such as shellfish tropomyosin and fish parvalbumin, can lead to co-reactions between crustaceans and mollusks as well as low cross-reactivity with fish. As a result, studies of molecular allergens in seafood species from Vietnam are needed. Comorbid reactions should be considered by physicians when providing dietary advice to patient.

There is a paucity of data regarding the age at the time of first reaction to seafood and resolution of allergy with age among the Vietnamese population. Our findings indicate that most SFA events occurred during childhood and adolescence. The persistence of SFA until adulthood was consistent with previous studies.[35,36] Our results are in line with studies from the US, which showed that the average age at the time of shellfish diagnosis in adult and pediatric populations was 15.9 years.[25] In another survey conducted in Singapore and the Philippines, the age at the time of onset of shellfish allergy was lower (6–10 years) than in our study.[18] This may be because the age at the time of first introduction to shellfish and fish was during late childhood (6–10 years) or adulthood in our study.

Cutaneous symptoms were the most common symptoms triggered by seafood consumption in different populations.[7,14,18–20,25,28] In our study, the prevalence of severe symptoms was similar to that reported from Singapore and the Philippines[19] but higher than that among Vietnamese adults.[14] This may be because we focused on participants with SFA, whereas previous studies conducted among Vietnamese adults included participants with all FAs. Shek et al hypothesized that cross-reaction with dust mite allergy contributes to mild cases of shellfish allergy.[20] Interestingly, sensitization to house dust mites is common in Vietnam, about 6.3–30.9% in the population and even higher in patients with allergic diseases (49.6–59.8%)[37,38] Therefore, it can lead to primary sensitization with dust mite tropomyosin, a panallergen and a major allergen in shellfish and mollusk. Other pan-allergens were highlighted, such as arginine kinase, troponin C, and triosephosphate isomerase, etc. The mentioned proteins also share homology with other invertebrate allergen sources, such as mites, insects, and parasites.[39–41] Further studies of SFA should evaluate the cross-reactivity with dust mites in Vietnam.

It is unanticipated that half of the participants did not receive treatment for SFA. Antihistamines were commonly used by all participants for rash/urticaria following seafood consumption. Among participants with shellfish reactions, emergency department visits, hospitalizations, and use of steroids and epinephrine were common. However, most participants did not undergo the oral food challenge test, the gold standard method for the diagnosis of FA, or receive autoinjector epinephrine due to unavailability. These issues make the management of patients with SFA challenging and should be given more attention in the future.

The severity of SFA is affected by the presence of comorbidities and epidemiological factors. Histories of asthma, anaphylaxis, comorbid peanut and nut allergy, and allergy to ≥3 seafood species were associated with increased odds of life-threatening symptoms in any SFA and shellfish allergy. Conversely, male sex was associated with lower odds of severe seafood allergy. In a study from the US, comorbid asthma, peanut, and tree nut allergy and severe FA were associated with increased odds of FA-related emergency department visits and epinephrine prescriptions.[17] Female adults are more likely to have FAs than males.[14,17] The number of allergenic seafood species is also a strong predictor for severe symptoms and should be recorded during patient consultations.

Several limitations of our study should be considered when interpreting the results. First, SFA was recorded on the basis of symptoms rather than allergic tests. We stratified the participants into convincing allergy, probable allergy, and self-reported allergy based on their history, symptoms, and time of onset, similar to previous studies.[18–20] Second, the possibility of selection and recall bias cannot be excluded. This study was performed among university students, who have convenient access to the Internet. To enhance the accuracy of our results, each response was checked twice by two

independent researchers, and suspicious responses were removed. Thirdly, the participation rate was less than 50%, and there might be a participation bias for those who had history of shellfish or fish, which led to over-estimation of SFA.

Conclusions

In conclusion, our results enhance understanding of SFA among adults from Vietnam. Shellfish accounted for most cases of SFA, whereas a minority of patients had allergy to both shellfish and fish. The seafood causing reactions differs from other countries' reports according to local species. Half of the participants did not receive any treatment for SFA. SFA tended to occur late and persisted into adulthood. Female sex, asthma, anaphylaxis, comorbid peanut and nut allergy, and reactions to ≥3 seafood species increased the odds for severe SFA. Our results provide a reference for patient management and highlight the need for further studies.

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Disclosure

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