

Original Article



Shellfish/crustacean oral allergy syndrome among national service pre-enlistees in Singapore

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ABSTRACT

Background: All Singaporean males undergo medical screening prior to compulsory military service. A history of possible food allergy may require referral to a specialist Allergy clinic to ensure that special dietary needs can be taken into account during field training and deployment.

Objective: To study the pattern of food allergy among pre-enlistees who were referred to a specialist allergy clinic to work up suspected food allergy.

Methods: Retrospective study of all pre-enlistees registered in the Clinical Immunology/Allergy New Case Registry referred to the Allergy Clinic from 1 August 2015 to 31 May 2016 for suspected food allergy.

Results: One hundred twenty pre-enlistees reporting food allergy symptoms other than rash alone were referred to the Allergy Clinic during the study period. Of these, 77 (64.2%) had food allergy. Among those with food allergy, mean age was 19.1 ± 1.5 years. They comprised predominantly Chinese (66.2%) and Malays (20.8%). The most commonly reported foods were shellfish/crustaceans (78%), peanut (15.6%), and egg (6.5%). Self-limiting oral allergy syndrome, OAS (itchy lips and throat with/without lip angioedema) was the most common manifestation ($n = 33$, 42.9%) followed by anaphylaxis ($n = 23$, 29.9%). Majority of OAS was from shellfish/crustacean (90.6%); of which shrimp (30.3%), crab (15.2%), and lobster (3.0%) were the most common. Mild childhood asthma (69.7%), allergic rhinitis (6.3%), and eczema (6.1%) were the most common atopic conditions among individuals with shellfish/crustacean OAS. This pattern was similar for shellfish/crustacean anaphylaxis. Skin prick tests were most commonly positive for shrimp (OAS 87.1% vs. anaphylaxis 100%), crab (OAS 95.8% vs. 90.9%), and lobster (OAS 91.7% vs. 63.6%).

Conclusion: OAS to shellfish/crustaceans was more common than anaphylaxis among this study population of young males referred for food allergy symptoms other than rash alone.

Keywords: Anaphylaxis; Hypersensitivity; Shellfish

INTRODUCTION

Prior to compulsory military service after the age of 18 years, Singaporean males are screened in the military and referred to our Allergy Clinic for confirmation of food allergy if they declare a history of suspected food allergy, with symptoms other than rash alone.

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Allergic diseases are highly prevalent among children and adolescents in Singapore. This includes asthma, allergic rhinitis, atopic dermatitis, anaphylaxis, and food allergy. Screening pre-enlistees for food allergy allows special dietary needs to be catered for in military camps and during outfield training. The aim of this study was to describe the pattern of food allergy among pre-enlistees who reported a history of suspected food allergy.

MATERIALS AND METHODS

All pre-enlistees registered in the Clinical Immunology/Allergy New Case Registry who were referred to the Allergy Clinic from 1 August 2015 to 31 May 2016 for suspected food allergy were retrospectively studied. Their demographic profile, suspected food allergy/allergies, concomitant atopy, and outcomes of skin prick tests (SPTs), blood tests for allergen specific IgE and/or oral food challenges (OFCs) were studied. Patients who had a definite diagnosis of food allergy in childhood based on clinical history and SPT and/or specific IgE measurements did not have the tests repeated. OFC were offered to patients where childhood history was equivocal, and SPT/specific IgE were negative, or to demonstrate tolerance following dietary elimination over time. This study was part of the Clinical Immunology/Allergy New Case Registry's approved domain specific review board reference number TTSH/2005-0016 for which additional informed consent was not required as this was a retrospective registry review with minimal risks to research subjects.

RESULTS

There were 120 male pre-enlistees comprising 26% of all referrals to the Allergy Clinic during the study period, of whom 77 (64.2%) had food allergy. Among those with food allergy, mean age was 19.1 ± 1.5 years. They comprised predominantly Chinese (66.2%) and Malays (20.8%) followed by 6.5% Indians and other ethnicities respectively. The most commonly reported foods were shellfish/crustaceans (78%), peanut (15.6%), and egg (6.5%).

Self-limiting oral allergy syndrome, OAS (itchy lips and throat with/without lip angioedema) was the most common manifestation ($n = 33$, 42.9%) followed by anaphylaxis ($n = 23$, 29.9%). The remaining 27.2% had urticarial and/or periorbital angioedema or food sensitive eczema. Among those with anaphylaxis, the most common manifestations were dyspnoea/wheeze (73.9%), angioedema (65.2%) most commonly of the lips, urticaria (60.9%), and diarrhoea (34.8%).

Majority of OAS was from shellfish/crustacean (90.6%); of which shrimp (30.3%), crab (15.2%), and lobster (3.0%) were the most common. Mild childhood asthma (69.7%), allergic rhinitis (6.3%), and eczema (6.1%) were the most common atopic condition among individuals with shellfish/crustacean OAS. This pattern was similar for shellfish/crustacean anaphylaxis.

SPTs were most commonly positive for shrimp (OAS 87.1% vs. anaphylaxis 100%), crab (OAS 95.8% vs. 90.9%) and lobster (OAS 91.7% vs. 63.6%). Two pre-enlistees had food sensitive eczema to cow's milk and peanut respectively. There were no cases of food-dependent exercise-induced anaphylaxis. The above information is summarized in **Table 1**.

Table 1. Most common foods and concomitant atopy among patients with food induced oral allergy syndrome and anaphylaxis

Variable	Oral allergy syndrome (n = 33)	Anaphylaxis (n = 23)
Culprit food		
Prawn	10 (30.3)	8 (34.8)
Crab	5 (15.2)	4 (17.4)
Squid	2 (6.1)	0 (0)
Lobster	1 (3.0)	0 (0)
Other foods		
Peanut	0 (0)	5 (21.7)
Egg	0 (0)	1 (4.3)
Abalone	0 (0)	1 (4.3)
Limpet	0 (0)	1 (4.3)
Bird nest	0 (0)	1 (4.3)
Buckwheat	0 (0)	1 (4.3)
Atopy		
Asthma	23 (69.7)	11 (47.8)
Allergic rhinitis	10 (30.3)	7 (30.4)
Eczema	2 (6.1)	1 (4.3)
Positive skin prick tests		
Shrimp	27/31 (87.1)	11/11 (100)
Crab	23/24 (95.8)	10/11 (90.9)
Lobster	22/24 (91.7)	7/11 (63.6)
Squid	11/20 (55.0)	1/8 (12.5)
Clam	9/20 (45.0)	2/9 (22.2)
Oyster	6/19 (31.6)	3/4 (75.0)
Scallop	6/20 (30.0)	1/9 (11.1)
Mussel	0 (0)	4/10 (40.0)

Values are presented as number (%).

Skin prick tests denominators vary with each respective food allergen as not all patients had all the skin tests done to the same panel of food allergens.

DISCUSSION

Allergic diseases are common in Singapore among children and adolescents (defined as up to 21 years old in the Singapore content), especially asthma [1], allergic rhinitis [2], and atopic dermatitis [3]. House dust mite is the most important inhalant allergen driving allergic sensitization in these 3 conditions in Singapore and Southeast Asia [4, 5], more so than grass and tree pollen. Anaphylaxis from food allergy (especially seafood/shellfish) and drug allergy/hypersensitivity (especially nonsteroidal anti-inflammatory drugs) are also common [6, 7].

In the international study of asthma and allergies in childhood (ISAAC) published in 1996 [8] and 2004 [9], the Singapore prevalence of doctor-diagnosed asthma was 20%, parent-reported rhinitis 44%, and chronic rashes 12% in 1996. In 2009, the Growing Up in Singapore Towards healthy Outcomes (GUSTO) study was initiated [10]. This is a large birth cohort study comprising 1,163 pregnant mothers and their children, with an integrated Allergy domain describing the epidemiology of allergic manifestations, phenotype, and the association between the development of metabolic diseases and allergy. Some of the key findings from the GUSTO cohort to date are as follows. Firstly, early childhood rhinitis up to the age of 18 months was associated with a history of parental atopy; atopic comorbidities of eczema and wheeze, but not allergen sensitization [11]. Secondly, early onset (before 18 months of age) eczema and wheeze are risk factors for later allergen sensitization as demonstrated by positive SPT to inhalant allergens (house dust mites: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blomia tropicalis*) and food allergens (egg, peanut, and cow's milk) [12]. Thirdly, there is a possible influence of maternal diet during pregnancy

on the development of allergic outcomes (eczema, rhinitis, and wheeze) in offspring up to the first 36 months of life [13]. Fourthly, delayed introduction of allergenic foods (egg, peanut, and shellfish) after 10 months in 50% or more of infants did not increase the prevalence of food allergy between the ages of 12–18 months: egg allergy 0.35%–1.8%, peanut allergy 0.1%–0.3%, and shellfish allergy 0.2%–0.9% [14]. This contrasts with the recent recommendation of early introduction of peanuts to prevent the onset of peanut allergy in high risk infants based on the “Learning Early About Peanut” study [15].

Food allergy in Singapore is relatively common among children and adolescents where shellfish allergy is overall more common than egg, cow's milk, and peanut allergy [16, 17]. Some unusual food allergens have also been reported locally, namely bird's nest [18], galactooligosaccharide – a prebiotic found in milk formulas [19], dust-mite contaminated flour [20], and tropical fish (threadfin, Indian anchovy, pomfret, and tengirri) [21]. Case series of food-dependent exercise induced anaphylaxis from shellfish [22] and wheat [23] have also been reported. A novel OAS from crustacean-shellfish allergy presenting with predominantly oral symptoms (tingling, lip swelling) has also been described in Singapore [24], with tropomyosin in house dust mites believed to be a possible cross-reactive sensitizing inhalant allergen [25]. This is consistent with the findings in our study.

There is paucity of literature on allergic disorders experienced by military servicemen or pre-enlistees in the Asia-Pacific region. Most of the literature in military medicine describe case reports/series on the epidemiology of insect venom hypersensitivity [26–28], asthma [29]/ exercise-induced bronchoconstriction [30], anaphylaxis [31, 32], and skin disorders [33, 34]. The literature on therapeutics in allergic diseases in the military covers mostly venom immunotherapy (VIT) and the use of epinephrine autoinjectors in anaphylaxis. VIT is the definitive treatment for insect venom anaphylaxis, enabling active duty servicemen to remain medically fit and ready for deployment around the world [35, 36]. Epinephrine autoinjector use in military patient populations [37, 38] has also been described. From the Asia-Pacific region, there has only been a single study describing the prevalence of allergic disease and wheezing among Korean military personnel [39] using a modified ISAAC questionnaire. The prevalence of current wheeze (10.5%), allergic rhinitis (14.0%), and eczema (9.7%) confirmed a significant prevalence of allergic disease in young adults in the Korean military.

Food allergy can be a limiting factor in the deployability of servicemen, as providing for a range of allergen-free rations in the field can be challenging; and there is an ever-present risk of a severe allergic reactions occurring in training areas with limited access to tertiary medical care.

Self-declaration of food allergy at pre-enlistment was implemented in 2015 as there appeared to be an increasing prevalence of food allergy among pre-enlistees. Servicemen with food allergies have their food allergy documented in their electronic personnel records, such that they can be supplied with suitable allergen-free diets in their camp cookhouses.

OAS to shellfish/crustaceans among pre-enlistees is consistent with the phenotype described in recent studies on shrimp allergy in Singapore [24]. The risk of accidental shrimp ingestion in a shrimp OAS patient triggering off anaphylaxis is unknown, and there are no studies presently to identify and risk-prognosticate such patients. Shrimp allergic individuals react to several high-molecular weight allergens, making molecular diagnosis with component resolved diagnostics difficult [40]. Tropomyosin and sarcoplasmic-calcium binding protein sensitization has been

shown to be associated with clinical reactivity to shrimp, arginine kinase and hemocyanin appear to be cross-reacting allergens between shrimp and arthropods [41]. In contrast in pollen-fruit OAS, the primary sensitizing and cross-reactive allergens are more clearly defined, and reactions are generally mild with little risk for anaphylaxis [42, 43]. For servicemen with shellfish anaphylaxis, the risk of accidental ingestion when outfield vis-à-vis difficulty in obtaining early access to emergency medical services continues to pose a risk to them being field-deployable [44]. However, for the majority of shellfish/crustacean-allergic pre-enlistees who have mild oropharyngeal symptoms, the avoidance of seafood ingredients in field rations should be sufficient to allow them to be field-deployable, as the risk of anaphylaxis in this group is likely to be low.

Oral immunotherapy (OIT) for food allergy may in future become a therapeutic option in achieving long-term tolerance (rather than just desensitization) with daily ingestion of the culprit food allergen [45]. For now, OIT remains a research tool, limited mainly to cow's milk, egg, and peanut allergy even though they have been mentioned in recently written clinical practice guidelines from Spain [46] and Japan [47]. More well designed randomized clinical trials are needed before OIT can become standard of care (like VIT). Although house dust mite sublingual immunotherapy has been reported to improve symptoms of shrimp allergy [48], this alone is unlikely to be effective where nontropomyosin allergens are involved. T-cell epitope peptide immunotherapy [49] and addition of other adjuvants may be needed to improve the efficacy and safety of immunotherapy.

A limitation of this study was that all pre-enlistees with shellfish/crustacean OAS were not contemporaneously offered repeat SPT (regardless how long before they had last been done), followed by confirmatory OFC to determine their threshold of reactivity, as in a previous local study [24]. The variability of the threshold of reactivity between individuals may pose a risk of systemic reactions following accidental ingestion. OFCs may play a role in determining the anaphylaxis-risk and thus field-deployability of an individual with OAS.

In conclusion, allergy to shellfish/crustaceans was the most common food allergy among pre-enlistees, and OAS to shellfish/crustaceans was more common than anaphylaxis.

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