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ORIGINAL ARTICLE

Clinical characterization of Chilean patients with IgE-mediated food allergy

Caracterización clínica de pacientes chilenos con alergia alimentaria mediada por IgE

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Abstract

Background: Food allergy (FA) is an entity of high and growing prevalence, which can be mediated by IgE or cellular immunity. It can have a wide range of symptoms and be triggered by multiple food antigens, which vary in different geographical areas. Objectives: To describe clinical characteristics of Chilean patients with IgE-mediated FA. Patients and Method: Retrospective review of patients with IgE-mediated FA treated at a tertiary healthcare center in Santiago, Chile, between 2006 and 2016. Demographic characteristics, clinical manifestations, and trigger foods were evaluated. Results: A total of 282 patients diagnosed with IgE-mediated FA were included. 89% had FA onset before 18 years of age and most of these before one year of age (median of age: one year; range: one month-55 years). The most common clinical manifestations were hives, angioedema, dyspnea, and vomiting. 40% had symptoms compatible with anaphylaxis. The foods most frequently involved were egg, cow's milk, peanut, shellfish, walnut, tomato, wheat, avocado, fish, and legumes. Egg, cow's milk, and peanut allergies were the most frequent at pediatric age, while seafood allergy was the most frequent among adults. Conclusion: Foods causing IgE-mediated FA in Chile were similar to those described in other countries, although the frequency of tomato and avocado allergy, which are unusual in international series, stands out. Anaphylaxis incidence was high, emphasizing the need for epinephrine autoinjectors in Chile.

Keywords: Food allergy; immediate hypersensitivity; anaphylaxis; Chile; egg allergy;

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Introduction

Food allergy (FA) is a specific abnormal and reproducible immunological response, which occurs in a person after the intake of a particular food¹. The immune response to food antigens can be mediated by specific IgE antibodies (IgE-mediated or immediate hypersensitivity) or by T lymphocytes (non-IgE-mediated or cellular hypersensitivity)².

Clinical manifestations of FA include various symptoms, which depend on the underlying immunological mechanism (IgE-mediated or non-IgE-mediated)3. Acute-onset symptoms (presenting within minutes up to two hours after the food intake) are usually IgE-mediated and may involve the skin (urticaria, angioedema, erythema), gastrointestinal tract (oral pruritus, colics, vomiting, and diarrhea), respiratory system (rhinitis, shortness of breath) and/ or cardiovascular system (hypotension, cardiogenic shock), being anaphylaxis the most severe manifestation⁴. On the other hand, subacute or chronic presentation of symptoms (within minutes up to days after the food intake) generally reflect non-IgE-mediated cellular responses, which mainly occur at the gastrointestinal tract (vomiting, diarrhea, abdominal pain, rectal bleeding) and skin (exacerbation of atopic dermatitis)5.

The risk of acute and potentially fatal reactions, which are fortunately infrequent, and the marked effects on the quality of life of patients with IgE-mediated FA and their families indicate that this disease is a global public health problem^{6,7}. In the last decades, an increase in FA prevalence has been reported worldwide, however, the epidemiology of this disease is still largely unknown, in part due to the variety of diagnostic criteria and FA definitions used by researchers⁸. Despite these limitations, it is estimated that FA affects from 1% to 10% of the global population, with a prevalence of 6% to 8% in children younger than three years and 2% to 4% in the adult population^{6,9}.

The most common foods that cause IgE-mediated FA globally are cow's milk (CM), egg, peanut, walnut, soy, wheat, seafood, and fish, although FA-causing foods vary by age group and geographic region^{10,11}.

Recent data obtained by our group showed that 5.5% of schoolchildren in Santiago, Chile, had a history that was compatible with IgE-mediated FA¹². Based on this data, the main foods reported were walnut, peanut, avocado, banana, seafood, CM, citrus fruits, wheat and fish¹². However, there is still little information regarding the clinical and demographic characteristics of the patients with IgE-mediated FA of different age groups in our country.

The objective of this study is to describe the clinical

and demographic characteristics and the most common foods involved in Chilean patients with IgE-mediated FA treated at a tertiary health center in Santiago, Chile.

Patients and Method

A retrospective review of the clinical records of patients with IgE-mediated FA treated at the immunology and allergy clinics of the UC Christus Health Network between 2006 and 2016 was performed. IgE-mediated FAs were diagnosed by a compatible clinical history and demonstration of food-specific IgE antibodies, through prick test with food extracts (Leti®, Spain) and/or serum-specific IgE (Immulite®, Siemens, Germany or ImmunoCap®, Phadia, Sweden).

The demographic data, clinical characteristics, and test results were registered in a database.

Anaphylaxis was defined as a severe systemic allergic reaction of acute onset associated with at least one of the following previously reported clinical criteria¹³: 1) Acute onset of an illness with involvement of the skin, mucosal tissue, or both, and respiratory compromise or hypotension, without a clear relation to a food allergen; 2) two or more of the following manifestations, which occur quickly after the intake of a likely food allergen, a) skin and/or mucosal involvement, b) respiratory compromise, c) hypotension or associated symptoms or d) persistent gastrointestinal symptoms; and 3) hypotension after the exposure to a food allergen known to the patient.

The Scientific Ethics Committee of the Faculty of Medicine of the Pontificia Universidad Catolica de Chile approved this study.

Statistical analysis

The frequency (percentage) was calculated for qualitative variables, while for quantitative variables, the mean and standard deviation were estimated. For the quantitative variables with high dispersion and atypical distribution, the median, range and interquartile range were calculated. The Kruskal Wallis test was used for independent samples in order to compare differences in the FA age of onset of patients allergic to different foods.

Results

Two hundred eighty-two patients with IgE-mediated FA diagnosis were included (Table 1). Eighty-nine percent had FA before age 18, and most of them before age one year (age median: 1 year; range: 1 month – 55

Table 1. Demographic characteristics of patients		
	n (%)	
Total	282	
Male gender	166 (58.8)	
Age group		
0 - 5 years	204 (72.3)	
6 - 11 years	30 (10.6)	
12 - 17 years	16 (5.6)	
≥ 18 years	32 (11.3)	

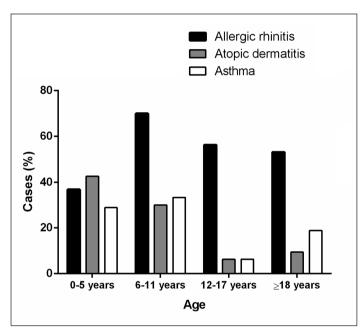


Figure 1. Frequency of atopic comorbidities at different ages.

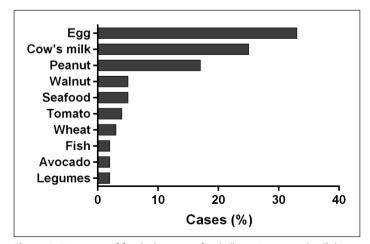


Figure 2. Frequency of foods that cause food allergy. Legumes: lentil, bean, green bean and pea; shellfish: shrimp, mussel, crab and abalone; fish: hake, salmon, codfish, herring and mackerel.

years). Pediatric patients had a median age of 1 year (interquartile range 0.5-4 years) and 62% were male. Adult patients (≥ 18 years) had a median age of 29 years (interquartile range 25-37 years) and 69% were females.

Of the total number of patients, 68% (n=192) had an atopic comorbidity, allergic rhinitis (AR) in 45%, atopic dermatitis (AD) in 35% and asthma in 27%. Of these, 64 patients (33%) had two atopic comorbidities and 21 (11%) had AR, AD, and asthma. Asthma and AR were the most frequent atopic comorbidities (15%). On the other hand, after analyzing the frequency of atopic diseases in different age groups, AR was more common in patients older than 6 years, while AD was more common in patients younger than this age (Figure 1).

Sixty-two percent of the patients had a first-degree relative with allergic diseases and 19% had at least one first-degree relative with family history of FA. The most commonly reported clinical manifestations of IgE-mediated FA were urticaria (90%), angioedema (57%), dyspnea (30%) and vomiting (21%). Forty percent had a history compatible with anaphylaxis.

In the study sample, the most common foods causing FA were: egg (33%), CM (25%), peanut (17%), and seafood (5%) (Figure 2), which were related to high levels of specific IgE and/or food prick test. Therefore, patients with egg, CM, peanuts and seafood allergy had on average: a 7 mm papule and 80.2 kUA/L specific IgE to egg, an 8.4 mm papule and 67.5 kUA/L specific IgE to CM, a 6.5 mm papule and 74.7 kUA/L specific IgE to peanut, and a 6.8 mm papule and 100 kUA/L specific IgE to seafood. Due to the great variety of clinical manifestations and that not every patient had a specific IgE and prick test, it was not possible to estimate if there was a statistical correlation between clinical manifestations and the levels of specific IgE and/or prick test to the involved food

On evaluating the FA-causing foods in relation with patient age, it was possible to observe that egg, CM and peanut were the main causes of IgE-mediated FA in patients younger than 12 years, with a clear decrease in frequency at older ages, in which these almost disappear as causal food in patients older than 12 years (Figure 3). The opposite is observed with seafood, where it was possible to observe an increased frequency in older patients, being almost inexistent in patients younger than 6 years and the main cause of FA in patients older than 18 years (Figure 3). Therefore, the age of onset of FA was significantly different between patients allergic to CM, egg, peanut, and seafood (p < 0.001). Twenty-nine percent of the patients had IgE-mediated FA to two or more foods.

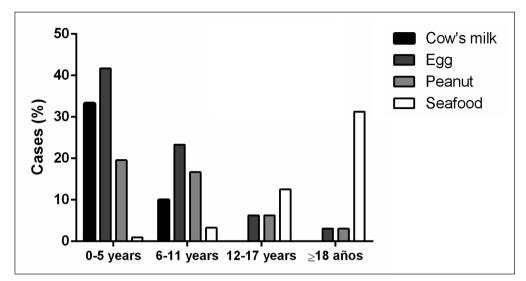


Figure 3. Frequency of foods that cause food allergy at different ages. Shellfish: shrimp, mussel, crab and abalone.

Discussion

This study describes a large series of IgE-mediated FA cases in Chile and establishes the most common causal foods at different ages. Similar to other FA studies, most of the patients had comorbid atopic diseases, being AD the most frequent in patients younger than 6 years and AR in patients older than 6 years (Figure 1)^{14,15}.

The IgE-mediated FA causal foods identified in this study were similar to those described in other countries. However, the presence of avocado and tomato is noteworthy, as these are uncommon foods in international FA series^{10,16,17}. Allergy to these foods usually occurs due to cross-reactions with seasonal pollen in patients with oral allergy syndrome. However, additional studies that delve into the causes of these allergies in our population are required.

IgE-mediated FA has been previously identified as the main cause of anaphylaxis during childhood^{18,19}. In this study, 40% of the patients had a history compatible with anaphylaxis, which is in line with previously obtained data¹². This indicates that the anaphylaxis incidence in our population is frequent and is an important manifestation of IgE-mediated FA. These data highlight the need for education, both for patients and their relatives and for health personnel regarding how to identify and to treat this clinical manifestation accurately²⁰. Adrenalin is the first-line treatment for anaphylaxis and it must be administrated early since it has been demonstrated that a delay in its use is associated with a higher risk of a fatal outcome^{20,21}. This, and the high incidence of FA-induced anaphylaxis in our country makes it necessary to have adrenalin auto-injectors in Chile, a medication that is hard to obtain in our

country and is not available in the public system²².

One of the main limitations of this study is that the clinical information of this study was collected retrospectively from clinical records, and that often patients and families report confusing information regarding the symptoms and their temporality. Another limitation of this study is that the FA diagnosis was based on a suggestive clinical history and confirmation of the presence of food-specific IgE (through prick test or serum specific IgE), while the gold standard corresponds to the oral food challenge test^{6,23}. Both limitations could be solved with the implementation of oral food challenges, however, the associated costs and the contraindication of performing it in a large number of patients with acute anaphylaxis risk would make it impossible to evaluate a significant number of patients due to the characteristics of our population and the available resources. Another limitation emerges from the fact that, in our experience, the FA-affected adults in Chile tend to consult for this condition less often than children, thus, the adult sample of this series is probably underrepresented. Some of the strengths of this study are the large number of patients included in the study and the inclusion of children and adults.

In conclusion, this study characterizes IgE-mediated FA in a large series of patients in Chile. The most common manifestations were urticaria and angioedema, with a high incidence of anaphylaxis. The most common foods involved were similar to those described in other countries, with the exception of avocado and tomato, which are infrequent in international series. The high anaphylaxis incidence emphasizes the need for education and for availability of adrenalin auto-injectors in Chile.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients

and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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