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Clinical and Laboratory Investigation of Food Allergies

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Abstract

Background: We retrospectively analyzed data from 1090 referrals for investigation of allergies.

Methods: Detailed clinical history, skin tests, specific IgE.

Results: Food allergies accounted for a significant percentage of the referrals (27.17%). IgE and non-IgE allergies were detected in 20.02% and 7.15% of cases, respectively. The prominent symptom of IgE mediated allergies was generalized urticaria and/or angioedema, while anaphylaxis was detected in 12.58% of cases. The most common sensitizations were to milk, egg, and tree nuts with a significant sensitization to peanuts. Comorbidities such as eczema, allergic rhinitis and asthma were not frequently reported (18.58% and 12.89% respectively). Among patients with IgE milk allergy and allergic proctocolitis, a significant number responded to extended hydrolyzed milk.

Conclusions: Food allergies in children are an important focus for the Department of Allergy. Our results are not consistent with in previous reports on food allergies in Athens, Greece. We report the incidence of anaphylaxis and systemic reactions, as well as high incidence of tree nut allergies, especially to peanuts and walnuts, in addition to milk and egg allergies. We also observed a high incidence of FPIES syndrome in fish. We report the incidence of concomitant diseases including allergic rhinitis/asthma and eczema, and compare our findings with existing literature.

Key Words: Food allergy, Athens, Greece.

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1- INTRODUCTION

Food allergy prevalence is related to eating habits and lifestyle, resulting in a geographical distribution of allergens that are the culprit. In westernized countries, the prevalence of food allergies has rapidly grown in the last twenty years, leading specialists to support the notion of a new allergy epidemic (1). Therefore, food allergy is a significant reason for referral to an Allergy Department. The clinical presentation varies from mild rashes to life threatening episodes of anaphylaxis. The cornerstone of treatment is avoiding the culprit food.

We present data from patients with food allergies referred to our department for investigation between 2013 and 2017. Overall, 1090 children were examined either on an outpatient basis or as hospitalized patients in the Pediatric Clinic. The aim of the study is to present data regarding food allergies in a sample of the pediatric population with allergies in Athens.

2- MATERIALS AND METHODS

This study was conducted retrospectively and ethical approval is not applicable. We analyzed data from 1090 patients routinely examined in the Allergy department in Greece during the period 2013-2017. The department functions as a referral unit for outpatients and inpatients within the 1st Pediatric Clinic of the University of Athens. Detailed clinical history regarding age, gender, the first appearance of symptoms, clinical presentation, concomitant diseases, follow-up, and physical examination were conducted.

Sensitization measurements, such as Skin Prick tests or Prick to Prick tests, were performed by the same experienced nursing staff and recorded. Results were considered positive, when a wheal ≥3mm was measured. Histamine, as a control, was measured at ≥3mm, and the negative control showed no sensitization, both provided by HAL Allergy commercial allergens.Specific IgE was measured using the ImmunoCap method and a titer ≥0.35 was considered positive for all allergens. Analysis was performed by a specialist in Excel using our data.

3- RESULTS

3-1. Incidence of Patients with Reported Food Allergy Among Referrals from Pediatricians

The number of patients presenting with food allergy was 296 out of the total 1090 referrals standing at 27.15%. Patients suffering from IgE mediated food allergy were 218 out of 1090 (20.02%), while patients with non-IgE mediated allergy were 78 out of 1090 (7.15%) of the total, including 60 patients with allergic proctocolitis (5.51%), 8 with eosinophilic esophagitis (0.73%), and 10 with FPIES (0.92%). The distribution of food allergy among other referrals for allergy investigation are presented in Figure 1. The distribution of the diagnosis of food allergy in different ages is presented in Figure 2, showing a decrease in incidence in older ages with a cut off at the age of 3.

Regarding patients with reported food allergy, 168 were boys (56.75%) and 128 were girls (43.24%). Thirty immigrants of different origins were included (10.49%), as well as 3 Roma (1.05%). Roma is a marginalized society that maintains its own traditions and a nomadic lifestyle.

3-2.Clinical Presentation of Patients with a Food Allergy

Anaphylaxis, based on clinical criteria was diagnosed in 36 out of 218 (12.58%) cases. The culprit foods in anaphylaxis cases were as follows: 13out of 36 (36.46%) were tree nuts, 7 out of 36 (19.44%) were cow milk, 5 out of 36 (13.88%) were egg, and 5 out of 36 (13.88%) were legumes.

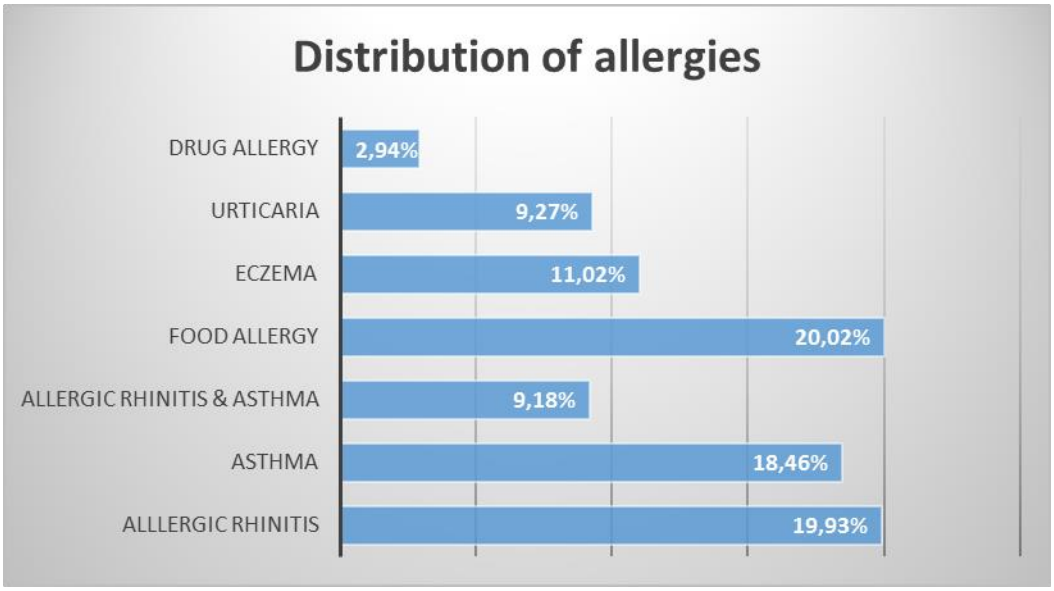

Figure-1. Distribution of allergies in our sample.

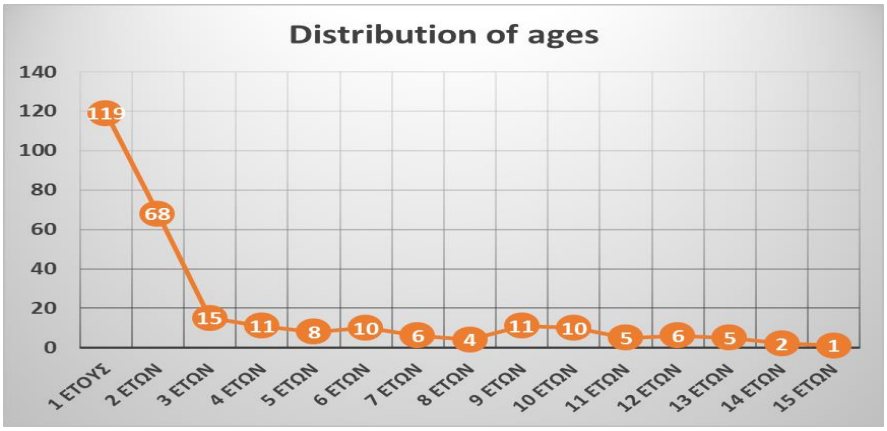

Figure-2. Distribution of age of diagnosis of food allergy implying the incidence of food allergy in different ages.

No fatalities were reported. Generalized reactions with significant angioedema or generalized urticaria or both were detected in 42 out of 218 children (14.69%), 22 out of 218 children (7.69%) and 13 out of 218 children (4.55%), respectively (Figure 3). Mild reactions with rash were detected in 53 out of 218 (18.53%) children, while 53 out of 218 children had concomitant eczema (18.53%). Although children with eczema who were sensitized to food allergens rarely developed symptoms apart from a mild deterioration of their skin problem, the culprit food was generally not avoided (Figure 3).

Clinical presentation from the gastrointestinal tract included 41 out of 218 children presenting with vomiting (14.34%) and 8 out of 218 with diarrhea (2.80%). Three children presented with dysphagia (Figure 3).

In our sample, cases of non-IgE mediated food allergy were included. We observed 60 out of 296 cases of allergic proctocolitis (20.27 %), 8 out of 296 cases with eosinophilic esophagitis (2.70%), and 10 out of 296 patients with FPIES syndrome (3.37%).

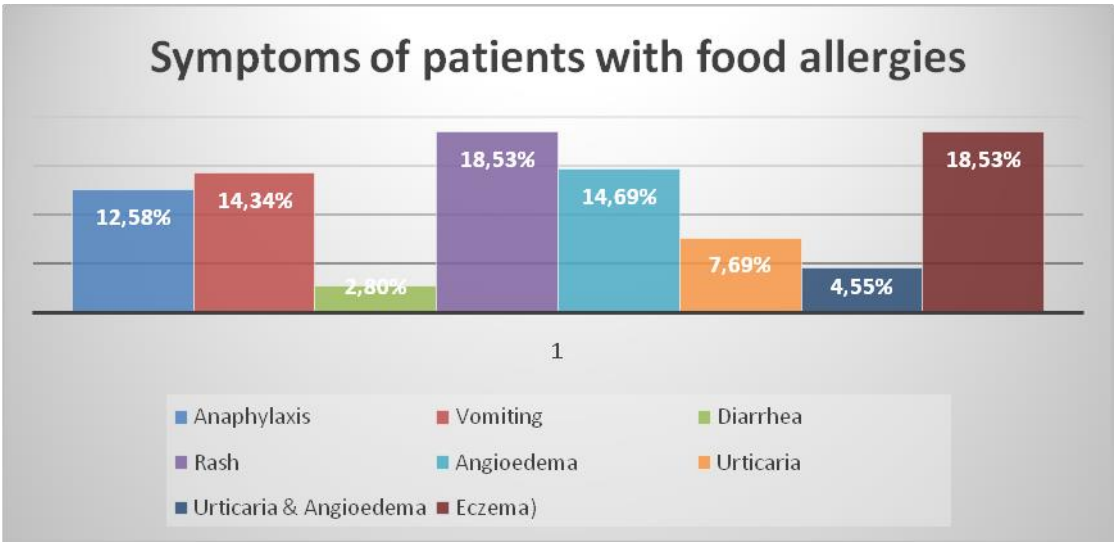

Figure-3. Data regarding the symptoms of the patients.

Comorbidities were eczema in 53 out of 296 patients (18.53%) and allergic rhinitis or/and asthma in 37out of 296 patients (12.89%).

3-3.Sensitization to Food Allergens

Most of the patients were tested with Skin Prick Test or Prick to Prick Test (82.51%). Most patients with negative tests were referred for milk allergy, while extended measurement of specific IgE was included in more severe cases.

Our data show that sensitizations to allergens were as follow as: 79 out of 218 to milk (27.62%), egg (egg white=52 out of 218, 18.18%, egg yolk=25 out of 218, 8.74%), peanut 39 out of 218 (13.64%), walnut 23 out of 218 (8.04%), hazelnut 22 out of 218 (7.69%), almond 22 out of 218 (7.69%), cashew 18 out of 218 (6.29%), fish 20 out of 218 (6.99%), and shrimp 6 out of 218 (2.10%) (Figure 4). Overall, the most common sensitizations were to milk, egg, and peanut. It is worth mentioning that 175 out of 218 patients (61.19%) were sensitized to more than one allergen.

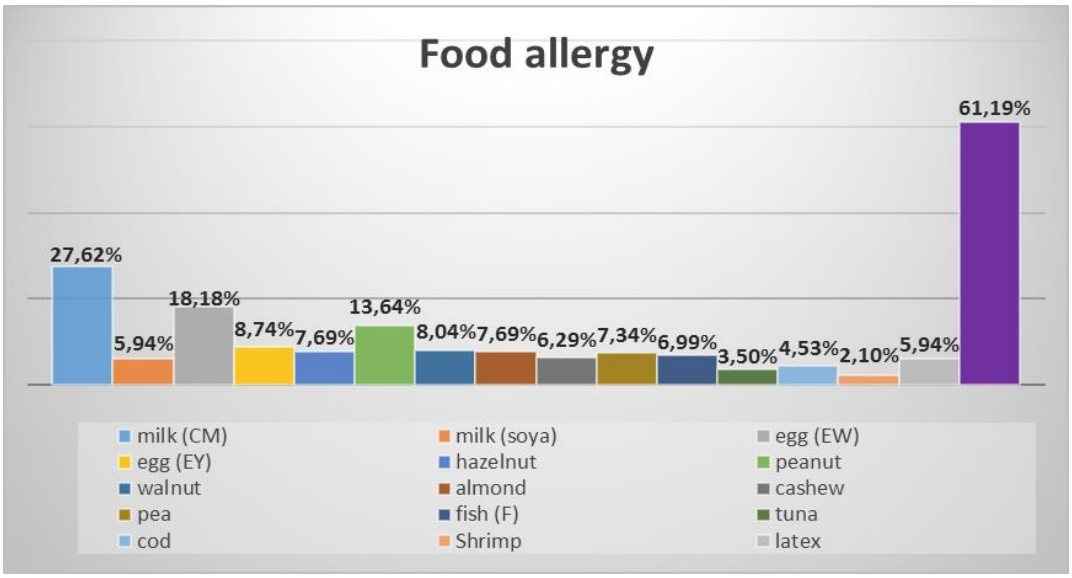

Figure-4. Data regarding the distribution of sensitization to different food allergens among patients with food allergy.

Furthermore, we measured IgE titers in 29 out of 286 patients due to the severity of the clinical presentation. Thus, 3 out of 29 had a titer>1500mg, 4 patients >1000mg/dl, 3 patients between 500-1000, 7 patients between 100-500, and 15 patients with a titer <100.

3-4. Treatment

It is well known that avoidance is the cornerstone of treatment for food allergies. A challenge test is performed either to diagnose the allergy, when tests are inconclusive or to detect a state of tolerance. We performed 24 negative challenge tests in patients with cow milk allergy and 17 negative tests in patients with egg allergy. None of the challenge procedures were positive regarding milk and egg. The mean age at which patients tolerated milk, as documented by a challenge test, was 20.54 months (ranging from 1 month to 5 years) and egg was 3.18 years (ranging from 15 months to 6 years). In more severe cases, a partially hydrolyzed milk, included in the milk ladder by many departments in Greece, was given to 12 children until a mean age of 30.75 months. Similarly, baked egg, included in the egg ladder, was given successfully to 13 out of 17 patients with severe egg food allergy at a mean age of 21 months. The mean age of tolerance to milk in children with allergic proctocolitis was 13 months.

It is noteworthy to mention that 28 out of 79 mothers with a child with IgE mediated milk allergy decided to offer breastfeeding (35.44%). The rest of the children were fed with different kinds of formulas. Particularly, an amino acid formula was given to 20 out of 79 children (25.31%), extensively hydrolyzed to 17 out of 79 children (21.51%), extensively hydrolyzed without casein to 25 out of 79 children (31.64%) and partially hydrolyzed to 12 out of 79 children (15.18%).

Regarding children with allergic proctocolitis, 16 out of 60 mothers decided to continue breastfeeding while avoiding dairy products (26.67%), 6 out of 60 children (10%) were fed with an amino acid formula, 17 children (28.33%) with extensively hydrolyzed milk and 10 children (16.66%) with extensively hydrolyzed milk without casein (Figure 5).

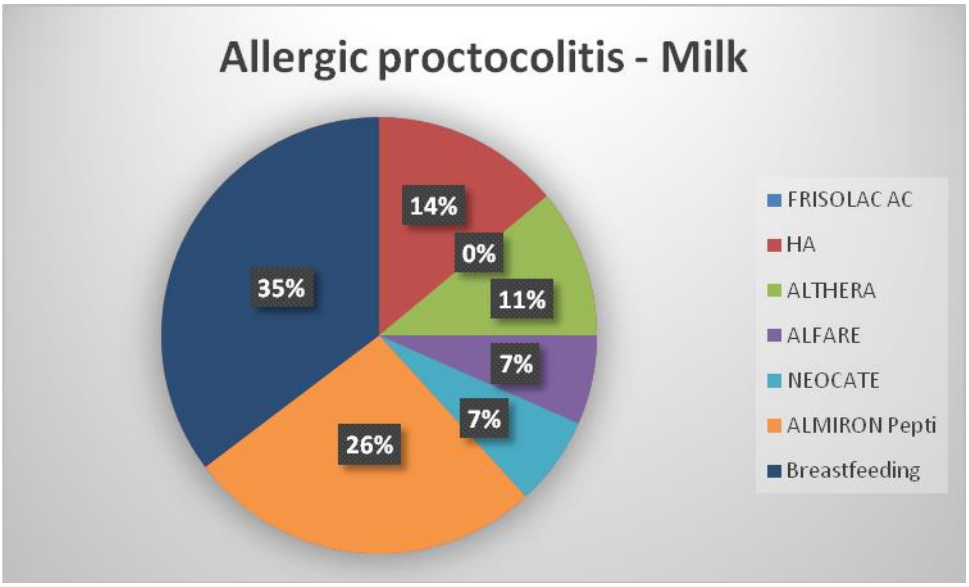

Figure-5. Milk substitution in children with allergic proctocolitis. The above graph shows that a significant percentage of patients respond to extensive hydrolyzed formulas.

3-5. Hereditary History

Our data did not detect any difference regarding the family history from the mother or the father. More specifically, 83 out of 296 patients had an atopy history from the father (28.04%) and 87 out of 296 patients from the mother (29.39%). However, 129 out of 296 patients did not mention any history of atopy in the family (43.58%). The distribution of allergic diseases of the father was asthma (20.48%), allergic rhinitis (50.60%), eczema (13.25%), and food allergy (15.66%). The distribution of atopy of the mother was asthma (28.73%), allergic rhinitis (48.72%), eczema (16.09%), and food allergy (2.29%).

4- DISCUSSION

Food allergies are becoming an increasing burden in industrialized countries. In the USA the increase has been around 18% and the ambulatory care visits per year soared by 73% between 2007 and 2017 (1). However, accurate prevalence estimations range between different reports due to elusive factors such as definition, study population, methodology, geographic variation, age, and dietary exposure. Similarly, in the UK, the estimated prevalence in children was 8% (2), and the EACCI reports lifetime and point self-reported prevalence in the general population as 17% and 6%, respectively. However, challenge testing confirmed food allergy in less than 1% of reported cases. The frequency, as expected, is higher in children and in North-West Europe (3).

Regarding clinical presentation in our sample, anaphylaxis and systemic reactions with generalized urticarial /angioedema were the main symptoms standing at 12.58% and 14.69%, respectively. The majority of patients presented with mild symptoms, including a rash (18.56%) and eczema (18.53%), and a significant proportion presented with symptoms from the gastrointestinal tract (14.34%).

In the literature, anaphylaxis is described in 13% to 65% of patients with food allergies, depending on the strict application of the diagnostic criteria (4). In the EACCI position document, the prevalence of food induced anaphylaxis in Europe ranged from 0.4% to 39.9%. Regarding the food allergens implicated in anaphylaxis, cow's milk was reported to be the culprit food in 29% of cases, hen's egg in 25%, hazelnut in 5% and peanut in 4% (3). In our sample, the culprit food in cases with anaphylaxis or systemic reaction was tree nuts (36.46%), cow milk (19.44%) and egg white (13.88%). None of the cases was fatal.

A significant percentage (27.27%) of patients suffered from non IgE mediated food allergy. Most of them were diagnosed with allergic proctocolitis (20.79%), as described in the literature (5). Interestingly, 10 patients were diagnosed with FPIES syndrome. Among patients with FPIES 6out of 10 (60%) had recurrent vomiting after the consumption of fish. A higher percentage for FPIES to fish was reported in a survey from Italy in which 65% of patients had a single fish FPIES and 35% had multiple fish FPIES (6).

The most frequent sensitizations among patients with food allergies were cow milk, egg, and peanut. The incidence of different food allergies in the random sample of 1090 patients examined was: milk 79/1090 (7.2%), egg white 52/1090 (5.41%), egg yolk 25/1090 (2.2%), peanut 39/1090 (3.57%), walnut 23/1090 (2.11%), hazelnut and almond 22/1090 (2.01%). A significant proportion of the patients, 175/218 (61.19%), were polysensitized. These results may not represent the incidence of these allergies in the general population, but they could illustrate the incidence of allergy to different foods and suggest an increased incidence of peanut allergy.

The European RedAll telephone survey reports that cow milk allergy represents 22.6% of food allergies in children (7). According to data in the general population, 3.5% of people suffer from milk allergy, 1.3% from egg allergy, 0.75% from peanut and 0.6% from fish allergy (7). However, the point prevalence is 2.3% for milk, 1.5% for egg, 1.5% for wheat, 1.7% for peanut and 0.6% for fish (3). In the US, the prevalence of food allergens in the general population is reported to reach 0.4% for milk, 0.2% for egg, 1.3% for peanut and 1% for shrimp (8).

From our results, it is interesting that children with IgE food allergy and allergic proctocolitis respond to extended hydrolyzed milks and do not need amino-based formula. In the literature amino-based formula is suggested for allergic proctocolitis, but we had good results with less extended hydrolyzation products.

As far as concomitant atopic disease is concerned, 18.53% of patients in our sample suffered from eczema while 12.89% developed allergic rhinitis and/or asthma. Results reported in the literature reveal a higher percentage of concomitant diseases in patients with food allergies. In the US, it is reported that food allergic children have a 4-fold increased likelihood of developing asthma and a 2.4 likelihood of developing eczema. It is estimated that 35-71% develop eczema, 33-40% develop allergic rhinitis and 34-49% develop asthma (8).

The investigation of the hereditary history of patients gave interesting results. In 1/3 of patients it was reported a negative family history for atopy, while positive history was equally referred from the father and the mother. That is to say, 2/3 of the patients had an atopic predisposition. In the literature, maternal allergy is considered a stronger determinant of allergic risk. In a survey, 13% of atopic mothers will have a child with a food allergy (9). Our data do not detect such a predisposition. One could question maternal predisposition in the development of food allergy in different ethnic populations, which could be an interesting finding for further research.

Although results are interesting regarding food allergies in Greek children, our study has limitations. The sample is random, but it may not be representative, since the number of children is limited, and referrals are not in an organized system in Greece.

5- CONCLUSION

This is a retrospective analysis of patients with food allergies. Therefore, we propose that our results are not biased, as they include a random, and non-selected population.

To the best of our Knowledge, this is the first presentation of data from children in Greece who suffer from multiple food allergies that are not included in European surveys (10, 11). In the Europrevall study, the prevalence of egg allergy in the general population was found to be 0.7% (10). Hazelnut Cor 9 was more frequently detected in the Greek population. An internet survey in adults suggested an increased frequency of allergies to fruits (14.9%), seafood (10.7%), and nuts (9.2%) (12).

Our results indicate that, in addition to milk and egg allergies, peanut allergies are significant food allergens in the Greek pediatric population. One in ten children present with anaphylaxis, two-thirds have an allergic predisposition, one-fifth suffer from eczema, and one in ten will develop another allergy.

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