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SHORT COMMUNICATION

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Single food allergy and reasons for multiple exclusions: A prospective study

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Abstract
Food Allergies (FA) presents an increasing global challenge, influenced by factors such as genetic predisposition, ethnicity, age, and cultural dietary practices. Patients diagnosed with IgE-mediated FA must adhere to strict dietary restrictions to avoid potential life-threatening anaphylactic reactions. Such restrictions are crucial but come with significant consequences as increased nutritional risks, higher costs for special meal preparations and medical care with potential social and psychological impacts on both the individual and their family The impact of FA on quality of life is frequently surrounded by persistent fear of adverse reactions after consuming certain foods. To better understand the behavior of patients with FA this study aims to explore whether patients with confirmed IgE-mediated FA tend to exclude other foods and to identify possible reasons for such exclusions.
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Food allergies (FA), influenced by factors such as genetic predisposition, ethnicity, age, and cultural dietary practices, present an increasing global challenge.[1,2] Patients diagnosed with IgE-mediated FA must adhere to strict dietary restrictions to avoid potential life-threatening anaphylactic reactions. Such restrictions are crucial but come with significant consequences as increased nutritional risks, higher costs for special meal preparations, and medical care with potential social and psychological impacts on both the individual and their family.[3-6] The impact of FA on quality of life is frequently accompanied by persistent fear of adverse reactions after consuming certain foods.[3]

To better understand the behavior of patients with FA, this study aims to report if patients with confirmed IgE-mediated FA tend to exclude other foods and if so, reasons for this exclusion.

This is a cross-sectional analysis that was conducted at a tertiary referral outpatient setting in Brazil with patients from 2011 to 2022. Patients were considered to be truly FA patients if they had a recurrent clinical

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history consistent with IgE-mediated reactions or anaphylaxis, associated with positive specific IgE or a positive oral challenge test with IgE-mediated reactions. Patients with anaphylaxis because of nonfood allergens, mixed or non-IgE-mediated FA, or comorbidities requiring restrictive diets unrelated to IgE-mediated reactions were excluded.

Of the 305 patients followed,180 met the inclusion criteria. Data on the epidemiology and allergens excluded were extracted from medical records, with supplementary data obtained through telephonic interviews when necessary. The primary diagnosticated allergen was categorized as F1, and secondary excluded foods were classified as F2. Descriptive statistical analyses were taken via SAS 9.4 software. Qualitative variables were reported as frequencies and percentages, and quantitative variables as means and standard deviations. The study was approved by the local Ethics Commitee (Comitê de ética do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo—CAAE number: 77471224.7.0000.0068), and all persons involved had provided their informed consent to participate in the study.

Most of the patients (59% were diagnosed with allergies before 6 months of age. The most common F1 was milk (77.78%), followed by egg (17.22%). Anaphylaxis was reported in 70.56% of the patients, with a complete F1 epidemiological profile seen in Table 1.

Of the patients, 55% excluded at least one F2, with an average of 1.57 exclusions per patient, ranging from 1 to 12; 14 types of food were considered as F2s. The primary reasons for excluding additional foods were an isolated positive specific IgE test (32.24%) and symptoms attributed to foods without diagnostic confirmation (21.86%), as detailed in Table 1.

This can be considered a pioneer study in Latin America, as it reveals different FA patterns depending on cultural aspects. There was a high number of secondary exclusions in patients with IgE-mediated allergies. Milk and eggs are prevalent in Brazilian dietary guidelines, both as whole foods and in preparations since the start of complementary feeding,[1,2] which could explain why milk was the most described F1, followed by eggs, reinforcing the nutritional risk as it impacts growth.[7]

Among children with secondary exclusions, the most frequent was egg. In this context, excluding such a common food from the daily diet increases the risk of negatively impacting nutritional development and quality of life, especially for children's neuropsychomotor development. This highlights the importance of understanding the reasons for food exclusions in order to mitigate the risks, as well as the consequences associated with their removal from the diet.[1,3,5,6]

Surprisingly, the primary cause of excluding a second food was not a second IgE-mediated allergy, as in the FARE study[8], but the existence of positive laboratory tests without symptoms or symptoms without laboratory confirmation/criteria for IgE-mediated allergies. As there are no pathognomonic symptoms of FA, an accurate diagnosis is needed. Also, likely misdiagnosis through indiscriminate requests for unproven diagnostic tests or specific IgEs without clinical correlation have to be avoided, which can by itself lead to the development of an IgE-mediated FA upon reinsertion of an unnecessary food exclusion, as seen in patients with atopic dermatitis.[1]

Table 1 Demographic and Clinical Profile of Patients with a Confirmed Food Allergy (F1)

Variables	Frequency	(%)
Sex		
Feminin	72	40,45
Masculin	106	59,55
Diagnostic age (months)		
≤ 6	107	60,11
7–12	48	26,97
13-24	16	8,99
>24	7	3,93
Anaphylaxis		
Yes	127	70,56
Diagnosis		
Anaphylaxis + Positive Specific IgE	42	23,33
Positive TPO	8	4,44
Clinical History + Specific IgE	130	72,22
F1		
Peanut	3	1,67
Milk	140	77,78
Egg	31	17,22
Fish	1	0,56
Soy	1	0,56
Banana	3	1,67
Shrimp	1	0,56
F2		
Milk	14	7,78
Egg	57	31,67
Wheat	13	7,22
Peanut	29	16,11
Shrimp	18	10,00
Cashews	20	11,11
Brazil Nut	20	11,11
Soy	13	7,22
Nuts	18	10,00
Fish	14	7,78
Others*	41	22,78

Reason for F2 exclusion

All F2 (N=366)	(%)
Positive specific IgE, asymptomatic	32,2
Fear of ingestion with positive IgE, asymptomatic	8,2
Confirmed IgE-mediated allergies	18,6
Solely fear of ingestion	18,6
Symptoms attributed to foods without diagnostic confirmation	21,9

Exclusions without previous ingestion (N=39)	(%)
Positive specific IgE, asymptomatic	51,3
Fear of ingestion with positive IgE, asymptomatic	0
Confirmed IgE-mediated allergies	5,1
Solely fear of ingestion	35,9
Symptoms attributed to foods without diagnostic confirmation	7,7

*Others: kiwi, papaya, banana, strawberry, avocado, grapes, mango, corn, yam, ham, pork, vegetables, beans, peas, lentils, red and purple dye

The ongoing fear of severe allergic reaction can prevent patients and their families from trying new foods (neophobia) and may result in a cycle of unnecessary food exclusions, which could further exacerbate nutritional deficiencies and contribute to the development of additional allergies. In fact, the combination of fear and indiscriminate specific IgE testing can pose a risk of misdiagnosis of FA.

This profile of secondary exclusions could be the starting point toward an indication for the medical community that there are no reasons to alter the age and pattern of complementary feeding introduction, with no restriction of potentially allergenic foods, preventing unnecessary food exclusions, which could increase the risk of selective eating and neophobia.[1,2,3,6,9,10] In this scenario, patients who started excluding foods based only on sensitization are at risk of becoming truly allergic to those foods upon reinsertion, increasing the risk of FA in a potentially preventable manner.

Only about 20% of patients were truly F2 allergic, suggesting the possibility of associations among some allergies, more than just antigenic similarity. This needs to be explored in future research, like the association between allergies related to milk and eggs or eggs and nuts. It is important to understand IgE-mediated symptoms and to recognize when to value symptoms arising from nonimmunological situations, such as food contamination, viral urticaria, and worsening of atopic dermatitis lesions because of the risk of incorrect diagnosis and unnecessary food exclusions.[2]

This study has limitations. It was conducted at a single center, despite being a regional reference, and relied predominantly on secondary data, which may introduce information bias and limit the generalizability of the findings. However, the elevated percentage of exclusions can serve as an inspiration for future studies. The sample was obtained through convenience sampling, and not all food exclusions were confirmed through standardized diagnostic methods such as oral food challenges, even though strong selection criteria were used to avoid selection bias.

In addition, this study highlights the need for follow-up research to investigate the long-term consequences of food elimination on children's growth, nutritional status, and psychological well-being. Further studies employing prospective designs and standardized diagnostic criteria that contribute to a more robust and generalizable evidence of cause and effect aspects in this field are required.

This study demonstrates that patients with IgE-mediated FA frequently exclude additional foods for reasons other than food allergy, leading to unnecessary nutritional, social, and economic consequences. A comprehensive approach to FA management, incorporating accurate diagnostic and parental conversation to overcome fears, is crucial for improving patient outcomes and quality of life.

Competing Interests

The authors had no relevant financial or nonfinancial interests to disclose.

Author's Contribution

All authors contributed equally to this article.

Conflict of Interest

None.

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