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Experiences and attitudes of parents of children with cow's milk and other food-allergy

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Abstract

Introduction and objective: The attitude and behaviors of parents are important in the management of children with food allergy (FA). The aim of this study is to evaluate the experiences and attitudes of parents of children with allergy to cow's milk and other FA.

Materials and methods: The parents of children with FA were asked to complete an 18-item questionnaire to evaluate the FA history and experiences during diagnosis, treatment, and follow up.

Results: The data from 558 (91.2%) survey questionnaire that were filled completely were analyzed. The mean age of the parents was 33.4±4.9. It was found that most common food allergen was cow's milk (85.3%). The mean time to diagnosis from the onset of symptoms was 10.9±18.4 months. Around 229 parents (41.6%) admitted to at least four different physicians and 68 (12.3%) parents admitted to at least five different physicians before diagnosis. The median time to diagnosis from the onset of symptoms was five (1-108) months in the patients admitted to four or more physicians, but it was one (1-48) month in the patients that admitted to less physicians ($p<0.001$). The most common symptoms were dermatitis and mucus-bloody stool, the least common ones were cardiovascular symptoms. Only 21.1% of the patients were able to use hypoallergenic formulas (HAF) in accordance with the recommendation of the physician.

Conclusions: Delayed diagnosis of FA is a major concern, and during this period the patients admit many physicians. A majority of the patients with CMPA experience difficulties while using HAFs, and only one-fifth of them is able to use formula regularly.

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Introduction

Food allergy (FA) is an important public health problem that affects children and adults, and it has been increasing in prevalence in the last two to three decades.¹ The most commonly implicated foods for it are cow's milk, egg, peanut, soy, tree nuts, fish, shellfish, and wheat.²⁻⁴ The symptoms can vary from mild to severe, and in extreme cases FA can lead to anaphylaxis, which is a life-threatening allergic reaction. Currently, there is no cure for FA. The management of FA usually includes responsible food avoidance, patient/parent education, and emergency treatment. Diet elimination including multiple food and especially cow's milk may cause stunting and growth retardation.^{5,6} Therefore, infants with FA should be monitored for growth and development closely during this fast growing period, and hypoallergenic formulas (HAFs) may be needed to support nutrition.⁷ In addition to its comorbidities, FA puts significant psychosocial and economic burden on parents, society, and the healthcare system.¹ It is important to increase the awareness and knowledge of both physicians and all healthcare providers, patients, and/or parents to minimize the multidirectional problems. It will be helpful to evaluate the real-life experiences of the parents about FA to develop optimal strategies. The aim of this study is to evaluate the attitudes and behaviors of the parents of children with FA to cow's milk and other FA.

Materials and Methods

The parents of children with FA were asked to complete an 18-item questionnaire to evaluate FA history and experiences during the diagnosis, treatment, and follow up. The questionnaire was posted on the official website of Life with Allergy Association (<https://www.alerjidernegi.org.tr>) as an application from 1 Aug 2020 - 15 Aug 2020. Incomplete questionnaires and the children with FA who were not diagnosed by a physician were not included in the analysis. Simultaneously, on the website (<https://www.alerjidernegi.org.tr>), the purpose of this study and the scope of the questions in the questionnaire was explained in detail, and assurance was given that the personal information will not be used for any other purpose. The ethics committee approval was obtained for the study, and their approvals have been requested. Life with Allergy Association has more than 40,000 members at present, and it was founded by parents with FA in 2016 to raise the awareness of allergy in society and increase quality of the children with FA. It is still the most comprehensive association operating in this field in Turkey.

The questionnaire had two main parts. The first part of questionnaire included parents' demographic characteristics [age, sex, education level (primary-secondary, high school, university), number of children], the onset of FA symptoms, the symptoms/complaints, how long after exposure to food the symptoms occur [acute onset (complaints occur in minutes or a few hours after exposure); delayed onset (complaints occur more than 2 hours or days after exposure)], when the diagnosis of food allergy is made by the physician (pediatrician, pediatric allergy, pediatric gastroenterologist, family practitioner or others), and

how many different physicians have been consulted before the correct diagnosis. The second part included the questions to determine which food is allergic [cow's milk and/or other food; one or multiple food allergy], to whom (mother and/or child) the diet elimination treatment was applied, which food it covered, whether a HAF is recommended for childrens' CMPA [cow's milk based partially, extensively hydrolyzed (EHF) or amino acid formula (AAF)], the problems encountered in the use of this HAF, how long the HAF support was used, and whether regular follow-up with physicians were carried out. Before the study, the protocol was approved by the Scientific Research Ethics Committee of Inonu University Faculty of Medicine (Year/number: 2020/715).

Statistical Analysis

The statistical analysis was performed with the MedCalc Statistical 12.7.7 software (MedCalc Software bvba, Ostend, Belgium; 2013) and normality was evaluated by the Shapiro Wilks test. Descriptive statistics were expressed as the frequency and percentage for categorical variables, whereas quantitative data were expressed as mean ($\pm$ SD) for normally distributed data, and median (min-max) for non-normally distributed data. The categorical and quantitative variables were compared using the chi-square test and/or the Mann-Whitney U test. A two sided $p < 0.05$ was considered statistically significant.

Results

Of the 612 parents of children with FA that were members of "Life with Allergy Association" who responded all the questions, 558 parents were included in the analysis. The mean age of the parents was 33.4 ± 4.9 , out of which 532 (95.3%) of them were mothers, 447 (80.1%) of them were university graduates and 41.4% had more than one child. Around 38.9% of the parents with more than one child also had a history of FA in another child.

The mean time to diagnosis from the onset of symptoms was 10.9 ± 18.4 months. About 229 (41.6%) parents stated that they have admitted at least four and 68 (12.3%) at least five different physicians before FA diagnosis. FA was diagnosed by a pediatrician in 50.8% of the patients, a pediatric allergy specialist in 34.8% of the cases, and a pediatric gastroenterologist in 12.4% of the cases. A family physician diagnosed it in 2% of cases. Around 81% of the patients followed up with the physician who made the diagnosis. Three hundred forty-five children (61.8%) had multiple FA, and it was revealed that the most common food allergen was cow's milk (85.3%). 72.1% of the children with CMPA had an allergy to another food. The parents stated that 54.3% of their children had FA symptoms in the first three months, 84.4% in the first six months, and 93.4% in the first year of their life. The demographic characteristics of patients were summarized in Table 1.

While onset of symptoms was in the first six months in 87% of children with CMPA, the frequency of symptom onset with food other than cow's milk was significantly higher in children over the age of one ($p < 0.001$). There was

Table 1 Demographic characteristics of the children with food allergy (n:558).

	n (%)
Age at symptoms onset	
0-3 month	303 (54.3)
3-6 month	168 (30.1)
6-12 month	50 (8.9)
>12 month	37 (6.6)
Time of the diagnosis, mean $\pm$ SD, month	10.9 $\pm$ 18.4
Diagnosis of multiple food allergy	345 (61.8)
Only breastfeeding at the time of the onset of symptoms	368 (65.9)
Number of siblings $\geq$ 2	231 (41.4)
History of food allergy in the sibling	90 (16.1)
Number of admitted physicians $\geq$ 4	229 (41.6)
Specialty of the physician that made the diagnosis	
Family practitioner	11 (2)
Pediatric gastroenterologist	68 (12.4)
Pediatric allergist	191 (34.8)
Pediatrician	279 (50.8)
Number of patients with regular follow up visits	455 (81.5)

a significant association between the number of physicians admitted before diagnosis and time to diagnosis ($p < 0.001$). The median time to diagnosis from the onset of symptoms was five (1-108) months in the patients admitted to 4 or more physicians, but it was 1 (1-48) month in the patients that admitted to less physicians ($p < 0.001$). The mean time to diagnosis did not differ significantly between parents with a history of FA in another child (9.2 ± 18.1 months) and those (11.8 ± 18.5 months) without a history ($p = 0.056$).

The frequency of the symptoms and in children with FA is shown in Table 2. The symptoms and clinical findings of dermatitis and mucus-bloody stool were the most common, and cardiovascular system symptoms were at least common (7.5%). The symptoms were acute onset in 46.8% of the patients, and the parents also stated that 10.1% of the children had anaphylaxis history. While gastrointestinal system symptoms developed significantly and more frequently in patients with CMPA (87.4%) than those without (68.8%), the frequency of urticaria and/or angioedema (45.2% and 60%, respectively) was found to be significantly lower ($p < 0.001$ and $p = 0.014$, respectively). FA symptoms occurred in 65.9% of the children while breastfeeding. While the frequency of CMPA was higher in the infants who were exclusively breastfed, the frequency of other food allergies was significantly higher in children who were introduced to complementary food ($p < 0.001$) (Table 3).

Both maternal and infant diet elimination was recommended in 82.3% of children with FA, and only infant diet elimination was recommended in others. HAF was provided to 67.2% of children with CMPA. HAF was recommended by their physicians to 59.8% of children with only CMPA, and 74.2% of children with multiple FA with CMPA. HAF was provided to 70.1% of the children who developed symptoms in the first six months, and 36.4% of the children in the other

Table 2 Symptoms and signs of children with food allergy.

	n (%)
Gastrointestinal system	
Mucus-bloody stool	301 (53.9)
Severe gas pain	263 (47.1)
Vomiting	220 (39.4)
Diarrhea	197 (35.3)
Persistent diaper rash	158 (28.3)
Loss of appetite	151 (27.1)
Growth retardation	113 (20.2)
Constipation	101 (18.1)
Skin and mucosa	
Dermatitis	320 (57.3)
Urticaria	205 (36.7)
Angioedema (lip, tongue, eyelid)	202 (36.2)
Respiratory system	
Wheezing	215 (38.5)
Sudden onset of cough	154 (27.6)
Shortness of breath, difficulty in breathing	112 (20)
Cardiovascular system	
Fainting, syncope/hypotension/cyanosis	42 (7.5)

Table 3 Nutritional characteristics of children with cow's milk protein and other food allergy at the time of symptom onset.

Nutritional characteristics	Cow's milk protein allergy n (%)	Other food allergy n (%)
Only breastfeeding	*327 (68.7)	41 (51.2)
Breastfeeding and formula	79 (16.6)	13 (15.9)
Breastfeeding and complementary food	53 (11.2)	*15 (18.8)
Only complementary food	9 (1.9)	*7 (8.8)
Formula and complementary food	8 (2.5)	*6 (7.5)
Total	476	82

* $p < 0.05$

age group ($p < 0.001$). Amino acid formula (AAF) was recommended for 85% of these cases, and extensively hydrolyzed formula (EHF) was recommended for others. Around 73.1% of the parents that were HAF stated that they had difficulty in using the formula (Table 4). The problems identified by the parents were rejection of the formula, difficulty of obtaining the formula due to cost, finding the formula, and symptom persistence. Only 21.1% of the patients were able to use HAF in accordance with the recommendation of the physician.

Discussion

The present study which evaluates the experiences of parents of children with FA in the diagnosis and management of FA, showed that delayed diagnosis of FA was a major

Table 4 Data on use of hypoallergenic formula in cow's milk protein allergy (n:320)

	n (%)
Number of patients who were recommended extensively hydrolyzed formula	272 (85)
Number of patients who were recommended amino acid formula	48 (15)
Number of patients who had difficulty using hypoallergenic formula	234 (73.1)
Problems identified by the parents	206 (88.1)
My child rejected formula/did not like its taste	18 (7.7)
I had difficulty obtaining it for regular use (cost, difficult obtaining, cannot find the formula)	10 (4.2)
Symptoms continued	
Number of patients who use it regularly according to physician's recommendation	68 (21.1)

problem, and more than half of the patients admitted at least four different physicians with the same symptoms before the diagnosis, and that three-fourth of children that were recommended hypoallergenic formula had difficulty to use the formulas, and only one-fifth of them were able to use formula regularly.

The increase in the incidence of FA in the world in the last two decades is accepted as the second allergy epidemic.⁸ Today, the economic and psychosocial burden on the patient, the family, and the society has made FA an important public health problem.⁹ It is extremely important to increase the awareness of physicians working in all healthcare settings and the society, especially among parents, on FA and how to solve this problem. It is necessary to provide future physicians up-to-date information on the diagnosis and management of FA during their education and post graduate education. Therefore, both international and national FA guidelines and algorithms have been published in the recent years.¹⁰⁻¹³ However, only 2% of the patients were diagnosed by family physicians working in primary care, and the fact that more than half of the patients admitted to four or more physicians before the diagnosis suggest that the desired success has not yet been achieved in this regard. In addition, the fact that the time to diagnosis in our study was similar between parents who had a history and experience of FA in another child and those who did not, suggests that the awareness among parents about FA is not at the desired level. These parents are the members of the Life with Allergy Association, which is a non-governmental organization founded to increase public awareness about FA, and it further increases the importance of this situation. The inadequacy of the physicians to whom the parents admit in the diagnosis of FA may be related to this situation.

The present study suggests that there is a delayed diagnosis in children with FA, a result similar to the previous studies that have also showed that children with FA can be diagnosed late, depending on the FA symptoms of the patients, the characteristics of the study centers, and study methodology.¹⁴⁻¹⁷ As in 94% of the cases, FA symptoms mostly

manifest in the first year of life.¹⁻¹⁸ The growth and development of a child is the fastest in first year of his/her life. Problems due to delayed diagnosis may be more important especially in these cases. At the same time uncontrolled inflammation and symptoms due to delayed diagnosis may cause new allergen sensitization and development of other atopic diseases.^{19,20} Moreover, re-exposure to food in a patient with food associated anaphylaxis can result in death. The delayed diagnosis may be associated with the lack of physicians' knowledge, as well as the lack of diagnostic features of any of the symptoms and clinical findings that develop in FA, and the lack of high diagnostic efficiency of the laboratory investigations used in clinical practice today. The gold standard of FA diagnosis is food provocation tests.^{1,18} The risks of these tests due to their nature and the necessity to be performed by experienced physicians may also be associated with delayed diagnosis. The fact that the FA diagnosis in more than half of the surveyed patients was made by pediatric allergists or gastroenterologists who are experts in tertiary health institutions and the patients do not have direct access to these physicians support this.

Although IgE-mediated immediate type reactions are the most common form of FA in childhood, FA can range from non-IgE mediated food allergy such as proctocolitis to IgE mediated FA, such as urticaria. IgE mediated FA is acute onset (within 2 h of exposure), and the presenting symptoms are often skin, respiratory, and gastrointestinal related, whereas non-IgE mediated FA has a delayed onset (usually 2 to 24 h) of symptoms.²¹ Half of our patients had acute onset, and the other half had delayed onset symptoms. Skin and gastrointestinal symptoms and clinical findings are the most common symptoms associated with FA.^{1,18} In the present study, dermatitis and mucus-bloody stool were the most common symptoms, and the least common ones were cardiovascular disease symptoms.

Although, theoretically every food can trigger FA, cow's milk, eggs, peanuts, shelled nuts, wheat, soy, fish, and shellfish are the cause of more than 90% of FA.^{1,18} In Turkey, cow's milk and egg are the most common causes of FA. In the present study, the most common FA was found to be CMPA, and this ratio is higher than other studies, as the incidence of CMPA is 51.4-62.7% in other recent studies.^{14,22-24} The incidence of multiple FA can vary in the studies.^{2,4} However, approximately two-thirds of the parents in our study stated that their children had multiple FA, and this rate is higher than the previous studies. These varying results may be due to several factors. Most importantly, this was a questionnaire-based study and was conducted through an association website where parents of children with FA can convey their correct knowledge and experiences to each other, and exchange views on solving their children's nutritional problems. Cow's milk is the most widely used food in our country's cuisine. By eliminating cow's milk and/or multiple food items from the diet of their children, parents may have at hand a serious problem in their daily life. They may need right experiences, suggestions, and practices to provide their children with a balanced diet, which they may share with each other, and solve the problem at hand. A significant number of the members most likely have problems with the nutrition and management of their children with FA. At the same time, parents think that diet elimination effects their children's

growth and development. The fact that three-quarters of the children of the parents participating in the present study had another FA along with FA to cow's milk also supports this situation. Although not diagnosed by a physician, the parents who hold other foods responsible for the development of symptoms may be one of the reasons for the high frequency of multiple FA in the present study.

Cow's milk and dairy products are the most important nutritional source for the infants.²⁵ In order to meet the growth and development needs of children with FA, it is necessary to include the essential macro and micro-nutrients in their diet with age-appropriate complementary nutrition.^{1,18} At the same time, a balanced diet of the mothers post their diet elimination is important as these children need more breast milk than healthy ones.^{1,18} Previous studies have shown that growth failure develops in 7-25% of the children with FA, especially at early age, and have multiple symptoms and FA.^{5,6} This rate is higher in the children with multiple FA in combination with CMPA.²⁶ Therefore, it is necessary to closely monitor the growth and development of children with FA, and support their nutrition with a HAF, with proven efficiency in CMPA as needed.^{1,18} In the present study, four out of every five patients have regular follow-up visits to the physician who made the diagnosis. Hypoallergenic formula was recommended to approximately 70% of children with CMPA. Formula use was recommended by the physician in approximately one-third of the children with CMPA alone, and in three-fourths of the patients with multiple FA in combination with CMPA. AAF was recommended to 85% of the patients as a HAF. In approximately two-thirds of our patients, the symptoms initiated while only breastfeeding, and approximately three-quarters of children with CMPA had multiple FA, which may be associated with the preference of AAF.

Only one-fifth of the patients were able to use the recommended HAF regularly. Approximately, three-quarters of the parents who were recommended the HAF stated that they had trouble using the formula. The most common reason was rejection of the formula because of its taste. Therefore, it is important that the physician recommending the HAF provide information to the parents about the problems they may experience while using the formula and the potential solutions.

This study has certain important limitations. Most importantly, there was a limited participation in the study from an association with 40,000 members. Therefore, the results of the study may not reflect the experiences of all the parents that have children with FA in our country, Turkey. Secondly, although the parents were asked to answer the questions based on the recommendations of the physician, their answers, especially regarding the treatment, may differ from the physician's recommendation. Third, retrospective questioning may reduce the reliability of the parents' responses regarding the onset of FA symptoms, and the age of diagnosis due to difficulties of remembering past information.

In conclusion, diagnosis is delayed after the onset of symptoms in FA, and during this period, patients admit many physicians. The majority of the patients with CMPA experience difficulties in the use of HAFs. Therefore, the awareness of FA among physicians, parents, and the society should be increased, and the parents who are

recommended HAF should be informed about the problems they will experience with it.

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