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Original article

Screening of Immunoglobulin E mediated Food Allergies among Children

Dépistage des allergies alimentaires à médiation par immunoglobuline E chez les enfants

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ABSTRACT

Background. – Food allergy is a major public health concern all over the world. Data are lacking on the number of affected children, severity of food allergy, and burden of the disease.

Objectives. – The current research aims at exploring the most common sensitization patterns of food allergy as well as collecting data on clinical presentation among pediatrics.

Methods. – The sensitization pattern of the most common 21 food allergens through Immuno^{LINE} IgE Nutritional assay as well as total serum IgE test were assessed. The assessment was conducted on a group of 188 children aged from one to five years who visited the pediatric outpatient clinic of Suez Canal University hospital.

Results. – One or more specific allergen components related IgE antibodies were found in 74.5% of the study participants. The mean level of total IgE in serum was 122.86 ± 72.93 IU/ml. In addition, the percentage of children who were diagnosed with food allergy reached 22.3% whereas the percentage of those who were confirmed with food allergy was 4.3%. Furthermore, Egg yolk was represented as the most frequently food allergen with a percentage of 27.7% whereas egg white and cow milk amounted to 23.4%.

Conclusion. – Most of the children were found to be poly-sensitized. The frequent food allergies confirmed via Immuno^{LINE} IgE Nutritional assay were caused by cow's milk and egg yolk allergens.

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R É S U M É

Contexte. – L'allergie alimentaire est un problème de santé publique majeur dans le monde entier. On manque de données sur le nombre d'enfants touchés, la gravité de l'allergie alimentaire et la charge de morbidité.

Objectifs. – La recherche actuelle vise à explorer les schémas de sensibilisation les plus courants de l'allergie alimentaire ainsi qu'à recueillir des données sur la présentation clinique en pédiatrie.

Méthodes. – Le profil de sensibilisation des 21 allergènes alimentaires les plus courants a été évalué par le test nutritionnel Immuno^{LINE} IgE ainsi que par le test des IgE sériques totales. L'évaluation a été menée sur un groupe de 188 enfants âgés de un à cinq ans qui ont visité la clinique pédiatrique ambulatoire de l'hôpital universitaire du canal de Suez.

Résultats. – Un ou plusieurs anticorps IgE spécifiques liés à des composants allergènes ont été trouvés chez 74,5 % des participants à l'étude. Le niveau moyen d'IgE total dans le sérum était de $122,86 \pm 72,93$ UI/ml. En outre, le pourcentage d'enfants chez qui une allergie alimentaire a été diagnostiquée a atteint 22,3 %,

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alors que le pourcentage de ceux chez qui une allergie alimentaire a été confirmée était de 4,3 %. En outre, le jaune d'œuf était représenté comme l'allergène alimentaire le plus fréquent avec un pourcentage de 27,7 % alors que le blanc d'œuf et le lait de vache représentaient 23,4 %.

Conclusion. – La plupart des enfants se sont avérés être poly-sensibilisés. Les allergies alimentaires fréquentes confirmées par le test nutritionnel Immuno LINE IgE ont été causées par les allergènes du lait de vache et du jaune d'œuf.

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1. Introduction

Food Allergy (FA) affects the quality of life for pediatric patients and their families. The economic burden of the disease and its related health problems are of increasing medical importance [1]. The incidence of FA in children less than 4 years was estimated to be 6%–8% [2]. The prevalence of food sensitization ranges from 10% in normal children to 30% in atopic children with increased incidence in preschool Egyptian children. It was recognized that children living in cities have a prevalence rate of FA that is larger than their counterparts who live in rural areas [3].

FA is commonly classified into immunoglobulin E (IgE) and non-IgE-mediated based on the time elapsed from the food ingestion to the onset of clinical manifestation, within or later than 2 hours [1].

IgE mediated FA is associated with atopic manifestations such as angioedema, vomiting, urticaria, anaphylaxis, aphonia, rhinitis, wheezes, dyspnea and diarrhea. Data suggest that IgE-mediated food allergies are common, affecting up to 10% of children with increasing prevalence in the last decades [4].

The immunopathogenesis of various food allergies is the breakdown of immunologic and clinical tolerance to an ingested food. It results in IgE-mediated reactions or non-IgE-mediated disorders. Sensitization to food allergens can occur through the gastrointestinal tract, the skin, and, less commonly, the respiratory tract, in conjunction with impaired and/or inflamed barrier function [5].

Many types of food could induce allergic reactions. There are about eight types of food that cause over 90% of allergic reactions in vulnerable persons. Specifically, they are cow's milk, eggs, soya, wheat, fish, shellfish, peanuts, and tree nuts [6].

In Egypt, little is known about children allergy, with few research studies done. The objective of this research is to identify the most common food allergens through Immuno^{LINE} IgE Nutritional assay. The current research aims also to find out about the food allergy rates in pediatrics and their correlation to total serum IgE levels in children from the Suez Canal area.

2. Patients and methods

A total of 188 children, aged from one to five years presented to the out-patients pediatric clinic, Suez Canal University hospital, Ismailia, Egypt, in the period from January 2019 to December 2019. The children were screened for FA. Detailed present and family histories were taken with focus on symptoms of FA as urticaria, dermatitis, vomiting, diarrhea, abdominal pain, both upper respiratory (aphonia or rhinitis) and lower (wheezes, dyspnea). Acute urticaria occurs with IgE mediated food allergy, however, atopic eczema occurs with non-IgE mediated food allergy and some patients have both presentations [7]. Physical examination was performed for all the children. Then allergic tests; total serum IgE and Immuno^{LINE} IgE nutritional test were done. The children with positive reaction to Immunoline IgE nutritional test, have high levels of total serum IgE with clinical allergic symptoms were diagnosed with food allergy. On the basis that some patients will tolerate food despite high levels of specific IgE against that food allergen, while, others will

react with positive test, so food challenge test is complementary to diagnose food allergy. For our patients who were enrolled in this study. The Food challenge test was performed as follows: First, the patients stopped taking the suspected food allergen that had been diagnosed by Immuno^{LINE} IgE nutritional test for two weeks. Next, Patients visited the hospital for re-examination and reassessment for the pre-existing symptoms and signs of FA. At that time, suspected food allergens were introduced to patients during their hospital visit under medical supervision of a pediatrics and followed up for possible severe adverse reactions such as anaphylaxis, severe wheezy chest or severe urticaria. Finally, within few hours, the patients were allowed to return home and followed up for two weeks. FA is diagnosed when symptoms and signs stop or improve by avoiding the suspected food allergen and reappear when it was reintroduced to the patients [8].

2.1. Immuno^{LINE} IgE Nutritional assay

The allergen specific IgE test is an Enzyme Immunoassay test (Immunolab GmbH, Kassel, Germany) for the qualitative detection of specific allergen-related IgE antibodies in serum. The surface of nitrocellulose membranes of test strips is coated with specific allergens. During testing, the specimen is added to the test strip and then incubated. If the specimen contains allergen-specific IgE antibodies, it can react with the allergens and bind to the nitrocellulose membrane of the strip. Unbound material is removed by washing. Detector antibodies (Anti-human IgE antibody) are then added to the strip and incubated. The Detector antibodies will bind to the respective specific IgE, which are bound to the strip in the first incubation. Unbound Detector antibodies are removed by washing. Next, the substrate solution; 5-bromo-4-chloro-3-indolyl phosphate/p-nitroblue tetrazolium chloride (BCIP/NBT) is added to the test strip and incubated which caused a specific enzymatic color reaction. The color intensity is directly proportional to the amount of allergen specific IgE and is interpreted by comparison with a color chart. To serve as a procedural control, a colored line will always appear in the control line region which indicates the correct procedure.

2.2. Total serum IgE assay

The VIDAS Total IgE (IGE) kit was used with the instrument of MiniVIDAS (Immunoassay Analyzer, U.S.) to assess the total IgE levels in serum of all participants. It is an automated quantitative enzyme linked fluorescent immunoassay to help in the diagnosis of allergic diseases. The results were analyzed and calculated automatically using calibration curves by the computer and expressed in IU/ml. The detection limit for the VIDAS Total IgE assay is 0.5 IU/ml.

2.3. Statistical analysis

The data was analyzed, by SPSS program version 25 software, as frequencies and percentage or means and standard deviation.

Table 1
Demographic characteristic, clinical and laboratory data of studied children.

	Participants n = 188	100%
Age(months)(mean± SD)	36.47	± 21.96
Age of allergy onset(months) (mean± SD)	7.24	± 2.21
Gender (n%)		
Male	86	45.70%
Female	102	54.30%
Type of feeding (n%)		
Breast feeding	70	37.20%
Artificial feeding	68	36.20%
Complementary	50	26.60%
Family history (n%)		
Positive	50	26.60%
Negative	138	73.40%
Allergy Symptoms (n%)		
No	116	61.70%
Yes	72	38.30%
Organ system (n%)		
Systemic	6	3.20%
Gastro-intestinal	40	21.30%
Dermatological		
Urticaria	5	2.60%
Eczema	49	26.10%
Respiratory	18	9.60%
Food allergy history (n%)		
Negative	116	61.70%
Positive	72	38.30%
Diagnosed food allergy (n%)		
Yes	42	22.30%
No	146	77.70%
Confirmed food allergy (n%)		
Yes	8	4.30%
No	180	95.70%
Immuno ^{line} IgE nutritional test		
One or more allergen specific IgE antibodies	140	74.50%
No allergen specific IgE antibodies	48	25.50%
Total serum IgE levels IU/ml (mean± SD)	122.864	± 72.9397

Chi² test was used to compare between two qualitative variables. Spearman's rank correlation coefficient was done to evaluate the strength and direction of association of nonparametric variables.

3. Results

An entire cohort of 188 children was included in this study. The mean age of participants was 36.47 ± 21.96 months and 45.7% (86/188) were male and 54.3% (102/188) were female. Participants with suspected allergy symptoms represented 38.3% (72/188). One or more specific allergen related IgE antibodies were found in 74.5% (140/188) of the studied children and the mean level of total IgE in serum was 122.86 ± 72.93 IU/ml. The demographic and clinical characteristics of participants are detailed in Table 1.

The study reported 51.4% (72/140) of children who had specific allergen-related IgE antibodies had no allergic manifestations while 48.6% (68/140) of them had allergic symptoms. In sensitized children, the most common allergic manifestations were dermatological symptoms (35.7%); 32.1% (45/140) eczema, 3.6% (5/140) urticaria, and gastrointestinal symptoms 28.6% (40/140). A reported history of FA was detected in 48.6% (68/140) of sensitized children and total serum IgE levels were elevated in 40% (56/140) of them. Only 27.1% (38/140) of sensitized children were diagnosed of having a FA as shown in Table 2.

The study investigated the prevalence of food allergens in sensitized children by Immuno^{line} IgE nutritional test. Egg yolk represented 27.7% (52/188) then each of egg white and cow milk showed 23.4% (44/188) and then peanut was 21.3% (40/188) as shown in (Fig. 1). Needs revision.

Table 3 illustrates the frequency of raising total immunoglobulin E levels and sensitization to tested food allergens according to the

Table 2
Relationship of clinical data of the study sensitized children and Immuno^{line} IgE nutritional test (n = 188).

	Sensitization to food allergen (by Immuno ^{line} IgE nutritional)		P-value
	Yes (140)	No (48)	
Gender			
Male	64 (45.7%)	22 (45.8%)	0.989
Female	76 (54.3%)	26 (54.2%)	
Type of feeding (n%)			
Breast feeding	48 (34.3%)	22 (45.8%)	0.330
Artificial feeding	54 (38.6%)	14 (29.2%)	
Complementary	38 (27.1%)	12 (25%)	
Symptoms (n%)			
No symptoms	72 (51.4%)	44 (91.7%)	< 0.001 ^a
Symptomatic	68 (48.6%)	4 (8.3%)	
Organ system (n%)			
Systemic	6 (4.3%)	0 (0%)	0.145
Gastro-intestinal	40 (28.6%)	0 (0%)	< 0.001 ^a
Respiratory	16 (11.4%)	2 (4.2%)	< 0.001 ^a
Dermatological			
Urticaria	5 (3.6%)	0 (0%)	0.001 ^a
Eczema	45 (32.1%)	4 (8.3%)	
Food allergy history			
Yes	68 (48.6%)	4 (8.3%)	< 0.001 ^a
No	72 (51.4%)	44 (91.7%)	
Diagnosed food allergy (n%)			
Yes	38 (27.1%)	4 (8.3%)	0.007 ^a
No	102 (72.9%)	44 (91.7%)	
Total serum IgE levels			
Normal	84 (60.0%)	20 (41.7%)	0.027 ^a
Elevated (> 100 IU/ml)	56 (40.0%)	28 (58.3%)	

^a Statistical Significance at $P < 0.05$

presented allergic manifestations while Fig. 2 presents monosensitization and polysensitization rates according to presented allergic manifestations.

There was a significant positive correlation between egg white with gastrointestinal symptoms ($r = 0.267$, $P = 0.010$). In addition, there was a significant positive correlation between the egg yolk with dermatological and gastrointestinal symptoms ($r = 0.272$, $P = 0.008$; $r = 0.202$, $P = 0.049$ respectively) and also cow milk with dermatological and gastrointestinal symptoms ($r = 0.517$, $P = < 0.001$; $r = 0.526$, $P = < 0.001$ respectively). However, strawberry was significantly negatively correlated with age ($r = -0.272$, $P = 0.008$) and positively correlated with dermatological and gastrointestinal symptoms ($r = -0.250$, $P = 0.015$; $r = 0.258$, $P = 0.013$ respectively) and also there was significant negative correlation between codfish with age ($r = -0.205$, $P = 0.048$) and positive correlation with dermatological symptoms ($r = 0.204$, $P = 0.048$) as shown in Table 4.

4. Discussion

The presentation of FA ranges from mild to severely life-threatening reactions, so proper diagnosis is necessary to provide life-saving preventive measures and prevent unjustified dietary restrictions [9]. The prevalence of FA for children below 5 years old was found to be 3.5%–7.7% in China, 6.8% in Norway, 3.6% in Denmark, 4% in the United Kingdom (UK) and Australia, 2.5%, South Africa and 1% in Thailand [2]. Interestingly, in our study, the challenge-proven FA was 4.3%.

The role of specific IgE for food allergens has been well recognized in asthma, allergic rhinitis, urticaria, anaphylaxis, and gastrointestinal allergies [10]. In the current study, the top allergy symptoms in sensitized children were dermatological symptoms (35.7%) followed by gastro-intestinal symptoms (28.6%).

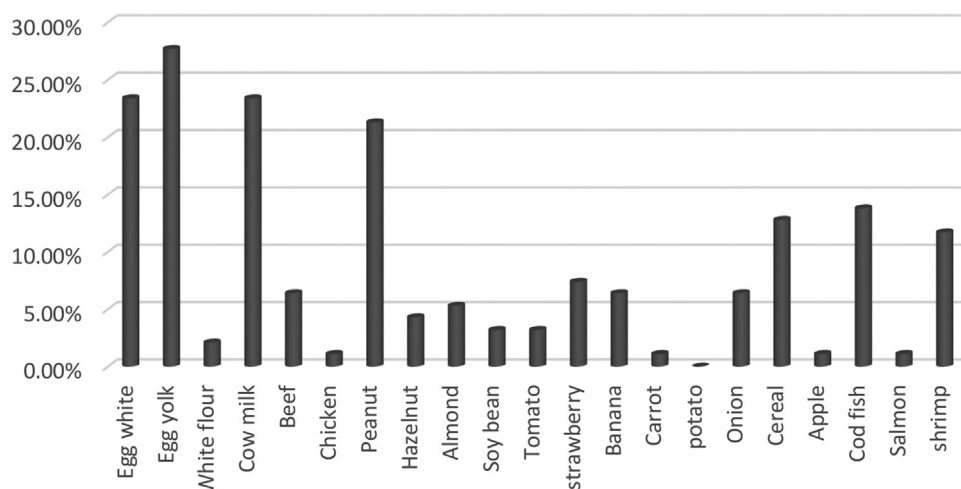


Fig. 1. Food allergen percentages in sensitized children by Immuno^{line} IgE nutritional test.

Table 3

Frequency of raising total serum immunoglobulin E levels and sensitization to common food triggers among patients according to allergic manifestation (n = 188).

	Dermatological (eczema n = 49)	Respiratory (n = 18)	Gastrointestinal (n = 40)
Raised total serum IgE level (> 100 IU/ml)	39 (79.6%)	12 (66.7%)	32 (80.0%)
Egg white	14 (28.6%)	4 (22.2%)	16 (40.0%)
Egg yolk	19 (38.8%)	8 (44.4%)	16 (40.0%)
White flour	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cow milk	20 (40.8%)	4 (22.2%)	14 (35.0%)
Beef	4 (8.2%)	4 (22.2%)	2 (5.0%)
Chicken	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peanut	9 (18.4%)	2 (11.1%)	8 (20.0%)
Hazelnut	3 (6.1%)	0 (0.0%)	2 (5.0%)
Almond	5 (10.2%)	0 (0.0%)	0 (0.0%)
Soy bean	3 (6.1%)	0 (0.0%)	2 (5.0%)
Tomato	2 (4.1%)	0 (0.0%)	2 (5.0%)
Strawberry	5 (10.2%)	0 (0.0%)	4 (10%)
Banana	5 (10.2%)	2 (11.1%)	2 (5.0%)
Carrot	0 (0.0%)	0 (0.0%)	0 (0.0%)
Potato	0 (0.0%)	0 (0.0%)	0 (0.0%)
Onion	1 (2%)	0 (0.0%)	2 (5.0%)
Cereal	6 (12.2%)	2 (11.1%)	6 (15.0%)
Apple	2 (4.1%)	0 (0.0%)	2 (5.0%)
Cod fish	10 (20.4%)	0 (0.0%)	6 (15.0%)
Salmon	2 (4.1%)	0 (0.0%)	0 (0.0%)
Shrimp	8 (16.3%)	0 (0.0%)	8 (20%)

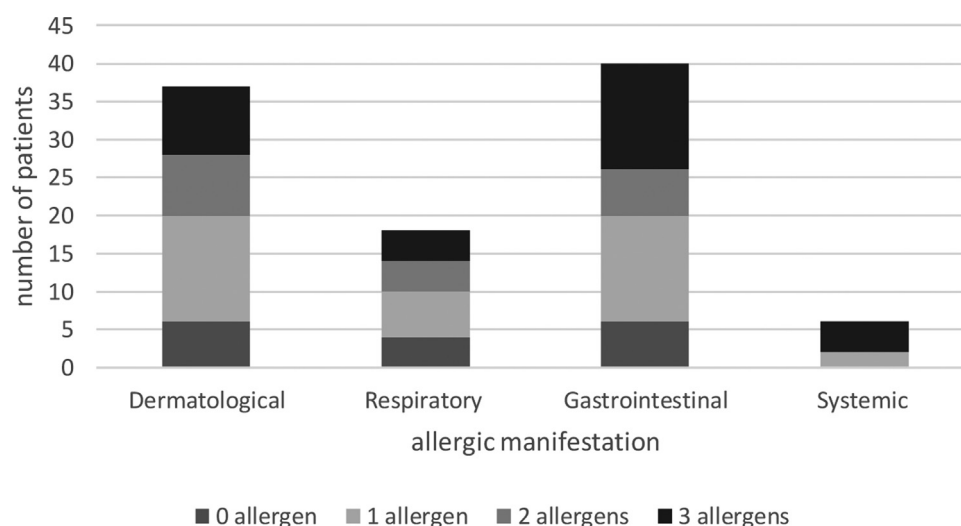


Fig. 2. Monosensitization and polysensitization rates according to allergic manifestations.

Table 4
Correlations of Age and system affected by food allergens of sensitized children.

	Age		Respiratory		Dermatological		Gastro-intestinal	
	r	P-value	r	P-value	r	P-value	r	P-value
Egg white	0.103	0.324	0.025	0.809	0.152	0.143	0.267	0.010 ^b
Egg yolk	−0.080	0.444	0.087	0.402	0.272	0.008 ^b	0.202	0.049 ^a
Cow milk	−0.021	0.844	0.144	0.166	0.517	<0.001 ^b	0.526	<0.001 ^b
Peanut	0.045	0.670	−0.081	0.439	0.072	0.490	−0.016	0.877
strawberry	−0.270	0.008 ^b	−0.016	0.877	0.250	0.015 ^a	0.258	0.013 ^a
Cereal	0.032	0.761	−0.016	0.877	0.039	0.709	0.035	0.739
Cod fish	−0.205	0.048 ^a	−0.180	0.083	0.204	0.048 ^a	0.081	0.438
Shrimp	0.063	0.545	−0.124	0.232	0.113	0.278	0.116	0.266

r: spearman's rank correlation coefficient; Statistical Significance at $P < 0.05$.

^a Statistically significant.

^b Highly significant P -value ≤ 0.01 .

Total serum IgE levels were elevated in 40% of sensitized children. Due to cost, special equipment and skills related to issues, most clinicians request total IgE assays for allergy suspected cases, and only then will proceed to specific IgE testing if the total IgE level exceeds a certain cutoff point. A previous study revealed no significant association of total serum IgE levels in children with FA ($P < 0.210$) [11]. In another study, to assess the diagnostic usefulness of total serum IgE in different allergies, sensitivity and specificity of total serum IgE in FA were 55.8% and 83.9%, respectively [12]. Al-Tamemi et al. reported an increased total serum IgE levels in 54.9% of patients with allergic manifestations, while other patients had normal total serum IgE levels [13]. All of these findings strengthen our findings and emphasize the importance of testing for specific allergens in the presence of allergic manifestations even with normal total serum IgE levels.

Sensitization to one or more of food allergens was reported in 140/188 (74.5%) of our studied children. In Iranian children, the reported rate of food sensitization was 51% by food allergen-specific IgE and 40% by skin prick test [14]. Lower sensitization rates were found in children in Honduras (23%) and in Germany (20%). The Honduran children were sensitized to various types of food allergens with different percentages. The most common food allergens were 9% for milk, 6.9% for eggs and 4.9% for peanut [15,16]. In an Australian 1-year-old cohort, more than 10% of infants had IgE-mediated FA [17]. In a comparative study, the prevalence of food specific IgE sensitization were 19.1% in India, 16.8% in rural Shaoguan, 16.6% in Hong Kong, 8.0% in Tomsok and 7.0% in Guangzhou [18]. Racial, environmental, food habits and the age of participants may account for this great variability in rates of sensitization in different studies.

The most frequent food allergens in our study group were egg yolk (27.7%) followed by egg white and cow milk (23.4% each) then peanut (21.3%). These food allergens were also the commonest in Liu et al. study where milk and egg caused 73.96% and 54.79% of allergies, respectively [19]. Despite the diverse methodologies and difference in prevalence rates, egg and cow milk were the most common food allergens in young children in different regions. In the study performed in an Egyptian Hospital, the most common food allergens were; soya beans, milk and strawberry 38.4% for each while mix nut were 23.1% [20]. According to a meta-analysis, included approximately 51 studies; milk and egg were the most common allergens in Europe. They showed the prevalence of food allergens, which was different from one food allergen to another as for milk (1.2% to 17%), for egg (0.2% to 7%), for peanuts and fish (0% to 2%) and for shellfish (0% to 10%) [21]. A descriptive analysis of 43 children had a history of strawberry allergy in the Mediterranean Area, reported approximately 67% had positive results to strawberry allergen [22]. In young Asian children and infants, egg allergy (0.15 to 4.4%), followed by cow milk allergy (0.33 to 3.5%) which represented the most common food allergies

[23]. The obvious difference in the prevalence of food allergen sensitization type may be explained by differences in the used method for diagnosis, differences in food habits among different regions, variation in the sample's sizes and differences in the age range of participants. The low sample size in our study and the use of a qualitative test for detection of specific allergen related IgE antibodies might have influenced the results.

Correlations of age with sensitization patterns to the tested food allergens were variable with strawberry and cod fish sensitizations were significantly negatively correlated with age. It has been reported that the prevalence of strawberry allergy peaks at two years of age and then falls progressively until late childhood [24]. In a high-risk cohort in Australia, prevalence of food sensitization is highest in infancy (26.3%) and drops after 12 months of age. Colonization pattern with gut microbiome may influence this variable sensitization with age [25].

Strong positive correlation was detected between cow milk sensitization and gastro-intestinal, dermatological and systemic manifestations. Literature review reported variable presentation of cow milk allergy affecting one or more organ system with the gastrointestinal tract and/or skin mostly involved. Cow's milk has been implicated as an important cause of severe reactions in children less than 6 years old [26]. In one study, the most common symptoms in children with suspected cow milk allergy were gastrointestinal symptoms followed by eczema [27]. In another study, gastrointestinal symptoms were the most common associated with suspected cow milk allergy (61%) followed by respiratory symptoms (41%) then skin complaints (33%) [28].

Another strong positive correlation in our study was detected between strawberry sensitization and both gastro-intestinal and dermatological manifestations. Allergy to strawberry in the Mediterranean area is generally rare with the most frequently reported symptoms of oral allergy syndrome, cutaneous symptoms and gastrointestinal symptoms [22].

In conclusion, we detected food specific IgE in the studied children with and without allergy. This just represents a state of sensitization rather than clinical allergy which possibly related to the early introduction of these foods in their diet. We correlated the sensitization pattern with their age and clinical presentation, but whether these patients with elevated specific IgE will develop food allergy or remain in sensitization phase; this is to be verified with long term follow up.

Ethics approval and consent to participate

All authors have seen and approved the manuscript, contributed significantly to the work, and also that the manuscript has not been previously published in or is not being considered for publication elsewhere. Verbal consent has been taken from each child parent.

The study was approved by the Ethics Committee at the faculty of medicine, Suez Canal University, Egypt.

Consent for publication

Done.

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Authors' contributions

Dr Hanan Omar: design of the study, analysis of the data, editing and final revision.

Dr maha Anani: design of the study, interpretation of data, drafting the article and final approval.

Dr Amany EL-kilany: acquisition of data, analysis of the data, editing and final revision.

Dr Asmaa hashem: acquisition of data, interpretation of data, drafting the article and final revision.

Dr Shereen Ahmed: acquisition of data, design of the study, analysis of the data, editing and final revision.

Disclosure of interest

The authors declare that they have no competing interest.

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