



Risk factors of Atopic dermatitis in 1- to 4-Years Old Children in Al-Bayda city, Libya

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Abstract: Atopic dermatitis (AD) is common among pre-school children worldwide. Food allergy may be an important factor in children with atopic eczema under 4 years. Our objective was to assess the extent and characteristics of confirmed and unconfirmed diagnoses of AD in 112 children who were diagnosed by Pediatric Allergy Clinic at Al-Bayda's hospital with a high possibility of having AD at some point in their lifetimes. Sera from the patients were analyzed for specific IgE antibodies to 20 allergens. About 95% of children with AD have IgE-mediated clinical reactivity. The prevalence of positive cases with food allergens ranged from 19-20%, and environmental factors ranged from 11-14% for boys and girls respectively. Positive cases of environmental factors in this population were recorded against some species of plants. As a result, a combined sensitization to food and environmental allergens not only has an additive increase in serum IgE antibody production, but also increases the risk of developing allergic diseases such as asthma during childhood. An evaluation for AD should be considered to these children.

Keywords: Atopic dermatitis (AD), Food allergy, environmental factors, children, Al-Bayda and Libya

INTRODUCTION

Atopic dermatitis (AD) is the most common inflammatory skin disease in children, particularly in young children. The prevalence of AD has tripled over the past three decades and affects 15% to 30% of children in industrialized countries (Larsen, 1996) (Bieber, 2010). This growth has been too speedy to be explained by genetic changes and alteration environmental elements have been proposed as the possible explanation for the increased prevalence of AD (McNally et al., 1998). There are also many factors demonstrated to be associated with AD: personal factors including, age, gender, nutritional status, lifestyle, allergy status and family history

(McNally et al., 1998) and changes in environmental factors (e.g. house dust mite, animal dander, molds, cockroach infestation, occupational exposure, environmental tobacco smoke, air pollution, aeroallergens, and climate change) (Lee et al., 2012; McNally et al., 2001; Schäfer et al., 2008). Since the first documented report of food allergy-provoking AD in 1915 (Schloss, 1915), parents and patients with AD continue to implicate food in disease flares (Greenhawt, 2010), an idea backed by the fact that food allergy is more common in children with AD. 30% of them are affected compared with 4% to 10% in the general pediatric population (Suh, 2010). Roughly one-third of kids with severe AD suffer from food allergy. In childhood, food

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allergies and food allergens such as cow's milk or hen's egg are mainly responsible for allergic reactions, when compared with adolescents and adults (Wassmann & Werfel, 2015). The diagnosis of eczematous reactions to food demands a careful diagnostic procedure, taking into account the patient's history and sensitization patterns. Despite the large types of food that can cause IgE-mediated reactions, most prevalence studies have concentrated on the most common allergenic foods, namely cow's milk, hen's egg, peanut, tree nut, wheat, soya, fish, and shellfish. Such allergens account for up to 90% of food allergy reactions (Eigenmann et al., 1998). Various diagnostic tools for atopic dermatitis (AD) have been proposed due to the lack of definitive biomarkers and the marked diversity of its clinical features (Brenninkmeijer et al., 2008; Deleuran & Vestergaard, 2014). The aim of our study was to screen serum of a group of children with AD to determine the course of sensitization and the development of clinical allergy which include a common allergic food and some environmental factors.

MATERIALS AND METHODS

The study protocol was reviewed and approved by Bioethics Committee at Biotechnology Research Center (BEC-BTRC) with Ref No: BEC-BTRC 04-2017. A group of 112 children (age: 6 months -48 months) with atopic eczema (inflammatory skin disease characterized by an itchy red rash) diagnosed by a doctor in Pediatric Allergy Clinic and Outpatients department at Al-Bayda's Hospital, Libya. The physicians involved in the study protocol determined the diagnosis of AD as a high possibility to have food allergies. Questions included demographic information, age of onset of allergy, number of accidental exposures, and history of concurrent food allergies. Then, a specific kit was used to determine main causes of these symptoms. Serum samples from all patients were collected at the time of the visit in Razi Med Lab in Al-Bayda and analyzed for allergen-

specific IgE antibodies using the ImmunoCAP Specific IgE (TÜV Rheinland, Germany) (Maloney et al., 2008). In brief, venous blood samples were collected and analyzed with the automated ImmunoCAP System. Fifty microliters of standards or patients' sera were added to the solid matrix (ImmunoCAP) and incubated for 30 minutes at room temperature. After washing, enzyme-labeled anti-IgE was added to the ImmunoCAP and incubated for 2.5 hours at same temperature, after which it was washed again. Then, 50 mL of developing solution was added to each sample. After a 10-minute of incubation, a stopping solution was added and fluorescence was determined and compared with values from the standard curve using biocheck imaging software. With the help of Biocheck Imaging Software (BIS) and a PC, the Polycheck cassettes were interpreted (TÜV Rheinland, Germany). In comparison with the standard curve, the amount of allergen-specific IgE for each allergen was given as relative kilo units per liter (kU/l) and results were determined based on their concentration of IgE. In this test, we used a pediatric screen for 20 individual allergens for children, designed as a screening test for the most relevant inhalation and food allergens. Histamine (10 mg/ml) was used as a positive control and glycerine as a negative control. Allergen-specific IgE (sIgE) concentrations in the serum were determined for the following allergens: milk, casein, α -laktalbumin, β -laktoglobulin, Bovine serum albumin, egg yolk and egg white, rice, soybean, banana, pork, beef, chicken, flour mix, bakers-yeast, *D.pteronysinus*- *D.farinaemix*, Cladosp herb.-Altern.altern.mix, Birch-Oak pollen mix, Alder-Hazel pollen mix, six Grass mix and level of IgE in serum. Degree of reaction for each allergen separately was ranged from 0.15 as a negative result (no specific antibody detection) to 100 as a positive result (very strong antibody concentration) that obtained as a result of collaboration of soft program with Polycheck kit.

RESULTS

From January to December 2016, 112 cases were screened for specific serum IgE for 20 different allergens. The majority of children were having atopic dermatitis or asthma at some point in their lifetimes. Of the children with reported symptoms of AD, the patients ranged in age from 6 months to 4 years (median, 2.5 years), and the ratio of gender of patients was male/female ratio of 47:65. There was similarity of results found between couple of genders with a type of allergens and most of them have more than one positive reaction to different allergens. Results in Table 1 illustrated a comparison in numbers between percentages of negative and positive cases for food/environmental allergens in both genders. The prevalence of positive cases with food allergens ranged from 19-20%, and prevalence of environmental factors ranged from 11-14% for boys and girls respectively. Most cases got a positive reaction against more than one type of allergens, thus the total numbers for positive and negative cases of food allergens for boys were 252 and 723 respectively, whereas the total number of the boys and girls in this study were 47 and 65 respectively (Figure 1 showed an example of the results for one subject).

For more details, Table 2 presented the numbers with percentages of negative and positive cases, and the mean degrees of reaction for each gender. Overall boy/girl cases, the highest numbers of positive cases were found with Alder-Hazel pollen mix (38 boys/44 girls) and Birch-Oak pollen mix (31 boys/43 girls), and the lowest numbers were noted with α -Laktalbumin (2 boys/4 girls), Casein (3 boys) and Chicken (4 girls). Additionally, of these 47 boys, 27 had reacted to *D. pteronyssinus*-,*D. farinaemix*, banana, and 24 reacted to 6-Grass mix. Of these 65 girls, 36 had reacted to *D. pteronyssinus*-,*D. farinaemix*, 39 reacted to a banana, and 21 reacted to 6-Grass mix. The results also showed that the total numbers for positive and negative cases

of food allergens for boys were 252 and 723 respectively, whereas the total number of the boys/girls in this study was 47/56 subjects. This referred to the most case that had been found to be positive to more than one type of food/ environmental allergens at the same time. In the same table, the ranges of increased serum specific IgE levels for each allergen varied widely among patients with positive diagnoses, and the total mean level of IgE was 96 and 100% for boys and girls respectively. The same table showed levels of mean degree of reaction for each allergen that ranges between 0.15-100 kU/I (concentration of antibody detection). The highest value was recorded with *D. pteronyssinus*-*D. farinaemix* with 21.4 and 19.8 for boys and girls respectively, followed by 6-grass mix and banana.

Table (1). Numbers and percentages of negative and positive cases for food/environmental allergens in both genders

Parameters	Boys (47)		Girls (65)	
	cases	percentage	cases	percentage
Total cases of food allergens	252	(19.38)	723	(55.62)
Total cases of environmental allergens	149	(11.46)	176	(13.54)
Total positive cases	252	(19.38)	723	(55.62)
Total negative cases	104	(8.06)	194	(14.92)

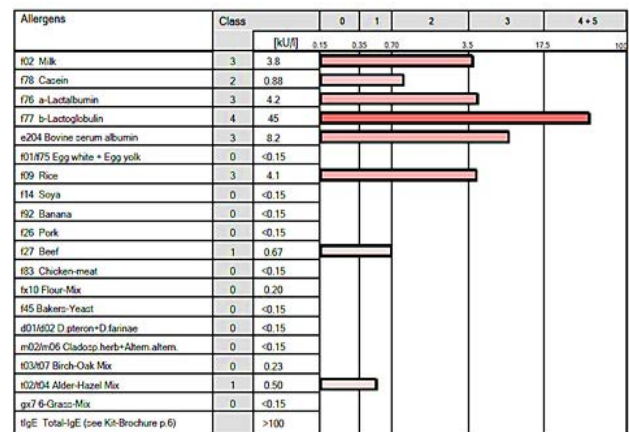


Figure (1). Results of Atopic test for one subject shown positive reaction for more than one type of allergens

Table (2) .Correlation between different twenty allergens with percentages of positive/negative cases and mean degrees of reaction in male and female subjects

No	Atopic	Boys (47)			Girls (65)		
		No of negative cases (%)	No of positive cases (%)	Mean degree of reaction	No of negative cases (%)	No of Positive cases (%)	Mean degree of reaction
1	Milk	41 (87.234)	6 (12.766)	0.197	57 (87.962)	8 (12.308)	0.282
2	Casein	44 (93.617)	3 (6.383)	0.169	57 (87.962)	8 (12.308)	0.181
3	α -Laktalbumin	45 (95.745)	2 (4.255)	0.181	61 (93.846)	4 (6.154)	0.279
4	β -Laktoglobulin	30 (63.830)	17 (36.170)	0.648	33 (50.769)	32 (49.231)	2.085
5	Bovine serum albumin	34 (72.340)	13 (27.660)	1.711	46 (70.769)	19 (29.231)	0.627
6	Egg white + Egg yolk	39 (82.979)	8 (17.021)	0.177	54 (83.077)	11 (16.923)	0.189
7	Rice	32 (68.085)	15 (31.915)	0.580	47 (72.308)	18 (27.692)	1.117
8	Soybean	38 (80.851)	9 (19.149)	0.625	56 (86.154)	9 (13.846)	0.593
9	Banana	20 (42.553)	27 (57.447)	3.627	26 (40)	39 (60)	2.808
10	Pork	38 (80.851)	9 (19.149)	1.064	51 (78.462)	14 (21.538)	0.535
11	Beef	35 (74.468)	12 (25.532)	0.207	57 (87.962)	8 (12.308)	0.18
12	Chicken	40 (85.106)	7 (14.894)	0.203	61 (93.846)	4 (6.154)	0.162
13	Flour-Mix	31 (65.957)	16 (34.043)	0.420	48 (73.846)	17 (26.154)	0.475
14	Bakers-Yeast	24 (51.064)	23 (48.936)	1.266	40 (61.538)	25 (38.462)	0.319
15	<i>D.pteronyssinus-D.farinaemix</i>	20 (42.553)	27 (57.447)	21.355	29 (44.615)	36 (55.385)	19.814
16	Cladosp.herb.- Altern.altern.mix	36 (76.596)	11 (23.404)	0.302	60 (92.308)	5 (7.692)	0.336
17	Birch-Oak pollen mix	16 (34.043)	31 (65.957)	0.575	22 (33.846)	43 (66.154)	1.086
18	Alder-Hazel pollen mix	9 (19.149)	38 (80.851)	0.420	21 (32.308)	44 (67.692)	0.916
19	6-Grass mix	23 (48.936)	24 (51.064)	3.980	44 (67.692)	21 (32.308)	2.886
20	Total IgE	2 (4.255)	45 (95.745)	58.42	0	65 (100)	59.351

DISCUSSION

AD/food allergy use had distinct risk factors. The prevalence of sensitization to food allergens appeared to occur and increase in early infancy (Kulig et al., 1998). In young children, the diagnosis of AD is mainly based on clinical evaluation. Although assessment of allergen-specific IgE antibodies provides helpful information to the clinician, a correct

interpretation of sensitization to common allergens is critical in determining susceptibility to allergic diseases (Chiu et al., 2014). This study attempted to estimate prevalence and risk factor profile of AD/food allergy that cause allergy in early childhood by comparing the distribution of different allergens in subjects suffers from AD. From our result, close to 95% of children with AD have IgE-mediated clinical reactivity. As a result, an

allergic reaction occurs when the immune system overreacts to the allergen by producing IgE antibodies. IgE is a type of antibody that is presented in small amounts in the body but plays a major role in allergic diseases (Galli & Tsai, 2012). In this study, the changes of serum IgE levels were consistent with the sensitization patterns of food. The lowest numbers of positive cases noted with α -Laktalbumin (2 boys/4 girls), Casein (3 boys) and Chicken (4 girls). On the other hand, the highest number of positive cases was recorded with banana followed by Bakers-Yeast, then β -Laktoglobulin, flour-mix, and rice for both genders. These results might refer to the fact that these types of food are considered as an important food for children at an early age. The total positive case with food allergens was found around 20% for both genders. These results were in agreement with other studies that found food allergy as an important factor in up to 20% of children with atopic eczema under 4 years (Oranje & De Waard-Van Der Spek, 2000; Tariq et al., 2000). These results were close to the finding of another study which stated that children (1 to 10 years old) in German were found to have a positive predictive value for eczematous reactions with food of 30% (Breuer et al., 2004). In another study, only 35% to 40% of food-sensitized children with AD have clinical signs and symptoms of food allergy (Greenhawt, 2010).

On the other hand, from our results, percentages of total positive cases with environmental allergens were found to be around 11-14% in both genders. In more details, 80 and 77% of subjects were found to have a high positive reaction with Alder-Hazel pollen mix, followed by Birch-Oak pollen mix and *D.pteronysinus* -*D.farinaemix* compared to food allergens. This might be attributed to the presence of these variety of plants in study area. Our results agreed with a study that found a prevalence of AD of (11.7%) from pediatric dermatosis in Benghazi, Libya (Elfaituri, 2015). They also agreed with a

study that found approximately half of young infants with food allergen sensitization were more likely to be allergic to inhalant allergens, and were at an increased risk of developing respiratory allergic diseases by the age of 4 years (Chiu et al., 2014). These environmental factors might play a role in increasing the risk of asthma which was reported in another study with children at age 1-14 years in the same city. Results of that study found a high number of children with severe smoke sensitivity and dust allergy and that the environmental factors might lead to the development of asthma in older children (Ali et al. 2016). To sum up, not only lifestyles but also environmental factors may be associated with the prevalence of AD in children at an early age in Al-Bayda city, which might lead to the increased risk of developing a respiratory allergy. This risk is high especially in children with early onset of food allergy.

CONCLUSION

The complex interplay between the variability of the environmental exposure and the interactions between the food allergies are likely to affect the development of AD. It is important to identify infants at risk to provide early intervention. Prevention should begin in early life, a critical window of vulnerability. Fixing of the epidermal barrier in infants with AD may prevent the subsequent allergic diseases.

Consent

It is not applicable.

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COMPETING INTEREST

Authors have declared that no competing interests exist.

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التهاب الجلد التأتبي (Atopic Dermatitis) وبعض العوامل المسببة له في الأطفال من سن 1-4

سنوات في مدينة البيضاء-ليبيا

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المستخلص : التهاب الجلد التأتبي (Atopic Dermatitis) هو أمر شائع بين الأطفال في مرحلة ما قبل سن الدراسة في جميع أنحاء العالم، والمسبب لالتهاب الجلد التأتبي ليس معروفاً. قد تكون الحساسية الغذائية من أهم العوامل المؤثرة والمسببة في معاناة الأطفال من هذا المرض أعمارهم من سنة واحدة إلى أربع سنوات. هدف هذه الدراسة هو تقييم مدى تشخيص المرض في عدد 122 حالة بعضها تم تأكيد التشخيص بها وأخرى مشكوك في تشخيصها حيث أن احتمال الإصابة تم تشخيصه في مرحلة ما من حياتهم من قبل عيادة حساسية الأطفال في مستشفى البيضاء. تم تحليل السيرم عند المرضى لتقدير نوع ومستوى الأجسام المضادة محددة لعدد 20 مسبباً من مسببات الحساسية، ما بين مسببات غذائية وأخرى بيئية. أظهرت النتائج أن حوالي 95% من الأطفال المصابين بالتهاب الجلد التأتبي لديهم تفاعل إيجابي للجسم المضاد IgE، وقد تراوحت نسبة الحالات الإيجابية مع المواد المسببة للحساسية الغذائية بين 19-20%، والحالات الإيجابية للعوامل البيئية بين 11-14% للذكور والإناث على التوالي، وقد كانت الحالات إيجابية لعوامل الحساسية الغذائية في فئة الدراسة ضد بعض أنواع النباتات. الخلاصة التي توصل لها الباحث هو التوعية المجتمع بالمكونات المسببة للحساسية في المواد الغذائية، فأى زيادة في إنتاج الأجسام المضادة IgE في المصل يمكن أن يزيد من خطر الإصابة بأمراض الحساسية مثل الربو في مرحلة الطفولة.

الكلمات المفتاحية : التهاب الجلد التأتبي، الحساسية الغذائية، الأطفال تحت سن 4 سنوات، البيضاء، ليبيا.