International Journal of Research in Medical Sciences
Khouzani M et al. Int J Res Med Sci. 2023 Aug;11(8):2875-2879
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20232415

Original Research Article

Influence of food allergy on atopic dermatitis in infants and children under 10 years: a study in Iran

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Received: 19 May 2023
Revised: 13 June 2023
Accepted: 19 June 2023

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ABSTRACT

Background: Based on the data collected from 220 cases of children and infants in Iran, aged under 2 months to 10 years, over a period of 6 months (2021-2022),there is evidence of a relationship between food consumption and the occurrence of Atopic dermatitis (AD).
Methods: It is an institution based Case-Control study. Analytical observational studies.
Results: It was found that 28.6% had IgE levels ranging between 150-250 u/ml. The majority of these patients consumed breast milk (n=83) or milk powders (n=75).In terms of the location of AD symptoms, 31.3% of the cases involved the chin and face.
Conclusions: The duration of treatment for these patients ranged from 6 to 8 months. Gastrointestinal problems and asthma allergies were also observed among the patients, which could be attributed to an increase in cytokines and pro-inflammatory factors. These findings highlight the influence of food consumption on the development of AD in Iranian children and infants. It suggests that certain foods, including breast milk and milk powders, may be associated with the occurrence of AD in this population.

Keywords: Atopic dermatitis, IgE, Immunity TH2, Th17, TSLPR, TSLP

INTRODUCTION

Atopic dermatitis (AD) is a common skin disorder that occurs in infants and children around six months after birth. This condition affects the skin, lungs, and stomach tissues, and can lead to kidney damage due to increased allergies. Given the rising prevalence of AD in developing countries, our research aims to explore the connection between food allergies and this disease. The immune system plays a crucial role in allergic diseases and Allergic diseases are commonly classified into three main types: Th1, Th2, and Th17. The Th1/Th2/Th17 concept is frequently employed to explain these conditions. Th1 cells are responsible for the production of interleukin-2 (IL-2) and interferon-gamma (IFN-γ), IL-4, IL-5, IL-13, and IL-31 are produced by Th2 cells.[1] Conversely, Th17 cells produce IL-17 and IL-22. In the case of AD, clinical manifestations include skin inflammation, itching (pruritus), elevated levels of eosinophils in peripheral blood, and increased serum IgE concentrations. These features can be attributed to Th2 immunity is characterized by the promotion of IL-4 and IL-13 the differentiation of Th2 cells and the generation of IgE. IL-5 is involved in the survival and proliferation of eosinophils, IL-31 is associated with the development of itchiness or pruritus, During In atopic dermatitis (AD), the dermis experiences infiltration of T cells that produce Th2-type cytokines, resulting in the formation of acute

skin lesions. Clinical studies have shown that dupilumab, a Th2 cytokine receptor antagonist, can alleviate AD symptoms[1]. However, chronic skin lesions in AD may also exhibit a bias towards Th1 or Th17 cells. Th17 cells, which play a crucial role in psoriasis, may contribute to the acute phase of AD but to a lesser extent compared to psoriasis. The exact role of Th17 immunity in the pathogenesis of AD remains uncertain, but it is hypothesized that IL-17 could enhance the development and exacerbation of skin symptoms in AD.[2]

Role of TSLP in AD

TSLP, IL-7-like cytokines, including one of its members, are expressed by various cell types such as epidermal keratinocytes, mast cells, dendritic cells (DCs), and fibroblasts. This cytokine family has gained significant attention and recognition. Attention plays a crucial role in the development of atopic dermatitis (AD). Elevated levels of TSLP are observed in Skin lesions observed in patients with AD are distinct from those seen in cases of allergic dermatitis triggered by nickel or lupus erythematosus.[3] Moreover, the expression There is a correlation between the severity scoring of AD and the levels of TSLP found in the stratum corneum. When allergens are injected into the skin of individuals with AD, it leads to rapid dermal expression. The production of TSLP in human keratinocytes can be induced by Th2 cytokines (IL-4 and IL-13), as well as pro-inflammatory cytokines (tumor necrosis factor [TNF]-α or IL-1α). Additionally, TSLP generation in keratinocytes can be triggered by innate immune responses mediated by Toll-like receptor 2/6 and 5 signals, as well as through activation of protease-activated receptor (PAR)-2, which is triggered by the proteolytic activity of house dust mite allergens.[4] Additionally, fibroblast-derived periostin, The expression of TSLP is induced by IL-4 and IL-13 stimulation in keratinocytes .Epidermal expression of TSLP is stimulated by skin injury or barrier disruption, which is particularly significant in the context of atopic dermatitis (AD). TSLP plays a crucial role in promoting Th2 immune responses. When naive CD4(+) T cells are activated by TSLP, it induces the transcription of the IL-4 gene, which in turn upregulates the expression of the Th2 cell activation is further enhanced by the presence of TSLP receptor (TSLPR) on these cells, creating a positive feedback mechanism. differentiation. TSLP also activates and promotes the Naive CD4(+) T cells can be differentiated into Th2 cells when CD11c (+) dendritic cells (DCs) migrate and prime them with a specific antigen, particularly in the absence of IL-12.[5] Additionally, TSLP stimulates dendritic cells (DCs) to produce chemokines such as CCL17 (thymus and activation-regulated chemokine, TARC) and CCL22 (macrophage-derived chemokine, MDC), which attract Th2 cells.[6] AD patients exhibit increased production of CCL17/TARC and CCL22/MDC. Patients compared to healthy individuals, and their serum levels correlate with disease activity. These chemokines are the production of CCL17/TARC and CCL22/MDC is not only generated by TSLP-primed dendritic cells (DCs), but also by activated blood mononuclear cells, endothelial cells, and epidermal keratinocytes.IL-31, produced by activated Th2 cells, is highly expressed in AD. There is a correlation between the clinical severity of AD and serum levels of IL-31. IL-31 functions as a pruritogenic cytokine and also triggers skin inflammation. When injected into the skin of mice, IL-31 induces specific effects leads to the infiltration of inflammatory cells. In response to IL-31, IL-18, and IL-33, which belong to the IL-1 family of cytokines, epidermal keratinocytes produce CCL17/TARC and CCL22/MDC, have implications in Th2 immunity.[7] Although IL-18 is generally considered a Th1 cytokine, it also contributes to Th2 immune responses. IL-18 stimulates basophils, mast cells, and CD4(+) T cells to produce IL-4 and IL-13. In AD patients, elevated serum concentrations of IL-18 are observed, and these levels correlate with disease severity and serum IgE levels. IL-33, on the other hand, promotes the maturation of mast cells and Th2 cells and enhances the production of IL-13 and other cytokines and chemokines from mast cells. High levels of IL-33 mRNA expression are observed in the lesional skin of AD.[8]

The objectives of the study were the possibility of a relationship between food allergy and atopic dermatitis, as well as the severity of the disease according to the IgE lab reports.

METHODS

It was an institution based case-control observational study. The area of the study was Razavi hospital in Mashhad of Iran. Patients of under 1 to 10 -years age group attending with AD and IgE lab reports and fulfilling inclusion and exclusion criteria were a part of the study population. The study period was from July 2021 to February 2022. Total 220 patients consisted of the sample size.

Inclusion criteria

All patients of age group between under1 to 10 years underwent, IgE lab reports holds and showing any range of atopic dermatitis were included were included.

Exclusion criteria

Patients having any infective disease such superficial skin infection, patients taking steroids for long time were excluded.

Methodology

Considering the increase of this disease among children, the expectations of the statistical community were high, but considering that our data was based on immunoglobulin E lab reports, we were able to find only 220 patients in Iran. Otherwise, our survey was uploaded on the internet from July 2021 to February 2022, we

reached only 220 patients by miss out the patients who did not answer the laboratory test (IgE lab reports).

Questionnaire

According to studies, we asked the patients for their IgE report range between 50 and 450 u/ml, Based on past studies more than 60% of patients with AD have IgE levels exceeding 200 u/ml.[9]

In the next question, I asked the participants about the body parts affected by AD, considering parameters such as the face, chin, face+chin, chin+back of hand, and the entire body. In separate questions, we inquired about the age of the patients (ranging from under 2 months to 10 years) and the types of food they consumed, including powdered milk, cow's milk, breast milk and solid food. We also asked about the duration of the illness, which varied from 1 month to 18 months.

RESULTS

In (n=220) a case study measuring IgE in 6 months (in Table 1), it was considered mid-range IgE=150u/ml -250 u/ml in result (n = 64 person, 28.6%) showed study had serum IgE above mid-range in 6 months period test 17.72% case study showed 50-150 u/ml IgE in serum and 9 person show > 450u/ml in serum. IgE lab reports show most patients had an IgE range between 150_250 by 28.6% and 250-350 by 29.9% and the lowest range is >450 by 4%.

Table 1: IGE lab reports.

<50	50-150	150-250	250-350	350-450	>450
39 person	39 person	63 person	46 person	22 person	9 person
17.7%	17.7%	28.6%	20.9%	10%	4%

About food consuming, n=30 patients use cow milk and n=75 use milk powder, 83 person breast milk and n=33 people used solid foods such as carbohydrates and n=53 select other food.

The resulting data show most patients consume breast milk by 30% and milk powder by 27% and lower range is solid foods by 12%, 31.3% (n=69) of patients showing AD (2)in face +chin, 18.1% (n=40) only in chin and 26.3% in only face (n=58), 17.7% (n =39) in chin +back of hand and 6.8% (n=15) showing in full of body (Figure 1).

Locate AD in body in n=220 patients than showing AD in chin+face most occurs in body by 31.3% and lowest about full body by 6.8% (2021_2022) (Figure 2).

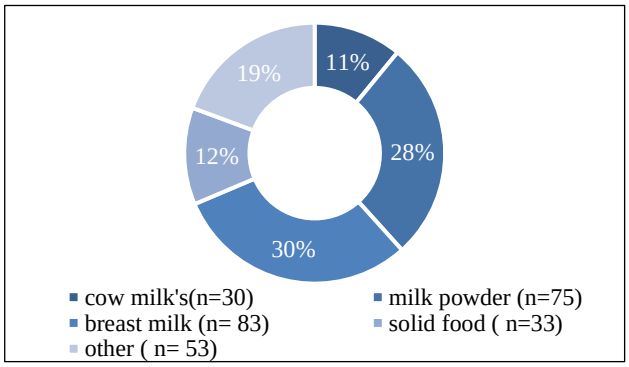

Figure 1: Food consumed by patients last month before showing AD.

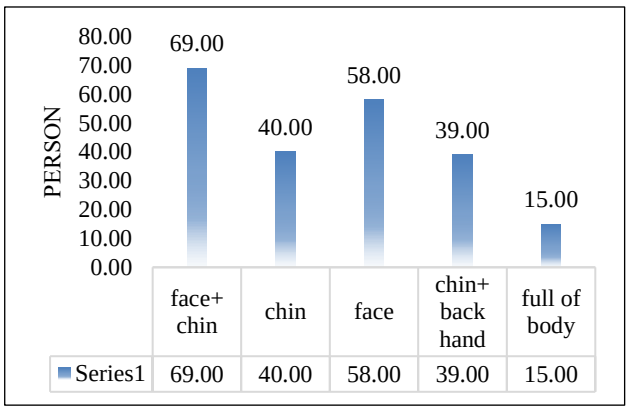

Figure 2: Locate AD in body in n=220 patients.

Result data for age patients (Table 2) is under 2 months 19% n= 42, under 1 year 35.4% n=78, under 5 years n=76 34.5%, and patients under 10 years (5_10 years) are n=24 11.3%.

Table 2: Age of patients showing AD.

Under 2 months	Under 1 years	Under 5 years (1_5)	Under 10 years (5_10)
42 persons	78 persons	76 persons	24 persons
19%	35.4%	34.5%	11.3%

Table 3: Schedule of treatment.

Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16 17,	18
Person	5	27	27	5	24	34	15	33	27	4	7	6	2	1	2	0	1
Percentage	2.2	12.2	12.2	2.2	10.9	15.4	6.8	15	12.2	1.8	3.1	2.7	0.9	0.4	0.9	0	0.4

Age of patients showing most AD in range under 1 year by 35.4% and lowest year in range under 10 years by 11.3% (Table 2).

Data collected from 63.6% n= 140 from urban region and 35.9% n=79 from rural region and data showing mid-range for schedule of treatment are 6 months to 8 months.

Schedule of treatment showing most months for treatment patients is 6 months by 15.4% and 8 months by 15%, and a small number of patients have been treated for more than 14 months to 18 months (Table 3).

DISCUSSION

Recent research has indicated a significant link between food allergies and atopic dermatitis (AD). Around 35% of children diagnosed with AD have been found to have concurrent food allergies. Cow's milk, eggs, peanuts, soy, wheat, and fish are among the commonly reported allergenic foods associated with AD.[10] In neonatal and infantile allergies, there can be an increase in IgE levels, particularly in the context of food allergies. These allergies can also have an impact on gastrointestinal diseases, leading to symptoms such as vomiting, diarrhoea, and bloody stools. IgE can be secreted in response to cytokines such as IL-4 and IL-5, and it can contribute to the development of allergic conditions like asthma, leading to symptoms such as coughing. This pattern is often observed in clinical practice.[11]The concept of "allergic (atopic) march" refers to the sequential occurrence of various allergic diseases in infants, including food allergies, atopic dermatitis (AD), asthma, and allergic rhinitis (AR). AD typically precedes food allergies, and other allergic diseases develop over several years. Recent research has highlighted the role of filaggrin and thymic stromal lymphopoietin (TSLP) in the progression of atopic march.[12] Filaggrin is an important component of the skin barrier. Dysfunction or loss-of-function Mutations in the FLG gene (FLG-LOF) have been identified as risk factors for allergic sensitization, atopic eczema, allergic rhinitis (AR) and asthma, These mutations play a role in the dysfunction of the epidermal barrier, leading to increased trans-epidermal water loss (TEWL).[13] The presence of increased trans-epidermal water loss (TEWL) can contribute to the development of clinical atopic dermatitis (AD) in individuals who are at a high risk of atopy. Furthermore, the combination of FLG-LOF mutations and allergic sensitization during childhood further amplifies the risk of developing eczema, particularly in relation to FLG-LOF mutations can contribute to the development of eczema, including food allergen sensitization (FAS), which, in turn, can increase the risk of developing food allergies (FA) later in life.[14] Immediate-type food allergies are characterized by symptoms that occur shortly after ingesting the allergenic food. In infants, FA can develop without AD, as some of the foods commonly associated with AD, such as carbohydrates, egg yolk, milk powders, and cow's milk, can also trigger food allergies.

This study has few limitations. In poor areas with basic economics, according to the high cost of testing, families did not want to be tested and were excluded from our data, which made the amount of data more focused on urban people.

CONCLUSION

In conclusion, atopic dermatitis (AD) is a disease that typically begins in the first months of life and can cause long-term itching, swelling, and inflammation in the skin and lungs. It is often associated with the development of asthma in patients. Controlling food allergies in infants and children has been shown to significantly decrease symptoms of AD by up to 80%. This highlights the importance of identifying and managing food allergies as a part of comprehensive treatment for AD. Overall, AD is a complex disease influenced by genetic factors, immune responses, and environmental triggers. Understanding these factors and implementing appropriate management strategies, including the control of food allergies, can greatly improve the symptoms and long-term outcomes for individuals with AD.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Khouzani MS, Krishnaveni K. Influence of food allergy on atopic dermatitis in infants and children under 10 years: a study in Iran. Int J Res Med Sci 2023;11:2875-9.