ACTA MEDICA SALINIANA

ORIGINAL PAPERS

ACCURACY OF POSITIVE SKIN PRICK TEST IN CHILDREN WITH ATOPIC DERMATITIS: A SINGLE CENTER EXPERIENCE

Amra Šerak[1], Almira Ćosićkić[2], Nina Mekić[1], Alma Trnačević[3]

ISSN 0350-364X

DOI: 10.5457/815

Amra Šerak
Almira Ćosićkić
Nina Mekić
Alma Trnačević

ABSTRACT

Aim: The aim of this study was to determine the incidence of positive SPT in children with atopic dermatitis and to show its diagnostic accuracy and correlation between postitive skin prick test (SPT) and severity of atopic dermatitis (AD), as well as emphasizing improtance of SPT as an important diagnostic tool in the diagnosis of AD.
Methods: The retrospective-prospective study was conducted at the Department of Rheumatology, Immunology and Allergology of the Clinic for Children's Diseases, University Clinical Center (UCC) Tuzla, from January 2015 to January 2020.
The skin prick test was performed by trained study personnel. Standard MWD ≥3 mm is proposed by the World Allergy Organization (WAO) and was used in our study.
Results: This study included 646 children. Atopic dermatitis was diagnosed in 126, while 114 children with atopic dermatitis met our study criteria. All 114 children were subjected to SPT. Positive results were found in 60 children (52.6%) with AD. SPT was positive in 11 of 23 children with mild form of AD (47.8%). In the same time, 36/70 (51.4%) children with moderate form of AD had positive skin prick test. Severe form of AD was found in 21 children. Thirteen children had food or aeroalergy (61.9%).
Conclusion: Our study showed that a significant number of children with AD showed sensitivity to dust, pollen, Dermatophagoides pteronyssinus, milk, eags and other alergens on SPT. It also showed strong correlation between postitive skin prick test and severity of AD.

Key words: Allergy; Atopic Dermatitis; Children; Skin Prick Test.

Affiliations:
[1]Pediatric Department, Health and Educational Medical Center Tuzla,
[2]Clinic for Children's Diseases Tuzla, University Clinical Center Tuzla,
[3]Clinic for Infective Diseases Tuzla, University Clinical Center Tuzla

Received:
01.08.2024.

Accepted:
01.09.2024.

Corresponding author:
Amra Šerak:
amraserak1989@yahoo.com;
+3876194731

Funding: none

Competing interests: none

INTRODUCTION

Atopic dermatitis (AD) is one of the most prevalent chronic inflammatory skin diseases in children [1]. It is a multifactorial inflammatory skin disease of complex etiology, resulting from the interaction of genetic, environmental and psychological factors. AD is characterized by the appearance of eczematous lesions, with pruritus and dry skin, associated with the disruption of epidermal barriers, abnormal immune responses, and immunoglobulin (Ig) E secretion [2]. AD onset is attributed to hypersensitive immune cells, including keratinocytes, monocytes, and dendritic cells, which overreact to environmental agents, such as house dust mite allergens, food, and bacteria, leading to overwhelming inflammatory responses [2,3].
The occurrence of AD is increasing rapid in children with an incidence rate of around 5-20% [4]. Cipriani reported in an American national study the total prevalence of 13% of AD in children with 67% being mild, 26% moderate and 7% severe form of AD [5]. The Canadian healthy infant longitudinal development study, found that children with AD and allergic sensitization had a greatly increased risk of food allergy, asthma and allergic rhinitis compared to non-sensitized children without AD [6]. Atopic dermatitis, food and aeroalergies and sensitivity are highly interconnected. Young children with AD tend to become sensitized to eggs, milk or peanuts, while older children and adults more often become sensitized to environmental allergens such as house dust mites (HDM), animal dander or pollen [7].
Infantile atopic dermatitis associated with food allergy, as a name, was proposed by the study group of the Ministry of Health, Labour and Welfare [8]. This type is the most common food allergy during childhood. It is associated with infantile atopic dermatitis. Eczema often remits with the elimination of allergen foods. The food allergy often improves with aging [9].
About 69% of infants who had AD during the first 3 months of life were sensitized

against aeroallergens and significant number of them showed sensitivity to dust, pollen, insects, Dermatophagoides farinae and fungi [9]. Commonly, AD and food and aeroallergy coexist in children with AD while in about 35% of children with AD food and aeroallergy is the provoking cause. Although the role of aeroallergens has been highlighted in studies, food allergens have been identified as the main external triggers in AD [9,10].

The skin prick test (SPT) is an indirect method for detecting IgE antibodies [11], commonly used in clinical practice and epidemiologic studies and has been used to screen infants before initiating interventions for primary prevention of food allergy [12-13].

The aim of this study were to determine the incidence of positive SPT in children with atopic dermatitis and to show its' diagnostic accuracy.

PATIENTS AND METHODS

The retrospective-prospective study was conducted at the Outpatient Clinic and Department of Rheumatology, Immunology and Allergy of the Clinic for Children's Diseases, University Clinical Center (UCC) Tuzla, from January 2015 to January 2020. Questionnaire was filled out including information about the age and sex of children, age of the child when the first signs of AD appeared, severity of the disease, background factors such as heredity of atopy and AD, respiratory manifestations of bronchial obstruction, feeding patterns during infancy, other possible allergic symptoms and data on sensitivity to food allergens and/or aeroallergens.

Diagnosis of AD was made by the Hanifin and Rajka diagnostic criteria for atopic dermatitis, and duration of the pruritic skin changes of at least 3 months. Children ages 0 to 15 were included. The inclusion criteria were satisfying at least three major and three minor criteria. The exclusion criteria were: children having more than 15 years, antihistaminics in therapy less than 10 days prior trial or corticosteroids less than 30 days prior trial, local corticosteroids less then 10 days, children with other acute or chronic diseases or systemic diseases and those children whoes parents refused to give writting consent to be included into trial. As we followed the stated criteria, 114 children met the criteria and were included in the study.

The SCORing Atopic Dermatitis (SCORAD) index was used to assess the severity of atopic dermatitis. We assessed the following: (A) spread of skin changes, expressed in a range of 0-100; (B) intensity of skin changes graded on a 0-3 scale, where 0 indicated absence of changes, 1 minor changes, 2 moderate changes, and 3 intense changes; (C) subjective signs were presented on a 1-10 scale, where 0 signifies "never better" and 10 "never worse". The intensity of the subjective signs was declared by the child (if it was an older child over 5 years old) or the child's guardian. The values of the SCORAD index were calculated according to the formula A/5+7B/2+C. The maximum SCORAD index value was 103. According to the SCORAD index values, the severity of the disease was assessed as mild (<15 points), moderate (15-40 points), or severe (>40 points).

Food allergen and aeroallergen testing by skin prick test (SPT) was performed at the Allergy Testing Department, Clinical Department for Children's Diseases, Tuzla UCC. Testing was carried out for groups of food allergens (cow's milk, eggs, flour, meat I and II, fruit I, II and III, vegetables I and II) and for groups of aeroallergens (grass pollen, weed pollen, tree pollen, house dust, Dermatophagoides pteronyssinus, animal hair-fur, feathers, vegetable fibers, fabrics, fungi, bacteria) using dialyzed extracts of allergens in a solution of a mixture of 50% glycerol solution in buffered saline solution (allergens preparations for SPT; Institute of Immunology, Zagreb, Croatia). Urticaria of >3 mm was taken as a positive test result.

RESULTS

Durin this period 646 children were examined in the outpatient clinic/departement of Rheumatology. Atopic dermatitis was diagnosed in 126, while 114 children with atopic dermatitis met our study criteria. Inclusion criteria weren't satisfied by 12 children because 7 used antihistaminics, three of them used system corticosterids, one had system deasease, while we didn't get one parents acceptance to include childs date to research. Among those 114 children, 56 were male (49.1%) and 58 were girls (50.9%). Positive anamnesis of food and/or respiratory alergy was found in 70 children (n=70, study group) (33 were boys (47.1%) and 37 were girls (52.9%)). In controled group (n=44) 23 were boys (52,3%) and 21 were girls (47,7%). Based on gender, there were no statistically significant difference between study and control groups (p= 0,91). We also analysed connection between gender and AD severity based on SCORAD index results (Table 1).

Table 1. Gender of children with different severities and forms of AD

	Form of disease			
	Mild form (n = 23)	Moderate form (n = 70)	Severe form (n = 21)	p
Male	13	29	13	NS
Female	10	41	8	

Study included children with average age of 26.5 months when they were admited to hospital, minimal of 1.5 months and maximum of 96 months. Out of all those children with AD, minimal age was 1.5 months and maximum age was 14.9 years. In the group of 70 children with food or respiratory alergies minimum was 4 months and maximum 14.9 years (MD at 31,25 months). In control group, youngest child was 1.5 months and oldest was 10.5 years (MD at 26 months). Based on age, there were no statistically significant difference between study and control groups (p= 0,15). We also analysed connection between children age and AD severity based on SCORAD index results (Table 2).

Table 2. Age of children with different severities and forms of AD

	Form of disease			
	Mild form (n = 23)	Moderate form (n = 70)	Severe form (n = 21)	p
Children age (months) median	26 (17-77)	29.5 (17-69)	18 (6-41)	NS

Most common maior criteria was itching and scraching (109/114). We found with typical localisation in 98/114 (85,9%) and chronic changes in 88/114 of children.
Most common localisation typical for AD was face (37.7%), than face and uper extremities (22.8%), lower extremities (14.9%), body (10.5%), neck skin folds (9.6%).
Most common skin changes were dray skin (103/114), scraching coused by swet (54/114), erythema (53/114).
Most common nonskin symptoms were: emotional factors (94/114), young age (92/114), increase of IgE (64/114).
Age of kids with AD on natural diet, had median around 6 months (0-12 months). For 46/114 (40,3%) kids with AD, first skin changes were reported while on natural diet, so positive and statistically significant correlation was found between lenght of natural diet and first skin changes (r=0,28, p=0,002; 95% CI: 0,10 - 0,44).
The introduction of cow's milk into the diet for kids with AD happened in interval between 0-13 months, with median at 6 months. Positive, light and statistically significant correlation between the age of introduction of cow's milk and apperance of first skin changes was found (r_0,27, p<0,003; 95% CI: 0,09-0,43).
The introduction of other food into the diet for kids with AD happended in interval between 0 and 9 months, with median at 6 months. Positive, light and statistically significant correlation between the age of introduction and apperance of first skin changes was found (r=0,19; p=0,03, 95%CI: 0,01, 0,36).
Disease severity was measured by SCORAD index. The most common subjective simptoms were: itching (109/114) and scraching coused by swetting (54/114).
Average SCORAD index was 28.5 points, with minimum of 4.7, and maximum at 102.8.
All 114 children were subjected to Skin Prick Test (SPT). Positive results were found in 60 children (52.6%) with AD. SPT was positive on aeroalergens in 23/114 children (20.2%) and most common alergen was home dust in 13/114 children (11.4%) and Dermatophagoides pteronyssinus in 5/114 children (4.4%). SPT on food alergens was positive in 37/114 (32.4%) children. Most common food alergen was cow milk in 17/114 (14.9%) children and eags in 8/114 (7%) children.
SPT was positive in 11 of 23 children with mild form of AD (47.8%). Six of them had been postitive on aeroalergens and 5 on food alergens. In the same time, 36/70 (51.4%) children with moderate form of AD were positive on aeroalergens (13) or food alergens (23).
Severe form of AD was found in 21 children. Thirteen children had food or aeroalergy (61.9%). Nine of them had food alergy and 4 had aeroalergy.
There is a significant correlation between postitive SPT for food or/and aeroalergens and severity of AD (r=0.21, t=2.28, p = 0.024) (Table 3).

Table 3. Correlation between positive SPT and severity of AD.

	Form of disease			
	Mild form	Moderate form	Severe form	p
Number of positive SPT (%)	11/23 (47,8)	36/70 (51,4)	13/21 (61,9)	p<0.05

Positive SPT was found at 60/114 (52,6%) of children with AD. In study group of children with AD, positive SPT was found at 52/70 (74.3%), while in control group 8/44 (18.2%). Statistically significantly more positive SPT tests were reported in group of children with AD (74.3 vs 18.2; $\chi 2=34.11$, p<0.0001; OR = 13; 95%CI: 5.10-33.11).

Point biserial correlation coefficient (PBC) was used to examine correlation between positive SPT and severity of AD. PBC showed strong positive correlation with r=0.21 between positive SPT and severity of AD. Contigency test ($\chi 2$) also showed significant correlation between positive SPT and severity of AD ($\chi 2$ =7.71; p=0.02; df=2; Contigency test =0.252). Based on paramethers of SCORAD index, we had different spred of changes and different intensity of changes and various subjective signs. Based on SCORAD index, intensity was messured. We had 103 children with dry skin, 98 with erythema, 71 with excoriations, 52 with lichenification, 51 with papulae and 46 with crusts.

DISCUSSION

According to worldwide researches atopic dermatitis, also known as atopic eczema, affects a large proportion of children and is most common in infants, where it occurs in 20% of those under two years of age [14]. Over the past 30 years, a twofold to threefold increase in paediatric atopic dermatitis has been reported [15]. Most children develop atopic dermatitis before the age of two years [16]. Significant morbidity associated with atopic dermatitis can be prevented with early diagnosis and treatment[17].

In our study both genders were equaly represented. Average age was 26.5 months on the day of admission to the Clinic, with the youngest child being 1.5 months odl and the oldest 96 months old.

The pathogenesis of AD involves the disruption of T helper (Th) 1/Th2 cytokine homeostasis towards Th2 skewed immune responses [3,12]. When Th2 cells are activated, cytokines such as thymic stromal lymphopoietin (TSLP), interleukin- (IL-) 4, IL-5, IL-10, and IL-13 are secreted, enhancing humoral immune responses and inhibiting the function of Th1 cells [12].

Atopic dermatitis can present in many different forms and, as such, the differential diagnoses are broad and can include contact dermatitis, impetigo, urticaria, scabies, psoriasis and seborrhoeic dermatitis. It is important to consider these diagnoses before a diagnosis of atopic dermatitis is established.

According to Dahr et al. in the childhood AD group, 74.50% had facial involvement, 35.53% had flexural involvement, 56.32% had extensor involvement and 8.24% had both flexors and extensors involved [19]. Our study shows that 109 out of 114 children had itching and scratching simptoms. At 98 out of 114 children we found tipical localisation, while we found chronic changes at 88 out of 114 children. Acute eczema was seen in 28.79%, subacute in 23.38%, chronic in 47.40% and follicular in 0.43% of the children [20]. In our study most common skin changes were dray skin (103/114), scraching coused by swet (54/114), erythema (53/114). Most common nonskin symptoms were: Emotional factors (94/114), young age (92/114), increase of IgE (64/114).

Food allergy (FA) represents the body's exaggerated immunological response to the ingestion of a particular type of food substance and it is characterized by itching, swelling, hives, eczema and wheezing in mild to moderate cases. In severe cases, there could also be associated difficulty in breathing, anaphylactic shock, light-headedness, and even death. The most common childhood foodallergies are typically outgrown by adolescence or adulthood [20].

SPT is recommended to determine the causes of food allergy. Avoid intradermal tests using food antigens because they are more likely to yield false positive results and cause anaphylactic reactions than the SPT. However, for children with a history of symptoms or high antigen-specific IgE antibody levels avoid even the SPT because it may cause systemic symptoms. Reportedly, an atopy patch test, in which a food antigen is applied on the skin, is useful for predicting nonimmediate reactions in the diagnosis of atopic dermatitis. However, no consensus has been reached on this finding. Before testing, the use of agents such as antihistamines, antiallergics and steroids should be withdrawed because these influence in vivo test [8]. The SPT wheal size is measured after 15–20 min in the standard procedure and is considered positive with a mean wheal diameter (MWD) of ≥3 mm larger than the negative control [9]. The SPT was performed by trained study personnel. Mean Weal Diametar (MWD) was derived as the sum of the longest diameter and the diameter perpendicular to this divided by 2 and reported in mm without decimals. An MWD of 10 mm or more was assigned 10+ mm.

A threshold of 2-mm MWD or more for AS is widely used in research [21,22,23] despite the standard MWD ≥3 mm proposed by the World Allergy Organization (WAO) [24] to define a positive SPT in the clinic, also in infants. We desided to use MWD≥3 mm threshold as proposed by WAO. An MWD ≥2 mm is likely to be of clinical relevance in infants, in line with the findings in the Learning Early About Peanut Allergy (LEAP) study [25] where 37.5% in the avoidance group with SPT 1–2 mm towards peanut at 4–10 months of age had a positive oral food challenge towards peanut at 60 months of age.

Our study showed that a significant number of children with AD showed sensitivity to dust, pollen, Dermatophagoides pteronyssinus, milk and eags on skin prick test. It also showed strong correlation between postitive skin prick test and severity of atopic dermatitis. It is an important diagnostic tool in the diagnosis of atopic dermatitis.

However, diagnostic approaches are rather complex for late onset reactions, because the role of allergens in the pathogenesis and clinical features of AD have not been explored in detail [14].

Allergic diseases are considered as important public health problem which significantly increase socioeconomic burden by lowering the quality of life and work productivity of affected children and their families [25]. The determination of sensitivity by SPT is one of the basic steps in the treatment of allergic diseases. In addition to the economic costs of allergic diseases they can cause social losses such as frequent absence

from school and work loss, impaired quality of life and reduction in productivity. Once the allergen sensitization has been determined by SPT, the children are kept away from the offensive allergen. Thus, the social losses could be reduced. Therefore, it is important to determine sensitivity and a change of sensitivity in people with allergic diseases.

Based on Gizem Atakul et al. study, clinical severity score increased, as the presence of food sensitization increased. Sensitization to egg white, egg yolk and cow's milk were the most frequent food allergens in their study group. Patients with multiple food sensitization were more likely to have higher SCORAD scores, vice versa [27].

Positive skin prick test was found in all form of AD but percentage was bigger in severe form of disease than in moderate or mild forms, with significant correlation between SPT results and severity of desease [28].

REFERENCES

1. Akiko Kijima, Hiroyuki Murota et al. Prevalence and Impact of Past History of Food Allergy in Atopic Dermatitis. Allergology International. 2013;62:105-112.
2. Boguniewicz M., Leung D. Y. M. Atopic dermatitis: a disease of altered skin barrier and immune dysregulation. *Immunological Reviews*. 2011;242(1):233–246.
3. Bieber T. Atopic dermatitis. *The New England Journal of Medicine*. 2008;358(14):1483–1494.
4. Yash Mehta, Darshna G. Fulmali. Relationship between atopic dermatitis and food allergy in children. Cureus 2022. 14(12): e33160.
5. Cipriani F, Dondi A, Ricci G. Recent advances in epidemiology and prevention of atopic eczema. Pediatr Allergy Immunol 2014; 25(7): 630-8.
6. Tran MM, Lefebvre DL, Dharma C, et al. Predicting the atopic march: results from the Canadian Healthy Infant Longitudinal Development study. J Allergy Clin Immunol 2018; 141(2): 601- 607.e8.
7. Risa Tamagawa-Mineoka, Norito Katoh. Atopic Dermatitis: Identification and Management of Complicating Factors. Int J Mol Sci. 2020. 21(8):2681.
8. Urisu A, Ebisawa M, Ito K et al. ; Committee for Japanese Pediatric Guideline for Food Allergy, Japanese Society of Pediatric Allergy and Clinical Immunology; Japanese Society of Allergology. Japanese Guideline for Food Allergy 2014. Allergol Int. 2014;63(3):399-419.
9. Almira Ćosićkić, Fahrija Skokić et all. Development of respiratory allergies, asthma and allergic rhinitis in children with atopic dermatitis. Acta Clin Croat 2017; 56: 308-317.
10. Pooja Bains, Alka Dogra. Skin prick test in patients with chronic allergic skin disorders. Indian J Dermatol. 2015 ; 60(2):159-64.
11. Ansotegui IJ, Melioli G, Canonica GW et al. IgE allergy diagnostics and other relevant tests in allergy aWorld. Allergy Organization position paper. World Allergy Organ J. 2020 ; 13((2)):100080.
12. Peters RL, Koplin JJ, Gurrin LC, et al. The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up. J Allergy Clin Immunol. 2017 ; 140((1)):145-–53.e8.
13. Alduraywish SA, Lodge CJ, Vicendese D, et al. Sensitization to milk egg and. peanut from birth to 18 years: a longitudinal study of a cohort at risk of allergic disease. Pediatr Allergy Immunol. 2016 ; 27((1)): 83–91.
14. Spergel JM, Paller AS. Atopic dermatitis and the atopic march. J Allergy Clin Immunol 2003;112(6 Suppl): S118–27.
15. Boguniewicz M, Leung DY. Recent insights into atopic dermatitis and implications for management of infectious complications. J Allergy Clin Immunol 2010;125(1):4–13; quiz 14–5.
16. Wolff K, Johnson RA. Atopic dermatitis: Fitzpatrick's color atlas and synopsis of clinical dermatology. 6th edn. New York: McGraw-Hill Medical, 2009.
17. Lewis-Jones S. Quality of life and childhood atopic dermatitis: The misery of living with childhood eczema. Int J Clin Pract 2006;60(8):984–92.
18. Spergel J. M., Mizoguchi E., Oettgen H., et al. Roles of TH1 and TH2 cytokines in a murine model of allergic dermatitis. *Journal of Clinical Investigation*. 1999;103(8):1103–1111.
19. Dhar S, Banerjee R. Atopic dermatitis in infants and children in India. Indian J Dermatol Venereol Leprol 2010;76:504-513.
20. Onyinye I Iweala, Shailesh K Choudhary, Scott P Commins. Food Allergy. Curr Gastroenterol Rep. 2018. 20(5):17.
21. Alduraywish SA, Lodge CJ, Vicendese D, et al. Sensitization to milk egg and. peanut from birth to 18 years: a longitudinal study of a cohort at risk of allergic disease. Pediatr Allergy Immunol. 2016 ; 27((1)):83–91.
22. Schoos AM, Chawes BL, Følsgaard NV, et al. Disagreement between skin prick test and specific IgE in young children. Allergy. 2015 ;70((1)):41–8.
23. Jøhnke H, Norberg LA, Vach W, et al. Patterns of sensitization in infants and its relation to atopic dermatitis. Pediatr Allergy Immunol. 2006 ;17((8)):591–600.
24. Ansotegui IJ, Melioli G, Canonica GW, et al. IgE allergy diagnostics and other relevant tests in allergy aWorld. Allergy Organization position paper. World Allergy Organ J. 2020 ;13((2)):100080.
25. Greenhawt M, Fleischer DM, Chan ES, et al. LEAPing through the looking glass: secondary analysis of the effect of skin test size and age of introduction on peanut tolerance after early peanut introduction. Allergy. 2017 ;72((8)):1254–60.
26. Remo Frei et al. Environmental influences on childhood allergies and asthma. Pediatr allergy Immunol. 2022 ; 33(6): e13807.
27. Gizem Atakul, MDa*, Sevgi Sipahi Çimen, MDb. The prevalence of sensitization to food allergens in children with atopic dermatitis. Allergol Immunopathol (Madr). 2023;51(3):85–90.
28. Kutlu, A., Karabacak, E., Aydin, E., et al. Relationship between skin prick and atopic patch test reactivity to aeroallergens and disease severity in children with atopicdermatitis. Allergol Immunopathol (Madr). 2013; 41(6):369---373.