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Food sensitivity in children with acute urticaria and the effect of age on sensitivity

Akut ürtikerli çocuklarda besin duyarlılığı ve yaşın duyarlılık üzerine etkisi

Velat ÇELİK[1], Fedli Emre KILIÇ[2], Hüseyin TANRIVERDİ[1]

[1]Adıyaman University, Faculty of Medicine, 02040, Adıyaman-Turkey
[2]Adıyaman University Training and Research Hospital, 02040, Adıyaman-Turkey

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Abstract

Aim: We aimed to determine the most common foods that cause sensitivity in children with acute urticaria (AU) in Adıyaman province.

Materials and Methods: The results of 70 children who underwent skin prick tests for AU between September 2021-May 2022 at Adıyaman Training and Research Hospital were analyzed.

Results: Sensitivity to at least one food was detected in 10 (14,3%) children. Five (7.1%) children were sensitized to egg, four (5.7%) to cow's milk, three (4.3%) each to peanut, walnut, pistachio, and hazelnut, two (2.9%) each to wheat and chicken meat and one (1.4%) child to beef. While 38.1% of children 24 months and younger had food sensitization 4.1% of children over 24 months had food sensitization (p=0.001).

Conclusion: The most common food sensitivities in Adıyaman province are egg, cow's milk, peanut, and tree nuts in children with AU. We found that the frequency of food sensitivities was higher in ≤24 months old children than older children.

Keywords: Acute urticaria; Anaphylaxis; Children; Food allergy; Skin prick test.

Öz

Amaç: Çalışmamızda Adıyaman ilinde akut ürtiker (AÜ) şikâyeti ile başvuran çocuklarda en sık duyarlılığa sebep olan besinleri belirlemeyi amaçladık.

Gereç ve Yöntem: Adıyaman Eğitim ve Araştırma Hastanesi'nde Eylül 2021-Mayıs 2022 tarihleri arasında AÜ tanısıyla deri prik testi yapılan 70 çocuğun sonuçları analiz edildi.

Bulgular: On (%14,3) çocukta en az bir besine duyarlılık saptandı. Beş (%7,1) çocukta yumurtaya, dört (%5,7) çocukta inek sütüne, üçer çocukta (%4,3) yer fıstığı, ceviz, antep fıstığı ve fındığa, ikişer çocukta (%2,9) buğday ve tavuk etine, bir çocukta (%1,4) ise kırmızı ete duyarlılık tespit edildi. Yirmidört ay ve altı çocukların %38,1'inde besin duyarlılığı bulunurken, 24 ay üzeri çocukların %4,1'inde besin duyarlılığı tespit edildi (p=0,001).

Sonuç: Adıyaman ilinde AÜ'li çocuklardaki duyarlılığa sebep olan en sık besinler yumurta, inek sütü, yer fıstığı ve ağaç kuruyemişleridir. ≤24 ay çocuklarda besin duyarlılık sıklığının daha büyük çocuklara göre daha yüksek olduğunu bulduk.

Anahtar Kelimeler: Akut ürtiker; Anafilaksi; Besin alerjisi; Çocuklar; Deri prik testi.

Yazışma Adresi/Address for Correspondence: Velat ÇELİK, Adıyaman University, Faculty of Medicine, 02040, Adıyaman-Turkey, E-mail: velatcelik@gmail.com

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Introduction

Urticaria is a common clinical status defined by the development of hives (wheals), angioedema, or both, mediated mainly by histamine.[1] Urticaria affects 20% of individuals throughout their lives. Occurrences of hives, angioedema, or both that last less than 6 weeks are classified as acute urticaria (AU), whereas those that occur on most days of the week for longer than 6 weeks are classified as chronic urticaria.[1,2] Urticaria has a high disease burden, high health care costs, and a significant negative impact on quality of life.[3]

Acute urticaria is frequently caused by an IgE–mediated allergic reaction. Viral infections, foods, drugs, and stinging-insect venoms are the most common causes of AU in children.[2] However, in cases with AU, it is not always feasible to identify the etiology, and in nearly 50% of cases, there is no known etiology.[3,4]

Food allergy (FA), is classified as IgE-mediated, non-IgE-mediated (cell-mediated), or mixed (IgE and cell-mediated) according to the type of immune response.[5] Acute urticaria is the most common clinical symptom of IgE-mediated FA and the most common cutaneous presentation of FA.[6] Skin prick test (SPT) can help to find the culprit food, especially in the presence of a significant history suggesting FA in IgE-mediated FAs.[2] Eggs, cow's milk, peanuts, and tree nuts are most commonly reported foods to cause AU in children.[6] But, the prevalence of the foods that cause the reaction most often varies between regions.[6,7] Although the prevalence of FAs seen in different regions of Turkey has been determined[8], data is still lacking in the southeast Anatolia region. There is no previous study on SPT data in AU in Adıyaman province located in the Southeastern Anatolia region.

The primary aim of our study is to investigate food sensitivity in children with AU attending the outpatient department of pediatric allergy in Adıyaman province. The second aim of our study is to investigate the relationship between the SPT results in children under the age of two and over the age of two.

Materials and Methods

This study was conducted at the Pediatric Allergy Department of Adıyaman University Medical School (Adıyaman, Turkiye).

A panel of 11 food allergens [cow's milk, whole egg (chicken), wheat flour, peanut, walnut, hazelnut, pistachio, chicken meat, beef, soybean, fish mix (flounder, codfish, halibut) (ALK, Madrid, Spain)] applied to children with AU. Histamine hydrochloride (10 mg/ml) was used as a positive control and saline solution was used as a negative control. Subjects' wheal diameters were evaluated after 15 minutes. Sensitization was defined as a mean wheal diameter of at least 3mm greater than the negative control for at least one of the tested allergens. Skin prick test was performed at least seven days after stopping drug(s) such as antihistamine that could interfere with the SPT.

Type of the study

The study was planned as a descriptive retrospective study.

The sample size of the study

The records of 70 children with AU who were admitted to the pediatric allergy outpatient clinic of Adıyaman University Training and Research Hospital between September 2021-May 2022 and underwent SPT were included in the study. Acute urticaria was diagnosed by a pediatric allergist (V.C.) according to the international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline.[1] Each child presenting with urticaria evaluated for anaphylaxis, as urticaria is the most common symptom of anaphylaxis. The presence of previous anaphylaxis in children was determined according to a consistent and clear history of anaphylaxis symptoms within 2 hours after the ingestion of the culprit food in accordance with the guidelines.[8]

Data collection tools

All SPT results of children with AU who were admitted to the pediatric allergy outpatient clinic of Adıyaman University Training and Research Hospital between September 2021-May 2022 were examined.

Data analysis

We performed statistical analysis using IBM SPSS Statistics for Windows, V.25.0 (IBM, Armonk, New York, USA). Continuous variables presented as median [inter quartile range (IQR)(Q3-Q1)] and categorical variables presented as numbers and percentages. Skin prick test results between groups were compared with the appropriate Chi-square test (Pearson, Yates, or Fisher exact). *p*-values <0.05, 2-sided, were considered statistically significant.

Ethics committee approval

The Ethics Review Committee at the Adıyaman University Medical Faculty approved the study (Approval number: 2022/7-4, date: 25/10/2022). We obtained written informed consent from all parents of participants. The principles of the Declaration of Helsinki conducted the research.

Results

Seventy children admitted with the diagnosis of AU included in the study. The median age of the children was 48 (94.5-24) months. Forty-six (65.7%) children were male and 24 (34.3%) children were female. Skin prick tests were performed on all children with a standard panel consisting of 11 foods explained above. Sensitivity to at least one food was detected in 10 (14.3%) children. Sensitivity to eight foods was detected in one (1.4%) child, to four foods in one (1.4%) child, to three foods in two (2.9%) children, to two foods in two (2.9%) children, and to one food in four (5.7%) children. Skin prick test results were found as follows: whole eggs sensitivity in five (7.1%) children; cow's milk sensitivity in four (5.7%) children; peanuts, walnuts, pistachio, and hazelnut sensitivities in three (4.3%) children; wheat, chicken meat sensitivities in two (2.9%) children, and beef sensitivity in one (1.4%) child. None of the children had a sensitivity to soybean or fish mix. Nine (12.9%) of the children who applied to the outpatient clinic with AU had a previous history of anaphylaxis. Sensitivity to at least one food was found in six (66.7%) of the children who had anaphylaxis, and three (33.3%) children had no food sensitivity. Food sensitivities were as follows: whole eggs in four (44.4%); peanut and pistachio in three (33.3%); cow's milk, wheat, walnut, hazelnut, and chicken meat in two (22.2%); and beef in one (11.1%).

Since FA is more common in younger ages,[9,10] sensitivities between ages compared. Children divided into two groups: ≤24 months old and >24 months old. While 21 children were 24 months and younger, 49 children were older than 24 months. Of the children under 24 months, 13 (61.9%) were male and eight (38.1%) were female. Of the children older than 24 months, 33 (67.3%) were male and 16 (32.7%) were female. There was no statistical difference between the groups in terms of gender (p=0.66). While eight (38.1%) children under 24 months had sensitivity to at least one food, two (4.1%) children older than 24 months had sensitivity to at least one food (p=0.001). We detected cow's milk sensitivity in one and hazelnut sensitivity in one of the children over 24 months. While all food sensitivities were more common under 24 months, this difference reached statistical significance in egg, peanut, walnut, and pistachio sensitivities (Table 1).

Table 1. Comparison of children 24 months and younger, and children over 24 months in terms of food sensitivities.

Skin prick test result	Children 24 months and younger (n=21)	Children over 24 months (n=49)	*p*
Food sensitivity	8 (38.1%)	2 (4.1%)	0.001
Whole Egg	5 (23.8%)	0 (0%)	0.002
Cow’s milk	3 (14.3%)	1 (2%)	0.078
Wheat	2 (9.5%)	0 (0%)	0.087
Peanut	3 (14.3%)	0 (0%)	0.024
Walnut	3 (14.3%)	0 (0%)	0.024
Hazelnut	2 (9.5%)	1 (2%)	0.212
Pistachio	3 (14.3%)	0 (0%)	0.024
Soybean	0 (0%)	0 (0%)	Can not calculate
Fish mix	0 (0%)	0 (0%)	Can not calculate
Chicken meat	2 (9.5%)	0 (0%)	0.087
Beef	1 (4.8%)	0 (0%)	0.3

While anaphylaxis observed in six (28.6%) children aged 24 months and younger, it observed in three (6.1%) children in the older age group, and this difference was statistically significant (p=0.018).

Discussion

In our study, we showed that the most common food sensitivities in AU in Adıyaman province were egg, cow's milk, peanut, and tree nuts, respectively. Food sensitivities were more common in children two years and younger age than in older children. Also, previous anaphylaxis accompanying AU was observed more frequently in younger children than in older children.

We found sensitivity to at least one food in 14.3% of the children with AU who participated in our study. Skin prick testing is a first-line test method to verify sensitization in IgE-mediated FA. It can generally help to confirm the diagnosis of a suspected IgE-mediated allergy, although it is not sufficient on its own. It is minimally invasive, cheap, and reproducible, and results are immediately available.[11,12] Since food sensitivity does not mean true FA and approximately half of SPT positivity is false positivity,[7,11] studies have conducted to determine regional FAs rather than regional food sensitization. The oral food challenge test is the gold standard diagnostic tool in the diagnosis of FA.[7,13] Therefore, there are few studies evaluating food sensitivity in acute urticaria. Guillet et al.[14] reported that food is responsible for 62% of infantile urticaria. In a study of children and adults older than 10 years with AU and chronic urticaria, sensitivity to any allergen found to be 88%.[12] Most of these sensitizations were of aeroallergen origin. Peanut sensitivity was the most common at 24%, followed by brinjal, chili, and mushrooms.[12] The fact that most of the patients in that study had chronic urticaria and the age group was older may explain the large difference between our results.

The prevalence of food allergy has been better studied. The frequency of self-reported FAs found to be between 3-35% in the general population.[15] Few studies used oral food challenge tests to confirm FA diagnosis and the frequency of FA found to be between 1-4% in these studies.[15] In studies conducted on children with FAs in the United States,[16] the most common food allergens were peanut, cow's milk, shellfish, tree nuts, egg, and fish, while cow's milk, egg, and peanut found in the United Kingdom,[17] and shellfish, egg, peanut, milk, fish and fruits in Hong Kong.[18] A recent study conducted in Turkey reported that the most common foods causing IgE-mediated FAs were eggs, cow's milk, hazelnuts, and sesame seeds, respectively in children aged 0–2 years.[10] In the same center, the most common foods causing FAs in children aged 3-18 years reported as tree nuts, cow's milk, seeds, egg white, and peanuts, respectively.[9] The frequency of FA and the foods that cause allergy vary according to age.[9,10,19] In a multicenter study in which 26 centers from Turkey participated, it was reported that the most common FA was IgE-mediated FA. This study reported that the most common food allergens were cow's milk, egg, tree nuts, and/or peanut, wheat, and seafood, respectively.[19] In this multicenter study, the frequency of FAs was investigated in all regions of Turkey except the southeast Anatolian region. While research on FA and food sensitivity in the Southeast Anatolian region is insufficient, FA or sensitivity has never been evaluated in the Adıyaman province before. As the frequency and distribution of FA etiology vary between populations, potentially based on dietary, ethnic, and cultural differences,[5,10] it is important to assess each region individually. Better management of FAs in children will be possible with knowledge of the population characteristics.[19] Consistent with previous studies, we showed that the most common sensitivities in AU were egg, cow's milk, peanuts, and tree nuts. Although our study does not show the frequency of FA in Adıyaman province, it may give a clue in this regard.

Among the children with AU who participated in our study, food sensitivity found to be almost 10 times higher in children aged 24 months and younger than in children older than 24 months. It is more likely to find the culprit factor in the etiology of AU at young ages. Arı et al.[4], in their study, determined the factor causing AU etiology in

65.1% of children under 2 years of age, while no culprit factor detected in 34.9% of them, and these patients accepted as idiopathic urticaria. The incidence of idiopathic urticaria increased to 51.7% in children over 2 years of age. But, the frequency of SPT positivity according to age was not given in this study[4]. Ricci et al.[20] found that while FA was responsible for approximately 15% of children under one year of age with AU in children referred to the emergency room, the rate of food causation decreased over the age of 2 years. Bezirganoglu et al.[21] reported that the rate of suspected food triggers for urticaria decreased significantly with increasing age. Arı et al.[4] emphasized that detailed tests may be necessary when investigating the etiology of AU in young children. Our study and previous studies show that FA is more likely to be the etiology of AU in young children and thus support a more careful evaluation of the etiology of AU in children under 2 years of age.

An immunoglobulin E (IgE)-mediated FAs can vary from common AU to even life-threatening anaphylaxis.[13] Urticaria is also the most common symptom of anaphylaxis.[6] Acute urticaria is a self-limited condition. Treatment is antihistamines and avoidance of any identified triggers.[2] However, there is always the possibility of anaphylaxis and allergic shock in the next encounter with the culprit food.[22] The most frequent cause of anaphylaxis in children is FAs.[23] For this reason, it is important to find the causative agent. In our study, 12.9% of the children had anaphylaxis and the frequency of anaphylaxis was higher in children under 2 years of age. In the study conducted by Kahveci et al.[10], the rate of children who had anaphylaxis at the first exposure to culprit food was 4.6%, whereas 18.7% of the children experienced at least one anaphylaxis after culprit food intake within two years. Food-induced anaphylaxis is more common in young children than in older children.[24] These results support the importance of demonstrating the presence of FA in AU in children under 2 years of age. If we miss the diagnosis of FA in a child presenting to our outpatient clinic with AU, the child may experience anaphylaxis the next time exposed to culprit food. Due to the higher sensitization under 2 years of age and the higher likelihood of anaphylaxis, it is important to accurately identify FA for management methods to reduce the risks of a possible life-threatening allergic reaction.

Guidelines recommend the same for all age groups, regardless of age: no routine testing is required in AU. If the history suggests allergy, investigation for the suspected causative factor recommended.[1,3,25] However, FA is more common in infantile age compared to other ages.[10] Also, the first 2 years of life is the age when first exposed to different foods. Aydoğan et al.[26] reported that food-induced urticaria observed in approximately 90% of children during the complementary feeding period. Families may not always give completely accurate stories. Children in this age group put everything in their mouth and try to eat. If the child has an older sibling, he/she can give food to the child without the parent's knowledge. In the first 2 years of life, the likelihood of accidental exposure to food is high. Since the likelihood of the child eating something without the parents' knowledge is high at this age, the history given by the family may be insufficient in AU caused by FA. Aydogan et al.[26] reported that the median time between the age of onset and the age of diagnosis of food-induced AU was 6 months. This delay can be prevented with SPT being performed in AU. For this reason, age should be considered as well as history in AU. We think that the possibility of FA should always be considered in children under 2 years of age with AU, and a SPT can be performed with suspicious foods in the history in addition to the routine FA panel.

The main limitation of this study was that it was a retrospective study and the number of cases in the study was small. Our second limitation is that we demonstrated food sensitivity, not FA in our study. The diagnosis of FA was not confirmed by an oral food challenge test.

Conclusion

We showed that the most common food sensitivities in Adıyaman province are egg, cow's milk, peanut, and tree nuts. We found

that anaphylaxis and food sensitivities were higher in children under the age of two years. Children presenting with AU under the age of two years may be routinely tested for allergy with a food panel prepared considering the most common food allergens in the region.

Ethics Committee Approval

The Ethics Review Committee at the Adıyaman University Medical Faculty approved the study (Approval number: 2022/7-4, date: 25/10/2022). We obtained written informed consent from all parents of participants. The principles of the Declaration of Helsinki conducted the research.

Informed Consent

Data for the study were collected with the permission of the Chief Physician of Adıyaman University Training and Research Hospital.

Authors Contrubituons

All of the authors contributed at every stage of the study

Conflict of Interests

There is no conflict of interest to declare.

Financial Disclosure

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Statements

The study was presented as an oral presentation at the 2nd Cerrahpaşa Pediatrics Days congress. Data related to the study is available on request.

Peer-review

Externally peer-reviewed.

References

1. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA(2)LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy.* 2022;77(3):734-766.
2. Stallings A, Dreskin S, Frank M, Sicherer S. Urticaria (Hives) and Angioedema. In: Kliegman M, St Geme J, Blum N, Shah S, Tasker R, Wilson K, eds. *Nelson Textbook of Pediatrics.* 21 ed. Philadelphia, PA: Elsevier; 2020:1222-1228.
3. Antia C, Baquerizo K, Korman A, Bernstein JA, Alikhan A. Urticaria: A comprehensive review: Epidemiology, diagnosis, and work-up. *J Am Acad Dermatol.* 2018;79(4):599-614.
4. Arı H, Guvenir H, Toyran M, et al. Etiological Assessment of Acute Urticaria in Children. *Turkish Journal of Pediatric Disease.* 2023;17:13-18.
5. Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol.* 2018;141(1):41-58.
6. Tam JS. Cutaneous Manifestation of Food Allergy. *Immunol Allergy Clin North Am.* 2017;37(1):217-231.
7. Peters RL, Krawiec M, Koplin JJ, Santos AF. Update on food allergy. *Pediatr Allergy Immunol.* 2021;32(4):647-657.
8. Muraro A, Worm M, Alviani C, et al. EAACI guidelines: Anaphylaxis (2021 update). *Allergy.* 2022;77(2):357-377.
9. Akarsu A, Ocak M, Koken G, Sahiner UM, Soyer O, Sekerel BE. IgE mediated food allergy in Turkey: different spectrum, similar outcome. *Turk J Pediatr.* 2021;63(4):554-563.
10. Kahveci M, Koken G, Sahiner UM, Soyer O, Sekerel BE. Immunoglobulin E-Mediated Food Allergies Differ in East Mediterranean Children Aged 0-2 Years. *Int Arch Allergy Immunol.* 2020;181(5):365-374.
11. Heinzerling L, Mari A, Bergmann KC, et al. The skin prick test - European standards. *Clin Transl Allergy.* 2013;3(1):3.
12. Lote S, Gupta SB, Poulose D, et al. Role of the Skin Prick Test in Urticaria Patients. *Cureus.* 2022;14(2):e21818.
13. Barni S, Liccioli G, Sarti L, Giovannini M, Novembre E, Mori F. Immunoglobulin E (IgE)-Mediated Food Allergy in Children: Epidemiology, Pathogenesis, Diagnosis, Prevention, and Management. *Medicina (Kaunas).* 2020;56(3).
14. Guillet MH, Guillet G. [Food urticaria in children. Review of 51 cases]. *Allerg Immunol (Paris).* 1993;25(8):333-338.
15. Mills EN, Mackie AR, Burney P, et al. The prevalence, cost and basis of food allergy across Europe. *Allergy.* 2007;62(7):717-722.
16. Gupta RS, Springston EE, Warrier MR, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics.* 2011;128(1):e9-17.
17. Venter C, Pereira B, Voigt K, et al. Prevalence and cumulative incidence of food hypersensitivity in the first 3 years of life. *Allergy.* 2008;63(3):354-359.
18. Leung TF, Yung E, Wong YS, Lam CW, Wong GW. Parent-reported adverse food reactions in Hong Kong Chinese pre-schoolers: epidemiology, clinical spectrum and risk factors. *Pediatr Allergy Immunol.* 2009;20(4):339-346.
19. Bingol A, Uygun DFK, Akdemir M, et al. Clinical phenotypes of childhood food allergies based on immune mechanisms: A multicenter study. *Allergy Asthma Proc.* 2021;42(3):e86-e95.
20. Ricci G, Giannetti A, Belotti T, et al. Allergy is not the main trigger of urticaria in children referred to the emergency room. *J Eur Acad Dermatol Venereol.* 2010;24(11):1347-1348.
21. Bezirganoglu H, Arik Yilmaz E, Sahiner UM, et al. The common triggers of urticaria in children admitted to the pediatric emergency room. *Pediatr Dermatol.* 2022;39(5):695-701.
22. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol.* 2014;133(5):1270-1277.
23. Dinulos J. Urticaria, Angioedema, and Pruritus In: *Habif's Clinical Dermatology.* 7 ed.: Elsevier 2019:176-214.
24. Jeong K, Lee JD, Kang DR, Lee S. A population-based epidemiological study of anaphylaxis using national big data in Korea: trends in age-specific prevalence and epinephrine use in 2010-2014. *Allergy Asthma Clin Immunol.* 2018;14:31.
25. Nettis E, Foti C, Ambrifi M, et al. Urticaria: recommendations from the Italian Society of Allergology, Asthma and Clinical Immunology and the Italian Society of Allergological, Occupational and Environmental Dermatology. *Clin Mol Allergy.* 2020;18:8.
26. Aydogan M, Topal E, Uysal P, et al. Proven Food-Induced Acute Urticaria and Predictive Factors for Definitive Diagnosis in Childhood. *Int Arch Allergy Immunol.* 2021;182(7):607-614.