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ORIGINAL ARTICLE
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Characteristics of Anaphylactic Reactions in Children: Evaluation from a Pediatric Allergy Clinic

Çocuklarda Anafilaktik Reaksiyonların Özellikleri: Pediatrik Alerji Kliniğinde Değerlendirme

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ABSTRACT

Aims: Anaphylaxis is a severe and potentially life-threatening hypersensitivity reaction characterized by rapidly developing multisystem involvement. By systematically evaluating the clinical features of anaphylaxis patients, we can obtain valuable information about the epidemiology and clinical spectrum of this life-threatening condition in children.

Material and Method: Between January 2016 and December 2022, data regarding patients aged 0-18 years who presented to the pediatric allergy clinic with the diagnosis of 'unspecified anaphylactic shock' were retrospectively screened, and a total of 186 patients with a history of anaphylaxis were included in the study. The patients' age at diagnosis, gender, allergy history, the potential allergen-causing anaphylaxis, and clinical manifestations during anaphylactic episodes were evaluated as part of the study.

Results: Of the patients, 55.4% were male, and the median age was 5.0 years. The probable allergen triggering anaphylaxis was food in 41.9% of patients, drugs in 40.3%, bee venom in 7.5%, and idiopathic in 10.2%. Among food triggers, tree nuts were the most common (35.9%), while antibiotics were the most common probable allergens among drugs. 24.7% of the patients had a known allergy history. Respiratory system involvement was observed in 85.5% of the patients, skin-mucosa involvement was observed in 82.3%, gastrointestinal system involvement was observed in 50%, and cardiovascular system involvement was observed in 4.3%.

Conclusion: Evaluating the clinical characteristics of anaphylaxis patients is of great importance in enhancing our understanding and clinical approach to this complex hypersensitivity reaction in children. This approach aims to optimize the diagnosis, proper management, and prevention of anaphylactic reactions, ultimately leading to better health outcomes and improved quality of life for children.

Keywords: Anaphylaxis, drug allergy, adrenalin, food-induced anaphylaxis

ÖZ

Amaç: Anafilaksi, hızla gelişen çoklu sistem tutulumu ile karakterize, şiddetli ve potansiyel olarak yaşamı tehdit edici bir aşırı duyarlılık reaksiyonudur. Anafilaksi öyküsü olan hastaların klinik özellikleri sistematik olarak değerlendirilerek, çocuklarda yaşamı tehdit eden bu durumun epidemiyolojisi ve klinik spektrumu hakkında değerli bilgiler edinebiliriz.

Gereç ve Yöntem: Ocak 2016- Aralık 2022 tarihleri arasında çocuk alerji polikliniğine 'anafilaktik şok, tanımlanmamış' tanısı ile başvuran 0-18 yaş arası hastalar ile ilgili veriler geriye yönelik taranmış, anafilaksi öyküsü olan 186 hasta çalışmaya dahil edilmiştir. Hastaların tanı yaşı, cinsiyeti, alerji öyküsü, anafilaksiyi tetikleyen muhtemel alerjen öyküsü, anafilakside görülen klinik bulgular çalışma kapsamında değerlendirilmiştir.

Bulgular: Hastaların %55,4'ü erkek, medyan yaş 5,0/yıl idi. Anafilaksi tetikleyicisi muhtemel alerjenler hastaların %41,9'unda besin, %40,3'ünde ilaç, %7,5'inde arı venomu, %10,2'sinde idiopatikti. Besinlerin içerisinde en sık kuruyemiş (%35,9), ilaçların içerisinde en sık antibiyotikler muhtemel alerjenlerdi. Hastaların %24,7'sinde öncesinde bilinen alerji öyküleri vardı. Hastaların %85,5'inde solunum sistemi, %82,3'ünde deri-mukoza, %50'sinde gastrointestinal sistem ve %4,3'ünde kardiyovasküler sistem tutulumu gözlendi.

Sonuç: Anafilaksi hastalarının klinik özelliklerinin değerlendirilmesi, çocuklarda bu karmaşık aşırı duyarlılık reaksiyonuna yönelik anlayışımızı ve klinik yaklaşımımızı geliştirmede büyük önem taşımaktadır. Bu sayede anafilaktik reaksiyonların tanısını, doğru yönetimini ve önlenmesini optimize etmeyi ve sonuçta çocuklar için daha iyi sağlık sonuçları ve daha iyi yaşam kalitesi hedeflenebilir.

Anahtar Kelimeler: Anafilaksi, ilaç alerjisi, adrenalin, gıda kaynaklı anafilaksi

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INTRODUCTION

Anaphylaxis is characterized by rapidly developing multisystem involvement and is a severe and potentially life-threatening hypersensitivity reaction (1). It represents a critical medical emergency that requires rapid diagnosis, immediate intervention, and long-term management (1). While anaphylaxis can affect individuals of all ages, its diagnosis and treatment pose greater challenges in childhood, making it even more critical in pediatric cases (2).

At present, there is no gold standard laboratory test or biomarker available for the diagnosis of anaphylaxis. The diagnosis of anaphylaxis is established worldwide using universally accepted clinical criteria, which relies on the patient's medical history and physical examination (1). The patient's medical history and clinical findings are the most crucial tools in determining whether a patient has anaphylaxis and identifying its underlying cause (3). However, none of the symptoms and signs manifested during anaphylaxis are specific to anaphylaxis alone. This situation can significantly lead to delayed or missed diagnosis in a considerable number of patients and subsequently result in delays in treatment. Therefore, the American National Institute of Allergy and Infectious Diseases (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) have developed clinical criteria to facilitate the diagnosis of anaphylaxis (4). Anaphylaxis typically presents with clinical manifestations involving at least two of the following systems: skin, respiratory, cardiovascular, or gastrointestinal system. Skin, mucosa, and respiratory system involvement are the most commonly observed in anaphylaxis (5). The absence of mucocutaneous symptoms, occurring in 10-20% of cases, may lead to underrecognition of anaphylaxis (6).

The incidence of anaphylaxis in children varies from country to country worldwide. In a systematic meta-analysis investigating the global incidence and prevalence of anaphylaxis in children, the reported incidence for total anaphylaxis ranged from 1 to 761 per 100,000 person-years, while for food-induced anaphylaxis (FIA), it ranged from 1 to 77 per 100,000 person-years (7). Furthermore, this meta-analysis also reported an increasing trend in the incidence of both total anaphylaxis and FIA over time (7). In a study conducted in Turkey, a screening based on diagnostic codes in patients attending hospitals in Istanbul estimated an annual incidence of 1.95 per 100,000 for anaphylaxis (8). This increase is believed to be influenced significantly by the rise in food allergies, particularly contributing to the increased frequency of anaphylaxis in children under the age of 5 (9). In another study conducted in our country, it was determined that children under the age of 2 accounted for 43% of all cases among those who experienced anaphylaxis (10). As the incidence of anaphylaxis increases worldwide and in our country, understanding the clinical characteristics and causes in children is important to improve patient care and clinical outcomes.

Our knowledge about the epidemiology of anaphylaxis is based on case series, patient records from healthcare centers and hospitals, and studies investigating the prevalence in the general population. By systematically evaluating the clinical features of anaphylaxis patients, we can gain valuable insights into the epidemiology and clinical spectrum of this life-threatening condition in children. This research article aims to investigate and analyze the clinical profiles of pediatric patients diagnosed with anaphylaxis, who presented to the pediatric allergy outpatient clinic, with the goal of understanding and improving the management of this potentially life-threatening condition.

MATERIAL AND METHOD

The study was carried out with the permission of University of Health Sciences, Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date: 23/02/2023, Decision No: 33). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Data on patients aged 0-18 years who presented to the University of Health Sciences, Ümraniye Training and Research Hospital Pediatric Allergy Clinic with a diagnosis of 'anaphylactic shock, undefined (International Statistical Classification of Diseases and Related Health Problems (ICD-10 code): T78.2)' between January 2016 and December 2022 were retrospectively retrieved from the hospital database. All patients with a history of anaphylaxis during the specified dates were included in the study. The patients' age at diagnosis, gender, allergy history, potential allergen history causing anaphylaxis, and clinical manifestations during anaphylactic episodes were evaluated as part of the study.

Statistics

The data were analyzed and recorded using SPSS (Statistical Package for Social Sciences for Windows 25.0) software. Descriptive statistics such as median, minimum, maximum values, as well as counts (n) and percentages (%) were utilized for presenting the data.

RESULTS

Between January 2016 and December 2022, a total of 186 patients presented to the Pediatric Allergy Clinic with a diagnosis of anaphylaxis. Among them, 55.4% (n=103) were male. The median age was 5.0 years (ranging from 0 to 18.0). In the majority of patients (74.7%, n=139), exposure to a potential allergen occurred through oral

contact. Among the probable allergens for anaphylaxis, food was responsible for 41.9% of patients (n=78), drugs for 40.3% (n=75), bee venom for 7.5% (n=14), and idiopathic/other causes for 10.2% (n=19) (**Table 1**).

Table 1. Demographic and clinical characteristics of the patients

Age (year), median (min-max)	**5,0 (0-18,0)**
Gender, n (%)	
Male	103 (55,4)
Female	83 (44,6)
Probable allergen exposure route, n (%)	
Oral	139 (74,7)
Subcutaneous	21 (11,3)
Intramuscular	14 (7,5)
Intravenous	12 (6,5)
Potential allergen, n (%)	
Food	78 (41,9)
Drug	75 (40,3)
Bee venom	14 (7,5)
Idiopathic/Others	19 (10,2)

In patients, 85.5% (n=159) had respiratory system involvement, 82.3% (n=153) had skin-mucosal involvement, 50% (n=93) had gastrointestinal system involvement, and 4.3% (n=8) had cardiovascular system involvement. All patients received adrenaline treatment upon admission to the emergency department. 24.7% (n=46) of the patients had a known allergy history. Among these patients with a history of allergies, 80.4% (n=37) had known food allergies, 17.4% (n=8) had inhalant allergies (pollen, dust mites, cat), and 2.2% (n=1) had drug allergies (**Table 2**).

Table 2. Clinical manifestations of anaphylaxis and allergy histories of the patients

Clinical findings	**n (%)**
Respiratory system involvement	159 (85,5)
Skin-mucosal involvement	153 (82,3)
Gastrointestinal system involvement	93 (50,0)
Cardiovascular system involvement	8 (4,3)
Administration of Adrenaline	186 (100)
Allergy history	46 (24,7)
Known allergens in those	
Food	37 (80,4)
Inhaled allergens (pollen, house dust mites, cat)	8 (17,4)
Drug	1 (2,2)

The most common probable allergens triggering anaphylaxis in patients who developed anaphylaxis were food items. Among food allergens, tree nuts were the most frequent probable trigger, accounting for 35.9% (n=28) of cases. Milk accounted for 16.7% (n=13) and hen's egg for 14.1% (n=11) of other probable triggers for anaphylaxis. Hazelnut (32.1%) and walnut (32.1%) were the most common triggers for anaphylaxis among the tree nuts. These were followed by peanut (21.5%), almond (7.1%), pistachio (3.6%), and cashew (3.6%). Among drugs, antibiotics were the most common triggering allergens (n=42, 56.0%). Within antibiotics, Amoxicillin/Clavulanic acid was the most frequent probable allergen (n=16, 21.3%) (**Table 3**).

Table 3. Allergens in patients (n=186)

	n (%)
1) Food (n=78)	
Tree nuts	28 (35,9)
Hazelnut	9 (32,1)
Walnut	9 (32,1)
Peanut	6 (21,5)
Cow's milk	13 (16,7)
Hen's egg	11 (14,1)
Fish	3 (3,8)
Legume	3 (3,8)
Pineapple	2 (2,6)
Others	18 (23,1)
2) Drugs (n=75)	
Antibiotic	42 (56,0)
Amoxicillin/Clavulanic acid	16 (21,3)
Clarithromycin	6 (8,0)
Ceftriaxone	6 (8,0)
Penicillin	5 (6,7)
Cefazole	5 (6,7)
Others	4 (5,3)
Non-steroidal anti-inflammatory drugs (NSAIDs)	22 (29,3)
Others	11 (14,7)
3) Bee venom (n=14)	
4) Idiopathic/Others (n=19)	

DISCUSSION

In this study, we aimed to evaluate the clinical characteristics of pediatric patients diagnosed with anaphylaxis who presented to the pediatric allergy outpatient clinic. Through the analysis of demographic data illustrating symptoms, triggers, medical history, and treatment strategies, we gained insights into the epidemiology and clinical spectrum of anaphylaxis in children.

Among the patients assessed in our study, 55.4% were male, and the median age was 5 years. Consistent with findings reported in other published studies (5,11-13), most anaphylactic reactions occur in younger children, and there is a male predominance across to all age groups. A meta-analysis compiling 54 studies investigating anaphylaxis in childhood showed that males had a higher incidence of anaphylaxis than females. However, as the older children (≥10 years), there was a tendency for a higher incidence of anaphylaxis in females compared to males, although this difference was not statistically significant (7).

Potential allergens triggering anaphylaxis were food items in 41.9% of patients, drugs in 40.3%, and bee venom

in 7.5%. Consistent with our study data, research from various countries identifies food as the most common trigger for anaphylaxis (5,11,12,14,15,16). Among food allergens, tree nuts were the most frequent allergen (35.9%), followed by milk (16.7%) and hen's egg (14.1%). The types of food triggers can vary based on age groups, different countries, and cultures. In a study conducted in China with a methodology similar to our study, milk was found to be the most common food trigger for anaphylaxis. This was followed by buckwheat, hen's egg, and fruits (15). In a study examining a multicenter anaphylaxis registry in Korea, the most common cause of FIA in children was hen's egg, followed by cow's milk, walnuts, wheat, and peanuts among 284 cases (14). In a study assessing children with a history of anaphylaxis in our country, cow's milk was identified as the most prevalent trigger for anaphylaxis among foods (16). Egg, hazelnut, lentil, and wheat were identified as the second most common triggers of anaphylaxis (16). In studies conducted in the United States, tree nuts are reported as the most common trigger for food-induced anaphylaxis (17). Dietary habits and cultural factors of the population may explain this difference between countries. The triggers of anaphylaxis can exhibit variations even among studies conducted within different regions of the same country.

In our study, respiratory system involvement was observed in 85.5% (n=159) of patients, skin-mucosa involvement in 82.3% (n=153), gastrointestinal system involvement in 50% (n=93), and cardiovascular system involvement in 4.3% (n=8). Previous studies have consistently reported that skin, mucosa, and respiratory system involvement are the most common manifestations in childhood anaphylaxis (11,18,19). In a recent study, gastrointestinal symptoms were observed to be significantly more common in infants and children with FIA (2). The distribution and severity of symptoms and signs comprising the clinical presentation of anaphylaxis can vary in each patient and even between different episodes of the same patient (1).

All of our patients received adrenaline treatment upon emergency room admission. Adrenaline is the life-saving drug in the treatment of anaphylaxis (20). The first and most crucial steps in managing all patients are ensuring airway, breathing, and circulation, followed by the prompt administration of adrenaline, the single life-saving treatment (1,6). There are also studies reporting that healthcare professionals have inadequate knowledge in diagnosing anaphylaxis and administering adrenaline (5,21-23). To increase anaphylaxis preparedness, the simplest precaution would be to conduct in-house training and develop a written anaphylaxis action plan that includes the diagnostic criteria for anaphylaxis.

In our study, the most common drug group triggering anaphylaxis was antibiotics, followed by non-steroidal anti-inflammatory drugs (NSAIDs). Among antibiotics, Amoxicillin/Clavulanic acid was the most frequently implicated drug. Antibiotics, especially those belonging to the beta-lactam group, have been consistently identified as the most common cause of drug-induced anaphylaxis in children in various studies (11,15,24). In a study conducted in the USA with one of the largest populations evaluated to date (19,836 drug-induced anaphylaxis patients), antibiotics were reported as by far the most common culprit drugs (25). Consistent with our study results, Amoxicillin/Clavulanic acid has been identified as the most commonly implicated agent among antibiotics (25). Overall, in previous studies, NSAID-induced anaphylaxis ranks second among drug triggers for anaphylaxis (15,25). Conversely, NSAIDs have been ranked first in a few studies as the leading cause of drug-induced anaphylaxis (12,14). Drug-induced anaphylaxis is more commonly observed in adults, and our knowledge regarding the role of drugs in anaphylaxis during childhood is limited (26). Beta-lactam group antibiotics and NSAIDs are likely the most commonly implicated drugs, possibly due to their high prescription rates (26).

Limitations

The fact that our study was conducted in a single hospital clinic poses a limitation to the generalizability of the research findings.

CONCLUSION

The evaluation of clinical features in anaphylaxis patients holds great significance in enhancing our understanding and clinical approach towards this complex hypersensitivity reaction in children. By systematically evaluating the clinical features and underlying triggers of anaphylaxis patients, we can gain valuable insights into the epidemiology and clinical spectrum of this life-threatening condition in children. This way, we can aim to optimize the diagnosis, proper management, and prevention of anaphylactic reactions and ultimately target better health outcomes and improved quality of life for children.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of University of Health Sciences, Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date: 23/02/2023, Decision No: 33).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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