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Characteristics of childhood anaphylaxis in different age groups

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Abstract

Background: Anaphylaxis is a severe systemic hypersensitivity reaction that usually has a rapid onset and can be fatal. Presentations of childhood anaphylaxis vary widely in accordance with the triggers and the patient's age, geographical region and dietary and lifestyle habits.

Methods: The medical records of 177 paediatric patients diagnosed with anaphylaxis between January 2021 and January 2024, whose disease progression was monitored at a single tertiary care centre, were reviewed retrospectively.

Results: The study included 177 patients diagnosed with anaphylaxis (107 males and 70 females with a median age of 48 months). The most common allergen responsible was food (53.7%). Egg allergy was the most common source of anaphylaxis, afflicting 35 patients (19.3%), while beta-lactam provoked the most common drug allergy, affecting 24 patients (13.6%). The most common organ involved was the skin (92.7%). When the patients were analysed by age group, there were more males in the infancy, preschool and school age groups, while there were more females in the adolescent group ($p = 0.44$). Food-induced anaphylaxis became less common with increasing age, whereas the rate of drug-induced anaphylaxis increased ($p = 0.01$ and $p = 0.01$, respectively). Cardiovascular system findings were observed more frequently in adolescents compared to other age groups ($p = 0.003$). Most cases stemming from a food allergy were mild, whereas most drug-induced cases were moderate or severe ($p < 0.05$). When severity was analysed by age group, mild cases in infants were more common than moderate to severe cases.

Conclusion: The aetiological and clinical manifestations of childhood anaphylaxis vary among different age groups.

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Introduction

Anaphylaxis is a severe systemic hypersensitivity reaction that has an acute onset, progresses rapidly, and is potentially life-threatening. According to a recent systematic review, the incidence of anaphylaxis in children ranges from 1 to 761 per 100,000 person-years.¹ Childhood anaphylaxis differs from adult anaphylaxis in terms of clinical findings and the allergens involved. Triggers of anaphylaxis vary depending on factors such as geographical region, age and diet.² The most frequent triggers are food, drugs and venom. While food frequently is a common cause of anaphylaxis in children, the frequency of reactions to drugs increases with age. Respiratory problems are common in food-associated anaphylaxis, while cardiovascular issues are more prominent in drug- and venom-associated cases. Clinical manifestations vary according to the patient's age. While respiratory problems are more frequent in children, cardiovascular issues become more prominent with increasing age.³ Diagnose anaphylaxis in infants can be challenging because the symptoms may be confused with normal behaviours of infants, making them difficult to recognise.⁴

Few studies have examined the varying manifestations of childhood anaphylaxis across different age groups. This study aims to address this gap.

Materials and Methods

We retrospectively reviewed the electronic files of children diagnosed with anaphylaxis who were evaluated by the Pediatric Immunology and Allergy Clinic of Istanbul Başakşehir Çam and Sakura City Hospital between January 2021 and January 2024. Patients aged 0-18 years were included in the study. Both patients who developed anaphylaxis during hospitalisation and those who experienced it outside the hospital were recruited. Each patient completed a questionnaire that gathered information on their age, gender, type of allergen, route of allergen intake, time of onset of reaction, location of reaction, severity of reaction, clinical findings, adrenaline administration, duration of observation and presence of comorbid atopic disease or familial atopic disease. Laboratory data, such as skin prick test results, eosinophil levels, serum total IgE levels, serum-specific IgE levels in response to suspected allergens and provocation test results, were obtained from the electronic patient files.

Anaphylaxis was diagnosed according to the diagnostic criteria by the World Allergy Organization as updated in 2020.¹ The study was approved by the Ethics Committee of Başakşehir Cam and Sakura City Hospital (file number KA EK/2022.04.128).

Statistical analysis

The questionnaire data were analysed using SPSS 22. Descriptive statistics are presented as numbers and percentages for categorical variables and as means \pm standard deviations or medians (least maximum value) for numerical variables. The presence of a normal distribution was

assessed using histograms, Q-Q plots and normal distribution tests (Kolmogorov-Smirnov or Shapiro-Wilk). Categorical variables were analysed using Pearson's chi-square test; if the assumptions were not met, comparisons were performed using Fisher's exact test. Z tests were used for tables larger than 2×2 with categorical variables. To compare numerical variables between two independent groups, either a t-test or Mann-Whitney U test was used, depending on the presence of a normal distribution. For comparisons involving more than two independent groups, one-way analysis of variance (ANOVA) or a Kruskal-Wallis test was used, depending on the presence of a normal distribution. A p-value < 0.05 was considered statistically significant.

Results

The study included 177 patients diagnosed with anaphylaxis (107 males and 70 females with a median age of 48 months). Thirty-seven (20.9%) of the anaphylaxis cases occurred in the hospital, and 140 (79.1%) occurred outside the hospital. The most common route of allergen exposure was oral (63.3%). Comorbid atopic disease was present in 102 patients (57.6%). Food was identified as the most common allergen responsible (53.7%). In terms of allergen distribution, egg allergy was the most common source of reactions, afflicting 35 patients (19.3%), while beta-lactam was the most common drug allergy, affecting 24 patients (13.6%) (Table 1). The most commonly involved organ was the skin (92.7%). The demographic characteristics of the patients are summarised in Table 2.

When the patients were analysed by age group, there were more males in the infancy, preschool and school age groups, while there were more females in the adolescent group ($p = 0.44$). The frequency of food-induced anaphylaxis decreased with increasing age, while the rate of drug-induced anaphylaxis increased ($p = 0.01$ and $p = 0.01$, respectively). Cardiovascular findings were more common in adolescence compared to other age groups ($p = 0.003$). The older the patient, the longer the required observation period after anaphylaxis ($p = 0.046$). Adrenaline administration after anaphylaxis was found to be more frequent in the 1-5- and 6-12 year age groups ($p = 0.005$). Serum IgE elevation, eosinophilia and specific IgE elevation were more frequently observed in the infantile period ($p = 0.001$, 0.001 and 0.002 , respectively). The results are summarised in Table 3.

Most of the anaphylaxis cases resulting from food allergies were mild, whereas most of the drug-induced cases were moderate or severe ($p < 0.05$). When analysing the severity of anaphylaxis by age group, mild cases were more common in infants compared to moderate to severe cases (Tables 4 and 5).

Discussion

Anaphylaxis is a potentially life-threatening allergic reaction characterised by sudden onset and rapid progression, accompanied by symptoms affecting the airway, respiratory, or circulatory. The most common triggers of

Table 1 Characteristics of children with anaphylaxis.

	n (%)
Age, month, median (min-max)	48 (2-256)
Gender, male	107 (60.5)
Anaphylaxis admission area, hospital/outpatient	37 (20.9)/140 (79.1)
Allergen exposure route	
Oral	112 (63.3)
Intravenous	26 (14.7)
Intramuscular	11 (6.2)
Subcutaneous	1 (0.6)
Inhalation	4 (2.3)
Physical contact	3 (1.7)
Insect bite	9 (5.1)
Unknown	11 (6.2)
Comorbid atopic disease	102 (57.6)
Suspected allergen	
Food	95 (53.7)
Drug	56 (31.6)
Venom	12 (6.8)
Others	14 (7.9)
Area of anaphylaxis	
Home	119 (67.2)
Hospital	41 (23.2)
Park/green area	11 (6.2)
School/kindergarten	2 (1.2)
Restaurant	1 (0.6)
Proportion of adrenaline administration	97 (54.8)
Clinical findings	
Skin	164 (92.7)
Respiratory system	147 (83.1)
Gastrointestinal system	61 (34.5)
Cardiovascular system	42 (23.7)
Neurologic system	14 (7.9)
Severity of anaphylaxis	
Mild	57 (32.2)
Moderate	95 (53.7)
Severe	25 (14.1)
<i>Observation period after anaphylaxis (Mean±SD), hour</i>	14.74±8.6
Biphasic reaction	5 (2.8)
Eosinophilia	69/161 (42.8)
Eosinophil level, median, (min-max)	4.0 (0.01-16.0)
Serum IgE elevation	93/145 (64.1)
Serum IgE level, median (min-max), IU/mL	142 (2-7316)
Specific IgE elevation	98 (55.4)
Specific IgE level, median (min-max), IU/mL	10 (0.4-100)
Total	177 (100.0)

anaphylaxis are food, drugs and venom, depending on the patient's age, diet and geographical region. In 30% of cases, the trigger cannot be identified. The first-line treatment is adrenaline, which should be administered intramuscularly. Mortality rates are high, especially in patients with asthma and those who experienced delays in receiving adrenaline

treatment. While food-related anaphylaxis progresses more slowly, drug-related anaphylaxis progresses rapidly.³

It has been reported that anaphylaxis is more common in males during childhood, with the proportion of males reported as 64.9% in Europe, 62.5% in Japan, 60.3% in Hong Kong, 59.7% in the USA, 61.0% in Portugal and 67.2% in Beijing.⁴⁻⁹ Similarly, it was previous reports from Turkey also indicate that childhood anaphylaxis occurs more frequently in males.^{2,10,11} One study hypothesised that this may be related to the frequent occurrence of food anaphylaxis in childhood.² Similarly, in our study, anaphylaxis was observed more frequently in males during infancy, pre-school and school periods (60.5%). However, during the adolescent period, anaphylaxis became more predominant in females.

A European study found that the most common triggers of anaphylaxis were food (66%), venom (19%) and drugs (5.1%) with milk and eggs being the main food triggers in children under 2 years of age.⁵ While food-induced anaphylaxis is generally common in young children, drugs and insect stings-related anaphylaxis are more common in older children.¹⁰⁻¹² Consistent with the literature, we observed a decrease in the food-associated anaphylaxis and an increase in drug-induced cases with increasing age. Although cow's milk was the most common trigger identified in previous studies of childhood anaphylaxis in Turkey, our study found that eggs and then nuts were the most common allergens.^{2,10,11} One recent study reported that allergenic foods, such as peanuts and eggs, should be introduced into the diet early in life. Differences in infantile feeding practices and the earlier introduction of these foods into the diet may explain why our findings differ from those of previous studies.¹³

It has been previously reported that a large proportion of severe anaphylaxis cases are drug related.³ Studies conducted in Turkey have shown that drug-related anaphylaxis tends to be more severe compared to food-related variant.^{10,11} In contrast, food-related cases have generally been milder in studies from Turkey.^{2,10} In our study, drug-related anaphylaxis were found to be more severe. Başkaya et al. also reported that drug-related anaphylaxis had a more severe course in school-aged children.² Although other studies in Turkey did not show differences in severity by age group, our study found that the condition was milder in infantile group.^{10,11} This may be because drug-related anaphylaxis is observed less frequently with decreasing age.

Venom is estimated to cause 1.5%-34% of all anaphylaxis cases.¹⁴ In our study, the rate of venom-induced cases was 6.8%, which is lower than the rates previously reported in Turkey (8.4%-37%).^{2,10,15} Notably, two of these studies were conducted in Adana and Ankara, where beekeeping is more compared to Istanbul. This higher prevalence of beekeeping in those two cities may account for the higher rates of venom-related anaphylaxis observed in those studies compared to our study.¹⁶

A European study conducted with children found that 92% of symptoms were skin related, 80% were respiratory, 41% were cardiovascular and 45% were gastrointestinal.⁵ In our study, 92% of cases in children were skin related, 83% were respiratory, 34% were gastrointestinal, 23% were cardiovascular and 7.9% were neurologic. It has been shown that respiratory symptoms occur more frequently

Table 2 Characteristics of children with anaphylaxis according to age groups.

	<1 years old n (%)	1-5 years old n (%)	6-12 years old n (%)	>13 years old n (%)	p
Gender, male	32 (68.1)	38 (60.3)	28 (66.7)	9 (36.0)	0.44
Anaphylaxis admission area, hospital/outpatient	6(12.8)/41(87.2)	16(25.4)/47(74.6)	10(23.8)/32(76.2)	5(20.0)/20(80.0)	0.41
Allergen exposure route					
Oral	41 (87.2)	43 (68.3)	16 (38.1)	12 (48.0)	
Intravenous	2 (4.3)	13 (20.6)	7 (16.7)	4 (16.0)	
Intramuscular	1 (2.1)	2 (3.2)	6 (14.3)	2 (8.0)	
Subcutaneous	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)	
Inhalation	2 (4.3)	1 (1.6)	1 (2.4)	0 (0.0)	
Physical contact	1 (2.1)	1 (1.6)	0 (0.0)	1 (4.0)	
Insect bite	0 (0.0)	1 (1.6)	6 (14.3)	2 (8.0)	
Unknown	0 (0.0)	2 (3.2)	6 (14.3)	3 (12.0)	
Comorbid atopic disease	94 (61.0)	40 (63.5)	24 (57.1)	14 (56.0)	0.626
Suspected allergen					
Food	44 (93.6) ^a	37 (58.7) ^b	11 (26.2) ^c	3 (12.0) ^c	0.001
Drug	3 (6.4) ^a	21 (33.3) ^b	16 (38.1) ^{b,c}	16 (64.0) ^c	0.001
Venom	0 (0.0)	2 (3.2)	8 (19.0)	2 (8.0)	
Others	0 (0.0)	3 (4.8)	7 (16.7)	4 (16.0)	
Proportion of adrenaline administration	24 (51.1)	49 (77.8)	30 (81.0)	14 (56.0)	0.005
Clinical findings					
Skin	46 (97.9)	55 (87.3)	40 (95.2)	23 (92.0)	0.175
Respiratory system	36 (76.6)	57 (90.5)	31 (73.8)	23 (92.0)	0.050
Gastrointestinal system	19 (40.4)	15 (23.8)	18 (42.9)	9 (36.0)	0.155
Cardiovascular system	4 (8.5) ^a	13 (20.6) ^{a,b}	14 (33.3) ^b	11 (44.0) ^b	0.003
Neurologic system	3 (6.4)	5 (7.9)	6 (14.3)	0 (0.0)	
Observation time during anaphylaxis (Mean±SD), hour	11.7±8.7	14.8±8.3	16.9±7.8	16.0±9.5	0.046
Eosinophilia	23/46 (50.0)	26/54 (48.1)	16 (38.1)	4/19 (21.0)	0.001
Eosinophil level, median, (min-max)	3.0 (0.01-16)	5.0 (0.01-16.0)	5.0 (0.01-16.0)	3.0 (0.01-16.0)	0.156
Serum IgE elevation	29/41 (70.7)	30/52 (57.6)	25 (59.5)	8/12 (66.6)	0.001
Serum IgE level, median (min-max), IU/mL	138 (5-3427)	114.5 (2-7316)	174.5 (10-1830)	108.5 (12-405)	0.744
Specific IgE elevation	42/47 (89.4)	35 (55.6)	26/40 (65.0)	21 (84.0)	0.002
Specific IgE level, median (min-max), IU/mL	15 (0.4-100)	10 (0.8-100)	10 (0.4-100)	50.6 (0.8-100)	0.982
Total	47 (100.0)	63 (100.0)	42 (100.0)	25 (100.0)	

Table 3 Comparison of severity of childhood anaphylaxis according to the responsible allergen.

	Mild n (%)	Moderate-severe n (%)	Total n (%)
Food	42 (76.4) ^a	51 (48.1) ^b	93 (57.8)
Drug	11 (20.0) ^a	45 (42.5) ^b	56 (34.8)
Venom	2 (3.6) ^a	10 (9.4) ^a	12 (7.5)
Total	55 (100.0)	106 (100.0)	161 (100.0)

The same superscript letters indicate that there is no statistically significant difference between the groups.

in younger children, while cardiovascular symptoms occur more frequently in adolescents.³ Consistent with these previous findings, cardiovascular symptoms were observed more frequently in adolescents in our study.

Although epinephrine is the first-line treatment for anaphylaxis, it remains underused. Epinephrine was reportedly administered to patients at rates of 25.0% in Europe, 44.0% in Japan, 49.6% in the USA, 46.0% in Portugal and 9.3% in

Table 4 Comparison of severity of childhood anaphylaxis according to age groups.

	Mild n (%)	Moderate-severe n (%)	Total n (%)
Infancy	23 (40.4) ^a	24 (20.0) ^b	47 (26.6)
Preschool, 1-5 years old	17 (29.8) ^a	46 (38.3) ^a	63 (35.6)
School age, 6-12 years old	9 (15.8) ^a	33 (27.5) ^a	42 (23.7)
Adolescence, >13 years old	8 (14.0) ^a	17(14.2) ^a	25 (14.1)
Total	57 (100.0)	120 (100.0)	177 (100.0)

The same superscript letters indicate that there is no statistically significant difference between the groups.

Beijing.^{4-6,8,9} In our study, epinephrine was administered to 54.8% of the patients. In a different study conducted in Turkey, the use of adrenaline in infants with food-induced anaphylaxis was found to be lower compared to other age groups.¹⁷ We found that adrenaline administration in the

Table 5 Distribution of suspected allergens.

	n (%)
Foods	103 (58.2)
Egg	35 (19.3)
Cow's milk allergy	20 (11.3)
Wheat	1 (0.6)
Tree nuts	22 (12.4)
Fish	3 (1.7)
Others	22 (12.4)
Drugs	50 (28.2)
Beta lactams	24 (13.6)
NSAID's	6 (3.4)
Macrolids	2 (1.1)
Others	18 (10.2)
Venom	8 (4.5)
Apis mellifera	2 (1.1)
Vespula	6 (3.4)
Others	16 (8.5)
Total	177 (100.0)

first year of life was less common than in other age groups. The fact that anaphylaxis is difficult to recognise in infants and that the symptoms overlap with some normal infant behaviours may help explain this.¹⁸

In a study by Başkaya et al., no statistically significant differences were found between age groups in terms of serum eosinophil and total IgE levels.² In our study, serum eosinophil levels, specific IgE levels and total IgE levels were found to be higher during infancy compared to other ages. The frequent occurrence of food allergies in this age group may have contributed to this finding.

In conclusion, the aetiology and clinical findings in children diagnosed with anaphylaxis differ by age group. Accordingly, childhood anaphylaxis should be evaluated with consideration of these differences between age groups.

Conflict of Interest

The authors declare no conflict of interest.

References

- Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World allergy organization anaphylaxis guidance 2020. *World Allergy Organ J.* 2020; 13(10):100472. <https://doi.org/10.1016/j.waojou.2020.100472>
- Baskaya N, Ertugrul A, Esenboga S, Ozmen S. Different age groups present different clinics in anaphylaxis with children: one size does not fit all children *Turk J Med Sci.* 2023; 53(2):495-503. <https://doi.org/10.55730/1300-0144.5609>
- Anaphylaxis Working Group of Resuscitation Council UK. Emergency treatment of anaphylaxis: guidelines for healthcare providers. May 2021. Available at https://www.resus.org.uk/sites/default/files/2021-05/Emergency%20Treatment%20of%20Anaphylaxis%20May%202021_0.pdf (Accessed April 20, 2024).
- Jiang N, Xu W, Xiang L. Age-related differences in characteristics of anaphylaxis in Chinese children from infancy to adolescence. *World Allergy Organ J.* 2021; 14(11):100605. <https://doi.org/10.1016/j.waojou.2021.100605>
- Grabhenrich LB, Dölle S, Moneret-Vautrin A, Köhli A, Lange L, Spindler T, et al. Anaphylaxis in children and adolescents: the European anaphylaxis registry. *J Allergy Clin Immunol.* 2016; 137(4):1128-37.e1. <https://doi.org/10.1016/j.jaci.2015.11.015>
- Kitamura K, Ito T, Ito K. Comprehensive hospital-based regional survey of anaphylaxis in Japanese children: time trends of triggers and adrenaline use. *Allergol Int.* 2021; 70(4):452-7. <https://doi.org/10.1016/j.alit.2021.04.009>
- Wang Y, Koplin JJ, Ho MHK, Wong WHS, Allen KJ. Increasing hospital presentations for anaphylaxis in the pediatric population in Hong Kong. *J Allergy Clin Immunol Pract.* 2018; 6(3):1050-2.e2. <https://doi.org/10.1016/j.jaip.2017.09.018>
- Kim SL, Suresh R, Mayampurath A, Ciaccio CE. Increase in epinephrine administration for food-induced anaphylaxis in pediatric emergency departments from 2007 to 2015. *J Allergy Clin Immunol Pract.* 2022; 10(1):200-5.e1. <https://doi.org/10.1016/j.jaip.2021.09.024>
- Gaspar Â, Santos N, Faria E, Pereira AM, Gomes E, Câmara R, et al. Anaphylaxis in children and adolescents: the Portuguese anaphylaxis registry. *Pediatr Allergy Immunol.* 2021; 32(6):1278-86. <https://doi.org/10.1111/pai.13511>
- Serbes M, Sasihuseyinoglu AS, Ozcan D, Ufuk Altıntas D. Clinical features of anaphylaxis in children. *Allergy Asthma Proc.* 2022; 43(1):50-6. <https://doi.org/10.2500/aap.2022.43.210089>
- Turgay Yagmur I, Kulhas Celik I, Yilmaz Topal O, Civelek E, Toyran M, Karaatmaca B, et al. Etiology, clinical features and severity of childhood anaphylaxis by age groups. *Int Arch Allergy Immunol.* 2022; 183(6):600-10. <https://doi.org/10.1159/000521063>
- Poor KM, Ducklow TB. Benefit of BP measurement in pediatric ED patients. *ISRN Nurs.* 2012; 2012:1-6. <https://doi.org/10.5402/2012/627354>
- Soriano VX, Ciciulla D, Gell G, Wang Y, Peters RL, McWilliam V, et al. Complementary and allergenic food introduction in infants: an umbrella review. *Pediatrics.* 2023; 151(2):e2022058380. <https://doi.org/10.1542/peds.2022-058380>
- Yu JE, Lin RY. The epidemiology of anaphylaxis. *Clin Rev Allergy Immunol.* 2018; 54(3):366-74. <https://doi.org/10.1007/s12016-015-8503-x>
- Orhan F, Canitez Y, Bakirtas A, Yilmaz O, Boz AB, Can D, et al. Anaphylaxis in Turkish children: a multi-centre, retrospective, case study. *Clinical and Experimental Allergy.* 2011; 41(12):1767-76. <https://doi.org/10.1111/j.1365-2222.2011.03859.x>
- Türkiye İller Bazında Arıcılık İstatistikleri (2022). Available at <http://arastirma.tarimorman.gov.tr/aricilik/Link/2/Arıcılık-İstatistikleri> (Accessed April 20, 2024.)
- Kahveci M, Akarsu A, Koken G, Sahiner UM, Soyer O, Sekerel BE. Food-induced anaphylaxis in infants, as compared to toddlers and preschool children in Turkey. *Pediatr Allergy Immunol.* 2020; 31(8):954-61. <https://doi.org/10.1111/pai.13320>
- Greenhawt M, Gupta RS, Meadows JA, Pistiner M, Spergel JM, Camargo CA Jr, et al. Guiding principles for the recognition, diagnosis, and management of infants with anaphylaxis: an expert panel consensus. *J Allergy Clin Immunol Pract.* 2019; 7(4):1148-56.e5. <https://doi.org/10.1016/j.jaip.2018.10.052>