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Retrospective evaluation of pediatric anaphylaxis cases according to WAO and NIAID/FAAN/EAACI criteria: A single center experience

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ABSTRACT

Background: Anaphylaxis is an emergency that must be correctly recognized and treated by every health care professional. With the update of the World Allergy Organization (WAO) criteria in 2020, differences between the European Academy of Allergy and Immunology (EAACI)/The National Institute of Allergy and Infectious Diseases (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) and WAO criteria have come to the fore.

Objective: The aim of our study is to compare the effectiveness of these 2 criteria in diagnosing anaphylaxis in pediatric patients.

Methods: Patients aged 0–18 years who applied to Ankara Bilkent City Hospital Pediatric Immunology and Allergy Clinic between September 1, 2020 and September 1, 2023 due to systemic allergic reaction and were diagnosed with anaphylaxis were evaluated retrospectively. The clinical findings of the patients were re-evaluated accordingto WAO 2020 and NIAID/FAAN/EAACI criteria.

Results: Included in the study were 492 patients who met the inclusion criteria. Median age was 3.8 years (IQR: 0.9–11.4). The majority of patients were male (59.6%). There were 466 patients (94.1%) diagnosed with anaphylaxis according to both NIAID/FAAN/EAACI and WAO criteria. Three patients (0.6%) with isolated laryngeal involvement and 23 (4.7%) patients with isolated respiratory findings (bronchospasm) were diagnosed only according to WAO Criterion 2, for a total of 26 patients (5.3%).

Conclusion: Although the majority of patients were diagnosed with both criteria, 5.3% were diagnosed only according to the WAO criteria. After contact with a suspected or known allergen, the presence of isolated respiratory or laryngeal findings without skin findings should be a warning before anaphylaxis progresses to more serious stages.

Keywords: Anaphylaxis, Triggers, Diagnosis, Children, Treatment

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INTRODUCTION

Anaphylaxis is an acute onset, life-threatening emergency involving different organ systems that healthcare professionals should recognize and treat appropriately.[1] Although mortality rates due to anaphylaxis are low, hospitalization rates due to anaphylaxis triggered by drugs or food have recently increased.[2]

An anaphylaxis diagnosis is based on clinical findings. Therefore, clinical criterias are crucial for consistent diagnosis and treatment.[3] The National Institute of Allergy and Infectious Diseases (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) met in April 2004 to establish consensus and resolve disagreements on the diagnosis and management of anaphylaxis. They established widely used criteria for anaphylaxis, which were updated in 2005.[4] The 2011 World Allergy Organization (WAO) criteria and the 2014 European Academy of Allergy and Clinical Immunology (EAACI) criteria were the same as those of the 2005 symposium.[5] However, in its 2020 update, the WAO made a significant change, accepting only laryngospasm or bronchospasm without typical skin manifestations as a finding of anaphylaxis as a result of "known or highly probable allergen exposure" in Article 2.[1] EAACI's 2021 update remains the same.[2] Therefore, differences between the 2 organizations' criteria for anaphylaxis diagnosis were raised.

This study aimed to evaluate retrospective data on the diagnosis, treatment, and triggers of anaphylaxis in pediatric patients and to compare the diagnostic value of WAO 2020 and NIAID/FAAN/EAACI criteria.

MATERIALS AND METHODS

Study design

Between September 1, 2020, and September 1, 2023, patients aged 0–18 years who were admitted to the Pediatric Immunology and Allergy Clinic of Ankara Bilkent City Hospital and diagnosed with anaphylaxis at the time of presentation were evaluated retrospectively. Anaphylaxis cases were identified from the electronic medical record with a query using admitting and/or discharge diagnoses with International Classification of Disease Tenth Edition (ICD-10) codes T78.0, T78.2, T80.5, and T88.6 (anaphylactic reaction or shock). Patients who were entered with an anaphylaxis diagnosis code were re-evaluated using standard patient follow-up forms by the same allergy and immunology specialist according to the WAO 2020 and NIAID/FAAN/EAACI criteria (Fig. 1). Demographic data, the responsible allergens, the organ systems involved, symptoms, the time interval between allergen exposure and symptoms, and comorbid allergic diseases were also recorded. Patients who did not meet the anaphylaxis criteria or who had incomplete clinical information were excluded from the study. Since the evaluation of the patients was done retrospectively, patients who could have anaphylaxis despite not having an anaphylaxis diagnosis code were not included in the study.

The severity of systemic allergic reaction was evaluated according to WAO criteria. Grade 3 and above were considered anaphylaxis. Patients were grouped into grades 3–4 and grade 5. Grades 3–4 were considered moderate anaphylaxis, while grade 5 was considered severe anaphylaxis.[1]

The clinical findings and organ involvement of the patients at the time of diagnosis were evaluated, and the diagnostic differences of the WAO 2020 and NIAID/FAAN/EAACI criteria were compared.

Ethics committee approval was obtained (NO: E2-23-5421). All authors signed the Declaration of Helsinki. Informed consent forms were obtained from the patients' relatives before diagnostic and provocation tests were performed.

Patient selection

Between September 1, 2020, and September 1, 2023, patients who diagnosed with anaphylaxis according to at least 1 of the WAO 2020 or NIAID/FAAN/EAACI criteria were included in the study. Patients who did not meet the criteria for anaphylaxis or whose file information was missing were excluded.

Diagnostic tests

No additional tests were performed for the study. Diagnostic tests performed on patients who had previously presented to our clinic were evaluated. Patients admitted to our clinic with a history

EAACI Anaphylaxis Diagnostic Criteria (2021)	WAO Anaphylaxis Diagnostic Criteria (2020)
1.Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue or both (eg generalized hives, pruritus or flushing, swollen lips–tongue–uvula *AND AT LEAST ONE OF THE FOLLOWING* a.Respiratory compromise (eg dyspnoea, wheeze–bronchospasm, stridor, reduced PEF and hypoxemia) b.Reduced BP or associated symptoms of end-organ dysfunction (eg hypotonia [collapse], syncope, incontinence)	1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula) *AND AT LEAST ONE OF THE FOLLOWING:* a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia) b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence) c. Severe gastrointestinal symptoms (eg, severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens)
2.Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): a.Involvement of the skin–mucosal tissue (eg generalized hives, itch-flush, swollen lips–tongue–uvula b.Respiratory compromise (eg dyspnoea, wheeze–bronchospasm, stridor, reduced PEF, hypoxemia) c.Reduced BP or associated symptoms (eg hypotonia [collapse], syncope, incontinence) d.Persistent gastrointestinal symptoms (eg crampy abdominal pain, vomiting)	2. Acute onset of hypotensiona or bronchospasmb or laryngeal involvementc after exposure to a known or highly probable allergend for that patient (minutes to several hours), even in the absence of typical skin involvement.
3.Reduced BP after exposure to known allergen for that patient (minutes to several hours): a.Infants and children: low systolic BP (age specific) or >30% decrease in systolic BP* b.Adults: systolic BP of <90 mmHg or >30% decrease from that person's baseline	

Fig. 1 Criteria for anaphylaxis according to EAACI and WAO. *EAACI: European Academy of Allergy and Clinical Immunology, WAO: World Allergy Organization, PEF: Peak expiratory flow; BP: blood pressure*

of anaphylaxis were evaluated by detailed questioning about the medications they used, the foods they consumed, their venom or latex exposure, and their exercise history until 24 h before the reaction. Diagnostic tests for suspected agents were planned accordingly. Serum-specific IgEs were used as *in vitro* tests (Siemens Immulite, 2000). Intradermal and skin prick tests (SPT) were also performed in appropriate patients. If the causative agent determined by specific IgEs or SPTs was compatible with the anamnesis, it was considered a sufficient criterion for anaphylaxis. In cases where this was impossible, provocation tests were performed with the suspected agent after obtaining the patient's consent. The diagnosis was confirmed in patients by findings compatible with anaphylaxis in the provocation test. In some patients, provocation tests were not performed even though

serum-specific IgE tests and skin tests were negative because the anamnesis was strong, and the index reaction was anaphylaxis. Moreover, provocation tests could not be performed in cases in which the patients did not give consent. These patients were considered to have anaphylaxis if their clinical histories were strong.

For inhaled allergens (grasses, rye, aspergillus, alternaria, tree mix [alder, platanus, and hazel], olecea, birch, artemisia, dermatophagoides farinae, dermatophagoides pteronyssinus, and cat and dog dander), the SPT was performed with panels using commercial allergens (ALK, Madrid, Spain).

Serum tryptase levels were evaluated using enzyme tryptase immune assey (Siemens). Serum tryptase levels measuring between 15 min and 3 h from onset symptoms in the presence of anaphylaxis were considered appropriate samples and included in the evaluation. If the tryptase level was measured at least 24 h after the resolution of all signs and symptoms, this value was considered the baseline tryptase level. The cut-off value for the serum tryptase level was determined to be11.4 ng/dl.[6]

STATISTICS

Data from medical records were analyzed using the IBM Statistical Package for the Social Sciences version 26.0 (SPSS Inc., Chicago, IL, USA). Descriptive data were given as 25 and 75 percentiles interquartile range (IQR). Categorical variables were presented as frequencies (n) and percentages. To compare categorical variables according to the cause of anaphylaxis, cross-tabulations were created, and numbers (n), percentages (%), and chi-square test statistics were provided. Logistic regresion analysis was performed to determine the risk factors for severe anaphylaxis. Parameters with p values of 0.20 and below in univariate analysis were included in the multivariate analysis. The results were given as odds ratio (Exp(B)) and 95% confidence interval. The statistical significance level was accepted as $p < 0.05$.

RESULTS

Patient demographic and clinical characteristics

A total of 492 patients who fulfilled the inclusion criteria were included in the study. Their median age was 3.8 years (IQR: 0.9–11.4), and the majority were male (59.6%).

A total of 212 patients had comorbid allergic diseases (43.1%). The most common concomitant allergic disease was asthma (22.2%). Concomitant allergic disease was present in 131 (47.6%) of patients with food-related anaphylaxis, 14 (45.1%) of patients with idiopathic anaphylaxis, 14 (26.9%) of patients with venom anaphylaxis, and 22 (25%) of patients with drug anaphylaxis.

A total of 292 patients underwent a skin prick test with an inhalant panel, and 102 were sensitized (102/292, 34.9%). Pollen atopy was the most common (76/292, 26%) (Table 1).

Twenty patients (4.1%) required hospitalization in the intensive care unit, while 5 (1%) developed a biphasic reaction. The demographic and clinical characteristics of the patients are summarized in Table 1.

The median time to onset of symptoms after exposure to the causative agent was 15 min (minimum, 5 min; maximum, 360 min).

Laboratory findings

The median serum total IgE level was 118 (IQR: 37.8–362.5)kU/L (n: 436). The median serum tryptase levels measured at baseline and during the reaction were 4.3 ng/ml (IQR: 3.1–7.8) (n: 144) and 7.4 ng/ml (IQR: 4.3–12.6) (n: 66), respectively (Table 1).The number of patients with a tryptase level of 11.4 ng/ml and above measured during the reaction was 21 (21/66, 31.8%).The suspected trigger was confirmed by diagnostic testing (SPT, IgE, or an oral provocation test) in 358 patients.

Signs and severity of anaphylaxis

The most commonly involved organ was the skin and mucosa (92.4%). The most common skin manifestation was urticaria (57.1%), while the respiratory system was the second most frequently involved system (69.5%) (Table 1).

An analysis of system involvement according to age groups indicated that gastrointestinal system involvement was more common in children under 5 years of age, and cardiovascular system involvement was more common in the adolescent group (Fig. 2).

Characteristics	N (%)
Male/Female	293/199 (59.6/40.4)
Age, years, median(IQR)	3.8 (0.9–11.4)
ConcomittanAllergicDisease	212 (43.1)
Asthma	109 (22.2)
AtopicDermatitis	97 (19.7)
AllergicRhinitis	79 (17.5)
ChronicUrticaria	9 (1.8)
AeroallergenAtopy(n: 293)	102 (20.7)
Pollen	76
House dust mites	26
Mold	16
Cat	41
Dog	13
Cochroach	3
Basal tryptase (ng/ml, n: 144)	4.3 (3.07–7.78)
Serum tryptase during reaction (ng/ml, n:66)	7.46 (4.34–12.6)
Total IgE (kU/L, n:436)	118 (37.8–362.5)
Biphasic reaction	5 (1.0)
Need for intensive care unit	20 (4.1)
Anaphylaxis grade	
Grade 3-4	433 (88)
Grade 5	59 (12)
Systemic involvement	
Skin andmucosa	455 (92.4)
Respiratory	342 (69.5)
Gastrointestinal	177 (36.0)
Cardiovascular	68 (13.8)
Treatment	
Antihistamines	317 (64.4)
Steroids	263 (53.4)
Adrenaline	260 (52.8)

Table 1. Demographic and clinical characteristics of the patients

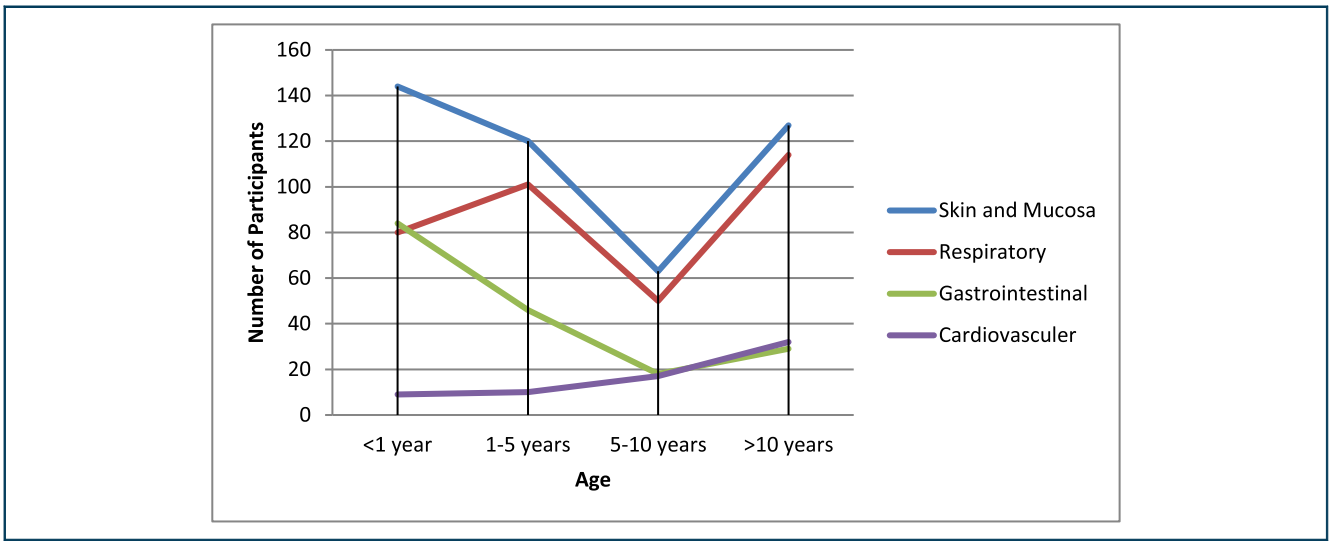

Fig. 2 Systemic involvement according to age groups

The severity of anaphylaxis was grade 5 in 59 patients (59/492, 11.9%). Of the grade 5 cases of anaphylaxis, 25 were drug induced (25/88, 28.4%), 11 were food induced (11/275, 4.0%), and 9 were venom induced (9/52, 17.3%). 5 were idiopathic (5/31, 16.1%), and 9 were due to other causes.

Drug-induced anaphylaxis was associated with a higher risk of grade 5 anaphylaxis ($p = 0.04$, OR = 2.85, CI = 1.20–8.11) (Table 2).

Anaphylaxis triggers and distribution by age groups

The most common trigger was food (275, 55.8%). Among foods, cow's milk was the most common cause of anaphylaxis (94/275, 34.2%). Other common food triggers were nuts (69/275, 25.1%) and eggs (46/275, 16.7%). Other main causes were drugs (88, 17.9%) and venoms (52, 10.5%). Among drugs, anaphylaxis with beta lactam (28/88, 31.2%) and nonsteroidal anti-inflammatory agents were the most common (27/88, 27.2%). In 31 (6.3%) patients, no trigger could be determined and they were considered idiopathic anaphylaxis.

The distribution of the causes of anaphylaxis according to age groups is shown in Table 3. When anaphylaxis triggers were evaluated according to age groups, a significant difference was found ($p < 0.001$) (Table 3). Food anaphylaxis was more common, especially in the infant group.

Distribution of patients according to WAO and NIAID/FAAN/EAACI criteria

A total of 466 patients (94.1%) were diagnosed with anaphylaxis according to both NIAID/FAAN/EAACI and WAO 2020 criteria, and 26 patients were diagnosed only according to WAO criteria. Of the 492 patients, 451 (90.9%) were diagnosed according to WAO Criterion 1, and 41 (9.1%) were

Triggers of anaphylaxis	Univariate			Multivariate		
	OR	%95 CI	P value	OR	%95 CI	P value
Food	0.40	0.16–0.96	**0.040**	**0.30**	**0.10–0.91**	**0.03**
Drug	4.83	2.45–9.38	**<0.001**	**2.85**	**1.20–8.11**	**0.04**
Venom	2.82	1.68–6.94	**0.001**	1.82	0.42–2.60	NS
Idiopathic	2.24	1.48–7.42	**0.008**	1.12	0.36–2.24	NS

Table 2. Comparison of anaphylaxis severity according to the triggers of anaphylaxis. *OR: odds ratio, CI: confidence interval, NS: non significant*

	Age Groups					
	0–1 years (n = 149)	1–5 years (n = 134)	5–10 years (n = 66)	>10 years (n = 143)	Statistics	
	n (%)	n (%)	n (%)	n (%)	$\chi 2$	p
Elicitors						
Food	138 (92.6)	97 (72.4)	17 (25.8)	23 (16.1)	$\chi 2 = 223.279$	**<0.001**
Drug	5 (3.4)	20 (14.9)	14 (21.2)	49 (34.2)		
Venom	3 (2.0)	9 (6.7)	12 (18.2)	28 (19.6)		
Idiopathic	1 (0.7)	1 (0.7)	9 (13.6)	20 (14.0)		
Others	2 (1.3)	7 (5.3)	14 (21.2)	23 (16.1)		

Table 3. Elicitors of anaphylaxis accordingto age groups. χ^2:*chi square test*

diagnosed according to WAO Criterion 2. Among patients diagnosed only according to WAO, 3 had isolated laryngeal involvement (0.7%) and 23 had isolated respiratory findings (4.7%); these 26 patients (5.3%) were diagnosed according to WAO Criterion 2.The characteristics of patients diagnosed only according to WAO Criterion 2 are shown in Table 4.

Characteristics	N (%)
Male/Female	13/13 (50/50)
Age, years, median(IQR)	5.5 (1.9–12.1)
Anaphylaxis triggers	
Food	13 (50)
Drug	9 (34.6)
Venom	2 (7.7)
Immunotherapy	2 (7.7)
Symptoms	
Bronchospasm	23 (88.4)
Larengeal involvement	3 (11.6)
Concomittan allergic disease	14 (53.8)
Asthma	9 (34.6)
Allergic rhinitis	9 (34.6)
Atopic dermatitis	4 (15.3)
Total IgE (kU/L, n:23)	218 (66.2–1019.0)
Treatment	
Steroid	12 (46.1)
Adrenaline	10 (38.5)

Table 4. Characteristics of patients diagnosed only accordingto WAO Criterion 2

A total of 352 patients (70.3%) were diagnosed according to EAACI Criterion 1, 110 patients (22.9%) were diagnosed according to EAACI Criterion 2, and 4 patients (1%) were diagnosed according to EAACI Criterion 3 (Fig. 3).

Anaphylaxis treatment

A total of 260 patients received adrenaline (52.8%), 317 received antihistamines (64.4%), and 263 received steroids (53.4%) (Table 1) as anaphylaxis treatment. Only 10 of the 26 patients diagnosed with WAO Criterion 2 were administered adrenaline (38.5%).

DISCUSSION

In our study, patients aged 0–18 years who were followed up with diagnoses of anaphylaxis were retrospectively evaluated, and their diagnoses were examined according to WAO and NIAID/FAAN/EAACI criteria.

Anaphylaxis severity, triggers, treatments administered, and risk factors for severe anaphylaxis were analyzed.

Most patients were male (59.6%). Male gender predominance was also present in the European Anaphylaxis Registry, the largest study on anaphylaxis in children (64.9%).[7] In a multicenter study involving 137 children between the ages of 4 months and 17 years from 11 different centers

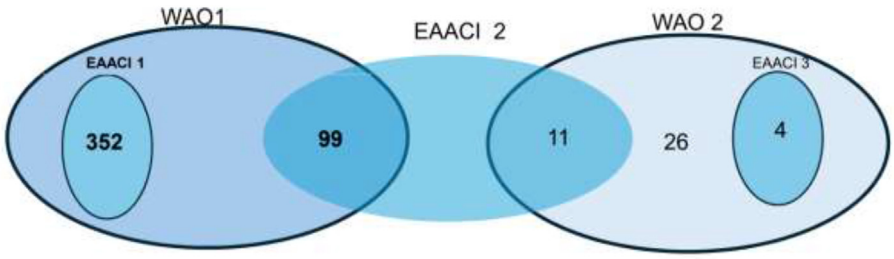

Fig. 3 Distribution of patients diagnosed with anaphylaxis according to EAACI and WAO criteria

in Turkey, the frequency of anaphylaxis was similarly found to be higher in boys.[8] However, female gender dominance has been identified in adult studies.[9] The reason anaphylaxis is more common in girls as their age increases is unknown, but studies with animal models have indicated that estrogen increases mast cell activation and allergen sensitization.[10] The predominance of the male gender in children and the female gender in adults may be related to this.[11]

Concomitant allergic disease has been defined as a risk factor for anaphylaxis. In our study, 43.1% of the patients had comorbid allergic diseases. The most common concomitant allergic disease was asthma (22.2%), while atopic dermatitis was the second-most common (19.7%). In another study conducted in Turkey, the rate of allergic disease was 59.1%.[8] In a Portuguese study, the rate was 79%, and in an Israeli study, it was 52%.[12,13] In the European Anaphylaxis Registry, 26.3% of patients had atopic dermatitis, 22.9% had asthma, and 21.2% had allergic rhinitis.[7] Our findings are consistent with other studies in the literature in this respect.

The skin was the most commonly affected system, followed by the respiratory, gastrointestinal, and cardiovascular systems. The most common skin finding was urticaria. Our findings are consistent with other studies in the literature.[7,8] The rate of skin involvement was reported as 92% in the European Anaphylaxis Registry study, 99.1% in a multicenter study conducted in our country, and 91.7% in a South African study.[7,8,14] Although skin involvement was the most common warning finding, we observed that 7.6% of our patients had no findings involving the skin. In this respect, we emphasize that clinicians should remember that anaphylaxis may occur without skin manifestations and be alert to other signs of anaphylaxis.[15,16]

Although skin and respiratory symptoms are the most common symptoms according to age groups, gastrointestinal system findings are most common in infants, and cardiovascular system findings are more common in adolescents. In a study conducted among North African children, no correlation was found between systemic involvement and age, whereas in another study in China in which children aged 0–16 years were evaluated, cardiovascular system findings were more frequently found in infants.[17,18] This situation may be related to the presence of food as a triggering factor in infants and drugs and venom in adolescents.

In 2020, the WAO made a significant change to Criterion 2, which caused diagnostic differences: the addition of "isolated laryngeal involvement or bronchospasm without skin findings as a result of known or highly probable allergen exposure".[1] In our study, 26 of the 492 patients (5.3%) had only laryngeal involvement or bronchospasm without skin manifestations. These patients were considered to have anaphylaxis on clinical evaluation. They were only diagnosed according to Criterion 2 of the WAO 2020 criteria and were not considered to have anaphylaxis according to the NIAID/FAAN/EAACI criteria.[1,2] Similarly, Yeğit et al (2023) diagnosed only 45 of 774 patients according to WAO 2020 Criterion 2 (5.7%).[19] No other study has evaluated the diagnostic criteria for pediatric patients, but as with the adult study, patients not diagnosed with anaphylaxis according to the previous criteria were diagnosed according to WAO 2020 criteria.

The WAO 2020 criteria may allow for early intervention by recognizing anaphylaxis findings before they progress to more severe stages, such

as respiratory failure or arrest. Considering the isolated laryngeal involvement or bronchospasm as criteria for anaphylaxis may raise concerns that anaphylaxis could be confused with non-anaphylaxis conditions, such as vocal cord dysfunction, asthma attacks, or angioedema. However, when differential diagnosis is made carefully in these cases, overdiagnosis can be prevented and missed anaphylaxis cases can be diagnosed before they progress to more serious conditions. In our study, as in the previous adult study, pediatric patients who were not diagnosed with the previous criteria were also diagnosed.[19] In this respect, we emphasize the importance of the WAO 2020 criteria in early diagnosis and treatment.

When all age groups were evaluated together, the most common trigger was food (55.8%), with cow's milk as the most common trigger (34.2%). In infants under 1 year of age, cow's milk and eggs were the main causes of anaphylaxis, while nuts were the most frequent in older children. These findings were consistent with those of the European Anaphylaxis Registry and other studies.[7,20] However, seafood anaphylaxis was rare in our country, a finding that may be explained by the low consumption of seafood due to regional dietary habits.

In our study, drug (17.9%) and venom anaphylaxis (10.5%) were the second and third most common triggers, respectively. The most common trigger among drugs were NSAIDs (5.5%) and beta lactams (5.7%). In the European Anaphylaxis Registry, antibiotics (n:41) and analgesics (n: 22) were the most common agents. In that study, unlike ours, venom was the second most common trigger, while food and drugs were the third most common.[7] In a multicenter study performed in our country, venom was the second most common after food, and drugs were the third most common.[8] The reason drug anaphylaxis was more frequently identified in our study could be due to our hospital being a tertiary care center, in which drug allergies occurring outside of it are referred to it.

When analyzed in detail according to age groups, food anaphylaxis was more common in patients younger than 5 years of age, whereas drug and venom anaphylaxis were predominant in adolescent patients older than 10 years of age, as it was in adults. Similarly, a study conducted in China including patients aged 0–16 years found that food anaphylaxis was more common in preschool children, and drug and venom anaphylaxis was more common in older children.[18,21]

In our study, 11.9% of patients had severe anaphylaxis. Severe anaphylaxis was observed in 4.0% of patients with food anaphylaxis, 28.4% with drug anaphylaxis, 17.3% with venom anaphylaxis, and 16.1% with idiopathic anaphylaxis. Drug-induced anaphylaxis is considered a risk factor for severe anaphylaxis. In a study by Turgay Yagmur et al evaluating the characteristics of severe anaphylaxis in children, the rate of severe anaphylaxis was reported to be 25%. It was also found that drugs were the main etiologic factor in severe anaphylaxis cases.[22] In the Yeğit et al study of adults, venom, and drug anaphylaxis were associated with more severe reactions, whereas in the European Anaphylaxis Registry, no significant relationship was identified between triggering factors and anaphylaxis severity in pediatric patients.[19] Only an association between egg anaphylaxis and mild symptoms was established.[7] Our study is significant for emphasizing the risk of drug-induced severe anaphylaxis in pediatric and adult patients. As in previous studies, no relationship was established between age groups and gender and anaphylaxis severity.[9,19,23]

The biphasic reaction rate in pediatric studies in the literature was between 1 and 20%.[14,24] In our study, biphasic reactions were observed in 1% of patients. In this respect, the data for our study were consistent with the literature.

Both guidelines recommend intramuscular adrenaline as first-line treatment for anaphylaxis.[1,2] In our study, adrenaline was administered to 260 patients (52.8%).This rate was 44% and 48.1% in pediatric anaphylaxis cases in Japan and China, respectively (18, 26); 25% in Europe, 46% in the USA, and 88% in Singapore.[7,25,26] In our study the rate of adrenaline administration was lower in patients diagnosed with WAO's criterion 2 (38.5%). Steroids were given to 53.4% of patients. The role of steroids in the treatment of anaphylaxis is controversial. Despite the recommendations of recently updated guidelines, studies have shown

that the rate of adrenaline administration at the time of anaphylaxis is low.[27] The main reasons for this low rate are as follows: not recognizing the symptoms, believing that the findings are mild and transient, fear of the side effects of adrenaline, and not knowing the dose and location of adrenaline administration.[28,29] These findings emphasize that educating healthcare professionals, patients, and their relatives about anaphylaxis diagnosis and treatment is essential.

A limitation of our study is that it was a retrospective study and anaphylaxis was diagnosed clinically, the effect of which was minimized by having the same allergy and immunology specialists perform a standardized examination of the medical records and excluding patients suspected of meeting the criteria or whose file records were incomplete. The strength of our study is that it is the first pediatric study to compare the diagnostic status of patients according to the WAO and NIAID/FAAN/EAACI criteria. Our study established that WAO criteria enabled the diagnosis of 26 (5.3%) patients with isolated laryngeal findings or bronchospasm without skin manifestations. We hope that our study will guide future prospective studies.

Abbreviations

EAACI: European Academy of Allergy and ClinicalImmunology; FAAN: Food Allergy and Anaphylaxis Network; IgE: immunoglobulin E; NIAID: The National Institute of Allergy and Infectious Diseases; NSAID: nonsteroid anti-inflammatory drug; WAO: World Allergy Organization

Editorial policy confirmation and agreement

All authors have approved the publication policy and agreement.

Data availability statement

The data that support the findings of this study are not publicly available due to the fact that their containing information could compromise the privacy of research participants but are available from the corresponding author upon a reasonable request.

Author contributions

Funda Aytekin Güvenir: Organization of the letter and substantial contribution to the acquisition of data.
Gökhan Yörüsün, Ragıp Dere, Ahmet Selmanoğlu: Collecting data and entering it into the registration system.
Zeynep Şengül Emeksiz: Organization of the letter and revision critically for intellectual content.
Emine Dibek Mısırlıoğlu: Organization of the letter and revision critically for intellectual content.

Statement of ethics

This study protocol was reviewed and approved by the ethics committee of Ankara Bilkent City Hospital, approval number, E2-23-5421. All authors signed the Declaration of Helsinki and approved the ethical statement. Written informed consent was obtained from all participants.

Consent for publication

All authors agreed to publication of the study.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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