Allergol Immunopathol (Madr). 2025;53(1):139-145 eISSN:1578-1267, pISSN:0301-0546

Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

REVIEW ARTICLE

OPEN ACCESS

Anaphylaxis in infancy: An area that needs to be highlighted

Evanthia Chiampou[a]*, Konstantinos Douros[b], Anastasios Serbis[a], Fani Ladomenou[a], Alexandros Makis[a], Ekaterini Siomou[a], Sophia Tsabouri[a]

[a]*Department of Pediatrics, University Hospital of Ioannina, Ioannina, Greece*
[b]*Pediatric Allergy and Respiratory Unit, 3rd Department of Pediatrics, "Attikon" University Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece*

Received 10 September 2024; Accepted 2 December 2024
Available online 1 January 2025

KEYWORDS
anaphylaxis;
diagnosis;
infants;
management

Abstract
Anaphylaxis, the most severe end of the spectrum of allergic reactions, has shown increasing incidence globally over recent years. This hypersensitivity reaction can occur at any age, including infancy. Recent data, although scarce, show that anaphylaxis is increasingly reported in infancy, with food identified as the leading cause of anaphylaxis cases in this age group. Infants constitute a unique subgroup with specific challenges regarding diagnosis of anaphylaxis due to a variety of factors, such as lack of age-specific diagnostic criteria, inability of infants to describe their symptoms, and the broad spectrum of clinical manifestations that may be mistaken as normal findings. Additionally, there are special issues in reference to the treatment of anaphylaxis during infancy, such as the limited availability of weight-appropriate epinephrine autoinjectors for infants weighing <15 kg. In this study, we review the current literature regarding specific characteristics of anaphylaxis in infants as well as unique challenges in terms of diagnosis, acute treatment, and long-term management of this medical emergency in this vulnerable age group.

***Corresponding author**: Evanthia Chiampou, MD, Department of Pediatrics, University Hospital of Ioannina, Ioannina, Greece. *Email address*: echiam88@yahoo.gr

https://doi.org/10.15586/aei.v53i1.1212

Introduction

Anaphylaxis is an acute life-threatening hypersensitivity reaction resulting from the release of inflammatory mediators from mast cells and basophils, following exposure to an offending agent.[1] As a growing public health issue and given the unpredictable and possibly lethal nature of anaphylaxis, it is crucial for healthcare providers to promptly recognize and manage this medical emergency. Epinephrine constitutes the cornerstone of anaphylaxis treatment and should be administered without any delay.[1]

Infancy has been the least investigated age group.[2,3] In infants, anaphylaxis is likely to be under-recognized, as diagnosis is challenging due to a variety of factors, such as lack of age-specific diagnostic criteria, inability of infants to verbalize their symptoms, and atypical and nonspecific manifestations that may overlap normal infant's behavior.[4-7] Moreover, in most countries, the limited number of premeasured doses of epinephrine autoinjectors has led to the undertreatment of anaphylaxis in this age group, especially in infants weighting <15 kg.[2,8]

The aim of this study is to provide an overview of the characteristics of anaphylaxis in infants as well as specific challenges regarding its diagnosis and treatment in this age group, with a view to increasing awareness of this medical emergency that may lead to improved management and prevention of recurrences. Raising awareness among healthcare professionals is fundamental to promptly recognize and manage anaphylaxis in infants, contributing to proper and comprehensive care of this vulnerable age group.

Epidemiology of Infant Anaphylaxis

It is difficult to precisely estimate the incidence and prevalence of anaphylaxis as there is heterogeneity among studies due to differences in definitions used, study methodology, and geographical areas. A 2019 systematic review conducted by Wang et al. focusing on children reported that global incidence rates of anaphylaxis vary widely, ranging from 1 to 761 per 1,00,000 person-years, while the prevalence estimates of anaphylaxis is 0.04–1.8%.[9]

Recent evidence suggests a global increase in both emergency department (ED) visits and hospitalizations due to anaphylaxis over the past two decades, particularly for food-induced reactions, aligned with a parallel increase in food allergies over the past years.[2,9-11] According to different studies, the highest incidence rates of anaphylaxis are recorded during the first years of life, especially in children aged 0–2 years.[10-12]

In infants, the exact prevalence of anaphylaxis is unknown, as the data available are limited, but it is reported to be increasing.[6] Variable range of anaphylaxis rates were observed among different studies. A study done by Samady et al. reported that 13% of food-induced anaphylaxis cases presenting to ED between 2015 and 2017 occurred in infants aged <12 months.[13] A 2-year nationwide study in the Greek pediatric population noted that 26.8% of anaphylactic reactions occurred in infants up to 2 years,[14] while a retrospective study conducted by Jiang et al. revealed that 57.6% (102/177) of the first episode occurred at the age group 0–2 years.[15] Moreover, according to another study, the number of infant anaphylaxis cases in South Korea quadrupled from 2009 to 2013, and this could be attributed to an increase in food allergies, and thus increase in food-induced anaphylaxis and increased awareness among patients and guardians regarding anaphylaxis.[16]

Triggers of Anaphylaxis in Infants

The leading triggers of anaphylaxis globally are foods, drugs and insect venoms. During infancy, food allergens account for the majority of anaphylaxis cases. Virtually, any food could be implicated in anaphylaxis, but cow's milk and hen's egg comprise the most frequently reported culprits during the first year of life. It is noteworthy that there are variable distributions in food allergens due to different eating habits among countries (Table 1).

Less commonly, anaphylaxis in infants may be triggered by drugs (mostly antibiotics and nonsteroidal anti-inflammatory drugs), natural rubber latex found in bottle nipples, pacifiers, rubber bands, and some toys as well as vaccinations.[19]

Risk factors

Comorbidities and cofactors of anaphylaxis are not well defined in infancy. There are comorbidities that possibly increase the risk of developing severe anaphylactic reactions, such as atopy, mastocytosis, and respiratory diseases, such as asthma, bronchiolitis, and croup.[4,6,19] Additionally, cofactors that may contribute to severity of the reaction include acute upper respiratory tract infections, fever, physical exertion, and emotional stress.[6,19-21] More studies are needed to better specify risk factors during infancy in order to prevent possible recurrences in future.

Diagnosis of Anaphylaxis in Infants

The diagnosis of anaphylaxis is primarily based on clinical presentation and history of a recent exposure to an offending agent because there is no specific laboratory test for accurate diagnosis.

No age-specific anaphylaxis diagnostic criteria are available, and it is therefore suggested to use the current criteria of National Institute of Allergy and Infectious Diseases–Food Allergy and Anaphylaxis Network (NIAID/FAAN)[22] or the recently published World Allergy Organization's (WAO)[1] anaphylaxis criteria to establish the diagnosis of anaphylaxis in all age groups, including infants (Table 2).

In case of anaphylaxis, the infant age group presents a diagnostic challenge, and hence a high index of suspicion is needed to make correct diagnosis during infancy. First, infants cannot describe their symptoms, such as pruritus, throat tightness, lightheadedness, or feeling of impending doom, which makes diagnosis of anaphylaxis difficult.[6,20] Additionally, in infants, it is difficult to interpret some of the symptoms of anaphylaxis, as they are nonspecific and could easily be attributed to normal infant's behavior, including behavioral

Table 1 Common triggers of anaphylaxis in infants.

Authors	Study	Study period	Age	Number of patients (N)	Triggers
Gaspar et al. (2021)[17]	Nationwide notification system for anaphylaxis by SPAIC (Portugal)	2007-2017	0-2 years	149	Cow's milk (62%) Hen's egg (19%) Fish (13%)
Jiang et al. (2021)[15]	Retrospective study in a tertiary hospital (China)	2014-2020	0-2 years	134	Cow's milk (32.9%) Hen's egg (21.4%) Wheat (20.7%)
Kahveci et al. (2020)[18]	Retrospective analysis of medical records in hospitals (Turkey)	2015-2020	<12 months	160	Cow's milk (51.4%) Tree nuts (16.6%) Hen's egg (15.4%)
Pouessel et al. (2020)[5]	Retrospective study of cases recorded by AVN (France)	2002-2018	≤12 months	61	Cow's milk (59%) Hen's egg (20%) Wheat (6%)
Jeon et al. (2019)[16]	Retrospective study in 23 secondary or tertiary hospitals (South Korea)	2016- 2018	0-2 years	338	Cow's milk (43.8%) Hen's egg (21.9%) Walnut (8.3%)
Samady et al. (2018)[13]	Retrospective study in ED of a tertiary hospital (USA)	2015-2017	<12 months	47	Hen's egg (28%) Cow's milk (17%) Peanut (13%)
Topal et al. (2017)[3]	Retrospective study in ED (Turkey)	2007-2011	≤12 months	23	Cow's milk (61%) Hen's egg (21%) Walnut (9%)
Misirlioglu et al. (2017)[7]	Prospective study on patients visiting an allergy clinic (Turkey)	2010-2015	0-2 years	63	Cow's milk (40.4%) Hen's egg (25%) Tree nuts (25%)

AVN: Allergy Vigilance Network; SPAIC: Portuguese Society of Allergology and Clinical Immunology.

Table 2 Anaphylaxis criteria of World Allergy Organization (WAO).[1]

Anaphylaxis is highly likely when any of the following criteria is fulfilled[1]:

1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, and swollen lips/tongue/uvula) and at least one of the following:
   i. Respiratory compromise (e.g., dyspnea, wheezing-bronchospasm, stridor, reduced PEF, and hypoxemia).
   ii. Reduced BP or associated symptoms of end-organ dysfunction (e.g., hypotonia [collapse], syncope, and incontinence).
   iii. Severe gastrointestinal (GI) symptoms (e.g., severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens.
2. Acute onset of hypotension[a] or bronchospasm, or laryngeal[b] involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement.

changes, such as irritability, inconsolable crying, regurgitation, or incontinence (Table 3). A study conducted among caregivers of infants who experienced food-induced anaphylaxis reported that signs such as eye rubbing and ear pulling were present in about 40% and 16% of cases, respectively.[18] Of equal importance is the interpretation of vital signs, such as heart rate, respiratory rate, and blood pressure, which must be done according to the age of the patient. In particular, measuring of blood pressure is a difficult procedure in infants, and it is usually omitted, as referred by studies.[6,7,19,23]

Symptoms of Anaphylaxis in Infants

Several studies have reported that there are age-related differences in the clinical presentation of anaphylaxis in children.[7,13] During infancy, most common symptoms involve the skin (generalized urticaria, flushing, and angioedema), the GI system (vomiting), and the respiratory system (cough, wheezing, and stridor). Less frequently observed symptoms of infant anaphylaxis are cardiovascular symptoms (tachycardia and hypotension) and neurologic symptoms (change in behavior and irritability) (Figure 1).

Differential Diagnosis

The differential diagnosis of anaphylaxis in infancy is often complicated due to the fact that many of the symptoms are common with other childhood illnesses or conditions (Table 4).

Table 3 Clinical manifestations of anaphylaxis in infants.[4,20,24]

Specific symptoms	Nonspecific symptoms
Skin: Hives, rashes, itching, and angioedema.	*Skin*: Eye rubbing, itching, or redness, ear scratching, tongue thrusting, tongue pulling, repetitive lip licking, or licking of hands.
Gastrointestinal: Vomiting, diarrhea, and abdominal pain.	*Gastrointestinal*: Spitting up/regurgitation, back arching, bringing knees to chest, colicky abdominal pain, hiccups, and loose stools.
Respiratory: Cough, wheezing, and tachypnea.	*Respiratory*: Hoarse voice/crying, putting fingers in ears, ear pulling.
Cardiovascular: Hypotension and fainting.	*Cardiovascular*: Skin mottling and cyanosis.
	Neurologic: Sudden behavioral changes (crankiness, inconsolable crying, withdrawn/clingy).

Treatment of Anaphylaxis in Infants

Regardless of the patient's age, intramuscular administration of epinephrine is the cornerstone of anaphylaxis treatment and must be administered without delay, even in suspicion of impending anaphylaxis, because delayed use of adrenaline is related to increased rates of hospitalization and fatalities.[1,25,26]

The recommended dose of epinephrine is 0.01 mg/kg (max 0.3–0.5 mg/kg) and can be administered as an injection drawn up from an ampule containing 1 mg/mL by using a 1-mL syringe or by using an EAI. In most countries, EAI are available in two doses: 0.15 mg for children weighing <30 kg, and 0.30 mg for children and adults weighing ≥30 kg; however, most infants weigh between 10 and 15 kg. In 2018, the US Food and Drug Administration (US FDA) approved a dose of 0.1-mg EIA for children weighing 7.5–15 kg; however, it is available only in the United States.[6,27] Globally, the 0.15-mg EIA is often prescribed for infants, as this is the lowest available dose, but this may provide up to double the recommended dose in case of infants weighing <7.5 kg. However, this dose is recommended due to the unavailability of 0.1-mg dose and the favorable benefit-risk ratio of epinephrine in this life-threatening allergic reaction. Furthermore, using an EIA minimizes the risk of dosing errors and delays in the administration of injectable epinephrine, especially for caregivers without medical training.[1,6,18]

Given the ambiguity of symptoms of anaphylaxis during infancy and the fact that many clinical manifestations of anaphylaxis could be confused with normal infant's behavior, infants could be more vulnerable to delayed administration of epinephrine than children of other age groups.[6,28]

Many studies have reported that epinephrine is underutilized in general population, specifically in infants.[18,19,23,29] In a prospective observational study of 512 infants aged 3–15 months with known or likely allergy to milk or egg, 11.4% of anaphylactic reactions were characterized as severe, yet only 29.9% of the infants received adrenaline.[7] Another study that analyzed the medical records of infants aged 0–2 years diagnosed with anaphylaxis, demonstrated that almost half of the patients (46.8%) received epinephrine treatment as initial management.[16] The low rates of

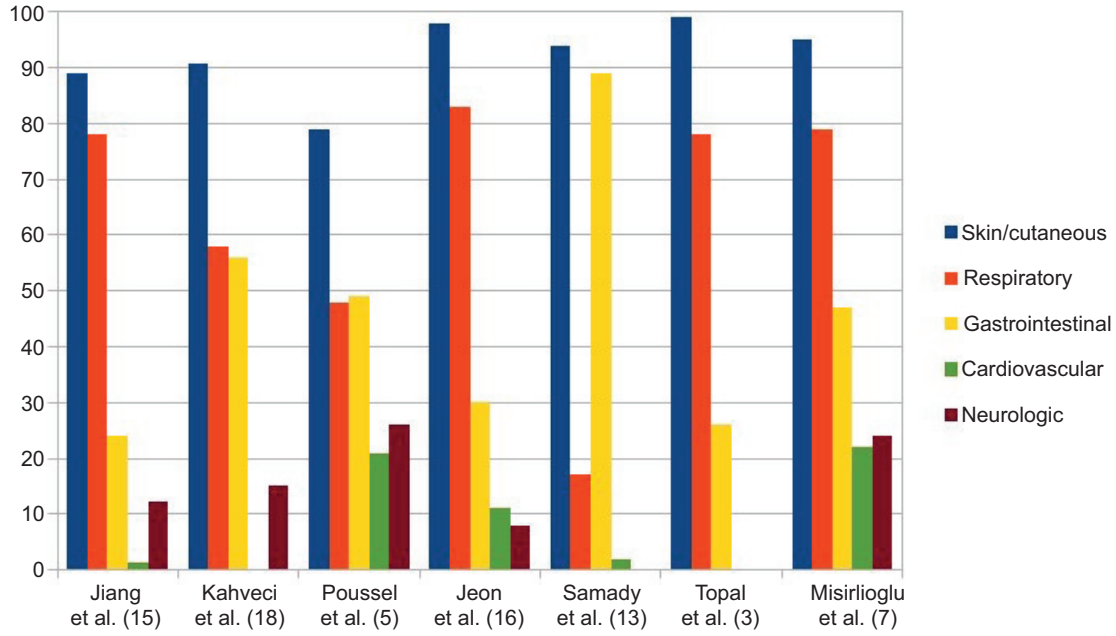

Figure 1 Comparison of manifestations of infant anaphylaxis by organ systems in reported studies.[3,13,5,7,15,16,18]

Table 4 Differential diagnosis of anaphylaxis in infants.[19,20]

Skin: Urticaria, urticaria pigmentosa/mastocytosis, contact dermatitis, viral exanthem, and hereditary angioedema.
Respiratory (upper or lower respiratory tract): Obstruction, congenital (e.g., laryngeal web, vascular ring, or malacias) or acquired (e.g., aspiration of foreign body, croup, bronchiolitis, or asthma), asphyxiation/suffocation, and breath holding.
Gastrointestinal: Obstruction, congenital, including pyloric stenosis and malrotation, or acquired, including food protein-induced enterocolitis syndrome with acute presentation, and intussusceptions.
Shock: Septic, cardiogenic, hypovolemic, distributive.
Central nervous system (CNS): Seizures, postictal state, stroke, trauma, child abuse, and increased intracranial pressure.
Metabolic disorders: Infectious diseases, such as pertussis, gastroenteritis, meningitis.
Ingestion of poison or toxin (e.g., food, drug, or plant); drug overdose.
Munchausen syndrome by proxy.
Sudden infant death syndrome, apparently a life-threatening event.

epinephrine administration could be attributed to several factors, such as failure to recognize anaphylactic reactions, fear of possible adverse reactions in infants, or uncertainty about the necessity of medication.[7,15,18,19,29]

Even though epinephrine is the first-line treatment for anaphylaxis, other medications, such as corticosteroids and antihistamines, often replace epinephrine in acute treatment of anaphylaxis, although there is little convincing data available to establish the effectiveness of these medications for treating anaphylaxis.[30] A retrospective review of a pediatric allergy department showed that of the 43 infants diagnosed with anaphylaxis in the first year of life, 68.3% received H1 antihistamines, 49.2% received corticosteroids, and only 36.5% received epinephrine as an acute treatment.[3]

Acute management

Acute treatment of anaphylaxis during infancy involves the following steps (Figure 2):

Additional medications, such as antihistamines, corticosteroids, or β-agonists, are prescribed as an acute treatment of anaphylaxis, although these are not first-line medications and will not rapidly lessen symptoms, such as laryngeal edema, bronchospasm, or hypotension.[6,19]

Written emergency protocol for anaphylaxis management
Remove any suspected trigger, if possible.
Assess airway, breathing, circulation, skin, and body weight.
Call Emergency Medical Service.

Place the infant in supine or semi-reclined position in the arms of an adult.

Inject epinephrine intramuscularly (0.01 mg/kg) in mid-outer thigh in healthcare settings
or
use EAI 0.15 mg in community settings. May repeat EAI every 5–15 min.

When indicated, consider the following:
1. Establish intravenous (i.v.) access and start fluid resuscitation with 0.9% saline, initially as a dose of 10–20 mL/kg over 5–10 min.
2. Provide high-flow oxygen (8–10 L).
3. Monitor vital signs, heart rate, blood pressure, and oxygenation (using pulse oximeter).

When indicated, cardiopulmonary resuscitation (CPR) at a rate of 100 chest compressions per minute and a depth of 4 cm and rescue breaths at a rate of 15–20/min.

Figure 2 Algorithm for the treatment of anaphylaxis in infants.[6,19]

Long-term management

In case of all infants with a history of anaphylaxis, long-term management is of paramount importance. Implementation of measures to prevent and effectively treat possible future reactions must include prescription of a weight-appropriate EAI, a personalized written anaphylaxis emergency action plan, and training of caregivers regarding prompt recognition of anaphylaxis manifestations as well as correct injecting of epinephrine. Moreover, the patient should be referred to an allergist/immunologist for identification of the suspected trigger via skin prick tests or by measuring allergen-specific immunoglobulin E (IgE) levels, prevention of recurrences by strict avoidance of the trigger(s), and allergen immunotherapy (AIT) if indicated.[19,31] Several studies have noted that EAIs are under-prescribed and underused in the treatment of anaphylaxis.[7,19,32] Fleischer et al. reported that among 512 infants aged 3 to 15 months with documented or likely food allergy, only 29.9% with severe anaphylaxis received adrenaline injections.[32] The possible reasons mentioned for not injecting epinephrine included the following: reactions not recognized by caregivers, unavailability of epinephrine, caregivers' fear or uncertainty to inject epinephrine, or waiting for more symptoms to develop.[32]

Future Directions

Although several studies are published over the years about anaphylaxis in infancy, additional research is required to address knowledge gaps in epidemiology, diagnosis, management, and prevention of recurrences in this age group.

Foremost, since no age-specific diagnostic criteria are available, it is important to create new infant-specific

diagnostic criteria, leading to prompt and accurate diagnosis of this medical emergency. Moreover, taking into consideration that anaphylaxis in the specific age group is often underdiagnosed and most of the data are underreported and do not reflect the real epidemiological pattern, a better understanding is of great importance regarding the true incidence of anaphylaxis in infants through more infant-specific and multi-institutional studies. Advance research is needed regarding identification of potential risk factors and cofactors that are crucial for proper management of patients with anaphylaxis, as they contribute to the development of personalized action plans to prevent possible recurrences in the future. As anaphylaxis is increasingly reported in infancy, healthcare professionals should focus on prevention of recurrences through parental education about avoidance of allergens, recognition of specific manifestations, and severity assessment of the allergic reaction as well as if indicated, appropriately epinephrine using an EIA. Last but not least, global availability of new types of autoinjectors containing 0.1-mg epinephrine is essential for its safe administration to infants.

Author Contributions

Evanthia Chiampou and Sophia Tsabouri equally contributed to the conception and design of the paper. Evanthia Chiampou drafted the manuscript. Konstantinos Douros, Anastasios Serbis, Fani Ladomenou, Alexandros Makis, Ekaterini Siomou and Sophia Tsabouri contributed to writing and critical revision of the paper. All authors approved the publication of the reviewed final paper.

Conflicts of Interest

The authors declared that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding

The authors declared that no financial support was received for conducting this review article.

References

1. 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
2. Robinson LB, Arroyo AC, Faridi MK, Rudders S, Camargo CA Jr. Trends in US emergency department visits for anaphylaxis among infants and toddlers: 2006–2015. J Allergy Clin Immunol Pract. 2021 May;9(5):1931–38.e2. https://doi.org/10.1016/j.jaip.2021.01.010. Epub 2021 Jan 21.
3. Topal E, Bakirtas A, Yilmaz O, Ertoy Karagol IH, Arga M, Demirsoy MS, et al. Anaphylaxis in infancy compared with older children. Allergy Asthma Proc. 2013 May–Jun;34(3):233–8. https://doi.org/10.2500/aap.2013.34.3658
4. 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 Apr;7(4):1148–56.e5. https://doi.org/10.1016/j.jaip.2018.10.052. Epub 2019 Feb 5.
5. Pouessel G, Jean-Bart C, Deschildre A, Van der Brempt X, Tanno LK, Beaumont P, et al. Allergy vigilance network. Food-induced anaphylaxis in infancy compared to preschool age: A retrospective analysis. Clin Exp Allergy. 2020 Jan;50(1):74–81. https://doi.org/10.1111/cea.13519. Epub 2019 Nov 21.
6. Carlisle A, Lieberman J. Clinical management of infant anaphylaxis. J Asthma Allergy. 2021 Jul 8;14:821–7. doi: 10.2147/JAA.S286692
7. Dibek Misirlioglu E, Vezir E, Toyran M, Capanoglu M, Guvenir H, Civelek E, et al. Clinical diagnosis and management of anaphylaxis in infancy. Allergy Asthma Proc. 2017 Jan 1;38(1):38–43. https://doi.org/10.2500/aap.2017.38.4009
8. Brittany G, Anna N, Julie W. Factors contributing to underuse of epinephrine autoinjectors in pediatic patients with food allergy. Ann Allergy Asthma Immunol, 2021;126(2):175–9.e3. https://doi.org/10.1016/j.anai.2020.09.012
9. Wang Y, Allen KJ, Suaini NHA, McWilliam V, Peters RL, Koplin JJ. The global incidence and prevalence of anaphylaxis in children in the general population: A systematic review. Allergy. 2019 Jun;74(6):1063–80. https://doi.org/10.1111/all.13732. Epub 2019 Mar 6.
10. De Filippo M, Votto M, Albini M, Castagnoli R, De Amici M, Marseglia A, et al. Pediatric anaphylaxis: A 20-year retrospective analysis. J Clin Med. 2022 Sep 7;11(18):5285. https://doi.org/10.3390/jcm11185285
11. Tejedor-Alonso MA, Moro-Moro M, Múgica-García MV. Epidemiology of anaphylaxis: Contributions from the last 10 years. J Investig Allergol Clin Immunol. 2015;25:163–75. PMID: 26182682.
12. Yu JE, Lin RY. The epidemiology of anaphylaxis. Clin Rev Allergy Immunol. 2018;54:366–74. https://doi.org/10.1007/s12016-015-8503-x
13. Samady W, Trainor JL, Smith BM, Gupta RS. Food-induced anaphylaxis in infants and children. Ann Allergy Asthma Immunol. 2018;121(3):360–5. https://doi.org/10.1016/j.anai.2018.05.025
14. Chiampou E, Douros K, Moriki D, Marina M, Anastasiou-Katsiardani A, Tanou K, et al. Evaluation of treatment and long-term management of anaphylaxis in pediatric departments of Greece: A 2-year nationwide survey. Allergol Immunopathol (Madr). 2024 May 1;52(3):8–16. https://doi.org/10.15586/aei.v52i3.1032
15. 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 Nov 18;14(11):100605. https://doi.org/10.1016/j.waojou.2021.100605
16. Jeon YH, Lee S, Ahn K, Lee SY, Kim KY, Kim HH, et al. Infantile anaphylaxis in Korea: A multicenter retrospective case study. J Korean Med Sci. 2019;34(13):e106. https://doi.org/10.3346/jkms.2019.34.e106
17. Gaspar Â, Santos N, Faria E, Pereira AM, Gomes E, Câmara R, et al. Portuguese Society of Allergology and Clinical Immunology (SPAIC) Anaphylaxis Interest Group. Anaphylaxis in children and adolescents: The Portuguese anaphylaxis registry. Pediatr Allergy Immunol. 2021 Aug;32(6):1278–86. https://doi.org/10.1111/pai.13511. Epub 2021 Apr 18.
18. 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;31:954–61. https://doi.org/10.1111/pai.13320

19. Simons FE, Sampson HA. Anaphylaxis: Unique aspects of clinical diagnosis and management in infants (birth to age 2 years). J Allergy Clin Immunol. 2015 May;135(5):1125–31. https://doi.org/10.1016/j.jaci.2014.09.014. Epub 2014 Oct 30.
20. Simons FER. Anaphylaxis in infants: Can recognition and management be improved? J Allergy Clin Immunol. 2007;120:537–40. https://doi.org/10.1016/j.jaci.2007.06.025
21. Anagnostou K. Anaphylaxis in children: Epidemiology, risk factors and management. Curr Pediatr Rev. 2018;14(3):180–6. https://doi.org/10.2174/1573396314666180507115115
22. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117(2):391–7. https://doi.org/10.1016/j.jaci.2005.12.1303
23. Cardenas-Morales M, Hernandez-Trujillo V. Infant anaphylaxis: A diagnostic challenge. Curr Allergy Asthma Rep. 2021 Feb 23;21(2):12. https://doi.org/10.1007/s11882-021-00990-4
24. Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, et al. Caregiver-reported presentation of severe food-induced allergic reactions in infants and toddlers. J Allergy Clin Immunol Pract. 2021;9(1):311–20 e2. https://doi.org/10.1016/j.jaip.2020.11.005
25. Fleming JT, Clark S, Camargo CA Jr, Rudders SA. Early treatment of food-induced anaphylaxis with epinephrine is associated with a lower risk of hospitalization. J Allergy Clin Immunol Pract. 2015 Jan–Feb;3(1):57–62. https://doi.org/10.1016/j.jaip.2014.07.004
26. Aun MV, Kalil J, Giavina-Bianchi P. Adults and children with anaphylaxis in the emergency room: Why it is not recognized? Curr Opin Allergy Clin Immunol. 2018 Oct;18(5):377–81. https://doi.org/10.1097/ACI.0000000000000469
27. Brown JC. Epinephrine, auto-injectors, and anaphylaxis: Challenges of dose, depth, and device. Ann Allergy Asthma Immunol. 2018;121(1):53–60. https://doi.org/10.1016/j.anai.2018.05.001
28. Robinson M, Greenhawt M, Stukus DR. Factors associated with epinephrine administration for anaphylaxis in children before arrival to the emergency department. Ann Allergy Asthma Immunol. 2017;119(2):164–9. https://doi.org/10.1016/j.anai.2017.06.001
29. Nunes FA, Zanini F, Braga CS, da Silva AL, Fernandes FR, Solé D, et al. Incidence, triggering factors, symptoms, and treatment of anaphylaxis in a pediatric hospital. World Allergy Organ J. 2022 Aug 21;15(9):100689. https://doi.org/10.1016/j.waojou.2022.100689
30. Delli Colli L, Al Ali A, Gabrielli S, Delli Colli M, Mule P, Lawson B, et al. Managing anaphylaxis: Epinephrine, antihistamines, and corticosteroids: More than 10 years of Cross-Canada Anaphylaxis REgistry data. Ann Allergy Asthma Immunol. 2023 Dec;131(6):752–8.e1. https://doi.org/10.1016/j.anai.2023.08.606
31. Shroba JA. Infant anaphylaxis: Diagnostic and treatment challenges. J Am Assoc Nurse Pract. 2020 Feb;32(2):176–83. https://doi.org/10.1097/JXX.0000000000000386
32. Fleischer DM, Perry TT, Atkins D, Wood RA, Burks AW, Jones SM, et al. Allergic reactions to foods in preschool-aged children in a prospective observational food allergy study. Pediatrics. 2012;130:e25–32. https://doi.org/10.1542/peds.2011-1762