ORIGINAL ARTICLE

Anaphylaxis fast-track system: a pilot project to enhance and standardize anaphylaxis patient care

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Summary

Background. Anaphylaxis is the most severe form of acute systemic allergic reactions. Several recommendations have been proposed to guide and standardize anaphylaxis approach and management. The objective of this study is to characterize a cohort of patients referred through an anaphylaxis fast-track system, to enhance and standardize anaphylaxis patient care. **Methods.** Observational study including patients with anaphylaxis admitted in the emergency department (ED) and/or referred through the fast-track system (June 2022 - June 2025). Collected data included demographics, clinical presentation, aetiology, treatment, adrenaline autoinjector (AAI) prescription, request for serum tryptase testing, biphasic reactions, diagnosis and follow-up care. **Results.** Over the 399 patients referred through the fast-track system for specialist evaluation, anaphylaxis was confirmed in 120 patients. Drug-induced anaphylaxis was the most prevalent, with nonsteroidal anti-inflammatory drugs the most reported (46.3%). Food-induced anaphylaxis was the second cause, with shellfish accounting for most cases (63.5%). The most common association of symptoms was mucocutaneous and respiratory symptoms (49.5%). Among the 120 confirmed cases, intramuscular adrenaline was administered in 68.4% (67/98) of patients admitted to ED and AAI in only 18.4% (18/98). Biphasic reactions were only reported in

three patients. No fatalities or recurrent episodes were documented. **Conclusions.** These findings highlight the importance of standardized protocols or fast-track systems for anaphylaxis diagnosis and management, allowing for a rapid recognition, treatment and management of patients. Nevertheless, the need to continually improve medical education and training remains. This study is limited by its selected cohort, the exclusion of primary-care emergency department data owing to coding limitations, and its inherently descriptive design.

Key words

Anaphylaxis; adrenaline; adrenaline autoinjector; emergency department; fast-track system.

IMPACT STATEMENT

This study highlights the effectiveness of an anaphylaxis fast-track system in improving diagnosis and management, while emphasizing the ongoing need for clinician education and standardized emergency care protocols.

Introduction:

Anaphylaxis is the most severe form of acute systemic allergic reactions. It constitutes a medical emergency, with the potential of fatal outcomes. Over the years, several recommendations and position papers have been proposed to guide and standardize anaphylaxis approach and management (1-4).

According to the literature, its estimated global incidence ranges from 50 and 112 episodes per 100 000 person-years, with a lifetime prevalence of 0.3-5.1% (5,6). Nonetheless, its real prevalence is estimated to be higher, as underreporting remains a significant issue in many regions. Additionally, recurrence occurs in nearly 26.5-54% of patients (7). Despite this, anaphylaxis-related mortality remains low (8,9).

In Portugal, a 10-year study, identified food allergens as the leading trigger of anaphylaxis, followed by drug-related event, findings consistent with previous studies (10-12). The recurrence of anaphylaxis events was documented in 41% of cases, with 21% of the patients reporting three or more episodes. The rate of intramuscular adrenaline administration was as low as 43%, highlighting the misrecognition and misdiagnosis of this entity. Adrenaline autoinjectors (AAI) were only used by 7% of patients (10).

Previous data from our department, have shown a steady increase in the diagnosis of anaphylaxis over time. More than a decade ago, confirmed cases accounted for only 1% to 6% of all cases. This percentage has since risen, currently ranging from 10% to 17%. This upward trend reflects our increasingly focused approach to the identification and management of this entity.

These findings highlight the ongoing need for increased awareness and updated protocols. The aim of the present study is to characterize a cohort of Portuguese patients admitted to the emergency department (ED) of a tertiary hospital on the island of Madeira, through an anaphylaxis fast-track system, implemented as a pilot project, to enhance and standardize anaphylaxis patient care. We aim to evaluate anaphylaxis emergency approach, treatment and management, as well as primary and specialist follow-up care.

Material and Methods:

Study Population

We conducted a mixed retrospective-prospective study to assess the occurrence of anaphylaxis in patients presenting to the ED of a tertiary hospital and/or referred through the anaphylaxis fast-track system (includes hospital ED, primary care centres ED, inpatient units, operating rooms and/or diagnostic facilities), between June of 2022 and June of 2025. All patients with a clinical history suggestive of anaphylaxis, who met the diagnostic criteria, were identified through the activation of the anaphylaxis fast-track system, previously developed for this purpose.

Following initial management, patients referred to our outpatient allergy clinic were prospectively followed until a final diagnosis was established. Data regarding demographic information, concomitant allergic diseases, clinical presentation, suspected or confirmed allergens, treatment administered in the ED, possession and use of AAI, and final diagnosis were collected from the clinical records. Additional variables as administration of anaphylaxis-specific treatment, serum tryptase testing, biphasic reactions, follow-up care and discharge recommendations were also evaluated.

To ensure clarity and consistency in data reporting, three nested populations were defined. The first included all ED activations for suspected anaphylaxis; the second comprised all subsequent referrals to our Immunoallergology outpatient clinic; and the third, the confirmed anaphylaxis cohort. For ED activations and the subsequent referrals, data were collected

retrospectively from clinical records. For the subset of patients with confirmed anaphylaxis, a prospective evaluation was performed during outpatient follow-up.

Anaphylaxis fast-track system

This pilot project was developed in accordance with the study protocol rules and followed the recommended framework models of the World Medical Association (Declaration of Helsinki revised in 2013). It was approved by the Ethics Committee and the hospital's Clinical Board and came into effect on July 12, 2022 and remains ongoing.

The main objective of this project is to facilitate the prompt identification of patients with suspected anaphylaxis, thereby enabling timely emergency intervention, minimizing the associated risks. This fast-track system integrates all key components of anaphylaxis emergency management, including the request for serum tryptase testing, acute treatment, and follow-up care, enhancing patient safety.

Additionally, it can be activated by any healthcare professional, at any time and in any location, regardless of whether it is in the ED, primary care centres, inpatient units, operating rooms or diagnostic facilities. It ensures care is provided within less than 10 minutes.

In its first year, training was provided to healthcare professionals working in the ED. A second recertification of training was conducted this year, expanding to include staff from the ED, as well as various surgical specialities, internal medicine and the radiology department. Training was provided to a total of 285 healthcare professionals.

Furthermore, this fast-track system was submitted to the quality certification process of the Portuguese Directorate General for Health (Direção Geral de Saúde, DGS), and received official certification in 2024.

Anaphylaxis diagnosis

Anaphylaxis diagnosis was made according to the consensus criteria published by the American Academy of Allergy, Asthma & Immunology (AAAAI), American College of Allergy Asthma and Immunology (ACAAI), European Academy of Allergy and Clinical Immunology (EAACI) and World Allergy Organization (WAO), based on the presence of at least one of the three established clinical criteria (1-4). Etiological allergen identification was performed in

conformity with the EAACI/European Network recommendations for IgE mediated reactions. Anaphylaxis severity was graded according to the Anaphylaxis Consensus Severity Grading System, proposed by Dribin et al., 2021 (13).

Statistical analysis

Descriptive analysis of demographic and clinical data was performed. Categorical variables were presented as absolute (n) and relative frequencies (%), and continuous variables as mean ± standard deviation (SD) (minimum and maximum) for parametric distribution, or as median value and interquartile range [IQR] for non-parametric distributions. Normality was assessed using the Shapiro-Wilk or Kolmogorov-Smirnov test. When applicable, 95% confidence intervals (95% CI) were calculated to provide an estimate of the precision of the mean or effect size. Differences between variables were assessed using the Pearson Chi-Square test, Fisher's Exact Test or the Mann-Whitney U test, with p-value < 0.05 considered statistically significant. The Kruskal–Wallis test was used to compare differences among non-parametric independent groups. All descriptive statistical analyses were performed using Software IBM SPSS (version 25.0, SPSS Inc., Chicago, III).

Results:

ED characterization

Over the past 3 years, a total of 506 patients were admitted to hospital ED for anaphylaxis treatment, through the activation of the anaphylaxis fast-track system. This population included mostly female patients (n=265, 52.4%) within mean age of 37.8±23.1 years (minimum 2 years; maximum 91 years). A quarter of these patients (n=125, 24.7%) were under 18 years of age (57.6% boys, mean age 9.8±4.8 years, minimum 2 years, maximum 17 years).

Referred population

Among patients evaluated through the anaphylaxis fast-track system, only 399/506 were referred to our Immunoallergology outpatient clinic. This population included mostly female patients (n=283, 70.9%) within mean age of 48.8±2.5 years (minimum 1 year; maximum 96 years). Twelve patients (3%) were under 18 years of age (58.3% boys, mean age 9.8±3.5 years, minimum 1 year; maximum 17 years). Most referrals originated from physicians in primary care

centres (n= 211, 52.9%), followed by the ED (n=125, 31.3%), other hospital specialities (n=37, 9.3%) and hospitalization/operating room (n=26, 6.5%).

Study population

Among all patients referred to our outpatient clinic, anaphylaxis was confirmed in 120 patients. The study population included mostly female patients (n=72, 60%) within mean age of 44.8±12.7 years (minimum 4 year; maximum 84 years). Only 6 of these patients (5%) were under 18 years of age (50% boys, mean age 9.3±7.8 years, minimum 4 year; maximum 15 years). Table I summarizes the baseline clinical characteristics of the study population.

Clinical manifestations and severity

Most patients reported mucocutaneous involvement (n=105, 87.5%), followed by respiratory symptoms (n=91, 75.8%), cardiovascular symptoms (n=54, 45%) and gastrointestinal manifestations (n=28, 23.3%). Seven patients reported laryngeal oedema and other three cardiac arrest. The most common association of symptoms was mucocutaneous and respiratory, observed in 52 patients (43.3%). In 15 patients (12.5%) mucocutaneous symptoms were not present.

Regarding anaphylaxis severity, the most prevalent classification was grade 4 (n=48, 40%), followed by grade 2 (n=42, 35%).

Patients often reported a median [IQR] of 30 [50] minutes (95% CI: 27.4-37.6) between allergen exposure and symptoms onset. The majority of episodes occurred at home (n=79, 65.8%) or at the hospital (n=27, 22.5%). Only a minority had taken any medication before arriving at the ED, including antihistamines or corticosteroids (n=6/120, 5%).

Anaphylaxis aetiology

A known or suspected allergen was identified in 96.7% (n=116/120) of cases. Most patients reported drug-related anaphylaxis (n=54, 45%), being the most prevalent NSAIDs (n=25, 46.3%), followed by antibiotics (n=17, 31.5%). Food-related anaphylaxis represented the second most common cause (n=52, 43.3%), with seafood being the most identified (n=35, 67.3%), with particular emphasis to limpet sensitization (n=14, 26.9%).

Emergency treatment

Among the 120 patients referred to our department, a total of 98 patients were admitted to the ED. Of these, 68.4% (n=67/98) received intramuscular adrenaline. Antihistamines were administered in 87.8% (n=86/98) of patients, and corticosteroids in 98% (n=96/98). Hospitalization was required in four cases (4.1%), but no fatalities were reported.

Considering adrenaline administration, most patients were treated accordingly, with only 1 intramuscular dose. Nonetheless, 11/67 (16.4%) patients needed 2 or more administrations. Intravenous adrenaline, performed in intensive unit care, was required in 7/98 (7.1%) patients, alongside with vasopressors. No statistically significant association was observed between anaphylaxis aetiology and the administration of adrenaline (p-value = 0.139).

Thirty-one (31.6%) patients did not receive adrenaline as part of their treatment, besides the correct clinical diagnosis. In these cases, patients were mainly treated with antihistamines and/or corticosteroids. No intravenous glucagon administrations were reported in this timeline, among patients potentially at risk for refractory anaphylaxis due to concomitant beta-blocker therapy.

Serum tryptase

This analysis, while not essential for establishing the diagnosis, was requested in 39/98 patients and yielded positive results in 29 cases, with a median [IQR] of 20.5 [21.7] ng/mL (95% CI: 12.8-47.1), according to the recommended formula, comparing its value in crisis and in basal state (at least 20% plus 2 ng/mL over the patient´s basal level) (12). The majority of positive cases reported drug-related anaphylaxis (n=19/39, 48.7%). No systemic mastocytosis was diagnosed. A statistically significant difference was found in tryptase levels across allergen categories (p-value = 0.038). Drug-induced reactions were associated with higher levels of serum tryptase (mean rank 24.39), collected in the event, whereas food-induced anaphylaxis presented with the lowest values (mean rank 13.61).

Biphasic reaction

Biphasic reactions were reported in 3/98 patients (2.5%), occurring mainly 4 to 6 hours after the initial episode. All patients were treated with a single additional dose of intramuscular adrenaline, antihistamines and corticosteroids, resulting in full symptom resolution. Curiously, these patients all belonged to the group that received 2 or more doses of adrenaline in the primary observation. In one of these patients, idiopathic aetiology was the final diagnosis. No statistically significant association was observed between anaphylaxis aetiology and the occurrence of biphasic reactions (p-value = 0.083).

Emergency follow-up care

The median [IQR] duration of ED observation was 4.5 [10] hours (95% CI: 8.6-18.1). There was no statistically significant association between anaphylaxis severity and the risk of hospitalization (p-value = 0.115). Nevertheless, all hospitalizations occurred among patients with reactions grade 3 to 5, suggesting a clinically relevant trend despite the lack of statistical significance. Nevertheless, patients with anaphylaxis grade 3 to 5 had significantly longer ED stays than those with grade 1 to 2 reactions (p-value = 0.009).

Most patients were discharged with the recommendation to avoid identified or potential triggers and were prescribed with both antihistamines and corticosteroids (n=65/98, 66.3%). Regarding AAI, they were only prescribed to 18.4% (n=18/98) of the population.

A previous history of anaphylactic episodes was documented in only one patient, who already carried an AAI, but did not administer it.

Allergology evaluation

Of the 120 patients followed in our allergology outpatient clinic, 37.5% (n=45) reported allergic comorbidities, with allergic rhinitis being the most prevalent (n=39, 86.7%).

Drug-induced anaphylaxis was the main reported cause of episodes (n=54, 45%), with NSAIDs being the most reported (n=25, 46.3%). Beta-lactam antibiotics were the second most frequent cause (n=16, 29.6%), followed by iodinated radiocontrast media (n=7, 13%). This etiology affected mostly adult patients (n=53, 98.1%).

Food-induced anaphylaxis was the second in line, confirmed in 52 patients (43.3%). Shellfish was the most stated, affecting 33 patients (63.5%). Tree nuts were positive in 4 patients,

fresh fruits in 5 and wheat in 3 other patients. Food-dependent exercise-induced anaphylaxis was concluded in 2 patients, one related to wheat, and the other to shrimp sensitization.

The third most common cause of anaphylaxis was hymenoptera venom hypersensitivity, reported in 9 patients (7.5%), with the majority showing sensitization to *Apis mellifera* venom (n=6, 66.7%). Latex-induced anaphylaxis was confirmed in one patient (0.8%). Idiopathic anaphylaxis remained the final diagnosis in 4 patients (3.3%). All four presented an elevated serum tryptase at the index event, with a normal basal serum tryptase, and the allergology study wasn´t able to solidly identify the main causative allergen. No further anaphylactic episodes were reported in this group. No statistically significant differences were observed between adult and paediatric patients regarding anaphylaxis´ aetiology, severity or adrenaline use (p-value > 0.05).

No recurrence of anaphylaxis episodes was registered for this population. Table II summarizes all aetiologies associated with anaphylaxis.

Discussion and Conclusions:

This study confirms drug-induced anaphylaxis as the most frequent cause of anaphylaxis in our population, with NSAIDs being more commonly implicated than antibiotics. This finding is consistent with findings from other published series (10,14,15). However, in several reports, antibiotics have been identified as the primary cause of drug-induced anaphylaxis, with the estimated risk of penicillin-induced anaphylaxis ranging between 0.7% and 10% (16). Regarding NSAIDs, the most frequently implicated agents were COX-1 inhibitors, notably acetylsalicylic acid, ibuprofen, and metamizole, in accordance with findings reported in the literature (14,15).

Nonetheless, food was the second most reported aetiology, mirroring previous literature on this subject (17,18). Seafood allergy is estimated to affect up to 10.3% of the global population, being more common in Asia region (19). In Portugal, it is estimated in about 27% of the population with food-induced anaphylaxis, aligned with mediterranean dietary patterns (10). Unlike shellfish (crustaceans/bivalves), limpet allergy is extremely rare and primarily reported in subtropical Mediterranean areas (20). However, in our population, it represented 26.9% of all food-related anaphylaxis episodes, contributing largely to food aetiology.

Idiopathic anaphylaxis may account for up to 20% of all anaphylaxis cases (21,22); however, in other series, its prevalence was as low as 2% (10), as it happens in our study,

reinforcing the importance of conducting a thorough etiological investigation in all cases of anaphylaxis.

The findings of this study indicate that anaphylaxis occurs across all age groups, as no statistically significant differences were observed between adult and paediatric patients regarding anaphylaxis´ aetiology, severity, biphasic reactions or adrenaline use. Nonetheless, as expressed in previous reports, a higher prevalence of anaphylaxis was observed among adults and female patients. Some authors have proposed endocrine factors as a major contributor to this prevalence (23,24).

The majority of our patients were admitted for emergency care. Unlike other studies, that reported low rates of intramuscular adrenaline administration (25,26), in our population it accounted for 68.4%. This might be due to the fact that training was provided every 2 years to all interested healthcare professionals in our hospital, alongside with supplementary explanative documents uploaded to the informatic fast-track system, that can be assessed whenever needed.

The absence or delay in the administration of adrenaline has been clearly associated with increased mortality in cases of refractory and biphasic anaphylaxis (21,27,28). In our population, biphasic reactions were only reported in a minority of patients (2.5%). Nonetheless, all of them belonged to the group that initially received 2 or more doses of adrenaline, reinforcing this factor as a clinical risk predictor, when considering emergency observation duration, as previously stated in the literature (3).

In some cases, within our cohort, the duration of physical observation following treatment in the ED was as short as one hour, which raises significant concerns about the potential oversight of biphasic reaction risks. Even though, one published study states that 1-hour symptom-free observation after resolution of the initial anaphylaxis was associated with a 95% negative predictive value for biphasic anaphylaxis (29), the same meta-analysis, that included 2890 adult patients with anaphylaxis, showed a median duration between the first episode resolution and the second reaction of 10.5 hours, aligning with other studies of biphasic anaphylaxis (3,30,31). Moreover, in our population, no statistically significant association was found between anaphylaxis severity and the risk of hospitalization. Nevertheless, all hospitalizations occurred among patients with reactions grade 3 to 5. These patients had also significantly longer ED stays than those with grade 1 to 2 reactions.

The rate of AAI prescription remained below recommended standards (18.4%). This under prescription is a well-documented issue, as previously demonstrated in the literature (12,32).

Serum tryptase request was also insufficient (32.5%). Even though it is not required to establish diagnosis, it can help to improve future management. Nonetheless, it is important to remember that a negative value does not exclude the diagnosis. Recommendations advise in favour of its request. However, they also state that the use of the serum tryptase equation alone is not advisable (4). In our cohort, drug-induced anaphylaxis was significantly associated with higher serum tryptase levels, whereas food-induced anaphylaxis exhibited the lowest values. This finding is consistent with previous reports on the subject (33).

The standardization of anaphylaxis diagnosis and management, through the fast-track system, allowed us to increase the number of patients referred to our department, thus increasing diagnosis and preventing further episodes. Like in other acute medical conditions, emergency fast-track systems provide a rapid patient-centred approach, that improves outcomes.

In the 10 years´ evaluation of anaphylaxis in our country, the authors reinforced that the voluntary report of cases may contribute to the underreporting of this entity (10). Considering this, the fast-track system increases awareness of this diagnosis and the need for specific follow-up, thereby indirectly enhancing reporting.

In conclusion, over the past 3 years, 120 patients were diagnosed with anaphylaxis in our department following referral through the anaphylaxis fast-track system. During this time, no recurrence episodes have been registered. Intramuscular adrenaline was administered to 68.4% of patients who presented to the ED, indicating a clear increase in the awareness of this entity. Nevertheless, the prescription for AAI were still low (18.4%), indicating room for improvement.

These findings highlight the permanent necessity to reinforce medical education and training, as well as to implement standardized anaphylaxis management protocols across emergency departments and health units. When addressing anaphylaxis, prevention is key. Patients and caregivers should be informed, orally and with a written action plan, how to avoid allergens and manage potential exposures. Patients should always carry an emergency kit, contemplating the AAI. Standard recommendations advise for a 2-device prescription, especially in patients living far away from the ED, idiopathic anaphylaxis and food–induced anaphylaxis triggered by trace amounts of a food allergen. Early administration of pre-hospital adrenaline can be of vital importance. Drug-induced anaphylaxis may dispense the obligation to carry an AAI, thus debatable. Nonetheless, all severe allergic reactions should be properly reported and signposted to all healthcare providers, and referred to allergy specialist evaluation, as exemplified by this anaphylaxis pilot system.

This study has some limitations in the extent that it is a retrospective study based on the analysis of clinical files. Second, the small sample of paediatric patients does not allow to extract further conclusions for this population. Nonetheless, the authors suggest that these results have important added value in clinical practice, contributing to further establishing data on this subject. To our knowledge, this fast-track system is the first ever created to fulfil the purpose of anaphylaxis management as a true medical emergency.

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Table I. Study population characterization. Abbreviations: n – total number; % - percentage; M - mean value; Md – median value; SD – standard deviation; min – minimum; max – maximum; IQR – interquartile range. *total of 39 patients.

Patients - n	120
Gender	
Female - n (%)	72 (60)
Male - n (%)	48 (40)
Adults - n (%)	114 (95)
Children - n (%)	6 (5)
Age (M+SD [min; max] years old)	44.8±12.7 [4; 84]
Clinical Manifestations – n (%)	
Mucocutaneous	105 (87.5)
Respiratory	91 (75.8)
Gastrointestinal	28 (23.3)
Cardiovascular	54 (45)
Anaphylaxis Severity Scale – n (%)	
Grade I	3 (2.5)
Grade II	42 (35)
Grade III	22 (18.3)
Grade IV	48 (40)
Grade V	5 (4.2)
Serum tryptase in the event (ng/mL) – Md [IQR]*	20.5 [21.7]

Table II. Anaphylaxis etiology. Abbreviations: NSAIDs - nonsteroidal anti-inflammatory drugs; PEG - polyethylene glycol.

Anaphylaxis etiology	Total (n=120)	<18 years (n=6)	≥18 years (n=114)
Drug-related anaphylaxis	**54**	**1**	**53**
NSAIDs	25	1	24
Beta-lactam antibiotics	16	0	16
Iodinated radiocontrast media	7	0	7
Others (ciprofloxacin – 1, midazolam - 1, rituximab – 1, carboplatin –1, oxaliplatin –1, PEG - 1)	6	0	6
Food-related anaphylaxis	**52**	**4**	**48**
Seafood	35	2	33
Tree nuts	4	2	2
Peanut	2	0	2
Fresh fruits	5	0	5
Wheat	3	0	3
Others (honey – 1, sunflower seeds – 1, fennel - 1)	3	0	3
Hymenoptera anaphylaxis	**9**	**0**	**9**
Apis melifera	6	0	6
Vespula spp.	3	0	3
Food-dependent exercise-induced anaphylaxis (wheat – 1; shrimp –1)	**2**	**0**	**2**
Latex anaphylaxis	**1**	**0**	**1**
Idiopathic anaphylaxis	**4**	**1**	**3**