S. Ruffoni[1], A. Furgani[1], I. Schiavetti[2], G. Ciprandi[3]

Anaphylaxis: a one-year survey on Medical Emergency Service in Liguria (Italy)

[1]Emergency Department and [3]Medicine Department, IRCCS - Azienda Ospedaliera Universitaria San Martino, Genoa, Italy
[2]Health Sciences Dpt, Genoa University, Genoa, Italy

Key words
Anaphylaxis; medical emergency service; Liguria

Correspondence:
Giorgio Ciprandi
Viale Benedetto XV 6, 16132 Genoa, Italy
Phone: + 39 010 35 33 8120
Fax: + 39 010 35 38 664
E-mail: gio.cip@libero.it

Summary
Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. The diagnosis is mainly based on clinical ground. This study aimed at evaluating the records of phone calls and medical visits for anaphylaxis occurred in Region Liguria during 2013. The phone call is managed in each headquarter, and classified according to a level of care intensity and a presumed level of criticality, according to established criteria. Criticality is then re-evaluated (detected criticality) at the end of medical visit, following the same score adding the black code defining died patients. Most of the phone calls (553) to the MES were recorded in summer (37.4%). Anaphylaxis was confirmed in about half of patients. There was a fair agreement between presumed and detected criticality ($k = 0.322$, $p < 0.001$). In addition, 530 patients (95.8%) were transported to Emergency Room. In conclusion, the present study shows that anaphylaxis represents a serious and relevant medical problem in the general population at any age, and should always be carefully managed.

Introduction

Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction (1). However, there is no definitive consensus about definition and diagnostic criteria. The most quoted work definition was proposed by Sampson and colleagues: anaphylaxis is likely when any of 3 criteria are fulfilled: i) acute onset of an illness with involvement of skin/mucosal tissue and airway compromise or reduced blood pressure or associated symptoms; ii) 2 or more of the following after exposure to known allergen for the patient: history of severe allergic reaction, skin/mucosal tissue, airway compromise, reduced blood pressure, gastrointestinal symptoms (for food allergy); iii) hypotension after exposure to known allergen for the patient (2). In Europe, the anaphylaxis incidence ranges from 1.5 to 7.9 per 100.000 person-years, so approximately 0.3% of the population experience anaphylaxis in their lives (1). Foods, drugs, stinging insects, and latex are the most common triggers. The updated World Allergy Organization Guidelines focuses on anaphylaxis diagnosis and management (3). Infants and teenagers have increased vulnerability to anaphylaxis. Comorbidity with severe or uncontrolled asthma, mastocytosis, and concurrent use of some medications increase the risk of severe or fatal anaphylaxis. Food is the most important trigger in childhood (4). Food anaphylaxis typically occurs after ingestion, more rarely after skin contact or inhalation. Drug anaphylaxis is most frequent in adults, whereas insect stings anaphylaxis may affect all ages.

The diagnosis of anaphylaxis is mainly based on a clinical ground. The clinical approach considers the presenting signs and symptoms and should exclude other sudden-onset multi-systemic diseases. Fortunately, only few food kinds, mainly including egg, milk, peanut, fish, soybean, wheat, are usually cause of anaphylaxis in children and adolescents, whereas shellfishes, crustaceans, and fresh fruits are relevant in adults. Their

relevance also depends on dietetic habits, different within each country. In this regard, there are some studies that addressed this topic, also considering the presenting clinical feature (4-7). About medications, b-lactam antibiotics and non-steroidal anti-inflammatory drugs (NSAID) are the most relevant cause of drug anaphylaxis. Finally, the timing, the clinical features, and the presence of co-morbidities (mainly asthma) and co-factors (e.g., NSAID, ACE-inhibitors, alcoholic drinks, and exercise) should be carefully evaluated.

In Italy, a medical emergency service (MES) exists to manage territorial emergency. MES is widespread distributed and is active h24. Recently, a study has been carried out to evaluate the medical emergency calls requiring attention for asthma and COPD exacerbations among the population of the territory of Genoa (Italy) in an 8-year period (8). Therefore, this study aimed at evaluating the records of phone calls and medical visits for anaphylaxis occurred in the Region Liguria during 2013.

Materials and Methods

Liguria is a North-Western Italian Region with about 1.6 million inhabitants. Medical Emergency Service (MES) is widespread in the territory, with 5 centrals and 18 medical stations. The service is available everyday h24.

The calls for suspected anaphylaxis occurred during the whole 2013 were evaluated.

The phone call is managed in each headquarter, and classified according to a level of care intensity and a presumed level of criticality, according to established criteria (http://www.emergencydispatch.org/it). Care intensity is scored according to a level ranging from Omega (the less relevant) to progressively more severe (Alpha, Bravo, Charlie, and Delta), up to the most critical Echo. The Academy indications are: Alpha level considers not-urgent dispatch of a basic BLS unit; Bravo level urgent dispatch of a BLS unit; Charlie level not-urgent dispatch of an ALS unit; Delta level urgent dispatch of an ALS unit. The care intensity definition is based on specific issues, including: vital parameters assessment, airways basic evaluation, presence of thoracic external compression, bleeding control, etc for BLS; advanced airways assessment (endotracheal intubation), medication use, manual defibrillators use, etc for ALS (http://www.mattoni.salute.gov.it/mattoni/documenti/MDS_MATTONI_SSN_milestone_1.4.1_Classificazione_attivit_118_v1.0.pdf).

Presumed criticality is initially defined at the headquarters on the basis of a score based on colours: white (mild), green (moderate), yellow (severe), and red (life-threatening). Criticality is then re-evaluated (detected criticality) at the end of the medical visit following the same score, adding the black code defining died patients.

The supposed diagnosis of anaphylaxis was based on clinical criteria (1,2,3), such as: suggestive clinical history consistent with presenting symptoms, i.e. the demonstration of a cause/effect dependence between exposure to potential causal trigger and occurrence of anaphylaxis clinical features (*post hoc ergo propter hoc*). Cardiovascular features were: hypotension, impairment of conscious state, pale and floppy presentation; respiratory features were: breathlessness, tongue or throat swelling, throat tightness, stridor, talking difficulty, wheezing, cough, and tachypnea; gastrointestinal features were: vomiting, colic, and diarrhea; skin features were: angioedema, urticaria, itching, and erythema.

Statistical analysis

Epidemiological, demographic and clinical profiles of patients are expressed as count and percentage or mean and standard deviation. Any relationship between detected criticality or season during which the event occurred, was evaluated by a chi-square test for goodness of fit. A non-parametric Kruskal-Wallis test was performed to check for significant differences in age distributions of detected pathologies. Cohen's Kappa coefficient was used for assessing the degree of agreement between alleged and detected criticality and between alleged and detected pathology. A $p \leq 0.05$ was considered statistically significant. SPSS (IBM Corp.) v.20 was used for computation.

Results

Table 1 shows the demographic and clinical characteristics of patients reporting anaphylaxis. Globally, 553 calls occurred during 2013.

Most of the phone calls to the MES were recorded in summer (37.4%), followed by autumn (23.7%), spring (20.6%), and winter (18.3%). Two hundred and fifty-two patients (45.6%) were males, and the mean age was 43.09 ± 23.32 years. **Figure 1** shows the distribution of ages per number of cases.

The most frequently registered levels of care intensity were Alpha (36.7%) and Charlie (28.2%). Breathing and/or swallowing difficulty were reported in 120 (21.7%) patients. As for the distribution of presumed criticality, yellow score was the most frequent (46.8%) followed by green (26.6%) and red (26.0%). On the other hand, about the detected criticality yellow score was the most frequent (49.9%), followed by green (44.8%).

Cohen Kappa value indicated a fair agreement between presumed and detected criticality ($k = 0.322$, $p < 0.001$). On 546 criticalities, 311 (56.96%) showed an exact correspondence between presumed and detected, 218 (39.93%) were presumed more serious than the real criticality verified, and 17 (3.11%) were presumed less serious than the real criticality detected (**table 2** and **figure 2**). The sub-analysis in children and adolescents showed super-imposable results ($k = 0.35$, $p < 0.001$).

In particular, 15 patients on 17 with presumed red code were confirmed as red level (88.2%), whereas only 2 were assessed as yellow code (11.8%).

There was no death for anaphylaxis during 2013 in Liguria. However, we cannot exclude that some case of death for anaphylaxis occurred in the Region during the period of observation as not registered through MES.
Finally, 530 patients (95.8%) were transported to Emergency Room.

Figure 1 *- Distribution of ages per number of cases.*

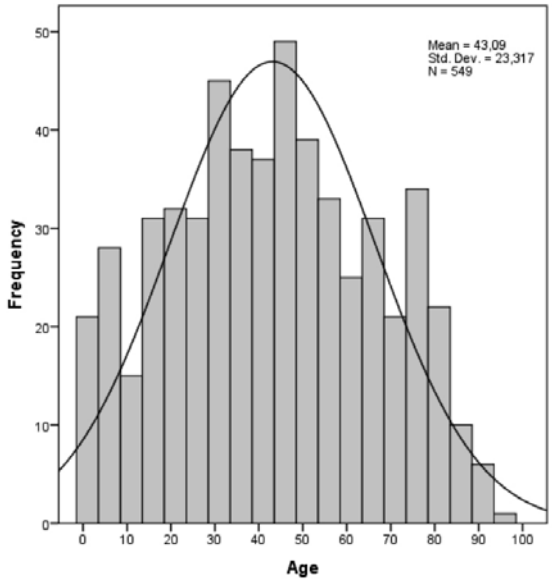


Table 1 *- (N = 553) - Descriptive analysis of the sample. Data are expressed as mean ± standard deviation and count (frequency).*

Season	*Spring*	114 (20.6)
	Summer	207 (37.4)
	Autumn	131 (23.7)
	Winter	101 (18.3)
Males, n (%)		252 (45.6)
Age (yrs)		43.09 ± 23.32
Care intensity level	*Alpha*	203 (36.7)
	Bravo	101 (18.3)
	Charlie	156 (28.2)
	Delta	91 (16.5)
	Echo	2 (0.4)
Presumed criticality	*White*	1 (0.2)
	Green	147 (26.6)
	Yellow	259 (46.8)
	Red	144 (26.0)
Detected criticality	*White*	7 (1.3)
	Green	248 (44.8)
	Yellow	276 (49.9)
	Red	17 (3.1)

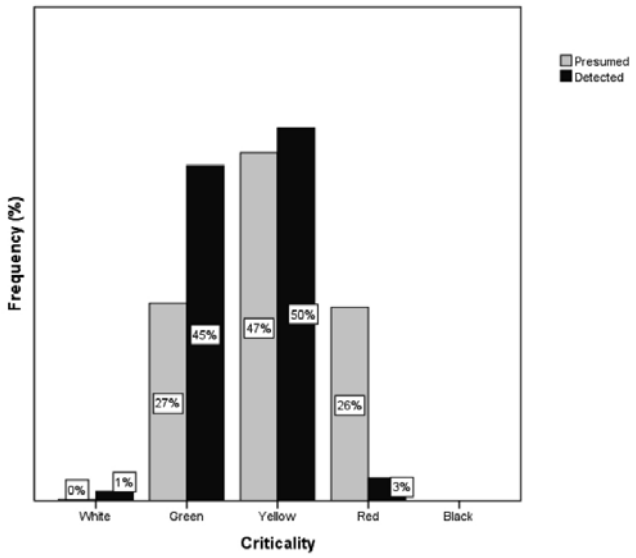
Table 2 *- Agreement between presumed and detected criticality.*

		Detected criticality				**Total**
		White	**Green**	**Yellow**	**Red**	
Presumed criticality	White	*1 (100.0)*	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
	Green	1 (0.7)	*130 (89.0)*	15 (10.3)	0 (0.0)	146 (100.0)
	Yellow	1 (0.4)	88 (34.4)	*165 (64.5)*	2 (0.8)	256 (100.0)
	Red	4 (2.8)	29 (20.3)	95 (66.4)	*15 (10.5)*	143 (100.0)
Total		7 (1.3)	247 (45.2)	275 (50.4)	17 (3.1)	546 (100.0)
Measure of agreement		k = 0.322; p < 0.001				

Table 3 *- Agreement between presumed and detected criticality in 86 minors.*

	Presumed criticality				
	White	Green	Yellow	Red	Total
age		7.97	7.84	8.84	
	0	29	38	19	86
	Detected criticality				
	White	Green	Yellow	Red	Total
age		8.95	6.98	11.0	
	1	41	42	2	86
Measure of agreement		k = 0.35; p < 0.001			

Figure 2 *- Presumed and detected criticality for anaphylaxis episodes.*



Discussion

The present survey demonstrates some interesting findings. Firstly, the highest frequency of phone calls for anaphylaxis occurred during summer (37.4%) and autumn (23.7%), such as about 2/3 of the global sample. This fact might be dependent on the prevalence of outdoor living in these seasons and the abundance of triggers, such as fruits and insects.

Secondly, mean age is nearly corresponding to half the survival rate. Indeed, anaphylaxis may occur at any age. This outcome is particularly relevant from a clinical point of view. Anaphylaxis should be always considered at any age.

Thirdly, anaphylaxis was confirmed in about half of cases, with a fair concordance between presumed and confirmed diagnosis, corresponding to red and yellow scores. Particularly, it is to note that there is a trend to overestimate the clinical severity by patients or observers. In fact, the severity of the red code was confirmed only in about 1/10 of cases. On the other hand, about half of calls corresponded to less severe allergic or non-allergic reactions. However, almost all subjects (95.8%) referred to the Emergency Room. This aspect underlines the relevance that this issue deserves.

The limitations of this study are the lack of details concerning the clinical presentation and the lack of triggers definition, in other words a definitive and correct diagnosis of anaphylaxis. These shortcomings depend on the particularity of medical records used by MES and, of course, on the peculiarity of MES deputed to emergency care. In fact, it has to be considered that there is a relevant diagnostic difficulty of this clinical picture during a MES intervention. In addition, several disorders should be considered in differential diagnosis, e.g. syncope, hearth infarction, stroke, vagal hypertonia, etc. Moreover, considering these limitations, mainly lack of details concerning clinical presentation and triggers definition, anaphylaxis can be only suspected and not confirmed, because diagnostic methods are very limited in the context of the emergency interventions.

On the other hand, the studies conducted in Italy about anaphylaxis were addressed to specific causes of anaphylaxis, such as food or hymenoptera allergic reactions, or concerned the experience of single Emergency Department. Therefore, the present study represents a further demonstration of the MES utility in

epidemiologic studies about several acute clinical pictures.
Obviously, further studies should be conducted addressing the limitations of the present survey.
In conclusion, the present study shows that anaphylaxis represents a serious and relevant medical problem in the general population at any age and should always be carefully managed.

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