

# What do Doctors Know About Anaphylaxis?

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## ABSTRACT

**Objective:** This study aims to assess the level of knowledge of doctors on anaphylaxis and its management at a tertiary care teaching hospital.

**Materials and Methods:** A pretested structured questionnaire was administered to the doctor, assistant doctor, and specialist doctor. Volunteers were asked to answer a questionnaire containing questions about anaphylaxis and its management. The questionnaire was administered face to face.

**Results:** Physicians from different branches of surgery and internal medicine participated in the study together with general practitioners, and the average age of 85 physicians participating in the study was 42.6 years. In the study, 8 of those participating were general practitioners, twenty six were medical residency students, and fifty one were working as specialist physicians in the tertiary hospital. The majority of the participants (83.5%) stated that they had encountered anaphylaxis before. There was no statistical difference between professional experience and the anaphylaxis encounter rate ( $p=0.76$ ). Only 4 participants correctly answered the diagnostic criteria of anaphylaxis. While 85% of the participants marked the combination of skin and respiratory signs and symptoms for the diagnosis, only 15% marked the combination of cardiovascular and gastrointestinal system signs and symptoms for the diagnosis. Unfortunately twenty participants did not administer intramuscular (im) adrenaline as first-line therapy in the treatment of anaphylaxis. After anaphylactic shock, sixty nine participants stated that the patient should be kept under observation for 8 to 24 hours.

**Conclusion:** Knowledge regarding anaphylaxis and its management is a basic requirement that every health care provider must acquire for the appropriate treatment of all patients. We show that there was no statistical relationship between professional experience and the diagnosis and treatment of anaphylaxis. We think that it would be beneficial to provide physicians with in service training regarding the diagnosis and management of anaphylaxis.

**Keywords:** Anaphylaxis, anaphylaxis management, physician knowledge

## INTRODUCTION

Anaphylaxis is a serious systemic allergic reaction, the incidence of which has increased in recent years, and which can occur rapidly and cause mortality (1). It has been reported that the incidence of anaphylaxis is between 50 to 112 per 100.000 persons and the prevalence varies between 0.3% and 5.1% (2). Anaphylaxis is a systemic reaction that develops due to mast cell and basophil derived mediators. The causes of anaphylaxis vary according to the age group. Anaphylaxis usually occurs with immunological mechanisms after exposure to foods, drugs and

bee venom. Non immunological mechanisms may also play a role in the development of anaphylaxis by causing mast cell and basophil degranulation. Non immunological factors include exercise, cold and various drugs (opioids, vancomycin, radiocontrast agent, cyclooxygenase (COX)-1 inhibitors). Drug induced anaphylaxis is more common in the adult age group. Anaphylaxis due to antibiotics is especially common. Beta Lactam group antibiotics are in the first place among the antibiotics that cause anaphylaxis. Non steroidal anti inflammatory drugs are the most common group of drugs that cause anaphylaxis after antibiotics. Due to the increase in the frequency of

use of chemotherapy and biological agents in recent years, the incidence of anaphylaxis has increased with both drug groups. Anaphylaxis can develop with all drugs. Therefore, anaphylaxis is common in hospitalized patients. Rapid diagnosis and correct treatment in anaphylaxis prevent possible mortality and morbidity.

Diagnosis of anaphylaxis; Diagnostic criteria determined in international guidelines are detected with the help of history and physical examination. Anaphylaxis diagnostic criteria are shown in Table I (3). Anaphylaxis usually occurs within the first 2 hours of encountering the trigger. Rarely, this period may take up to 4 to 6 hours. For this reason, in case of anaphylaxis, the drugs used and the foods consumed by the patient in the last 4 to 6 hours should be questioned (4). Skin symptoms and signs are most common in anaphylaxis. Skin signs and symptoms are followed by respiratory system signs and symptoms. Upper respiratory symptoms and signs such as rhinitis may occur, as well as lower respiratory tract symptoms and signs such as laryngeal edema or bronchospasm. Involvement of these two systems is followed by gastrointestinal and cardiovascular symptoms and signs (5). Respiratory system or cardiovascular system symptoms and signs are the most important indicators for mortality and morbidity (6). The World Health Organization has defined the development of bronchospasm alone after exposure to known allergens as anaphylaxis in 2019 (7). According to the Australasian Society of Clinical Immunology and Allergy 2023

anaphylaxis guidelines, acute hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient is considered anaphylaxis, even in the absence of typical skin findings (8). Anaphylaxis signs and symptoms are shown in Table II (3). Anaphylaxis diagnostic criteria are definite although the condition is difficult to diagnose because it shows clinical variability. Anaphylaxis may present as mild clinically without severe symptoms such as desaturation, hypotension, and loss of consciousness. The clinic, which starts with mild symptoms and signs, may worsen over time. For this reason, the physician's recognition of and intervention in mild anaphylaxis prevents the patient's clinical condition from worsening. The most common cause of fatal anaphylaxis is drugs, and a good anaphylaxis management can be lifesaving in hospitalized patients (9).

The most important laboratory test used in the diagnosis of anaphylaxis is the measurement of the tryptase level. The tryptase level measured 24 hours after the patient's symptoms have resolved should be considered the baseline value. An increase in tryptase level of 20%+2 ng/ml compared to the basal level during the reaction supports the diagnosis of anaphylaxis (10). Tryptase measurement is not done in every laboratory and unfortunately the results come out days or even weeks later in laboratories that can measure it. This increases the importance of the clinical picture in the diagnosis of anaphylaxis.

**Table I: Diagnostic criteria for anaphylaxis.**

<p><b>Anaphylaxis is highly likely when any ONE of the following three criteria is fulfilled:</b></p> <p><b>1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both. (E.g., †, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)</b></p> <p><b>And at least one of the following:</b></p> <p>A. Respiratory compromise. (E.g., †, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)</p> <p>B. Reduced *BP or associated symptoms of end-organ dysfunction. (E.g., †, hypotonia, collapse, syncope, incontinence)</p> <p><b>2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):</b></p> <p>A. Involvement of the skin mucosal tissue. (E.g., †, generalized hives, itch-flush, swollen lips-tongue-uvula)</p> <p>B. Respiratory compromise. (E.g., †, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)</p> <p>C. Reduced *BP or associated symptoms. (E.g., †, hypotonia, collapse, syncope, incontinence)</p> <p>D. Persistent gastrointestinal symptoms. (E.g., †, crampy abdominal pain, vomiting)</p> <p><b>3. Reduced *BP after exposure to a known allergen for that patient (minutes to several hours):</b></p> <p>A. Infants and children - Low systolic *BP (age-specific) or greater than 30% decrease in systolic *BP.</p> <p>B. Adults - Systolic *BP of less than 90 mmHg or greater than 30% decrease from that person's baseline.</p>
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\*BP: Blood Pressure, † E.g.: Example given, ‡ Table I is taken from 'Anaphylaxis: Turkish National Guideline 2018'.

**Table II: Anaphylaxis signs and symptoms.**

Systems	Symptoms and sings	Incidence (%)
<b>Skin</b>	Feeling of warmth, flushing (erythema), itching, urticaria, angioedema, and “hair standing on end” pilo erection, Itching or tingling of lips/ tongue/ palate, Edema of lips/tongue/ uvula, Periorbital itching/ erythema/ edema, tearing, and conjunctival erythema.	80-90
<b>Respiratory</b>	Nose - Itching, congestion, rhinorrhea, and sneezing Laryngeal - Itching and “tightness” in the throat, dysphonia, hoarseness, stridor. Lower airways - Shortness of breath (dyspnea), chest tightness, cough, wheezing, and cyanosis.	70
<b>Gastrointestinal</b>	Nausea, abdominal pain, vomiting, diarrhea, and dysphagia.	30-45
<b>Cardiovascular</b>	Feeling of faintness or dizziness; syncope, altered mental status, chest pain, palpitations, tachycardia, bradycardia or other dysrhythmia, hypotension, tunnel vision, difficulty hearing, urinary or fecal incontinence, and cardiac arrest.	10-45
<b>Neurologic</b>	Anxiety, apprehension, sense of impending doom, seizures, headache and confusion.	10-15
<b>Other</b>	Uterine cramps in women and girls, metallic taste.	

§ Table II is taken from ‘Anaphylaxis: Turkish National Guideline 2018’.

Anaphylaxis is the most severe allergic reaction that can result in mortality and should be treated promptly after diagnosis. It is very important to cut off contact with the antigen that causes anaphylaxis after the patient’s vital signs (blood pressure, heart rate, saturation measurement with pulse oximetry, etc.) are measured. To prevent the empty ventricle syndrome, the patient should be laid on his back and the legs should be raised. Thus, the venous return to the heart will increase and cardiac output will be preserved (11). Oxygen (8-10 L/min) support should be provided to the patient with a mask. The first drug to be given in treatment is adrenaline. With adrenaline; Alpha-1 adrenergic receptors are activated and vasoconstriction increases, peripheral vascular resistance increases, mucosal edema decreases, inotropy and chronotropy increase with activation of beta-1 adrenergic receptors, and bronchodilation develops with activation of beta-2 adrenergic receptors (12). Adrenaline is administered intramuscularly to the vastus lateralis muscle. The dose of adrenaline is 0.5 ml of 1 mg/mL (1:1000) in the adult patient, 0.01 mL/kg of 1 mg/mL (1:1000) in pediatric patients, and the maximum adrenaline dose is 0.30 mg. If symptoms and signs of anaphylaxis persist, im adrenaline is administered several times at intervals of 5-15 minutes. Intravenous (iv) adrenaline is given to patients whose signs and symptoms of cardiogenic shock persist despite at least 3 injections of im adrenaline. During iv adrenaline therapy, patients should be monitored for cardiac arrhythmias. Intravenous adrenaline is started at a dose of 2-10 µg/min in adult patients and at a dose of 0.1-1 µg/kg/min in pediatric patients. It can be increased up to 10 µg/min in pediatric patients (13).

After the adrenaline treatment, the patient is given iv fluid replacement. This can be started with 10-20 ml/kg saline in 10 minutes and fluid replacement up to 100 ml/kg can be administered according to the patient’s clinic. After adrenaline, the patient is given H1 antihistamine treatment. This treatment can be administered iv, im, or orally. If necessary, antihistamine treatment can be repeated in 4-6 hours. 2 mg/kg of methylprednisolone (maximum 50 mg) can be administered im, iv, or orally. If necessary, the treatment can be repeated at intervals of 4-6 hours.

The European Society of Allergy and Clinical Immunology (EAACI) recommends monitoring for 6-8 hours in cases with respiratory complaints due to anaphylaxis, and monitoring for 12-24 hours in patients presenting with circulatory disorders (14). Depending on the severity of anaphylaxis, patients should be kept under observation in the emergency room or intensive care unit.

Anaphylaxis is the most severe allergic reaction that is also life threatening and its prevalence is increasing so that physicians will encounter it in almost every branch. It has been shown that there are deficiencies in the definition and management of anaphylaxis. There is confusion about the dose and the route of adrenaline administration, especially the fact that adrenaline is the first choice in treatment.

In this study, our aim was to measure the awareness of anaphylaxis diagnosis and treatment of doctors working in different branches of a 3<sup>rd</sup> Stage Training and Research Hospital. Doctors from twenty different branches participated in the study.

### Subject of Study

This study was designed as a cross sectional study. From July 2022 to August 2022, a questionnaire was administered to 85 doctors from different branches working at the Training and Research Hospital, a tertiary medical institution in Erzurum, about the diagnosis and treatment of anaphylaxis. Eligibility criteria were as follows: Volunteering to participate in the study and working as a doctor in Erzurum Training and Research Hospital.

### Research Methods

Written consent was obtained from the all participants. The content of the questionnaire consisted of two parts, demographic characteristics and questions about the diagnosis and treatment of anaphylaxis. Evaluation questionnaire for anaphylaxis;

- 1) Age?
  - a) 24-30
  - b) 31-40
  - c) 41-50
  - d) 51-64
  - e) Over 65
- 2) Gender?
  - a) Female
  - b) Male
- 3) How many years of professional experience do you have?
  - a) 1-3
  - b) 4-10
  - c) 11-15
  - d) 16-20
  - e) Over 20
- 4) What is your professional title?
  - a) General Practitioner
  - b) Specialist Physician (..... Specialist)
- 5) Have you ever received training on anaphylaxis before?
  - a) Yes
  - b) No (Please proceed to Question 7)
- 6) Where did you receive the training on anaphylaxis?
  - a) Faculty of Medicine
  - b) Medical residency training
  - c) Pharmaceutical meetings
  - d) Other .....
- 7) What are the diagnostic criteria for anaphylaxis? (You can write more than one option)
  - I. Involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
  - II. Respiratory compromise (e.g., dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
  - III. Reduced blood pressure or associated symptoms (e.g., hypotonia, collapse, syncope, incontinence)
  - IV. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)
- 8) What is the first medical treatment you will apply to the patient you have diagnosed with anaphylaxis? (tick only one option)
  - a) Antihistamine
  - b) Steroids
  - c) Fluid replacement
  - d) Intravenous adrenaline
  - e) Intramuscular adrenaline
- 9) How long do you keep the patient under observation for anaphylaxis
  - a) Until the patient's complaint is improved
  - b) 1-2 hours
  - c) 6-8 hours
  - d) 24 hours

The questionnaire was administered face to face and the subjects were asked to complete the questionnaire without a time limit. The study was conducted with the decision of the ethics committee of Erzurum Training and Research Hospital, numbered E-37732058-514.99.

Export to IBM SPSS Statistics for data analysis, 23.0 (IBM Co., Armonk, NY, USA) was used. We used chi-square test for categorical variables. Categorical variables were given as “%” and parametric ones were expressed as “mean  $\pm$  standard deviation”.  $P < 0.05$  was regarded as statistically significant

## RESULTS

Physicians from various branches of surgery and internal medicine participated in the study together with general practitioners, and the average age of the 85 physicians participating in the study was 42.6 years. The participation rate in the study was 65% for men and 35% for women. In the study, 8 of the doctors participating were general practitioners, twenty six were medical residency students, and fifty one were working as specialist physicians in the tertiary hospital. The demographic characteristics of the participants are shown in Table III. The majority of the participants (83.5%) stated that they had encountered anaphylaxis before. There was no statistical difference between professional experience and the anaphylaxis encounter rate ( $p=0.76$ ). The majority of the participants (89.4%) stated that they received training on anaphylaxis throughout their medical education life. The number of participants who stated that they received anaphylaxis training during their specialty training in medicine was 20%, and the only 1 participant stated that he received anaphylaxis training at the pharmaceutical company meeting.

Only 4 participants correctly marked the anaphylaxis diagnostic criteria. While 85% of the participants marked the combination of skin and respiratory signs and symptoms for diagnosis, only 15% marked the combination of cardiovascular and gastrointestinal system signs and symptoms for diagnosis. A statistically significant difference was found between the branches and the correct diagnosis ( $p=0.03$ ). There was no statistically significant difference between professional experience and correct diagnosis ( $P=0.92$ ). When the participants with and without anaphylaxis experience were compared in terms of the diagnosis, no statistically significant difference was found ( $p=0.48$ ).

**Table III: The demographic characteristics of the participants.**

<b>Gender</b>	<b>Female (N=30, 35%)</b>	<b>Male (N=55, 65%)</b>
<b>Age of doctors</b>	<b>n</b>	<b>%</b>
24-30 Years	21	25
31-40 Years	44	52
41-50 Years	16	19
51-64 Years	4	4
<b>Branch</b>	<b>n</b>	<b>%</b>
Emergency Room	11	13
Family physician	1	1
Allergy and immunology	2	2
Anesthesia	1	1
Internal medicine residency students	26	31
Internal medicine	1	1
Dermatology	3	4
Endocrinology and metabolic diseases	2	2
Infectious diseases and clinical Microbiology	2	2
Gastroenterology	3	4
General surgeon	3	4
Pulmonary disease	1	1
Hematology	2	2
Nephrology	1	1
Neonatology	1	1
Orthopedics and traumatology	4	5
Pediatrics	5	6
Plastic surgeon	1	1
General practitioner	8	9
Radiology	3	4
Rheumatology	1	1
Urology	3	4
<b>Professional experience (years)</b>	<b>n</b>	<b>%</b>
1-3	12	14
4-10	37	44
11-15	21	25
16-20	7	8
20	8	9
<b>Anaphylaxis education</b>	<b>n</b>	<b>%</b>
Medical school	31	36
Medical school and medical residency training	25	30
Medical school and medical residency training, pharmaceutical meetings	2	2
Medical residency training	17	20
Pharmaceutical meetings	1	1
Not trained in anaphylaxis	9	11

In the treatment of anaphylaxis, fifty five participants stated im adrenaline, and ten participants im adrenaline and fluid replacement as the first medication option. Unfortunately twenty participants did not administer im adrenaline as first line therapy. When we excluded allergy physicians, there was no statistically significant difference between the branches and correct treatment ( $P=0.19$ ). There was no statistically significant difference between professional experience and correct treatment ( $P=0.39$ ).

The majority of the participants (81%) recommended that the patient be kept under observation for at least 8-24 hours due to the risk of biphasic anaphylaxis. There was no statistical difference between the branches and the observation time due to the risk of biphasic anaphylaxis ( $p=0.09$ ).

## DISCUSSION

The incidence and prevalence of anaphylaxis increased over time. In our study, the anaphylaxis observance rate of new physicians was 83%. It was observed that the physicians who stated that they did not encounter anaphylaxis did not know the diagnostic criteria for anaphylaxis. The fact that 14% of the physicians with 16-20 years of professional experience stated that they had not encountered anaphylaxis suggests that the diagnosis of anaphylaxis was missed. Knowing the diagnosis and treatment of anaphylaxis, which is the most severe allergic reaction, by all branch physicians prevents anaphylaxis-related mortality and morbidity. For this reason, it is necessary to provide training on the diagnosis and treatment of anaphylaxis, both during medical education and during residency training.

The majority of the physicians participating in the study stated that they received training on anaphylaxis during their medical education. When the training fields are examined, thirty one received training at the medical school, twenty five during the medical school and specialization training, seventeen during the specialization training, two at the specialty training and pharmaceutical company meetings, and 1 physician at the pharmaceutical company meetings. In medical school education, the diagnosis and treatment of anaphylaxis is explained to all students within the curriculum. The fact that only thirty one physicians stated that they received anaphylaxis training at the medical faculty shows that the education provided is not permanent (15). Unfortunately nine physicians stated that they did not receive any training on anaphylaxis.

In the study conducted by Baççioğlu and Yılmaz, 992 (84.7%) participants answered the questions about the symptoms of anaphylaxis correctly. In our study, this rate was only 4.7% (16). Most of the participants (85%) did not accept gastrointestinal and cardiovascular system symptoms and signs as anaphylaxis criteria. However, respiratory and cardiovascular systems are most frequently affected in cases of fatal anaphylaxis (6). Apart from allergy specialists, one emergency specialist and one internist marked the correct diagnostic criteria, these answers showing that the training that should be given about anaphylaxis was independent of the branches.

The majority of the participants (70%) stated that the first medical treatment to be administered during anaphylaxis is adrenaline. The most common mistake in the treatment of anaphylaxis is not administering adrenaline or the incorrect administration of iv adrenaline (17, 18). As a matter of fact, 8 physicians who participated in our study marked iv adrenaline as the first treatment option for anaphylaxis.

The incidence of biphasic anaphylaxis ranges from 0.4% to 21%. Due to the possibility of biphasic anaphylaxis, it is recommended to keep patients under observation for at least 8 hours in international guides (19). Sixty nine (81%) physicians stated that patients should be kept under observation for 8-24 hours.

## CONCLUSION

Every physician may encounter anaphylaxis. Therefore, all physicians should be knowledgeable about the diagnosis and treatment of anaphylaxis. In our study, we found that regardless of professional experience and branch, physicians had insufficient knowledge especially in terms of anaphylaxis diagnostic criteria, anaphylaxis treatment, and observation time. We think that it would be beneficial to provide physicians with in service training regarding the diagnosis and management of anaphylaxis.

### Ethics Approval

This study was approved by the institutional review board, College of Medicine Research Center, Erzurum Training and Research Hospital (reference number 2022/08-102). All patient data were confidential and used for research purposes only, and all the patients were coded with a serial number without mentioning their names. Informed consent was obtained from the patients. This study was conducted in accordance with the Declaration of Helsinki.

### Conflict of Interest

The authors have no conflicts of interest to declare.

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**Author Contributions**

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