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Azam Mohsenzadeh

Department of Pediatrics, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

Fatemeh Sohrabi

Department of Allergy and Clinical Immunology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

Masoud Movahedi

Department of Allergy and Clinical Immunology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

Nima Parvaneh

Department of Allergy and Clinical Immunology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

Mansoureh Shariat

Department of Allergy and Clinical Immunology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

Mohammad Gharagozlou (✉ tsabooteh@yahoo.com)

Department of Allergy and Clinical Immunology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

Toomaj Sabooteh

Department of Immunology, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

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Risk factors, clinical symptoms, diagnostic methods, management and treatment of patients with anaphylaxis in Tehran

Azam Mohsenzadeh^{1,2}, Fatemeh Sohrabi², Masoud Movahedi², Nima Parvaneh², Mansoureh Shariat², **Mohammad Gharagozlou***², Toomaj Sabooteh³

1- Department of Pediatrics, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

2- Department of Allergy and Clinical Immunology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

3- Department of Immunology, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

Azam Mohsenzadeh, mohsenzadehazam@gmail.com

Masoud Movahedi, movahedm1@gmail.com

Nima Parvaneh, nparvaneh@icloud.com

Mansoureh Shariat, m_Shariat@tums.ac.ir

Toomaj Sabooteh, tsabooteh@yahoo.com

Corresponder: Mohammad Gharagozlou, gharagoz@tums.ac.ir

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Abstract

Introduction: Recent studies have evaluated the risk factors, clinical symptoms, diagnostic methods, management and treatment of anaphylaxis in different populations, but the results of various studies are contradictory. The aim of this study was to evaluate the risk factors, clinical symptoms, diagnostic methods, management and treatment of anaphylactic patients referred to the Children's Medical Center of Tehran during the years 2015-2016.

Materials and Methods: In this cross-sectional study, 30 patients with anaphylaxis were studied. The study population included all patients who had been diagnosed with anaphylaxis without age limitation and during the period from 2015 to 2016 to undergo serum beta-tryptase examination were referred to the laboratory of the Children's Medical Center of Tehran. The sampling method was census-based and the information was collected through a pre-designed questionnaire by examining patient files or telephone contacts with patients. After collecting data, the data were entered into SPSS 22 software and analyzed statistically. Finally, $P < 0.05$ was considered statistically significant.

Results: In our study, we investigated 30 patients with anaphylaxis, an average age of 25 ± 15 years (range 2 to 60 years) among which 13 (43%) were men and 17 (57%) women. The most important cause of anaphylaxis in the studied patients was foods (57%), followed by drugs (20%), unknown (20%) and pollen plants (3%). About 33.7% of patients had allergies to specific allergens. The most routes of exposure with allergens were, oral (56.3%), intravenous (18.7%), unknown (12.6%) and cutaneous (3.1%), respectively. 33.6% of them had positive skin tests. The most common symptoms of anaphylaxis in order of frequency were respiratory (72.9%), cutaneous (48.8%), cardiovascular (18.6%) and gastrointestinal symptoms (6%). Eighty percent of anaphylaxis occurred at home. The most commonly prescribed medications were corticosteroids (83.3%), antihistamine (76%), epinephrine (60%) and beta-agonists (3%). Only 30% of the patients had access to Epipen.

Conclusion: According to the results of this study, since most anaphylactic reactions occur in the home and more than one-third of patients had allergic to certain allergens and two-thirds of patients had a history of anaphylaxis, it seems that by providing the necessary training and knowledge to individuals with regard to allergenic substances or allergenic drugs, as well as increased access for patients to Epipen, we can prevent the occurrence and risk of subsequent anaphylaxis in these people.

Keywords: Risk Factors, Clinical Symptoms, Diagnostic Methods, Management and Treatment, Anaphylaxis

1. Introduction

Anaphylaxis, the most severe manifestation of an acute allergic reaction which may involve life-threatening airway, breathing, or circulation problems, is a medical emergency and in rare cases may cause death (1). It typically causes more than one of the following: throat or tongue swelling, an itchy rash, vomiting, shortness of breath, low blood pressure and lightheadedness. These symptoms typically come on over minutes to hours (2). Although in many recent studies reported an increase in the incidence of anaphylaxis, it is difficult to establish the true incidence (3-5). Based on several studies, the estimated prevalence of anaphylaxis is 0.3-5.1% and the estimated incidence is between 50-112 episodes per 100.000 personyears (6). The mechanism involves the release of mediators from certain types of white blood cells triggered by other immunologic or non-immunologic mechanisms (7).

Several factors that may play a role in anaphylaxis; included host behavior-related factors (alcohol, risk taking, exercise, medication), allergen-related factors (host immunoglobulin IgE levels and binding affinity, food processing and matrix, type of food consumed, dose ingested, host cellular responses), as well as other intrinsic and extrinsic factors (age, gender, sex, allergic rhinitis, asthma, immune activation, cardiovascular disease) (8). In children, cow's milk is also a common cause (3) and Specifically, peanuts and tree nuts are most commonly reported as causes of severe anaphylaxis and have been associated with fatalities (9). Other causes include latex exposure and exercise. Additionally, cases may occur without an obvious reason (10).

Diagnosis is based on the presenting signs and symptoms after exposure to a potential allergen. Anaphylaxis diagnosis through biomarkers such as Tryptase and other inflammatory mediators, Skin testing, Serology and specific IgE, Specific IgE drugs, Basophil activation test and so on (11).

Based on several studies the causes of anaphylaxis indicates that drugs, insect venom and food are the most frequent triggers (12,13). Anaphylaxis can present with various clinical symptoms involving different organ systems including the respiratory tract, skin, the cardiovascular system and gastrointestinal. In 80–90% of reported episodes, most frequent symptom was the involvement of the skin (14,15). In up to 70% of patients, the respiratory tract is affected, and have been reported the gastrointestinal tract and the cardiovascular system to be less frequently involved (13,14).

Care of patients with anaphylaxis involves consideration of both the acute, emergency treatment of reactions and long-term care, which aims to reduce the risk of further reactions

and improve outcomes if, despite these measures, a further reaction ensues (16). The primary care and management of anaphylaxis is epinephrine injection into a muscle, positioning the person flat and intravenous fluids (17). In recent studies interventions for the acute management of anaphylaxis (such as Adrenaline (18), Glucocorticosteroids (19,20), Antihistamines (21), Methylxanthines (22) and etc) and pharmacological and nonpharmacological approaches for the long-term management of anaphylaxis (such as Venom immunotherapy (VIT) (23), Educational interventions (24), Psychological interventions (25), Prophylactic interventions (26), and etc) has been investigated.

The aim of this study was to evaluate the risk factors, clinical manifestations, diagnostic methods, management and treatment of anaphylaxis patients referred to Children's Medical Center of Tehran during the years 2015-2016. This article has been written based on the STROBE Guideline (27).

2. Materials and Methods

2-1. Study design

The present study was conducted in a cross-sectional study between 2015 and 2016.

2-2. Setting

In this study, all patients who had been diagnosed with anaphylaxis without age limitation and during the period from 2015 to 2016 to undergo serum beta-tryptase examination were referred to the laboratory of the Children's Medical Center of Tehran and had inclusion criteria and had not exclusion criteria. All patients were monitored by an allergist.

2-3. Participants

The inclusion criteria were all patients, including children and adults referring to the laboratory of the Children's Medical Center for measuring the serum level of beta-tryptase with the diagnosis of anaphylaxis. Also, patients who were not willing to cooperate for any reason for completing the questionnaire, were excluded.

2-4. Variables

In this study, patients' data including age, sex, risk factors, diagnostic methods, clinical symptoms and management and treatment methods were collected through a pre-designed questionnaire by examining patient files or telephone contacts with patients.

2-5. Data sources/ measurement

At the beginning of the study, the demographic information and clinical information of patients were obtained using a questionnaire.

2-6. Study size

The sampling method was census-based, so it was not necessary to determine the sample size.

2-7. Statistical methods

After collecting data, the data were entered into SPSS 22 software and analyzed statistically. Descriptive statistics, frequency, percentage and average of collecting data were presented in statistical tables. Analytical statistics (t-test and chi-square) were used to measure the association and the effect of variables. Finally, $P < 0.05$ was considered statistically significant.

2-8. Limitations

The limitations and problems of the implementation of this study include the limited number of patients, the failure to record the contact numbers of some patients in the laboratory, the inaccuracy in responding to the questionnaire by the patients, incomplete information in the records of patients and the lack of access to all records of files patients.

2-9. Ethics

The Ethics Committee of Tehran University of Medical Sciences approved this project. People were volunteered to enter this research. Also, all patient information was considered as a secret, and any disclosure was refused. Identification codes were used to prevent the registration of patients' names and surnames. The data were confidential and recorded as SPSS software as numerical codes.

3. Results

3-1. Study Participants

In this cross-sectional study, 30 patients with anaphylaxis with an average age of 25 ± 15

years (in the range of 2 to 60 years) were evaluated for risk factors, clinical symptoms, diagnostic methods, management and treatment of anaphylaxis patients referred to Children's Medical Center of Tehran during 2015-2016. In patients 13 (43%) were men with an average age of 20 ± 11 years and 17 (57%) were women with an average age of 28 ± 16.5 years. Based on t-test, there was no significant difference between the mean age of two groups ($P=0.128$). The mean age at the first anaphylactic reaction was 21.6 ± 14.9 years (range of 1.5-53 years), in men 17 ± 11 years and in women 25 ± 17 years ($P=0.125$).

3-2. Risk Factors

The results of the present study on the types of allergens and the risk factors for allergy in patients showed that the frequency of allergen types that caused allergies in patients were foods (57%), drugs (20%), unknown (20%) and pollen plants (3%) respectively ($P=0.001$). The incidence of allergies was more pronounced in autumn (56.7%), spring (26.7%), winter (10%) and summer (6.6%) respectively ($P=0.001$). Also, the month of November (47%) ($P=0.465$) had the highest incidence of allergy symptoms. The most ways of exposure to allergens were respectively oral (56.3%), intravenous (18.7%), unknown (12.6%), dermal (3.1%), inhalation (3.1%), intramuscular injection (3.1%) and Intrathecal (3.1%) ($P<0.001$). Also, the most common causes of lead to exacerbation of anaphylaxis symptoms in patients, respectively were stress (27%), temperature increase (17%), exercise (10%) and menstruation (3%) ($P=0.001$). Factors leading to recurrence of symptoms after epinephrine injection, were foods (75%) and drugs (25%). Also, In patients studied, family history of allergy was 57% ($P=0.456$), history of anaphylaxis was 60% ($P=0.273$), having symptoms of asthma before the onset of anaphylaxis symptoms was 3.3% ($P<0.001$), the use of Salbutamol Prior to the onset of anaphylaxis in 3.3% ($P<0.001$), history of previous allergies to a specific allergen was 33.7% ($P=0.144$) and symptom exacerbations was 46.7% ($P=0.633$). None of the patients had a positive family history of anaphylaxis. The most frequent symptoms of anaphylactic times, at 10 am (30%) and 17 pm (23.3%). About 43.3% of the cases of anaphylactic symptoms were in the time range of 10am to 12am ($P<0.001$).

3-3. Diagnostic Methods

The results of the present study on allergy diagnosis in patients showed that allergy was diagnosed in 11 (36.6%) patients, of which 10 (33.3%) were identified by skin test and 1 (3.3%) patients were diagnosed with RAST method ($P<0.001$). Also, the median duration of

exposure to allergen to symptoms was 30 minutes, with a time interval of between 0 and 4 hours. Figure 1 shows that the distribution of this interval time is not normal. For this reason, there was no possibility of reporting the mean time and the median index was used.

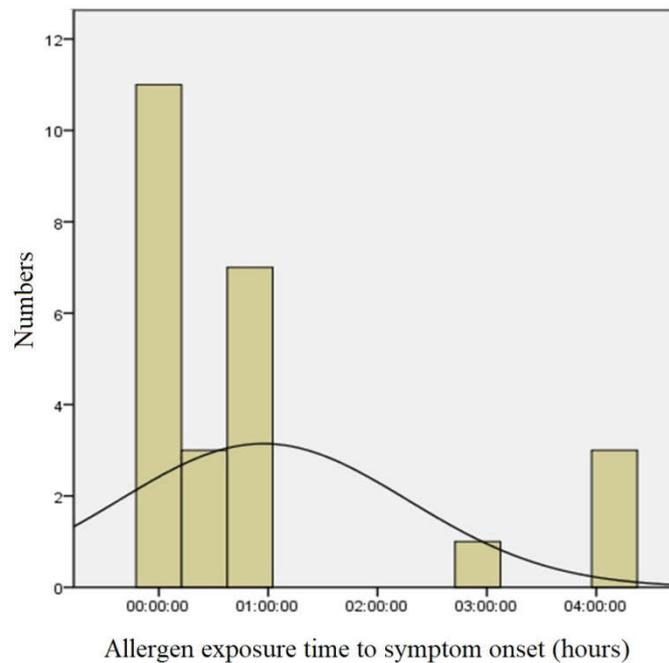


Figure 1. Histogram of the allergen exposure time to symptom onset

3-4. Clinical Signs and Symptoms

The results of this study showed that the most common symptoms were respiratory (72.9%), dermal (48.8%), cardiovascular (18.6%) and gastrointestinal (6%) respectively ($P < 0.001$). Also, the first symptom was erythema (50%), itching (20%), hives (10%), dyspnea (6.7%), tachypnea (3.3%), hypotension (3.3%), swollen throat and mouth (3.3%) and angioedema (3.3%) ($P < 0.001$). None of the patients had nightly waking with signs of asthma. The severity of the symptoms was severe in 93.3% of patients and moderate in 6.7% ($P < 0.001$). Anaphylactic symptoms occurred mostly at home (80%) ($P < 0.001$). The frequency distribution of the types of skin, cardiovascular and respiratory symptoms are listed in Table 1.

Table 1. Frequency distribution of types of skin, cardiovascular and respiratory symptoms in patients under study

Types of Symptoms	Symptoms	Number (n=30)	Percentage	P-value
Skin Symptoms	Erythema	23	76.7	0.001*
	Itching	23	76.7	0.003*
	Angioedema	10	33.3	0.068
	Hives	4	13.3	0.001*
Cardiovascular Symptoms	Hypotension	11	36.7	0.144
	Collapse	6	20	0.001*
	Tachycardia	2	6	0.001*
	Warmness	1	3	0.001*
Respiratory Symptoms	Wheezing	20	66.7	0.068
	Dyspnea	20	66.7	0.068
	Tachypnea	15	50	0.99
	Cyanosis	10	33.3	0.068
	Stridor	7	23.3	0.003*
	Cough	4	13.3	0.001*

* No statistically significant difference ($P < 0.05$)

3-5. Management and Treatment

The results of this study about management and treatment in patients showed that 93.3% of patients were treated in emergency departments ($P < 0.001$). Epinephrine injection was performed in 55.6% of patients by the patient, 33.3% by the parents and 11.1% by the physician ($P = 0.264$). Only one patient (3.3%) called to Emergency calls. Only 30% of patients with history of anaphylaxis, had access to an Epipen ($P = 0.001$). Also, the return of symptoms and the need for the second injection of epinephrine in 44.4% ($P = 0.754$), the referral to the hospital after epinephrine injection in 77.8% ($P = 0.144$), post-treatment follow up in 90% ($P = 0.001$), Epipen prescribing in 90% ($P = 0.001$), antihistamines prescribing in 84.3% ($P = 0.001$) and anaphylaxis symptoms training were observed in 84.3% ($P = 0.001$). The frequency distribution of effective factors in the management and treatment of patients is listed in Table 2.

Table 2. Frequency distribution of effective factors in the management and treatment of patients under study

Variables		Number (n=30)	Percentage	P-value
Types of treatments outside the health centers	Epinephrine	9	30	0.001*
	Antihistamine	5	16.6	
Types of treatments in health centers	Corticosteroids	25	83.3	0.001*
	Antihistamine	23	76	0.001*
	Epinephrine	28	60	0.273
	Agonist of beta 2 receptors	1	3	0.003*
The interval time between the use of Epipen after symptoms start	0-5 minutes	5	55.6	0.264
	5-15 minutes	3	33.3	
	15-30 minutes	1	11.1	
Feeling remission after injection	0-5 minutes	1	11.1	0.044*
	5-15 minutes	6	66.7	
	15-30 minutes	2	22.2	

* No statistically significant difference (P<0.05)

4. Discussion

Anaphylaxis can present with various clinical symptoms involving different organ systems including the respiratory tract, skin, the cardiovascular system and gastrointestinal (14,15). Care of patients with anaphylaxis involves consideration of both the acute, emergency treatment of reactions and long-term care, which aims to reduce the risk of further reactions and improve outcomes if, despite these measures, a further reaction ensues (16).

So far, various studies have been carried out to investigate the risk factors, clinical symptoms, diagnostic methods, management and treatment of patients with anaphylaxis in different populations, which reported different results. The aim of this study was to investigate the risk factors, clinical symptoms, diagnostic methods, management and treatment of anaphylaxis patients referred to the Tehran Children's Medical Center during the years 2015-2016.

4-1-1. Study Participants

In this study, which performed on 30 patients with anaphylaxis, it observed that most of the patients were female (43% male vs. 57% female). However, in some similar studies, most patients are male. In a study by Nogic et al. in 2016, in 55 children with anaphylaxis in Melbourne, Australia, most of the patients were boys (62% boys vs. 38% girls) (28).

Similarly, in other similar studies, 55-70% of the patients were boys (29-32). However, in none of these studies gender differences were statistically significant in patients.

4-1-2. Risk Factors

In this study, the most common cause of anaphylaxis was foods (57%). These results are consistent with the results of most similar studies. In a study by Gaspar et al. in 2015, on 64 children with anaphylaxis in Lisbon, Portugal, also the most important cause of anaphylaxis was food (84%) (30). Also in other similar studies, foods reported in 35-75% causes of anaphylaxis (28,29,31,33-36). On the other hand, in a study by Dibs et al. On 55 Pennsylvanian children with anaphylaxis, the most important cause of anaphylaxis, reported latex (27%) (37). Although in other studies, latex less than 6% of the anaphylaxis agent reported (33,36). In a study by Cianferoni et al. in 2004 on 76 Italian children, showed Food to be the most important cause of anaphylaxis in children with lower age, eczema and gastrointestinal symptoms. While exercise and physical activity are the most 10 important causes of anaphylaxis in children of higher age, hives and angioedema symptoms (36). Another study also stated that foods were the most important cause of anaphylaxis at lower ages, and insect bites and drugs were the most important cause of anaphylaxis in the higher ages (29). On the other hand, in a study conducted by Rolla et al in 2013 on 778 patients with anaphylaxis in Italy, reported that among the various foods, milk and eggs, the most important cause of anaphylaxis in lower ages and peaches, vegetables and sea foods were the most important cause of anaphylaxis in the higher ages (34).

In the present study, the drugs (20%) were the second leading cause of anaphylaxis. These results were in line with the results of a study by Sole et al., Conducted in 2012 on 191 Brazilian children. In this study, drugs (27.7%) were the second leading cause of anaphylaxis (29). In some studies, anaphylaxis with drugs reported to be between 10% and 16% (33,36,37). In some studies, insect bites caused anaphylaxis in 7-26% of cases (29,33,35,36). Also, In other studies, nuts caused anaphylaxis in 20-40% of cases (28,38). In the present study, idiopathic agents were cause for 20% of anaphylaxis cases. However, in other studies, 5-15% of anaphylaxis cases occurred by idiopathic agents (29,36).

In the present study, 33.7% of the patients were allergic to specific allergens. Similar studies also reported that 30-35% of patients were allergic to specific allergens (33,37). In the present study, the most common way of exposure to allergens was oral (56.3%), intravenous (18.7%), idiopathic (12.6%) and dermal (3.1%) respectively. In another study, the most common methods of contacting allergens were intravenous (38%), oral (27%) and cutaneous

(20%) respectively (37). In the present study, 60% of patients had a history of anaphylaxis. However, in other similar studies reported, 30-40% of patients had history of anaphylaxis (30,31,35).

4-1-3. Diagnostic Methods

In the present study, allergy detected in 11 patients (36.6%) with different diagnostic methods, of which 10 (33.3%) positive skin test and one (3.3%) had a positive RAST test. These results were in line with the results of Barzegar et al., Which conducted in 2010 on the Iranian population. In their study, 24% of patients had a positive skin test (31). Another study found that 79% of patients who had an anaphylaxis with at least one oral or inhaler allergen, had a positive skin test. Also, all patients who had anaphylaxis by insect bites, had a negative skin test (36).

4-1-4. Clinical Signs and Symptoms

In the present study, respiratory symptoms (72.9%) were the most symptoms of anaphylaxis in the studied patients. Respiratory symptoms in some other studies, the most common anaphylaxis symptoms reported (35,36). In a study conducted by Shokouhi et al in 2016 on 78 children in Tehran, respiratory symptoms (63.3%) were the most common anaphylaxis symptoms (32).

In the present study, skin symptoms (48.8%) were the second most common anaphylaxis symptoms in the patients. While in some other studies, dermatological symptoms reported as the first common anaphylaxis symptom (28,29,37). In a study by De Swert et al in 2008 on 48 children with anaphylaxis in Belgium, reported that 96.9% of patients had dermatologic symptoms (33). Also, in a study by Gaspar et al. In 2015, 94% of patients had dermatologic symptoms (30). In the present study, 18.6% of patients had cardiovascular symptoms. In similar studies, 15-25% of patients had cardiovascular symptoms (30,36). In the present study, 6% of patients had gastrointestinal symptoms. However, in some similar studies, 20-40% of the patients had gastrointestinal symptoms (30,32,33). Another study reported that lower age children, often have gastrointestinal symptoms and higher age children, often have respiratory and cardiovascular symptoms (34).

In the present study, 46.7% of patients had severe anaphylaxis. In another study, 27% of patients had severe anaphylaxis (37). In a study by Sicherer et al, in 2001 in New York, on 5149 children, showed that patients with a history of asthma and history of accidental

ingestion, have severe anaphylaxis (38). In the present study, 80% of cases of anaphylaxis occurred at home. In most similar studies, anaphylaxis has occurred most often at home (28,33,35). In a study by Grabenhenrich et al in 2016 on 1970 children in 10 European countries, reported that 81% of anaphylaxis occurred at home (35).

In the present study, the most commonly prescribed drugs in health centers for anaphylaxis patients were corticosteroids (83.3%), antihistamine (76%), epinephrine (60%) and beta agonists (3%). In another study in Belgium, antihistamine (71.9%), corticosteroids (45.6%) and beta-agonists (24.6%) were the most commonly prescribed drugs in the health centers (33). In the present study, 30% of patients had access to Epipen. In similar studies, access to Epipen reported at about the same level (10-35%) (29,30,33,35,38).

5. Conclusion

According to the results of this study, since most anaphylactic reactions occur in the home and more than one-third of patients had allergic to certain allergens and two-thirds of patients had a history of anaphylaxis, it seems that by providing the necessary training and knowledge to individuals With regard to allergenic substances or allergenic drugs, as well as increased access for patients to Epipen, we can prevent the occurrence and risk of subsequent anaphylaxis in these people.

It suggested that in future studies, this study should conducted with a larger sample size in different populations. Also, in future studies, in order to assess the knowledge of patients with anaphylaxis, about the risk factors, diagnostic methods, symptoms, and management and treatment of anaphylaxis, designed and implemented.

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7. Conflicts of interest

There are no conflicts of interest between the authors of the article.

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Figures

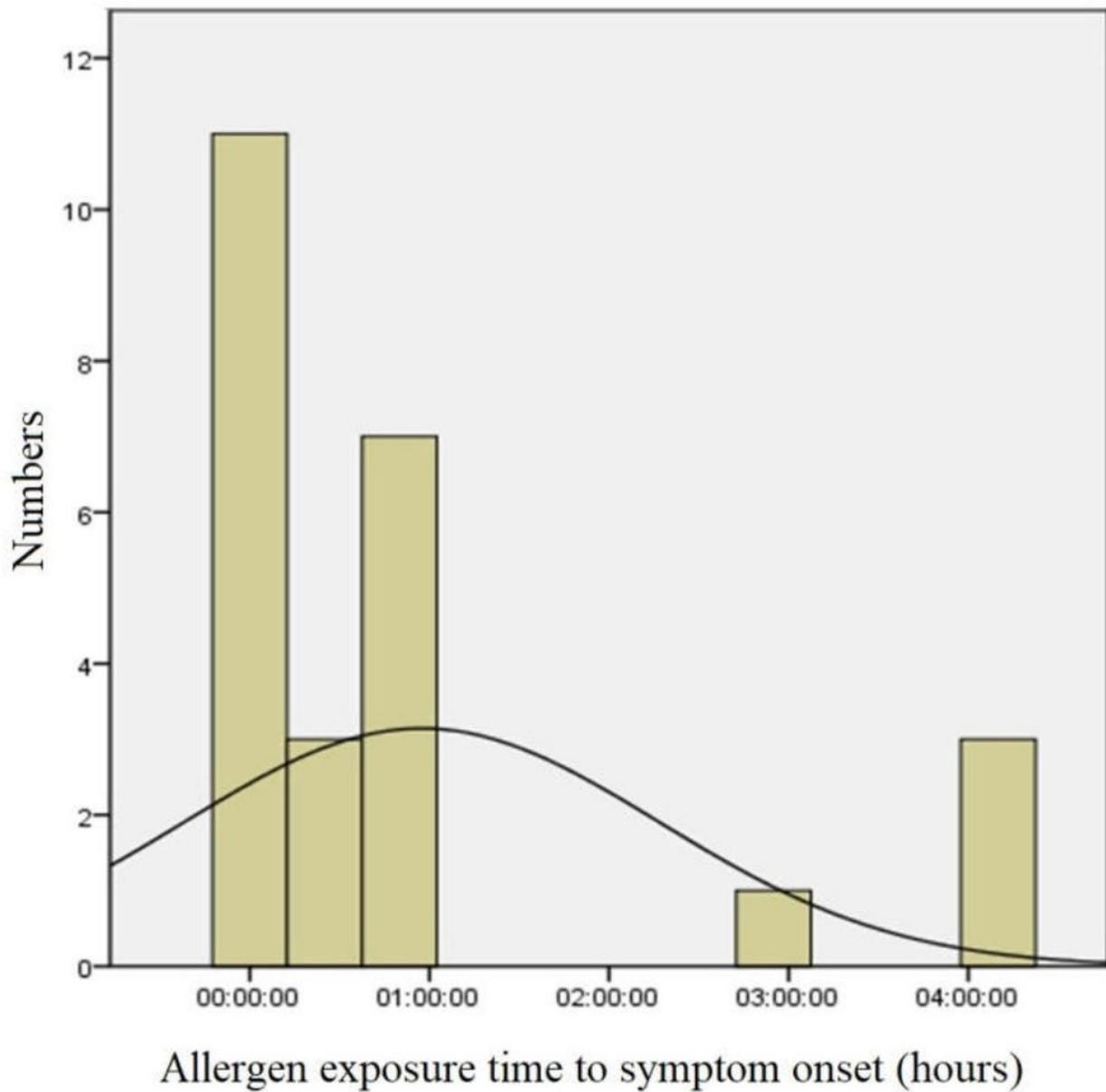


Figure 1. Histogram of the allergen exposure time to symptom onset

Figure 1

Histogram of the allergen exposure time to symptom onset