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# Clinical features of anaphylaxis according to age in a single university hospital in Korea

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## Abstract

**Background:** Prevalence of anaphylaxis is increasing steadily, but there is scant information about anaphylaxis.

**Objective:** To identify the prevalence of anaphylaxis and evaluate the cause and features of anaphylaxis according to age.

**Method:** The relevance of gender, age, history of allergic diseases, causes and clinical symptoms in the treatment and prognosis of anaphylaxis were retrospectively evaluated in patients diagnosed with anaphylaxis in Pusan National University Hospital from January 2009 to June 2014.

**Results:** The 161 patients included 30 children and 131 adults. The prevalence of anaphylaxis in both children and adults increased during the study period. The most common triggers were food in children, especially in those <5 years of age, and drugs in adults. All of the children with episodes of anaphylaxis presented with cutaneous symptoms and 90% had respiratory symptoms. For adults, cardiovascular symptoms were more common.

**Conclusions:** The prevalence of anaphylaxis increased in both children and adults, with a higher rate in children. The causes and symptoms of anaphylaxis may differ depending on age. Clinicians should understand the characteristics of anaphylaxis by age.

**Keywords:** Anaphylaxis, age, epidemiology, etiology, children, infant

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## Introduction

Anaphylaxis is a systemic allergic reaction with a rapidly progressive onset that can be fatal. It requires immediate diagnosis and treatment.[1-3] The incidence and severity of allergic diseases is steadily increasing in Korea, causing an intense awareness and an interest in anaphylaxis.[4-7] It is important to understand the epidemiology of anaphylaxis in order to manage patients properly and prevent recurrence. However, the range of prevalence and triggering factors of anaphylaxis varies worldwide.[7-10] The epidemiology of anaphylaxis in Asia is unclear.

The incidence of anaphylaxis in Korea, as reported by Lim[11] by analyzing the medical claim data of the Health Insurance Review and Assessment Service (HIRA) from 2001 to 2007 under the disease code 'anaphylaxis', was 0.7-1.0 cases per 100,000 persons under 18 years of age. Lee et al.[4] analyzed patients under 18 years of age who visited one of nine general hospital emergency rooms between June 2008 and March 2009 (10 months), and reported that 7.23 cases out of 10,000 pediatric patients were diagnosed with anaphylaxis. Yang et al. reported that among 978,146 patients, 138 (0.014%) patients had anaphylaxis in a single center.[12] However, there is no comprehensive research on the incidence and prevalence of anaphylaxis in Korea.

As anaphylaxis shows a variety of clinical symptoms and can be life threatening, many guidelines have been proposed for a rapid diagnosis and effective treatment; however, the diagnostic rate and level of epinephrine prescription or self-administration is still reported to be low.[13] In particular, children have difficulties expressing their symptoms. The younger the patient is, the harder it is to diagnose and treat them.[3] Also, there have been many studies on the characteristics of anaphylaxis in adults according to age, so efforts are needed to comprehend the characteristics of anaphylaxis by age. We analyzed the incidence of patients diagnosed with anaphylaxis in our hospital during 5 years and aimed to determine the cause and clinical characteristics of anaphylaxis according to age.

## Methods

A retrospective chart review was performed in anaphylaxis patients at Pusan National University Hospital, Busan, Korea from January 2009 to June 2014. Our university hospital is a reference center for a population of 6 million inhabitants in Busan and Gyeongnam. Information on sex, age, history of allergic diseases, cause of anaphylaxis, clinical symptoms, treatment, and prognosis were collected. Subjects under 19 years of age were defined as children, and those above 20 years of age were defined as adults. All patients were further classified into six age groups: under 5 years, 6-11 years, 12-19 years, 20-39 years, 40-59 years, and more than 60 years. Patients were first selected using the disease codes for anaphylaxis, anaphylaxis shock, allergy and anaphylaxis, hypersensitivity, food hypersensitivity, and drug hypersensitivity on the basis of the International Statistical Classification of Diseases, 10th Revision (ICD-10), and their medical records were analyzed so that only patients full filling the diagnostic criteria for anaphylaxis were included. Anaphylaxis was diagnosed if one of the following three criteria were met: the occurrence of respiratory or cardiovascular symptoms accompanied by an acute cutaneous reaction within a few minutes to a few hours; the occurrence of two or more systemic responses out of the cutaneous, respiratory, cardiovascular, or gastrointestinal system, after exposure to an allergic antigen; and the occurrence of hypotension after exposure to a known allergic antigen.[1] The study was approved by the Pusan National University Hospital Institutional Review Board.

Statistical analyses were performed using IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA), and the Chi-square test and Fisher's exact test were used to test the statistical significance in children and adults. Data were considered to be statistically significant if the p-value was < 0.05.

## Results

There were 161 subjects included in the study, with 30 children and 131 adults. Sixteen (53.3%) were male children and 65 (49.6%) were male adults. The average age at diagnosis was 9.5±5.7 years for children and 50.2±16.0 years for adults (**Table 1**). There were 22 children (73.3%) and 69 adults (52.7%) with a history of allergic disease (**Table 1**). Histories of atopic dermatitis, food allergy, allergic rhinitis, and asthma were higher in children, while drug allergy was higher in adults.

**Table 1. Demographic characteristics of patients with anaphylaxis**

| | Children (n=30) | Adult (n=131) | *P*-value |
|---|---|---|---|
| Sex | | | |
| Male | 16(53.3) | 65(49.6) | |
| Female | 14(46.7) | 66(50.4) | |
| Mean Age (yr) | 9.5±5.7 | 50.2±16.0 | |
| History of allergic diseases | 22(73.3) | 69(52.7) | |
| Atopic dermatitis | 13(43.3) | 2(1.5) | 0.000* |
| Food allergy | 13(43.3) | 28(21.4) | 0.019* |
| Allergy rhinitis | 10(33.3) | 9(6.9) | 0.000* |
| Asthma | 8(26.7) | 12(9.2) | 0.014* |
| Chronic urticaria | 2(6.7) | 12(9.2) | 1.000 |
| Drug allergy | 1(3.3) | 24(18.3) | 0.049* |

Values are presented as mean±standard deviation (range), number (%).
*$P$<.05 was considered statistically significant.

**Table 2. Underlying causes of anaphylaxis**

| Underlying cause | Children (n=30) | Adult (n=131) | *P*-value |
|---|---|---|---|
| Food | 15(50.0) | 29(22.1) | 0.003* |
| Cow's milk | 5(16.7) | 0 | |
| Egg white | 2(6.7) | 0 | |
| Sea foods | 1(3.3) | 9(6.9) | |
| Fruits/vegetables | 1(3.3) | 5(3.8) | |
| Wheat | 1(3.3) | 7(5.3) | |
| Nuts | 0 | 3(2.3) | |
| Soy | 1(3.3) | 2(1.5) | |
| Buckwheat | 1(3.3) | 1(0.8) | |
| Chicken | 1(3.3) | 0 | |
| Beef | 1(3.3) | 1(0.8) | |
| Pork | 1(3.3) | 1(0.8) | |
| Drug | 8(26.7) | 73(55.7) | 0.005* |
| IgE mediated | | | |
| Ampicillin | 0 | 3(2.3) | |
| Cephalosporin | 3(10.0) | 22(16.8) | |
| Muscle relaxant | 0 | 3(2.3) | |
| Methylprednisolone | 1(3.3) | 1(0.8) | |
| Non-IgE mediated | | | |
| Aspirin or NSAID | 4(13.3) | 23(17.6) | |
| Radio contrast | 0 | 8(6.1) | |
| Acetaminophen | 0 | 3(2.3) | |
| Other | 0 | 10(7.6) | |
| Exercise(food dependent) | 2(6.7) | 5(3.8) | 0.615 |
| Exercise(food independent) | 0 | 6(4.6) | 0.594 |
| Insect sting | 1(3.3) | 9(6.9) | 0.690 |
| Blood transfusion | 1(3.3) | 0 | 0.186 |
| Idiopathic | 3(10.0) | 9(6.9) | 0.698 |

Values are presented as number (%).
*$P$<.05 was considered statistically significant.

**Table 3. Signs and symptoms of anaphylaxis**

| | Children (n=30) | Adult (n=131) | *P*-value |
|---|---|---|---|
| Cutaneous | 30(100.0) | 98(74.8) | 0.001* |
| Urticaria | 25(83.3) | 58(44.3) | |
| Itch-flush | 22(73.3) | 42(32.1) | |
| Pruritus and swelling of lips-tongue-uvula | 7(23.3) | 6(4.6) | |
| Erythema | 7(23.3) | 18(13.7) | |
| Angioedema | 6(20.0) | 21(16.0) | |
| Respiratory | 27(90.0) | 82(62.6) | 0.004* |
| Dyspnea | 23(76.7) | 76(58.0) | |
| Cough | 14(46.7) | 5(3.8) | |
| Wheeze | 10(33.3) | 7(5.3) | |
| Stridor | 9(30.0) | 7(5.3) | |
| Coryza | 5(16.7) | 0 | |
| Cyanosis | 5(16.7) | 13(9.9) | |
| Cardiovascular | 8(26.7) | 81(61.8) | 0.000* |
| Hypotension | 7(23.3) | 70(53.4) | |
| Pallor | 5(16.7) | 0 | |
| Chest pain | 2(6.7) | 8(6.1) | |
| Collapse | 1(3.3) | 1(0.8) | |
| Diaphoresis | 0 | 8(6.1) | |
| Cardiac arrest | 0 | 7(5.3) | |
| Gastrointestinal | 14(46.7) | 36(27.5) | 0.049* |
| Nausea | 11(36.7) | 14(10.7) | |
| Vomiting | 10(33.3) | 17(13.0) | |
| Abdominal pain | 4(13.3) | 17(13.0) | |
| Neurologic | 14(46.7) | 73(55.7) | 0.420 |
| Dizziness | 8(26.7) | 32(24.4) | |
| Anxiety | 5(16.7) | 1(0.8) | |
| Confusion | 1(3.3) | 3(2.3) | |
| Loss of consciousness | 1(3.3) | 44(33.6) | |
| Death | 0 | 1(0.8) | |
| Biphasic response | 7(23.3) | 3(2.3) | 0.000* |

Values are presented as number (%).
*$P<.05$ was considered statistically significant.

The incidence of anaphylaxis increased during the study period in both children and adults (**Figure 1**). In children, the number of patients who visited the hospital increased steadily from 1.7 per 100,000 in 2009, 3.6 in 2010, 11.9 in 2011, 13.3 in 2012, and 30.9 in 2013, to 60.2 in 2014. For adults, the number of patients who visited the hospital also increased from 0.9 per 100,000 in 2009 to 14.7 in 2014.

Causes of anaphylaxis in children included food (50%), drugs (26.7%), food-dependent exercise-induced anaphylaxis (6.7%), blood transfusion (3.3%), insect bites (3.3%), and idiopathic causes (10%). Causes in adults included drugs (55.7%), food (22.1%), insect bites (6.9%), exercise (4.6%), food-dependent exercise-induced anaphylaxis (3.8%), and idiopathic causes (6.9%) (**Table 2**). Among the food allergens, milk and seafood were the most common causes in children and adults, respectively, and cephalosporin and non-steroidal anti-inflammatory drugs (NSAIDs) were the most common causative drugs for anaphylaxis (**Table 2**). Anaphylaxis due to food was the most common in children under 5 years old, at 88.9% (**Table 4**).

Cutaneous symptoms occurred in 30 children (100%) and 98 adults (74.8%), respiratory symptoms occurred in 27 children (90%) and 82 adults (62.6%), gastrointestinal symptoms occurred in 14 children (46.7%) and 36 adults (27.5%), and cardiovascular symptoms occurred in 8 children (26.7%) and 81 adults (61.8%). Cutaneous, respiratory, and gastrointestinal symptoms were significantly more common in children compared to adults (**Table 3**). Cardiovascular symptoms were more common in adults compared to children and were not seen in children under 5 years of age and increased in proportion to age (**Table 4**). A biphasic response was seen in 7 children (23.3%) and 3 adults (2.3%), which was significantly more common in children (**Table 3**). The time interval from exposure to a causal agent to the appearance of symptoms was within 10 minutes in 10 children (33.3%), under 30 minutes in 8 children (26.7%), within 10 minutes in 32 adults (24.4%), and under 30 minutes in 37 adults (28.2%).

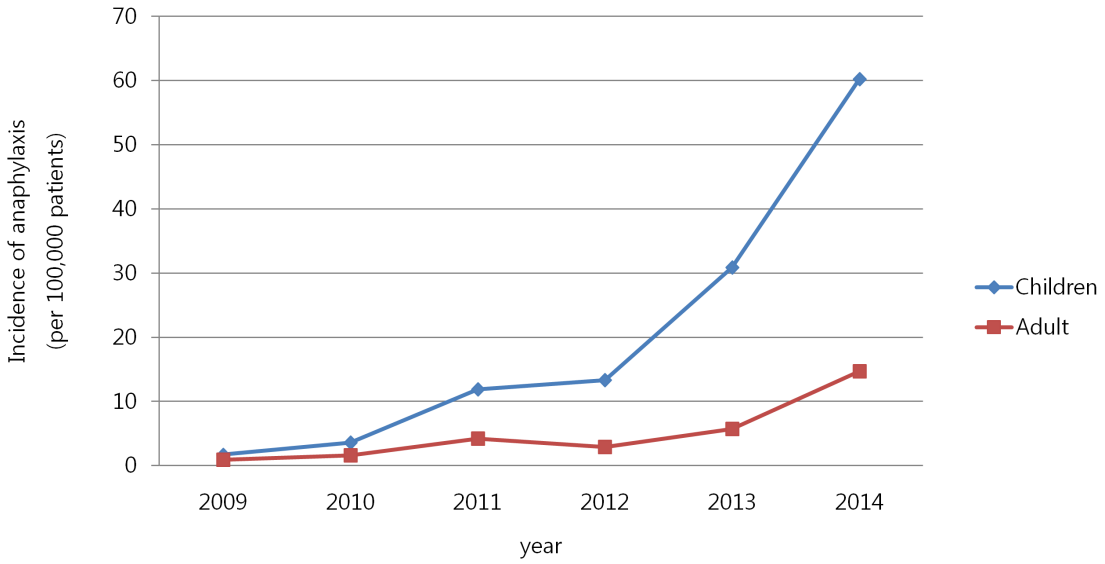


**Figure 1. Incidence of anaphylaxis in Pusan National University Hospital from 1.7 per 100,000 patients in 2009 to 60.2 per 100,000 patients in 2014 in children and 0.9 per 100,000 patients in 2009 to 14.7 per 100,000 patients in 2014 in adult group.**

**Table 4. Underlying cause, signs, symptoms and treatment according to age group**

| | Age groups | | | | | |
|---|---|---|---|---|---|---|
| | ≤5yr | 6-11yr | 12-19yr | 20-39yr | 40-59yr | ≥ 60yr |
| Number | 9(5.6) | 9(5.6) | 12(7.5) | 37(23.0) | 56(34.8) | 38(23.6) |
| Cause | | | | | | |
| Food | 8(88.9) | 3(33.3) | 4(33.3) | 9(24.3) | 10(17.9) | 10(26.3) |
| Drug | 1(11.1) | 3(33.3) | 5(41.7) | 19(51.4) | 32(57.1) | 22(57.9) |
| Exercise(food) | 0 | 0 | 2(16.7) | 3(8.1) | 2(3.6) | 0 |
| Exercise | 0 | 0 | 0 | 2(5.4) | 4(7.1) | 0 |
| Insect sting | 0 | 1(11.1) | 0 | 1(2.7) | 6(10.7) | 2(5.3) |
| Idiopathic | 0 | 2(22.2) | 1(8.3) | 3(8.1) | 2(3.6) | 4(10.5) |
| Signs and symptoms | | | | | | |
| Cutaneous | 9(100.0) | 9(100.0) | 12(100.0) | 32(86.5) | 40(71.4) | 26(68.4) |
| Respiratory | 9(100.0) | 9(100.0) | 9(75.0) | 28(75.7) | 34(60.7) | 20(52.6) |
| Cardiovascular | 0 | 3(33.3) | 5(41.6) | 18(48.6) | 34(60.7) | 29(76.3) |
| Gastrointestinal | 4(44.4) | 4(44.4) | 4(33.3) | 11(29.7) | 19(33.9) | 6(15.8) |
| Neurological | 4(44.4) | 4(44.4) | 6(50.0) | 10(27.0) | 36(64.3) | 27(71.1) |
| Treatment | | | | | | |
| Epinephrine | 4(44.4) | 9(100.0) | 9(75.0) | 4(10.8) | 15(26.8) | 8(21.1) |
| Prophylactic self-injectable epinephrine | 3(33.3) | 4(44.4) | 5(41.7) | 6(16.2) | 10(17.9) | 7(18.4) |

Values are presented as number (%).

**Table 5. Treatment of anaphylaxis**

| | Children (n=30) | Adult (n=131) |
|---|---|---|
| Emergency treatment | | |
| Epinephrine | 22(73.3) | 27(20.6) |
| Antihistamine | 20(66.7) | 63(48.1) |
| Systemic steroid | 18(60.0) | 62(47.3) |
| IV hydration | 18(60.0) | 44(33.6) |
| Bronchodilator | 12(40.0) | 10(7.6) |
| O2 inhalation | 13(43.3) | 43(32.8) |
| Prophylactic self-injectable epinephrine | 12(40.0) | 23(17.6) |
| Hospitalization | 17(56.7) | 16(12.2) |

Values are presented as number (%).

Twenty-two children (73.3%) and 27 adults (20.6%) received epinephrine treatment, and 12 children (40.0%) and 23 adults (17.6%) were prescribed a prophylactic self-injectable epinephrine (**Table 5**). In children, the younger they were, the less likely they received epinephrine and prophylactic self-injectable epinephrine prescription; no difference was seen in adult subjects (**Table 4**). Seven adults (6.8%) received treatment in the intensive care unit, 7 (6.8%) were hospitalized, and there was one death from a bee sting-induced anaphylaxis. One child (3.3%) received treatment in the intensive care unit and 16 (53.3%) were hospitalized, with no cases of death reported.

## Discussion

The lifetime prevalence of anaphylaxis is about 0.05-2%,[2,14,15] and clinical studies show that the incidence is steadily increasing.[3,12,16-21] In this study, the incidence of anaphylaxis for last 5 years also increased, especially at a higher rate in children. Recent nationwide data in Korean adults also showed that the incidence of anaphylaxis significantly increased from 7.74 cases per 100,000 in 2007 to 13.32 in 2011.[7] This increase in incidence is thought to be due to an increased diagnostic rate following the setup of guidelines, and also due to the increased prevalence of allergic diseases in general.[2,20,22] In our study, the reason for the increase in pediatric anaphylaxis incidence being even more prominent may be because of the active education and promotion of anaphylaxis following the initiation of pediatric allergist specialist clinics in 2009. However, more focus and continuous research is needed on the rapid increase of anaphylaxis incidence in children in this study.

In this study, the most common cause of anaphylaxis in children was food, especially in children under 5 years old. Although food is known a common cause of pediatric anaphylaxis, the type of food has differed between studies.[3,4,12,16,19,23-25] In Western studies including the United States, peanuts and other nuts are the most common causes.[3,16,20,23,25-27] In Korea, the most commonly reported causes have been buckwheat,[11] fish,[4] and eggs.[28] In this study, milk was found to be the most common cause. Such differences are generally thought to be due to the inclusion criteria of the subjects or to differences in the age or region of the subject.[18,20,29]

In the present study, as in other similar studies,[12,30-33] drugs, food, and insect stings were the most common causes of anaphylaxis in adults, with no difference according to age. Among the drugs, NSAIDs, and cephalosporin were most common. Seafood was the most common food to cause anaphylaxis in adults, in agreement with the results of a study on food anaphylaxis in adults living in the Southeastern seaside,[17] which can be presumed to be a characteristic of Korean adults living close to the shoreline.[30,34] In this study, the incidence of anaphylaxis due to insect stings is lower than in other studies.[7,12] We suggest the reason for this being that only

some of the patients referred to our university hospital resided in an urban area, because insect stings often occur in rural settings and cause mild anaphylaxis symptoms.[7]

Presently, 73.3% of children and 52.7% of adults had a history of allergic disease. The history of atopic dermatitis, food allergy, allergic rhinitis, and asthma was higher in children, while drug allergy was higher in adults. In other studies, allergy history was reported to be higher in children than adults, with prevalence rates of 64 to 82% in children[22,31,33] and 19 to 50% in adults.[7,10,12] These differences may reflect the increasing prevalence of allergy disease. As the hospitalization rate of children was higher than adults in our study, it might be possible to obtain a more detailed medical history.

The most common clinical manifestation of anaphylaxis has been reported to be skin reactions,[4,12,20,22,24,25,28-35] which is also the case in this study for both children and adults. Cutaneous, respiratory, and gastrointestinal symptoms were more commonly observed in children compared to adults, and cardiovascular symptoms were more common in adults. In particular, cardiovascular symptoms were not seen in children under 5 years of age and increased with age. It is hard to measure blood pressure in children and tachycardia is a more common accompanying symptom rather than hypotension, so caution is needed for diagnosis.[3,24,25] Also, the reason why cardiovascular symptoms are more common in adults may be because drugs are more frequently involved as a cause, and there are more patients with a history of cardiovascular disease as their age increases.[24,35] In contrast to previous reports that biphasic responses are uncommon in children,[20,31-33,36] they were more common in children in this study. These results may be influenced by the fact that there were more cases of hospitalization in children, so they were observed for a longer period of time.

In this study, the prescription rate of epinephrine and portable epinephrine was higher in children compared to adults. However, the prescription rate under 5 years of age was lower compared to the other pediatric age groups. This is because subjective symptoms are ambiguous and blood pressure measurement is difficult in this age group, meaning that diagnosis is not easy, and also because prophylactic self-injectable epinephrine is hard to use in children who weigh less than 10kg.

This study is limited as the sample size was small and was a retrospective study in a single university hospital. However, the study is relevant as the increasing incidence of anaphylaxis was found and the characteristics of anaphylaxis were analyzed by age. Clinicians should understand the characteristics of anaphylaxis by age and try to diagnose actively and prescribe epinephrine. Also, the development of a prophylactic self-injectable epinephrine that can be used in children less than 10kg is necessary.

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