Maternal Posttraumatic Stress Symptoms and Psychological Burden in Mothers of Korean Children With Anaphylaxis

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ABSTRACT

Purpose: Anaphylaxis is a severe allergic reaction that is potentially life-threatening, but post-traumatic stress symptoms (PTSS) in the caregivers of children with anaphylaxis have not been evaluated. This study aimed to investigate the psychological burden on mothers of children with recent anaphylaxis.

Methods: A total of 188 children with recent anaphylaxis was recruited from 13 hospitals in Korea. Validated questionnaires, including the Korean versions of the Beck Anxiety Inventory (K-BAI), the Beck Depression Inventory (K-BDI), and the Impact of Event Scale Revised-Korean version (IES-R-K), were used to evaluate maternal anxiety, depression, and PTSS.

Results: The median ages of children and their mothers were 4 and 36 years, respectively. PTSS (IES-R-K ≥ 25) were identified in 56.9% of mothers, and 57.9% of them showed severe PTSS. The proportions of mothers who had anxiety (K-BAI ≥ 22) and depression (K-BDI ≥ 17) were 18.6% and 33.0%, respectively. Multivariable logistic regression analysis indicated that the patient’s history of asthma (adjusted odds ratio [aOR], 5.46; 95% CI, 1.17–25.59) and the presence of central nervous symptoms (aOR, 3.27; 95% CI, 1.07–9.96) were associated with PTSS. Age of 2 or older (aOR, 2.87; 95% CI, 1.10–7.52) and eggs, milk, or wheat as the cause of anaphylaxis (aOR, 2.87; 95% CI, 1.10–7.52) increased the risk of severe PTSS.
Conclusions: The rate of PTSS among mothers of children with recent anaphylaxis was high at 56.9%. Clinicians who care for pediatric anaphylaxis patients should be aware of the psychological burden on their caregivers.

Keywords: Anaphylaxis; anxiety; depression; stress disorders, post-traumatic; psychological distress

INTRODUCTION

Post-traumatic stress symptoms (PTSS) are severe anxiety, flashbacks, and/or uncontrollable thoughts, key elements of post-traumatic stress disorder (PTSD), that occur after exposure to emotionally stressful events or experiences of serious medical conditions. PTSD manifests as persistence of intense, painful, and fearfully avoided responses to reminders of the traumatic events, altered mood and cognition, a pervasive sense of impending threats, sleep disturbance, and excessive vigilance after exposure to emotionally stressful events or experiences of serious medical conditions. The lifetime prevalence of PTSD varies from 1.3 to 12.2% depending on social background and country of residence. A recent meta-analysis reported that about 19% of parents of children with chronic physical illnesses suffered from PTSS, which is much higher than the 3.5% found in the general adult population in the United States. This indicates that diagnosis of serious chronic diseases in families can be recognized as a traumatic event.

Anaphylaxis is a severe, potentially life-threatening allergic reaction that is mostly triggered by foods, drugs, or insect venom. The lifetime prevalence of anaphylaxis ranges from 0.3% to 5.1%, and one-quarter of all cases occur in children and adolescents according to European data. The incidence of anaphylaxis is increasing in various regions, and the increase is particularly large in young age groups. Anaphylaxis typically occurs in unpredictable circumstances and is often accompanied by severe systemic symptoms such as respiratory difficulty or hypotension, causing psychological stress to patients and their caregivers.

Anaphylaxis can be a life-threatening situation and a lifetime traumatic event, and the experience of anaphylaxis in children can have a huge impact on their caregivers. Anaphylaxis has been considered a cause of PTSD because it can be felt as a threat to physical integrity in patients and family members. There have been several studies in adults showing that PTSS were significantly more frequent in patients who have experienced anaphylaxis, but no studies have been conducted on PTSS in the caregivers of children with anaphylaxis. Therefore, we used validated versions of related questionnaires to evaluate the psychological burden, specifically anxiety, depression, and PTSS, of mothers after their children had experienced anaphylaxis.

MATERIALS AND METHODS

Study population and design
A questionnaire-based, cross-sectional study was performed in 13 hospitals in Korea from October 2016 to December 2018. Children aged 0–17 who were diagnosed with anaphylaxis in emergency departments or outpatient clinics within the last two weeks to three months were recruited, and their mothers were given a detailed questionnaire to complete. Anaphylaxis...
was defined according to the diagnostic criteria proposed by the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network. The questionnaire included information regarding sex, age, maternal age, past medical history, family history of allergic diseases, prior anaphylaxis, and symptoms and causes of anaphylaxis. We classified the reported symptoms according to the affected organs: 1) Skin or mucosal symptoms such as urticaria, rash, itching, redness, or angioedema; 2) gastrointestinal symptoms such as vomiting, nausea, abdominal pain, or diarrhea; 3) respiratory symptoms such as cough, dyspnea, or wheezing; 4) cardiovascular symptoms such as chest pain, tachycardia, bradycardia, or hypotension; and 5) central nervous system (CNS) symptoms such as confusion, unconsciousness, hypotonia, dizziness, or seizure.

This study was approved by the Institutional Review Boards of Seoul Medical Center No. 2016-04-45, Kyung Hee University Gangdong Hospital No. 2016-07-003, Hallym University Dongtan Sacred Heart Hospital No. 2016-3574, Inha University Hospital No. 2016-07-015, Inje University Seoul Paik Hospital No. 2016-314, Soonchunhyang University Seoul Hospital No. 2016-08-029, Inje University Ilsan Paik Hospital No. 2016-11-007, Yonsei University Severance Hospital No. 4-2016-0569, Samsung Medical Center No. SMC-2016-06-071, Ajou University Hospital No. AJIRB-MED-SUR-16-357), Soonchunhyang University Bucheon Hospital No. 2016-07-020-003, National Health Insurance Service Ilsan Hospital NHIMC 2016-06-003-006, and Eulji University Nowon Hospital No. 2018-07-140. Written informed consent was obtained from each parent before his/her child participated in the study.

Evaluation of anxiety, depression, and PTSS
The Korean versions of the Impact of Event Scale (IES-R-K)-Revised, a modified Korean version of the IES-R, was used to detect PTSS. This self-rated questionnaire consists of 22 inquiries to evaluate the presence of PTSS, such as hyperarousal (feeling watchful and on guard), avoidance (an effort to avoid reminders of the event), and intrusion (dreaming about the event). IES-R-K scores were categorized into three groups: normal (IES-R-K ≤ 24), low risk of PTSS and mild-to-moderate (25 ≤ IES-R-K ≤ 39); and severe (IES-R-K ≥ 40).

The Korean version of the Beck Anxiety Inventory (K-BAI) and the Beck Depression Inventory (K-BDI) were used to assess anxiety and depression, respectively. These self-administered questionnaires consist of 21 questions, and each of the questions is scored with values ranging from 0 to 3. A K-BAI score ≥ 22 was considered as the existence of anxiety symptoms, while a K-BDI score ≥ 17 was defined as the presence of depressive symptoms.

Statistical analysis
Data were analyzed using SPSS for Windows (version 27.0, SPSS, Chicago, IL, USA). Data were presented as numbers (percentages) or median (range). Univariate and multivariate logistic regression analyses were used to test the associations between clinical characteristics and psychological distress. Variables with a P value < 0.1 in univariable analyses were chosen for the multivariable analysis. A P value less than 0.05 was considered significant.

RESULTS
Clinical characteristics of the study population
One hundred eighty-eight subjects were enrolled in the study. The median age of children was 4 years, ranging from 4 months to 17 years. Of the 188 mothers who conducted the survey, information on age was collected in 144, of which 23.9% were aged < 35, 33.5% were...
aged 35–39, and 23.4% were aged 40 years or older. Among the concurrent allergic diseases in children, food allergy (FA) (71.3%) was most common, followed by atopic dermatitis (43.6%), allergic rhinitis (28.2%), and asthma (15.4%). Anaphylaxis was caused by food in most cases, whereas drug-induced, food-dependent, and exercise-induced anaphylaxis were also reported. Other causes of anaphylaxis were physical stimuli or animal exposure. Among food-induced anaphylaxis, tree nuts, egg, grains and seeds, and milk accounted for 75%. The demographic and clinical characteristics are given in Table 1.

### PTSS and psychological burden in mothers of children with anaphylaxis

The median (range) IES-R-K score was 29 (0–88), and 107 (56.9%) mothers had PTSS (IES-R-K ≥ 25). The median (range) K-BAI score and K-BDI score were 8 (0–63) and 11 (0–68), respectively, and the proportions of mothers who had anxiety (K-BAI ≥ 22) and depression (K-BDI ≥ 17) were 18.6% and 33.0%, respectively (Fig. 1).

When classified according to age of the patients, the maternal PTSS rate was 42.9% at 0–1 years, 69.3% at 2–6 years, 56.5% at 7–9 years, and 51.2% at 10 years or older. The maternal anxiety rates for each age group of patients were 8.2% at 0–1 years, 24.0% at 2–6 years, 21.7% at 7–9 years, and 19.5% at 10 years or older. As with PTSS and anxiety, maternal depression was also highest in the 2–6-year group; 26.5% at 0–1 years, 37.3% at 2–6 years, 34.8% at 7–9 years, and 31.7% at 10 years or older.

According to the age of the mother, the psychological burden tended to be lower for those under 35 years of age. The PTSS rates were 46.7%, 63.5%, and 61.1% in those < 35, 35–39, and ≥ 40 years, respectively. Anxiety rates were 13.3%, 23.8%, and 25.0% in those < 35, 35–39, and ≥ 40 years, respectively, and depression rates were 31.1%, 34.9%, and 38.9% in the same age groups.

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**Table 1. Baseline characteristics of patients**

| Characteristics of children with anaphylaxis | Values         |
|---------------------------------------------|----------------|
| **Age (yr)**                                |                |
| Median (range)                              | 4 (4 mo–17 yr) |
| 0–1                                        | 49 (26.1)      |
| 2–6                                        | 75 (39.9)      |
| ≥ 7                                        | 64 (34.0)      |
| **Sex**                                     |                |
| Male                                        | 126 (67.0)     |
| Female                                      | 62 (33.0)      |
| **Allergic diseases**                       |                |
| Atopic dermatitis                           | 82 (43.6)      |
| Allergic rhinitis                           | 53 (28.2)      |
| Asthma                                      | 29 (15.4)      |
| Drug allergy                                | 3 (1.6)        |
| Food allergy                                | 134 (71.3)     |
| **Family history of allergic diseases**     |                |
| **Causes of anaphylaxis**                   |                |
| Food                                        | 171 (91.0)     |
| Drug                                        | 9 (4.8)        |
| Food-dependent exercise-induced anaphylaxis | 3 (1.6)        |
| Other causes                                | 5 (2.7)        |
| **Maternal age (yr)**                       |                |
| Median (range)                              | 36 (25–53)     |
| < 35                                        | 45/144 (23.9)  |
| 35–39                                       | 63/144 (33.5)  |
| ≥ 40                                        | 36/144 (23.4)  |

Data are shown as number (%).
Among the causes of anaphylaxis, the psychological burden tended to be higher in mothers of children with drug-induced anaphylaxis. The maternal PTSS rate was 66.7% in drug-induced anaphylaxis compared to 57.9% in food-induced anaphylaxis. In drug-induced anaphylaxis, maternal anxiety and depression rates were 22.2% and 44.4%, respectively, which were higher than the 18.7% and 32.7% in food-induced anaphylaxis.

In the analysis of the psychological burden according to the presence or absence of specific symptoms, maternal PTSS was more prevalent in the cases with CNS or cardiovascular symptoms. There was no difference in the prevalence of maternal PTSS in the cases with respiratory symptoms; in the cases with gastrointestinal symptoms, maternal PTSS tended to be fewer. Severe PTSS, defined as IES-R-K score of 40 or higher, was identified in 62 subjects, accounting for one-third of mothers, and 57.9% of those with PTSS.

**Correlation between IES-R-K, BDI, and BAI scores**

IES-R-K scores were positively correlated with BDI and BAI (rho coefficient = 0.581 and 0.680, respectively; all $P < 0.001$). In addition, there was a positive association between BDI and BAI scores (rho coefficient = 0.709; $P < 0.001$).

**Factors associated with maternal psychological distress in children with anaphylaxis**

Univariable analysis indicated that age of 2 or older (odds ratio [OR], 2.16; 95% confidence interval [CI], 1.12–4.19), previous history of asthma (OR, 2.74; 95% CI, 1.11–6.77), and CNS symptoms (OR, 2.50; 95% CI, 1.05–5.92) were associated with maternal PTSS (Table 2). Age of 2 or older (OR, 2.74; 95% CI, 1.23–6.10) and CNS symptoms (OR, 2.19; 95% CI, 1.00–4.80) were also related to severe PTSS (Table 2). The multivariable analysis revealed that history of asthma (adjusted OR [aOR], 5.46; 95% CI, 1.17–25.59) and CNS symptoms (aOR, 3.27; 95% CI, 1.07–9.96) were associated with PTSS (Fig. 2A). Additionally, age of 2 or older (aOR, 2.87; 95% CI, 1.10–7.52) and eggs, milk, or wheat as the cause of anaphylaxis (aOR, 2.87; 95% CI, 1.10–7.52) increased the risk of severe PTSS in multivariable analysis (Fig. 2B).

Age of 2 or older was the only risk factor for maternal anxiety in univariable and multivariable analyses. Although eggs, milk, or wheat as the cause of anaphylaxis were associated with an increased risk for maternal depression in univariable analysis (Table 3), no association between clinical characteristics and maternal depression was found after adjusting for sex,
Table 2. Univariable analyses for clinical characteristics influencing PTSS

| Variables                                | PTSS          | Severe PTSS   |
|-------------------------------------------|---------------|---------------|
|                                           | OR (95% CI)   | P value       | OR (95% CI)   | P value       |
| Age (≥ 2 yr)                              | 2.16 (1.12–4.19) | 0.022        | 2.74 (1.23–6.10) | 0.014        |
| Maternal age (≥ 35 yr)                    | 1.92 (0.94–3.91) | 0.074        | 1.69 (0.76–3.74) | 0.196        |
| Sex (male)                                | 1.03 (0.56–1.90) | 0.928        | 0.68 (0.35–1.32) | 0.257        |
| Past medical history                      |               |               |               |               |
| Atopic dermatitis (yes)                   | 1.23 (0.69–2.20) | 0.489        | 1.47 (0.80–2.71) | 0.217        |
| Allergic rhinitis (yes)                   | 0.98 (0.52–1.87) | 0.957        | 0.74 (0.37–1.48) | 0.394        |
| Asthma (yes)                              | 2.74 (1.11–6.77) | 0.029        | 1.54 (0.68–3.46) | 0.298        |
| Drug allergy (yes)                        | 1.52 (0.14–17.01) | 0.733        | 1.02 (0.09–11.43) | 0.989        |
| Food allergy (yes)                        | 1.65 (0.87–3.11) | 0.125        | 1.41 (0.70–2.81) | 0.337        |
| Family history of allergic diseases (yes) | 1.05 (0.56–1.97) | 0.888        | 1.41 (0.71–2.80) | 0.326        |
| Cause of anaphylaxis                      |               |               |               |               |
| Food                                      | 1.55 (0.57–4.20) | 0.392        | 1.67 (0.52–5.35) | 0.389        |
| Egg, milk, or wheat                       | 1.53 (0.83–2.81) | 0.169        | 1.74 (0.92–3.29) | 0.087        |
| Peanut or tree nuts                       | 0.84 (0.44–1.61) | 0.596        | 0.60 (0.24–1.50) | 0.277        |
| Seafood                                   | 0.50 (0.18–1.37) | 0.175        | 0.40 (0.11–1.44) | 0.161        |
| Drug                                      | 1.55 (0.37–6.37) | 0.548        | 1.02 (0.25–4.21) | 0.981        |
| Symptoms                                  |               |               |               |               |
| Respiratory                               | 1.01 (0.46–2.23) | 0.976        | 1.43 (0.60–3.42) | 0.424        |
| Cardiovascular                            | 1.41 (0.58–3.37) | 0.444        | 2.09 (0.89–4.89) | 0.091        |
| Central nervous system                    | 2.50 (1.05–5.92) | 0.038        | 2.19 (1.00–4.80) | 0.049        |
| Previous experience of anaphylaxis (yes)  | 1.30 (0.67–2.54) | 0.439        | 1.85 (0.94–3.63) | 0.076        |
| Prescription of epinephrine autoinjector (yes) | 1.54 (0.72–3.27) | 0.264        | 1.37 (0.63–3.00) | 0.431        |

PTSS, post-traumatic stress symptoms; OR, odds ratio; CI, confidence interval.

Fig. 2. Multivariable analyses for risk factors influencing maternal PTSS (A) and severe maternal PTSS (B).

aOR, adjusted odds ratio; CI, confidence interval; CNS, central nervous system; PTSS, post-traumatic stress symptoms.
past medical history of atopic dermatitis, or prescription of an epinephrine autoinjector in multivariable analysis.

**DISCUSSION**

To the best of our knowledge, this is the first study to investigate the association between anaphylaxis in children and maternal PTSS. We found that more than half of the mothers of children with anaphylaxis developed PTSS, and about one of three mothers suffered from severe PTSS. Additionally, 18.6% and 33.0% of mothers had anxiety symptoms and depression, respectively, after their children experienced anaphylaxis. These prevalence rates are higher than the 41.4% for PTSS, 23.2% for severe PTSS, and 28.1% for depression in Korean adult patients with anaphylaxis, whereas the rate of anxiety was not higher than that in an adult study.

This indicates that mothers of pediatric patients find anaphylaxis more psychologically frightening and painful than do adult patients. We enrolled only mothers of children with anaphylaxis because the occurrence and severity of PTSS could be influenced by sexual and social factors.

Previous studies also showed that mothers of children with chronic diseases tend to develop PTSS or PTSD more frequently than fathers.

As in our previous study, food was the most common cause of anaphylaxis, followed by drugs. Eggs, cow’s milk, and wheat, the most prevalent food allergens, are common in processed foods, which suggests why they affect severe PTSS in the present study. It is inferred that widespread presence of allergens can lead to anxiety about recurrence of serious allergic reactions by accident and subsequent PTSS. In accordance with the possible reasons, anxiety sensitivity was positively related to PTSS severity including avoidance and hyperarousal symptoms. Similarly, recent clinical studies suggest that FA is associated with impaired quality of life and increased level of anxiety in patients and caregivers. In Turkish

| Variables                                | Anxiety      | Depression   |
|------------------------------------------|--------------|--------------|
| **Age (≥ 2 yr)**                          | 3.21 (1.08–9.68) | 1.51 (0.73–3.11) |
| **Maternal age (≥ 35 yr)**                | 2.08 (0.79–5.51) | 1.27 (0.60–2.69) |
| **Sex (male)**                            | 0.65 (0.29–1.50) | 1.86 (0.94–3.70) |
| **Past medical history**                  |              |              |
| Atopic dermatitis (yes)                   | 0.72 (0.34–1.53) | 1.79 (0.97–3.31) |
| Allergic rhinitis (yes)                   | 0.86 (0.37–1.98) | 0.84 (0.42–1.66) |
| Asthma (yes)                              | 1.49 (0.58–3.82) | 1.29 (0.57–2.94) |
| Drug allergy (yes)                        | 0 (0–999.9) | 1.02 (0.09–11.43) |
| Food allergy (yes)                        | 1.77 (0.72–4.35) | 1.24 (0.63–2.46) |
| **Family history of allergic diseases (yes)** | 0.65 (0.30–1.42) | 0.67 (0.32–1.43) |
| **Cause of anaphylaxis**                  |              |              |
| Food                                     | 1.07 (0.29–3.96) | 0.89 (0.31–2.54) |
| Egg, milk, or wheat                      | 1.22 (0.57–2.63) | 1.94 (1.02–3.70) |
| Peanut or tree nuts                      | 0.60 (0.24–1.50) | 0.261 (0.30–1.27) |
| Seafood                                  | 0.93 (0.26–3.51) | 0.42 (0.12–1.53) |
| Drug                                     | 1.26 (0.25–6.36) | 1.67 (0.43–6.45) |
| **Symptoms**                             |              |              |
| Respiratory                              | 0.90 (0.34–2.40) | 1.43 (0.60–3.42) |
| Cardiovascular                           | 1.88 (0.72–4.91) | 1.17 (0.48–2.81) |
| Central nervous system                   | 1.34 (0.53–3.43) | 1.35 (0.61–3.00) |
| **Previous experience of anaphylaxis (yes)** | 1.25 (0.55–2.86) | 1.40 (0.71–2.77) |
| Prescription of epinephrine autoinjector (yes) | 1.67 (0.66–4.26) | 2.14 (0.98–4.65) |

OR, odds ratio; CI, confidence interval.
children with FA, scores related to emotional impact and food anxiety were particularly affected in those with previous anaphylaxis.26 Among caregivers of children with FA in the United States, low quality of life scores were associated with age at the most severe reaction, peanut or tree nut allergy, multiple FAs, and a history of anaphylaxis.27

In the present study, previous history of asthma and CNS symptoms in children increased the likelihood of PTSS in their mothers. The persistence of the fear response in PTSD patients is due to a dysregulated fear response, impaired safety signal learning, and fear-related memory formation.3,28 It is postulated that enormous events such as CNS symptoms and a past history of asthma in children can affect fear learning in their mothers. These results are different from those of Korean adults, which showed no association between PTSS and symptoms and severity of anaphylaxis.24 In addition, mothers of patients aged 2 years or older and who attended childcare facilities or schools had a high risk of severe PTSS in our current study. Previous Korean multicenter studies demonstrated that only one-quarter of pediatric patients were infants, and about 7.7% of food-induced allergic reactions occurred in childcare centers or schools.13,29 As severe PTSS in mothers of preschoolers and schoolchildren could have a negative impact on parental burden and maternal stress, social assistance is required for families of children with anaphylaxis.

In a recent meta-analysis, parents of children with epilepsy, diabetes, sickle cell disease, heart disease, and cancer had the highest risk of developing PTSS.5 PTSS was reported in 25%–48% and 32%–45% of the parents of children with epilepsy and cancer, respectively, although race and evaluation methods were not the same as those in the present study.20,21 Those findings indicate that Korean mothers of pediatric patients with anaphylaxis experience a similar prevalence of PTSS to that of parents of children with other chronic diseases. Parental PTSS can be caused by disease-related life threats, chronic illness-induced damage, serious complications associated with treatment, painful procedures, and emergency hospitalizations, which are also found in anaphylaxis.3 However, no studies have been conducted to investigate PTSS in children suffering from chronic diseases or their guardians in Korea, making it difficult to accurately compare maternal psychologic stresses among other chronic diseases. More than half of PTSD cases have mood, anxiety, and substance use disorders.30 Similarly, our present study also showed anxiety and depression symptoms in about 18.6% and 33.0% of mothers with PTSS, respectively. In this regard, careful monitoring of PTSS and psychiatric problems is critical in parents of children with anaphylaxis, as PTSS has been reported to have a relationship with suicidal behavior.3,31,32

There are limitations in this study. We did not evaluate biological correlates of PTSS including inflammatory markers and neuroendocrine profiles in the present study, and the diagnosis of PTSS and evaluation of other psychiatric conditions were performed through questionnaires rather than clinical interviews. However, our study is clinically meaningful in that these data are the first known attempt to show the significant association between maternal PTSS and anaphylaxis in children using validated questionnaires.

In conclusion, mothers of children with anaphylaxis are likely to have significant psychological burdens such as PTSS, anxiety, and depression. CNS symptoms and previous history of asthma were associated with PTSS, whereas age of 2 or older and food allergens such as eggs, milk, or wheat increased the likelihood of severe PTSS. Therefore, careful evaluation of emotional symptoms and psychological interventions is needed for mothers of pediatric patients with anaphylaxis.
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