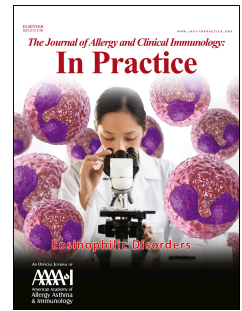


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Post-anaphylaxis acute stress symptoms: a preliminary study on children with food-induced anaphylaxis and their parents

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Competing interest

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Clinical Implications Statement: A meaningful proportion of children and parents showed acute stress symptoms after food-induced anaphylaxis. Clinicians may play an important role in preventing the long-term negative outcomes of this traumatic event.

Key words: anaphylaxis, stress, food allergy, trauma, children, parents

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Anaphylaxis is a serious, generalized or systemic, allergic or hypersensitivity reaction that can be life-threatening or fatal (1). It constitutes the most frightening allergic reaction, placing patients at high risk of death. Understandably, this can be an emotionally traumatic experience. Chung et al. (2) found that 12% of adults who had experienced anaphylaxis fulfilled the diagnostic criteria for post-traumatic stress disorder (PTSD). Weiss and Marsac (3) reported in a pilot study that children with food allergy (FA) may be at risk for post-traumatic stress symptoms and those with a history of anaphylaxis at even more risk. Although experiencing anaphylaxis has been linked to greater psychological complaints in children and families with FA (4,5) no data are available on the development of acute stress symptoms in children and parents after food-induced anaphylaxis.

Acute stress disorder (ASD) is characterized by acute stress reactions that may occur in the initial month after exposure to a traumatic event. It includes symptoms of intrusion, dissociation, negative mood, avoidance, and arousal and causes clinically significant distress or impairment in daily functioning (6) - for complete diagnostic criteria see Table E1 in the Online Repository. ASD diagnosis facilitates identification and treatment of severe acute stress responses. Treatment of ASD can have the additional benefit of limiting subsequent PTSD, which is diagnosed only four weeks after trauma (6,7).

This study aimed to investigate the development of acute stress symptoms among children with FA who experienced a food-induced anaphylaxis and parents who assisted them. Inclusion criteria were children aged between 3-13 years, a medical diagnosis of FA and food-induced anaphylaxis (1). Participants with serious concomitant non-allergic diseases were excluded. Patients were recruited both through the Emergency Department and follow-ups specifically due to anaphylaxis. It is worth noting that all patients are educated to inform the allergists in the event of a reaction using a phone number and/or an email address, also to ask a new prescription of adrenaline auto-injector (AAI) if

it has been administered. Thirty-four families attending the Food Allergy Referral Centre, Veneto Region (Italy) were contacted sequentially (over a period of 12 months) after anaphylaxis and were invited to participate in the study. A total of 31 children, 31 mothers and 10 fathers were recruited (91% participation rate) and parents signed written informed consent.

About twenty days after the child had experienced anaphylaxis, parents had a psychological interview and completed an *ad hoc* sociodemographic questionnaire and the following validated measures. The *Child Stress Disorders Checklist (CSDC)* (8) is an observer-rated measure of traumatic stress symptoms. The *Pediatric Emotional Distress Scale (PEDS)* (9) is a parent-report tool for screening emotional symptoms in children after a potentially traumatic event. The *Acute Stress Disorder Scale (ASDS)* (7) is a self-report questionnaire evaluating ASD in adults (6). Only the parents were interviewed regarding themselves and their children and completed questionnaires before the psychological interview. Diagnosis of ASD was performed by a Clinical Psychologist with expertise in FA based on clinical interview and questionnaire responses and in accordance with DSM-5 (6). Clinical information about patients was collected through a cross check between parents reports and hospital records.

The Padua University Ethics Committee of Psychological Research approved the research.

Statistical analysis was conducted using SPSS. Sample characteristics are shown in Table I. Results revealed that 61% of anaphylaxis occurred following an unintentional ingestion at home, restaurant or school, while 6% occurred at home during oral immunotherapy (OIT) and 33% during an oral food challenge in the hospital; 58% was mild and 42% was moderate anaphylaxis, while no severe anaphylaxis was reported. Among parents, 17% (all mothers) administered AAI to their children. This represents 33% of cases that occurred outside the hospital.

With regard to diagnosis of ASD, among *children*, 7 (22.6%) had symptoms that met the DSM-5 diagnostic criteria, while 8 (25.8%) had sub-threshold stress symptoms (5-8 symptoms of criterion B but all other criteria fulfilled - including D: clinically significant distress or impairment). Among *parents*, 6 (14.6%) had a diagnosis of ASD: 10% of fathers and 16.1% of mothers respectively.

128 Parents' diagnosis did not significantly correlate with children's diagnosis. Clinical and
129 sociodemographic variables showed in Table I were not associated with the development of ASD;
130 however, these findings must be interpreted with caution, because the study could be underpowered
131 in this regard and further research in larger samples is needed.

132 Secondly, mean scores and SD were calculated for CSDC, PEDS and ASDS scores (Table II).
133 Pearson's correlation was calculated to preliminarily explore possible associations with socio-
134 demographic and clinical factors. AAI use positively correlated with anaphylaxis severity ($r=.635$;
135 $p<.01$) and Immediate Response (IR) dimension of CSDC ($.383$; $p<.05$). Patient's gender correlated
136 with IR ($r=.493$; $p<.01$), with female mean scores higher than male mean scores, and Acting out
137 dimension of PEDS ($r=-.489$; $p<.01$), with males' scores higher than females'. Age inversely
138 correlated with Fearful dimension of PEDS ($r=-.384$; $p<.01$), Acting-out ($r=-.377$; $p<.01$) and PEDS
139 total score ($r=-.398$; $p<.01$). Since symptom presentation may vary based on patient gender and age,
140 clinicians need to be knowledgeable in identifying potential signals of ASD.

141 In addition to larger samples, future studies may also include other variables, such as possible
142 previous traumatic life experiences (including previous anaphylaxis) and coping strategies, as well
143 as other data sources in addition to parents' reports. Although not the subject of this study, the low
144 frequency of AAI parental use seems crucial and should be further explored. These limitations
145 notwithstanding, this is the first study reporting the frequency of ASD after food-induced
146 anaphylaxis among children and their parents. About half of children with FA showed acute stress
147 symptoms after food-induced anaphylaxis. Almost a quarter fulfilled the diagnostic criteria for
148 ASD, while a quarter had sub-threshold stress symptoms. Age and gender effects seem in line with
149 typical development and sociocultural aspects, but should be further investigated. Among parents,
150 the frequency of ASD is comparable to the percentage of PTSD in adults who experienced
151 anaphylaxis themselves (2). This highlights the need to assess parents' psychological wellbeing as
152 well as children's after an anaphylactic reaction. Allergists/immunologists must be aware of the risk
153 of ASD in children and families with FA. They could ask patients/parents how they feel after

anaphylaxis, if they are experiencing any uncomfortable or unusual behavior/emotion or any difficulty in daily life. In case of symptoms and impairment the allergist may address the patient/parent to a mental health professional for complete assessment, diagnosis and, if needed, opportune support. The possible use of brief validated instruments for ASD screening in the allergist's office should be explored in further research. Proactive education about anaphylaxis and the potential for ASD is also recommended for parents and patients. Further investigation and greater understanding of risk factors for ASD in children with FA may facilitate the design of acute interventions to prevent the long-term negative outcomes of traumatic events. Adequate assessment pathways, prompt psychological support and interventions tailored for children and for parents should be implemented. A multidisciplinary team that includes allergists/immunologists, pediatricians and mental health professionals is advisable.

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237 **Tables**

CHILDREN WHO EXPERIENCED ANAPHYLAXIS (N=31)				
Age	Min 3	Max 13	M 8.77	SD 4.137
Gender	Female 12	Male 19		
Accidental exposure	Yes 19	No 12		
Place	Home (or other) 21	Hospital 10		
Anaphylaxis severity*	Mild 18	Moderate 13	Severe 0	
PARENTS WHO ASSISTED ANAPHYLAXIS (N=41)				
Age	Min 32	Max 58	M 42.97	SD 5.695
Gender	Female 31	Male 10		
Education Degree	Middle/High School 20	University 11		
AAI use	Yes 7	No 34		
<i>All participants came from Veneto Region (Italy) and were Caucasian.</i> <i>All patients had a medical diagnosis of IgE-mediated FA and no serious concomitant non-allergic diseases.</i> <i>All parents were present at anaphylaxis.</i> <i>*Anaphylaxis severity was independently judged by two allergists with expertise in FA according to Muraro 2007 (1)</i>				

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239 **Table I: Participants' characteristics**

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Children's Scores		
Child Stress Disorders Checklist (CSDC)		
Response format: 0=Not true, 1=Somewhat or sometimes true, 2=Very true or often true		
CSDC Subscales	Mean	SD
<i>Immediate Response</i> (5 items on children's feelings or behaviors immediately after a frightening event: e.g. Child felt terrified)	3.68	2.713
<i>Reexperiencing</i> (7 items e.g. Child reports uncomfortable memories of the event.)	1.81	2.104
<i>Avoidance</i> (5 items e.g. Child avoids doing things that remind him or her of the event.)	1.68	2.315
<i>Numbing, Dissociation</i> (8 items e.g. Child seems "spaced out" or in a daze.)	1.55	2.321
<i>Increased Arousal</i> (6 items e.g. Child startles easily; for example, he/ she jumps when hears sudden or loud noises.)	2.87	2.277
<i>Impairment in Functioning</i> (4 items e.g. Child has difficulty getting along with friends, schoolmates, or teachers.)	0.74	1.210
CSDC-TOT (30 items – Immediate Response scale is not included) (Questionnaire range score: 0-60)	8.65	7.405
Pediatric Emotional Distress Scale (PEDS)		
Response format: 1=Almost Never; 2=Sometimes; 3=Often; 4= Very Often		
PEDS Subscales	Mean	SD
<i>Anxious/Withdrawn</i> (6 items e.g. Seems sad and withdrawn.)	9.84	2.945
<i>Fearful</i> (5 items e.g. Clings to adults/doesn't want to be alone)	7.10	2.948
<i>Acting-out</i> (6 items e.g. Has temper tantrums.)	10.74	4.809
<i>Talk-play</i> (4 items e.g. Creates games, stories, or pictures about the event)	5.29	2.003
PEDS-TOT (21 items) (Questionnaire range score: 21-84)	26.81	9.159
Parents' Scores		
Acute Stress Disorder Scale (ASDS)		
Response format: 1=Not at all; 2=Mildly; 3=Medium; 4=Quite a bit; 5=Very much		
	Mean	SD
ASDS-TOT (19 items) (Questionnaire range score: 19-95) (e.g. During or after the trauma, did you ever feel numb or distant from your emotions?; Have memories of the trauma kept entering your mind?)	39.97	15.961

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252 Table II: Participants' scores and Instruments' main details.

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