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ORIGINAL ARTICLE

First Attack of Acute Urticaria in Pediatric Emergency Department

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Received: Aug 1, 2007
Revised: Jan 3, 2008
Accepted: Jun 25, 2008

KEY WORDS:

acute urticaria;
children

Background: Management of a first attack of acute urticaria in children is dependent on the etiology of the disease. Knowledge of the various etiologies of urticaria will help primary physicians to perform appropriate clinical assessments. In this study, we analyzed the etiologies and their prevalence in first-attack acute urticaria in infants, children and adolescents in central Taiwan.

Methods: This was a retrospective study of 953 children who were admitted to the emergency department (ED) with a first attack of acute urticaria from January 2000 to December 2006. All patients were followed in the ED or outpatient department until their symptoms subsided. Patient demographics and detailed etiologies of the first attack of acute urticaria were analyzed. Furthermore, the prevalence of various etiologies in different age groups, as well as the etiologic trends of acute urticaria in children during the previous 7 years, was determined.

Results: The most common etiologies of a first attack of acute urticaria in children were various infections (48.4%), foods (23.5%), idiopathic causes (13.2%), and medications (11.5%). Among the three major etiologies above, upper respiratory tract infections (nasopharyngitis), seafood (shrimp) and nonsteroidal anti-inflammatory drugs (ibuprofen) were the most frequent causes. Moreover, the etiologies differed significantly with patient age ($p < 0.001$). Overall, infections were the major cause in infants (56.5%), whereas food (36.6%) and medications (26.8%) were the most common etiologies in adolescents. The prevalence of various infections dropped as the age of the children increased (56.5% in infants, 51.2% in preschool-aged children, 42.1% in school-aged children and 17.1% in adolescents). The etiologies of foods and medications were more prevalent in adolescents than in younger children.

Conclusion: Detailed etiologies of first-attack urticaria in children in central Taiwan were analyzed. Most importantly, we found that there was a decrease in the prevalence of various infections as causative factors as the age of the children increased. The etiologies of foods and medications were more prevalent in adolescents than in younger children.

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1. Introduction

Urticaria is a common disease in the pediatric emergency department (ED). Many parents ask for emergency medical treatment when their children experience first-time attacks of acute urticaria, especially when they develop severe clinical presentations including itchy, recurrent generalized wheals, edema of the lips or eyelids, and shortness of breath. The diagnosis of acute urticaria is usually based on detailed history taking and clinical manifestations; it presents as transient, geographic, circumscribed wheals and edematous areas involving the dermis and subcutaneous tissue. Urticarial lesions can be evanescent, disappearing within minutes to hours, but recurrence is not uncommon. The etiologies of acute urticaria frequently remain unknown,¹⁻⁴ even after detailed history taking and evaluation by physicians.

In general, acute urticaria in children can be caused by a wide variety of factors, and each etiology requires a different management strategy. A detailed understanding of the various etiologies of urticaria would help primary physicians to perform appropriate clinical assessments, and help parents to prevent their children from coming into contact with specific allergens, especially in the case of children with no past history of any form of urticaria. However, detailed information on the etiologies of first-attack acute urticaria in different age groups of children in central Taiwan is lacking. In this study, we aimed to analyze the prevalence of various etiologies based on different age groups, the average length of hospital stay associated with different etiologies, and the trends in prevalence of etiologies during a 7-year period in central Taiwan.

2. Methods

2.1. Patient population

This retrospective study was conducted from January 2000 to December 2006. During the study period, acute urticaria was diagnosed in 8528 children aged <18 years at the Changhua Christian Hospital, an 1800-bed medical center in central Taiwan. Among these patients, 2152 children underwent medical treatment in the pediatric ED, where 1346 children were identified as having had a first attack of acute urticaria. A first attack of acute urticaria was defined as urticarial symptoms presenting for less than 6 weeks in patients without any prior history of urticaria. To record their demographics and complete disease courses, 953 patients who had follow-up of their disease in the

ED or outpatient department (OPD) were included for further analysis.

2.2. Methods

Patient demographic information was obtained from the hospital records, and included onset date of disease, age at onset, gender, etiology, clinical presentation, treatment, and length of hospital stay. The total duration of symptoms, which was evaluated by physicians and family members, comprised the period between the onset and subsidence of symptoms. Patients were divided into four age groups: infant (1 month to 1 year), preschool-aged (2–6 years), school-aged (7–12 years) and adolescent (13–18 years).

The etiologies of first-attack acute urticaria were divided into seven major categories based on clinical assessment: (1) medications, (2) foods, (3) various infections, (4) inhalants, (5) insect bites, (6) contact materials, and (7) idiopathic causes. The clinical presentations of children with a first attack of acute urticaria in this study included six groups of constitutional symptoms: (1) skin lesions only, (2) respiratory tract symptoms (cough, rhinorrhea, sore throat, shortness of breath), (3) urinary tract symptoms (frequency, dysuria, pyuria), (4) neurologic symptoms (dizziness, vertigo, convulsion, headache, consciousness change), (5) gastrointestinal symptoms (nausea, vomiting, diarrhea, constipation, abdominal pain), and (6) others.

Personal allergy histories including asthma, allergic rhinitis and atopic dermatitis were obtained from hospital records and from patients' or family members' statements. The types of medical treatment that improved symptoms in patients were recorded. The length of hospital stay was obtained from the records of children who were admitted to hospital.

Seven major categories were selected from the detailed etiologies causing first-attack acute urticaria. Differences in the prevalence of these etiologies were analyzed among the four age groups (infant, preschool-aged, school-aged and adolescent). Moreover, the prevalence of each of these seven categories was recorded according to the date of onset of urticaria, to compare the changes in trends during the past 7 years.

2.3. Statistical methods

The prevalence of the etiologies in different age groups was analyzed by Chi-squared tests. The distribution of variables was reported as percentages, mean \pm standard deviation and median for detailed etiologies, age, length of hospital stay and total

duration of symptoms. A p value <0.05 was regarded as significant.

3. Results

3.1. Demographics, etiologies, clinical presentations and treatments

This study included a total of 953 children with a first attack of acute urticaria, who were followed in the ED or OPD for 7 years. There were 535 boys and 418 girls. They ranged in age from neonate to 18 years (mean, 4.92 ± 3.71 years). The majority of children were in the preschool-aged group (59%), followed by the school-aged (23.2%), infant (14.5%) and adolescent (4.3%) groups. Seven major etiologic categories were identified in our study. The most common etiology of first-attack acute urticaria in children was infection (48.4%), followed by foods (23.5%), idiopathic causes (13.2%), medications (11.5%), inhalants (1.7%), insect bites (1.5%), and contact materials (0.2%) (Table 1).

Detailed etiologies of first-attack urticaria are presented in Table 2. Nasopharyngitis and other upper respiratory tract infections were the most common infectious etiologies of acute urticaria in children (23.1%). Other infectious causes included acute gastroenteritis (5.5%), lower respiratory tract infections (4.4%) and urinary tract infections (1.4%). Foods were the second most common etiology in our study (23.5%), with shrimp and other types of seafood (13.3%) being the most common allergens. Milk (3.3%), eggs (1.9%) and peanuts (1.6%) were the least common food-related allergens. Medications were determined to be the cause of urticaria in 11.5% of children. Of the medication-related etiologies, ibuprofen and other types of nonsteroidal anti-inflammatory drugs (NSAIDs) were the most common (3.3%), followed by antibiotics (3.1%). Other etiologic agents, including inhalants (1.7%), insect bites (1.5%) and contact materials (0.2%), were less common, but among these, animal feathers, ant bites and nickel were the major allergens, respectively. In addition, the etiology of first-attack acute urticaria was idiopathic in 13.2% of the children in this study.

The mean duration of symptoms was 6.98 ± 4.05 days (Table 1). Clinical presentations included skin lesions alone (44%), respiratory tract symptoms (41.4%), gastrointestinal symptoms (11%) urinary tract symptoms (0.9%) and neurologic symptoms (0.4%). Allergic rhinitis (22.9%) was the most prevalent allergic disease, followed by asthma (8.1%) and atopic dermatitis (4.6%). The most common medical treatments were oral antihistamines (72.6%), followed by intravenous steroids (27.3%),

Table 1 Demographics, clinical presentations and treatments of first-attack acute urticaria in children ($n=953$)*

Gender	
Male	53.5 (56.1)
Female	418 (43.9)
Age (yr)	4.92 ± 3.71
Infant	138 (14.5)
Preschool-aged	553 (58)
School-aged	221 (23.2)
Adolescent	41 (4.3)
Etiology of urticaria	
Medications	110 (11.5)
Foods	224 (23.5)
Various infections	461 (48.4)
Inhalants	16 (1.7)
Insect bites	14 (1.5)
Contact materials	2 (0.2)
Idiopathic causes	126 (13.2)
Clinical presentations	
Skin lesions only	419 (44)
Respiratory tract symptoms	395 (41.4)
Urinary tract symptoms	8 (0.9)
Neurologic symptoms	3 (0.4)
Gastrointestinal symptoms	106 (11)
Others	22 (2.3)
Personal allergy history	
Asthma	77 (8.1)
Allergic rhinitis	218 (22.9)
Atopic dermatitis	44 (4.6)
Treatments	
Antihistamines (oral/ injection [†] /both)	682 (72.6)/15 (1.6)/ 229 (24.4)
Steroids (oral/ injection [†] /both)	177 (18.9)/255 (27.3)/ 48 (5.1)
Adrenalin (subcutaneous)	11 (1.2)
Admitted to hospital	294 (30.8)
Total duration of symptoms (d)	6.98 ± 4.05

*Data are presented as n (%) or mean \pm standard deviation; [†]included intravenous or intramuscular injections.

oral plus intravenous antihistamines (24.4%) and oral steroids (18.9%); only 1.2% of children received subcutaneous adrenalin injections. Of the 953 children enrolled in this study, 294 (30.8%) required hospitalization.

3.2. Length of hospital stay

Among the 294 patients who were admitted to hospital, infections were the most common etiology of acute urticaria (51%), followed by foods (20.5%), medications (17%), idiopathic causes (10.3%) and

Table 2 Detailed etiologies causing first-attack acute urticaria in children ($n=953$)*

Medications	
NSAID	31 (3.3)
Ibuprofen	10 (1)
Diclofenac (sodium)	9 (0.9)
Ketorolac (tromethamine)	7 (0.8)
Acetylsalicylic acid	3 (0.4)
Others	2 (0.2)
Antibiotics	30 (3.1)
Vaccine	11 (1.2)
Acetaminophen	3 (0.3)
Herbs	9 (0.9)
Antiepileptics	5 (0.5)
Antidiarrheals	5 (0.5)
Antiemetics	3 (0.3)
Sulfa drug	2 (0.2)
Other	11 (1.2)
Inhalants	
Feathers or dander	4 (0.4)
Duck	1 (0.1)
Dog	2 (0.2)
Chicken	1 (0.1)
Pollen	3 (0.3)
Other	9 (1)
Idiopathic causes	126 (13.2)
Foods	
Seafood	127 (13.3)
Shrimp	64 (6.7)
Crab	30 (3.1)
Fish	8 (0.9)
Oyster	5 (0.5)
Other	20 (2.1)
Milk	31 (3.3)
Egg	18 (1.9)
Peanut	16 (1.6)
Fruits	9 (0.9)
Others	23 (2.4)
Insect bite	
Ant	5 (0.5)
Flea	4 (0.4)
Bee	3 (0.3)
Other	2 (0.2)
Various infections	
Upper respiratory tract infections	335 (35.2)
Nasopharyngitis	220 (23.1)
Laryngitis	40 (4.2)
Rhinosinusitis	36 (3.8)
Epiglottitis	13 (1.4)
Others	26 (2.7)
Acute gastroenteritis	52 (5.5)
Lower respiratory tract infections	42 (4.4)
Urinary tract infections	13 (1.4)
Cellulitis	9 (0.9)
Skin infections	5 (0.5)
Acute otitis media	5 (0.5)
Contact materials	
Nickel	2 (0.2)

*Data are presented as n (%). NSAID = nonsteroidal anti-inflammatory drug.

insect bites (1%). Overall, infections led to the longest hospital stay (4.80 ± 3.08 days) and idiopathic etiologies were associated with the longest total duration of symptoms (8.96 ± 4.38 days) (Table 3).

3.3. Analysis of etiologies in different age groups

Infectious diseases were the predominant etiology in infants (56.5%), preschool-aged children (51.2%) and school-aged children (42.1%). Foods were the most frequent etiology in adolescents (36.6%). In addition, we found that the etiologies differed significantly between these four age groups. The prevalence of infectious etiologies decreased as the age of the children increased (56.5% in infants, 51.2% in preschool-aged children, 42.1% in school-aged children and 17.1% in adolescents). Food-related etiologies of acute urticaria were more predominant in older children than younger children (15.9% in infants, 22.4% in preschool-aged children, 28.5% in school-aged children and 36.6% in adolescents). The prevalence of medications as a cause of urticaria was also higher in adolescents (26.8%). Overall, the prevalence of the various etiologies differed significantly between the four age groups ($p < 0.001$) (Figure 1).

3.4. Etiologic trends of acute urticaria from January 2000 to December 2006

Various infections were not only the predominant etiologies in terms of patient numbers, but they were also the leading etiologies in each year of the study. Foods were the second most common etiology, followed by idiopathic causes and medications. Insect bites and inhalants were the least common etiologies of acute urticaria throughout the 7 years (Figure 2).

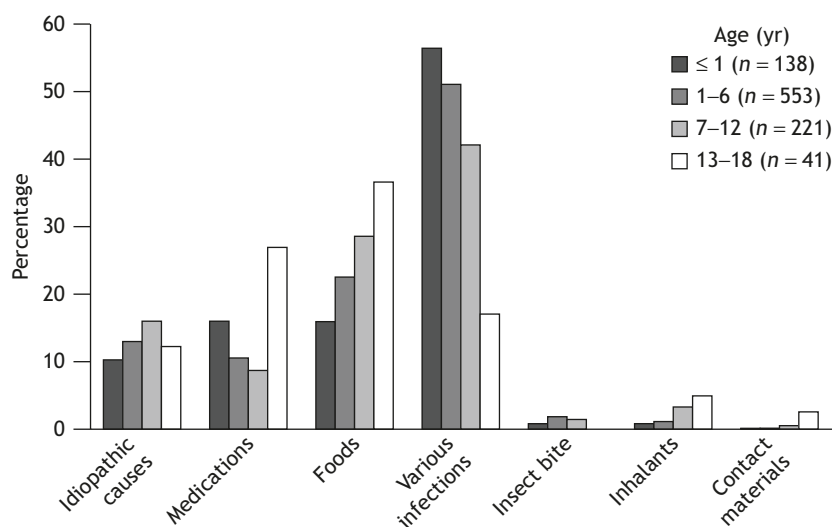
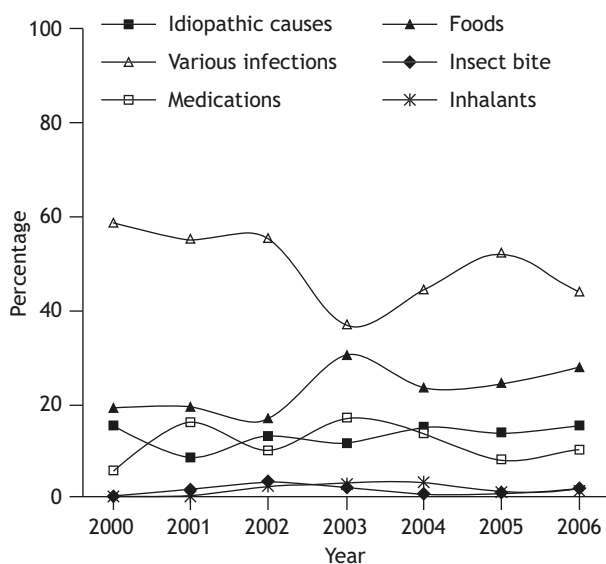
4. Discussion

Urticaria is a common disease in the ED and is estimated to affect 15–25% of people at some point in their life.¹ Many studies have analyzed the etiologies of acute and chronic urticaria,^{1–3,5,6} but the prevalence of different etiologies of a first attack of acute urticaria in children of different age groups has not been clarified. In this study, we identified the etiologies responsible for first-attack acute urticaria in children in central Taiwan, and analyzed their prevalence in different age groups.

Infections were the most common etiologies of acute urticaria in children (48.4%). This finding is compatible with those reported in previous studies.^{1,2,5,7–9} Sackesen et al reported that urinary

Table 3 Etiologies causing hospital admission in children with first-attack acute urticaria (n=294)

Etiologies	n (%)	Age (yr)	Hospital length of stay (d)	Total duration of symptoms (d)
Various infections	150 (51.0)	4.50±3.08	4.80±1.72	7.06±2.15
Foods	59 (20.5)	5.71±3.36	4.20±1.65	7.23±2.97
Medications	50 (17)	3.96±3.51	4.14±1.84	6.25±2.11
Idiopathic causes	31 (10.3)	5.18±3.50	4.55±1.71	8.96±4.38
Insect bite	3 (1)	2.06±3.07	4.67±0.58	6.33±1.52
Inhalants	1 (0.2)	8.5	4	5
Contact materials	0 (0)	0	0	0
Total	294	4.72±3.29	4.54±1.70	7.13±2.70

**Figure 1** Prevalence of etiologies causing a first attack of acute urticaria in children differed significantly between the four age groups ($p < 0.001$).**Figure 2** Prevalence of various etiologies of a first attack of acute urticaria in children from January 2000 to December 2006.

tract infections and upper respiratory tract infections were the most frequently documented infections associated with urticaria.² However, in our study, upper respiratory tract infections and acute gastroenteritis were the major infectious causes of a first attack of acute urticaria. This finding suggests that the respiratory and gastrointestinal tracts should be examined when investigating the etiology of acute urticaria in children. Epiglottitis has been rare in children since the introduction of the *Haemophilus influenzae* type b vaccine.^{10,11} In our study, epiglottitis was determined to be the cause of first-attack urticaria in 13 children. Eighty-five percent of these cases occurred in the first 3 years of our study period (2000–2002) and might have been related to the lower vaccination rate in the countryside of Changhua area at that time.

Although some studies have found foods to be the major cause of childhood urticaria (11–62% of cases),^{1,2,7,12} foods were only the second most common cause in our survey (23.5%). Eggs, milk,

peanuts and tomatoes have previously been reported to be the most frequent food-related causes of urticaria in children.^{1,7,12,13} But in our study, very few cases were due to peanuts and fruits; on the contrary, seafood was the major food-related etiology of acute urticaria in children. Medications, including NSAIDs (11.5%) and antibiotics (3.3%), were identified as the cause of first-attack acute urticaria in 110 patients (11.5%).

Confirmation of the relationships between these etiologies and first-attack acute urticaria was determined by detailed medical history taking and clinical assessments. The initial suspicion of the causative etiology of acute urticaria was based on life events or stresses reported in the patients' statement or statements of the patients' family members. These factors were then further investigated by physicians in the ED. For example, patients who suffered from urticaria after presenting with signs of infection were examined for infection sources. Various infections were suspected to be causative etiologies when patients or families denied any other particular life events or stresses (including special foods or medication intake, animal, plant or material contact). Also, particular foods or medications were suspected as etiologies when patients or families stated that they suffered from a skin rash after eating some of these foods or using the medications. Idiopathic causes were suspected when patients or families denied any special life events or stresses, and there were no positive findings after clinical assessments.

The different mechanisms causing acute urticaria due to different etiologies have been reported in previous studies:^{14,15} urticaria due to infections, either viral or bacterial, is thought to involve the complement system and plasma effector systems; food and medications cause urticaria via an IgE- and IgE receptor-dependent mechanism; while urticaria due to NSAIDs and aspirin are likely mediated by abnormalities of arachidonic acid metabolism.

The etiologies could not be easily determined in patients who presented with infectious signs and were concurrently taking medications before the onset of urticaria. In this study, there were 28 children in this situation. Medications could immediately be ruled out as the cause in 15 patients in the ED, because they had previously taken the same medications without any acute urticaria or allergic reactions, according to hospital records or the patients' statements. In 13 patients, however, the cause could not be determined immediately in the ED. According to the retrospective hospital records, however, medications could be ruled out as the cause in nine of them because they had taken the same medications either before or after this course of urticaria, without presenting with symptoms. In the remaining four

patients, infection could be retrospectively ruled out as the cause, because they suffered from acute urticaria again, after taking the same medications, without any infectious disease.

Although many studies have investigated the major etiologies of urticaria in children,^{1-3,5,7} none of them have investigated the prevalence of these etiologies among different age groups. In this study, we found that the prevalence of various infections as causative factors decreased as the age of children increased ($p < 0.001$), and that foods were the predominant etiology in older children. Medication-related etiologies were also prevalent in adolescents. These findings indicate that primary physicians should survey the underlying infections in younger children while treating their skin lesions. For most parents, first-attack acute urticaria can be a stressful cue, and can suggest the presence of an undiagnosed infection in their children, especially in younger children. In addition to infections, foods and medications are common causes of acute urticaria in adolescence. Therefore, histories of food and medication intake were more important in older children when exploring the possible causative etiologies.

From January 2000 to December 2006, infection was the leading etiology of acute urticaria. The prevalence of the various etiologies causing first-attack acute urticaria in central Taiwan did not change over time. According to this result, we suggest that primary physicians and parents should pay continuing attention to the origins of underlying infections in children who present with a first attack of acute urticaria.

In summary, the detailed prevalence of the etiologies responsible for first-attack acute urticaria in children was analyzed in our study. Various infections were the most common etiologies, followed by foods and idiopathic causes. Most importantly, we found that there was lower prevalence of infectious etiologies as the age of the children increased. Foods and medications as causative factors increased in prevalence in adolescents, compared with younger children. Therefore, we suggest that investigation of underlying infections is essential in younger children with first-attack acute urticaria, while medication and food history taking should be carried out in older children.

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