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Hospital admissions for urticaria in a pediatric emergency department of a tertiary care hospital

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Abstract

Background: Urticaria is a common disorder, estimated to affect 2.1 to 6.7% of children and adolescents, and is a frequent cause of emergency department (ED) admissions.

Methods: The aim of this study was to retrospectively characterize the clinical features of children and adolescents with a diagnosis of urticaria, evaluated in a tertiary care pediatric ED between 2015 and 2019. Statistical analysis was performed using IBM SPSS Statistics®, version 27.0.

Results: A total of 2254 episodes of urticaria were counted with 98.1% corresponding to acute urticaria (AU). A suspected trigger factor was identified in 51.6% of the episodes, namely infections (27.8%), drugs (9.9%) and food (7.6%). From these episodes, excluding infections, only 59.2% were referred to an Allergy Consultation for further study, with only 18.8% (drug) and 28.3% (food) confirmed as the AU trigger. Of the 43 episodes of chronic urticaria (CU), 79% were referred to consultation, with 23 being diagnosed with chronic spontaneous urticaria, 8 with inducible urticaria and 3 with both entities. Older age ($p < 0.001$), personal history of atopy ($p = 0.019$) and angioedema ($p = 0.003$) were factors associated with CU, while the presence of other accompanying symptoms ($p = 0.007$) was associated with AU. Older age (OR = 1.2; $p < 0.001$) and the presence of angioedema (OR = 2.7; $p = 0.007$) were identified as independent factors for CU.

Conclusion: The majority of episodes corresponded to AU. Infections were the main suspected trigger, followed by drugs and food, with an overall confirmation rate ranging from 18 to 30%, highlighting the importance of an allergologic follow-up evaluation.

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Introduction

Urticaria is a common nosological entity in clinical practice, with variable clinical presentation and severity. It has a wide range of etiological variety, and its diagnosis is based on the clinical history, physical examination and the evaluation of possible specific triggers.¹ Although it can affect all age groups, epidemiological data on urticaria is limited, especially studies focusing on the inherent particularities of the pediatric population.

Urticaria is characterized by the rapid onset of pruritic erythematous, circumscribed, discreetly elevated lesions, with a clear center, that are migratory and transient in nature, usually lasting 24 hours. On physical examination, lesions disappear with digit pressure and have a complete resolution without a residual skin lesion. Concomitantly, it may be accompanied by angioedema, defined by sudden and accentuated submucosal or subcutaneous edema, oftentimes more painful than pruritic, usually with a resolution within 72 hours.¹⁻⁶

Urticaria can be classified as acute or chronic, depending on whether it lasts less or more than 6 weeks, respectively, with these different entities requiring differentiated approaches.¹⁻⁶

In the pediatric age group, urticaria is estimated to affect 2.1 to 6.7%⁷ of children, and although it is most frequently mild and self-limited, it can be an anxious motive for parents, therefore being a frequent cause of emergency department (ED) visits.

In its initial approach, it is essential to obtain a complete clinical history focusing on the duration and distribution of lesions, potential triggering factors, and personal and family history of atopy. In addition to an objective examination with emphasis on the skin and mucous membranes, the presence of some relevant data compatible with other concomitant diseases should be identified,^{1,2,6} such as wheezing, cough, rhinorrhea, dizziness, flushing, gastrointestinal symptoms, fever, tachycardia, joint pain, among others.

Acute urticarial (AU), the most common form, rarely requires subsequent investigation, as recent studies show that its main cause in pediatric patients are infectious diseases, especially viruses.⁸⁻¹² Nevertheless, children with a suspected allergic etiology, like food or drugs, should be referred for an allergy consultation, in which a specific allergy investigation is crucial.^{1,13}

Although chronic urticarial (CU), in all its different subtypes, is significantly less frequent; due to its higher pathophysiological complexity, it is often challenging in terms of achieving therapeutic control and characterized by a significant negative impact on a patient's quality of life.¹

Regarding CU, the lack of overall information becomes more evident, particularly when compared to the acute forms of urticaria and especially when focusing on the pediatric population. CU can be subdivided into spontaneous (idiopathic, autoimmune or infectious) and physical/inducible (cold, delayed pressure, solar, heat, vibratory, symptomatic dermographism, aquagenic, cholinergic or contact urticaria).^{1,2,14,15} Being that the diagnosis of CU is essentially clinical, the request for further diagnostic tests to investigate its etiology should be based on the patient's clinical history and performed by an allergy specialist.

The treatment of urticaria should include both non-pharmacological and pharmacological measures. These are clustered into first-line therapy (antihistamines), second-line therapy (omalizumab) and third-line therapy (ciclosporin).¹ Although further treatment options other than antihistamines are not well studied in children. Second-generation, non-sedating antihistamines are the main treatment for episodes of AU; however, the most important course of action is to identify and avoid any potential triggering agent whenever suitable and possible.²

We aim to describe the prevalence, clinical, etiological and clinical characteristics and follow-up of urticaria episodes observed in a pediatric ED.

Material and methods

Type of study and study population

This was a retrospective observational, descriptive, non-intervention study carried out at a tertiary care pediatric ED that provides healthcare to children and adolescents under 18 years of age.

Data were obtained from the analysis of clinical records of all the patients observed in the ED who, at the time of discharge, had a diagnosis of urticaria (including all its subtypes - according to International Classification of Diseases - Ninth Revision codes), from January 1, 2015 to December 31, 2019 (5 years).

Clinical files that were found to have a differential diagnosis and those whose clinical description of skin lesions was not compatible with urticaria were excluded.

Patients were classified into acute or CU according to the temporal duration of their symptoms at the time of ED admission: AU if symptoms lasted less than 6 weeks and CU if recurrent symptoms were present for more than 6 weeks.

This study was approved by the Hospital Ethics Committee (internal reference OBS.SF.238/2021).

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics®, version 27.0.

The following variables were evaluated: gender, age, location of skin lesions (either widespread or local), concomitant presence of angioedema and its location, classification of the urticaria according to its temporal evolution into acute or chronic, personal history of atopy, presence of other symptoms, suspected etiological factor, treatment administered in the ED, prescription at discharge, destiny on discharge and later confirmation or exclusion of the suspected factor. The Kolmogorov-Smirnov test was performed to analyze continuous variables and the chi-square test (χ^2) and Mann-Whitney U test determined differences in the distribution of nominal and continuous variables, respectively. Statistical significance was considered at $p < 0.05$.

When comparing between groups (acute vs. CU), the variables with statistical significance were analyzed using a univariate and multivariate logistic regression model.

Results

In this 5-year period, there were 2254 episodes of urticaria concerning 2042 children, of whom 212 (10.4%) had recurring episodes within the selected time frame. The frequency of urticaria in our ED was about 0.7% and the incidence was 710.8/100,000 in 5 years, given the fact that 317,123 pediatric emergency episodes were recorded in this study period. There was no significant variation in the number of cases occurring over time from 2015 to 2019 (ranging 413-488 episodes/year).

The median age was 5.3 years, with a minimum age of 2 months and a maximum age of 18 years. The distribution

of patients by age group was: 124 patients were under 1 year of age (5.5%), 1123 were of preschool age (1-5 years; 49.8%), 618 were between 6 and 11 years (27.4%), and 389 were between 12 and 18 years (17.2%).

Table 1 presents demographic characteristics, distribution of lesions, presence of angioedema or concomitant symptoms, medical history, therapeutic approach and management of acute and CU episodes.

Classification of urticarial episodes according to duration was also done, and 98.1% were acute and 1.9% were chronic. A statistically significant difference in age was found between children with acute and CU [$p < 0.001$, OR = 1.2 (CI = 1.2-1.3)]. A slight predominance of the male gender

Table 1 Demographic and clinical characteristics of urticaria emergency episodes, acute vs. chronic.

Variable, % (n)	Total 100% (n = 2254)	Acute urticaria 98.1% (n = 2211)	Chronic urticaria 1.9% (n = 43)	p-value
Age (years)				
Median (IQR)	5.3 (2.5-9.8)	5.2 (2.4-9.6)	13 (8.8-16.2)	<0.001
Sex				
Male	55 (1239)	55 (1215)	55.8 (24)	0.91
Personal history of atopic diseases	26 (586)	25.7 (568)	41.9 (18)	0.017
Asthma	14	13.9 (308)	18.6 (8)	-
Allergic rhinitis	6.4	6.4 (142)	7 (3)	-
Atopic eczema	8.6	8.7 (192)	7 (3)	-
Food allergy	2.4	2.4 (52)	4.7 (2)	-
Drug allergy	0.6	0.5 (12)	4.7 (2)	-
Distribution of skin lesions				
Widespread	87.7 (1976)	87.7 (1938)	88.4 (38)	0.887
Angioedema				
Present	11 (247)	10.7 (236)	25.6 (11)	0.005
Other symptoms	34.5 (777)	34.9 (771)	14 (6)	0.004
Respiratory	21 (474)	21.4 (473)	2.3 (1)	-
Fever	8.6 (194)	8.6 (191)	7 (3)	-
Gastrointestinal	4.6 (104)	4.6 (102)	4.7 (2)	-
Discharge from ED				
Discharge home	99.8 (2249)	99.8 (2207)	97.7 (42)	-
Medical appointment	19.4 (438)	18.3 (405)	76.7(33)	-
Short-term hospitalization (<24 hours)	0.2 (5)	0.2 (4)	2.3 (1)	-
ED therapeutic approach				
No therapy	70.5 (1590)	70.3 (1555)	81.4 (35)	-
H1-antihistamine	24.8 (559)	25 (553)	14 (6)	-
Antihistamines in association with corticosteroids and/or adrenaline	4.7 (105)	4.7 (103)	4.7 (2)	-
Outpatient therapeutic approach				
No therapy	3.9 (87)	3.9 (86)	2.3 (1)	-
H1-antihistamine	92.3 (2080)	92.4 (2043)	86 (37)	-
Antihistamines in association with corticosteroids and/or adrenaline	3.9 (87)	3.7 (82)	11.6 (5)	-
Suspected etiology	51.6 (1164)	51.8 (1146)	41.9 (18)	0.195
Infection	27.8 (627)	28.1 (621)	14 (6)	0.041
Drugs	9.9 (223)	10 (220)	7 (3)	0.795
Food	7.6 (172)	7.7 (171)	2.3 (1)	0.252
Contact urticaria	2.6 (58)	2.5 (56)	4.7 (2)	0.304
Insect bites	2.4 (55)	2.5 (55)	0 (0)	0.625
Physical agents	1.3	1 (23)	14 (6)	<0.001

The values presented correspond to the percentage (n), unless otherwise indicated; n - number of cases; ED - emergency department; IQR - interquartile range.

was observed (55%), with a male-to-female ratio of 1.2, with no statistically significant difference between those with acute or CU ($p = 0.91$).

Five hundred and eighty-six children (26%) had a personal history of atopy: 55.2% had asthma, 25.3% had allergic rhinitis, 33.6% had atopic eczema, 9.4% had food allergy, 2.4% had history of drug allergy, three (0.5%) had eosinophilic esophagitis, four (0.7%) had cutaneous mastocytosis, two (0.3%) had history of anaphylaxis and two (0.3%) had previously been diagnosed with CU. The prevalence of atopy was significantly higher among those with CU [(41.9% vs. 25.7%, $p = 0.017$, OR = 2.08 (CI = 1.1-3.8)].

Regarding the distribution of lesions, 87.7% presented with widespread lesions, with 11% of those having angioedema. The majority of angioedema episodes were facial, with labial and periorbital edema being the most frequently reported. The occurrence of angioedema was significantly higher in children with CU than in those with AU [(25.6% vs. 10.7%, $p = 0.005$, OR = 2.9 (CI = 1.4-5.8)].

Other symptoms were present in 777 episodes: respiratory symptoms in 21%, fever in 8.6% and gastrointestinal symptoms in 4.6%. The presence of additional symptoms was higher in children with AU [(34.9% vs. 14%, $p = 0.004$, OR = 0.3 (CI = 0.1-0.7)].

As far as the ED management of the urticaria episodes is concerned, the vast majority of children were subsequently discharged (99.8%), with five cases requiring a short-term hospital stay for evolution monitoring. Out of those discharged from the ED, 19.5% were referred for an outpatient consultation, with 87.9% referrals to an allergy specialist.

When it came to the ED therapeutic approach to urticaria, medical treatment was administered to only 29.5% of children, the majority with just antihistamine therapy (24.8%) or in association with oral corticosteroids (3.6%) and/or intramuscular adrenaline (1%).

On the other hand, 96.1% of children were prescribed outpatient therapy, with antihistamines being the most often prescribed.

Suspected factor and etiological study

In 1164 episodes (51.6%), it was possible to identify a suspected triggering factor through the clinical history. Infections (27.8%), drugs (9.9%) and food (7.6%) stood out as

the main causes. The various suspected etiologies organized by age group: preschool age (<6 years) and school age and adolescent (≥ 6 years), are displayed in Table 2.

In terms of the distribution by age group, urticaria in an infectious context was predominantly in children less than 6 years of age (36.3% vs. 17.3%, $p < 0.001$). Of the 627 episodes, suspected infection-induced urticaria (27.8%), upper respiratory tract infections (URTIs) (45.6%) and viral gastroenteritis (17.5%) were more frequently involved. In cases where URTIs were implicated, the majority were common colds (84.3%), but otitis and pharyngitis/tonsillitis were also observed. In 12% of the episodes, the symptoms did not allow for the establishment of the source of infection, but in the presence of fever and lack of other culprit, we consider infection as the suspected etiology.

Of those in whom a suspicious factor could be identified, excluding infections ($n = 537$), only 59.2% ($n = 318$) were referred to outpatient consultation for further etiological study. In 627 episodes with an infection etiology identified, 5.1% ($n = 32$) were referred for outpatient consultation.

Of the 223 episodes (9.9%) of suspected drug-induced urticaria, antibiotics (81.6%; $n = 182$), nonsteroidal anti-inflammatory drugs (NSAIDs) and vaccines were the main culprit drugs involved. In cases where antibiotics were implicated, the majority ($n = 171$; 94%) were beta-lactams, particularly aminopenicillins, but also cephalosporins. Notably, amoxicillin was the main suspected cause of antibiotic-induced urticaria, present in 64.8% of cases. NSAIDs that are non-selective cyclooxygenase 2 inhibitors, particularly ibuprofen and paracetamol also had a large prevalence ($n = 10$; 4.4% and $n = 8$; 3.5%, respectively). Among those who were referred for etiologic study (76.2%), the suspected drug was later confirmed through an allergological study in 32 cases (18.8%), excluded in 113 cases (66.5%), and the remaining cases did not complete the investigation. Concerning the distribution, by age group, of urticaria due to suspected drug allergy, there was a predominance of cases in children less than 6 years of age (11.2% vs. 8.2, $p = 0.018$).

In children observed with urticaria and the possible association with food ingestion, leading to suspected food allergy, fresh fruits were the most frequently reported (18%), with particular emphasis on rosacea fruits, with nuts and seeds being the second most commonly implicated cause (17.4%). Other implicated foods were, in decreasing

Table 2 Suspected etiology according to age group: preschool age (<6 years) vs. school age and adolescence (≥ 6 years).

Suspected etiology, % (n)	Total 100 (2254)	Preschool age 55.3% (n = 1247)	School age and adolescence 44.7% (n = 1007)	p-value
Not identified	48.4 (1090)	38.4 (479)	60.7 (611)	<0.001
Infection	27.8 (627)	36.3 (453)	17.3 (174)	<0.001
Drugs	9.9 (223)	11.2 (140)	8.2 (83)	0.018
Food	7.6 (172)	9.1 (113)	5.9 (59)	0.004
Contact urticaria	2.6 (58)	1.7 (21)	3.7 (37)	0.003
Insect bites	2.4 (55)	2.4 (30)	2.5 (25)	0.906
Physical agents	1.3 (29)	0.9 (11)	1.8 (18)	0.058

The values presented correspond to the percentage (n); n - number of cases.

order of frequency: eggs, shellfish (mainly shrimp), cow's milk protein and fish, among others. Regarding suspected food-induced urticaria, there was a predominance of cases in children less than 6 years of age (9.1% vs. 5.9%, $p = 0.004$). In children under 6 years of age, the main culprit food was fresh fruits, followed by eggs, nuts and cow's milk protein; in contrast, in children aged more than or equal to 6 years, nuts and seafood were the most commonly reported possible allergens. The suspected culprit food was later confirmed to be a food allergy in 36 cases (28.3% of those referred) and excluded in 67 cases (52.8% of those referred), while in 24 cases (18.9%) it was not possible to complete the study due to loss of follow-up. The remaining 45 patients were not referred for consultation.

An insect bite was the suspected cause of the urticaria episodes in 55 cases (5.5%). Insects implicated as the urticaria culprit were not discriminated in most episodes, with only 5 patients reporting a hymenoptera sting.

Contact urticaria was considered in 58 episodes (2.6%). Cosmetics and hygiene products were the most frequently observed suspects ($n = 22$; 38%). Other factors implicated were animals and plants. Of the 6 that were referred for consultation, 2 did not complete the etiologic study, 3 were attributed to contact with animals and 1 suspected case contact urticaria was excluded.

In 29 episodes, (1.3%) physical factors/stimuli, namely heat/exercise ($n = 12$), dermatographism ($n = 8$), cold and/or hot water ($n = 5$), cold ($n = 2$) and sun exposure ($n = 2$) were identified as suspicious causes by clinical history and examination. The majority of patients were male (2.2:1) and were less than 6 years of age (62.1%). Of the 13 episodes that were referred to specialty consultation, 4 were diagnosed with cholinergic urticaria, 3 with symptomatic dermatographism and 1 with cold urticaria; the remaining 5 had no cause-effect relationship between the suspected physical stimulus and the clinical findings.

CU was responsible for 43 emergency episodes in this study period, out of which 34 (79%) were referred to outpatient consultation. Complementary diagnostic tests were requested in 27 cases: antinuclear antibodies (ANA) were positive in three patients (two with chronic spontaneous urticaria (CSU) and one with simultaneous CSU and physical urticaria); antithyroid antibodies were detected in two adolescents (both with CSU and autoimmune thyroid pathology). IgE total levels were elevated in 12 children. Regarding etiological diagnosis, 23 were diagnosed with CSU, 8 with inducible/physical urticaria (4 cholinergic; 3 symptomatic dermatographism, 1 cold urticaria) and 3 had

both CSU and inducible urticaria (cholinergic, pressure-induced and dermatographism).

In 43 emergency episodes of chronic urticarial, none of the patients were treated with either omalizumab or cyclosporine. Also, the 34 patients who were referred for outpatient consultation did not require these treatments during follow-up, and the disease was controlled with antihistamine therapy.

Logistic regression

In a comparative analysis, we observed that the cases with CU were significantly older (5.2 vs. 13 years, $p < 0.001$) and had a personal history of allergic diseases (41.9% vs. 25.7%, $p = 0.019$). The presence of angioedema was more frequent in children with CU (25.6% vs. 10.7%, $p = 0.003$), whereas the presence of concomitant symptoms was higher in children with AU (34.9% vs. 14%, $p = 0.007$).

After logistic regression, it was only possible to identify older age (OR = 1.2, $p < 0.001$) and the presence of angioedema (OR = 2.7, $p = 0.007$) as independent factors for CU (Table 3).

Discussion

This study aimed to describe, characterize and analyze urticaria admissions in a pediatric ED of a central hospital over a 5-year period, guided by electronic medical record review. The prevalence of urticaria in our sample was 0.7%, which is lower than previous pediatric studies reporting values between 2.1 and 6.7%,⁷ but slightly higher than a recent study in a Portuguese ED whose prevalence of AU was 0.58%.¹⁰ Similar to previously published data, most episodes were found to be AU with only 1.9% being CU.¹⁶⁻¹⁸

The median age of our sample was 5.3 years, with a predominance in the preschool age group. This may be justified by viral infections being the most common cause of AU and by the high prevalence of infections in this age group possibly associated with the attendance of kindergarten. Furthermore, CU was found to be more frequent in older age groups (median age, 13 years) compared to AU (median age, 5.2 years).

Males were slightly more affected (55%) with the absence of gender differences in pediatric age having already been described, in contrast to adults where there is a described female predominance, often attributed to endocrine factors and an immunological basis.¹⁶⁻¹⁸

Table 3 Univariate and multivariate logistic regression analysis of predictors for chronic urticaria.

Variable	Univariate		Multivariate	
	OR (95% - CI)	p-value	OR (95% - CI)	p-value
Age (years)	1.2 (1.2-1.3)	<0.001	1.2 (1.1-1.3)	<0.001
Atopy	2.1 (1.1-3.8)	0.019	1.9 (1-3.5)	0.052
Angioedema	2.9 (1.4-5.8)	0.003	2.7 (1.3-5.6)	0.007
Other symptoms	0.3 (0.1-0.7)	0.007	0.5 (0.2-1.3)	0.170

95% - CI - 95% confidence interval; OR - Odds ratio.

In contrast to previous studies in which AU was associated with allergic diseases rather than chronic urticarial, which had no association with atopic factors,¹⁹ in our sample, atopy was significantly more frequent in those with CU than in those with AU (41.9% vs. 25.7%).

In the group studied, there was a high percentage of cases of CU with associated angioedema (25.6%), as described in the literature^{7,19}; on the other hand, when the total sample was analyzed, only 11% presented angioedema associated with urticaria, lower than what was previously described (40%).³ Angioedema often affects the eyelids and lips, but it can also involve hands, feet, genitals, among other body parts.

The presence of concomitant symptoms suggestive of infection was higher in children with AU, mainly respiratory symptoms, reinforcing previous studies that showed that infections are the most common cause of AU in pediatric age.^{4,9,20,21}

Only five cases were hospitalized, which is consistent with the benign nature of this condition. Nevertheless, approximately 1/5 were referred for an outpatient consultation, mostly to a specialist allergy consultation. While children without referral criteria were referred for consultation (5.1% of all with infectious etiology), on the other hand, children with suspected allergic etiology were not properly guided to an investigation (40.8%) mainly, in order to clarify any possible food or medication allergies, thus avoiding a future of food restrictions or unnecessary therapeutic alternatives. These circumstances can have important social and quality of life repercussions, given that inappropriate contact with the potential allergen can put the allergic patient's life at risk.

In terms of the therapeutic approach, antihistamines were the gold standard, in line with international¹ and national²² guidelines. Still, it should be noted that in seven cases intramuscular adrenaline was used inappropriately in the treatment of urticaria, highlighting the need to implement and promote standardized protocols for the management of urticaria in EDs.

AU is known to be more likely to have a suspected etiology compared to CU, although in our sample there was no statistically significant difference found. In this study, a suspected etiology could not be identified in 48.2% of AU cases, which was higher than that reported by other authors.^{8,9}

Regarding the causes of urticaria in pediatric age, the results are similar to a previous study performed in Portugal.¹⁰ In that study, the main causes of urticaria were infections, followed by food, insect bites and drugs, whereas in this study, drugs were the second most common suspected culprit.

In suspected drug-induced urticaria, antibiotics, NSAIDs and vaccines were most frequently implicated, similar to what has been observed in other publications.^{10,23} A higher frequency of urticaria with amoxicillin was found, which may be explained by the beta-lactam prescription pattern in Portugal. According to previous studies,²⁴ amongst NSAIDs, the main drug implicated was ibuprofen. Paracetamol, which is a very commonly used drug, was also frequently implicated. Allergic drug-related events should be reported and well known by the patient and their caregivers, in order to avoid erroneous re-exposures.

Food was a suspected culprit in 7.7% of AU cases, while the prevalence reported in previous studies was variable (1.3-14%).^{4,8,9} Out of the different foods, fresh fruits and nuts and seeds stood out as the most frequently implicated. Cow's milk proteins were less implicated in our sample, diverging from findings reported by other authors,^{12,18} which highlights the importance of a thorough knowledge of the specific national and regional dietary particularities.

Less frequently, insect bites, contact urticaria, and physical or induced urticaria were implicated.

Older age, a personal history of allergic diseases and the presence of angioedema were factors associated with CU, while the presence of other accompanying symptoms was associated with AU. After logistic regression, older age and the presence of angioedema could be identified as independent factors for CU.

Regarding the classification of CU, the majority corresponded to spontaneous CU, the most common type of CU in pediatric age.⁷

It is well-known that CU may also be associated with systemic diseases and may precede other manifestations of the underlying disease by several years.¹³ CU is more common in children with autoimmune diseases,^{4,23} moreover, children with CU are more likely to be found to have autoantibodies. Although antibodies identification may not have pathological significance, they should be evaluated, allowing early identification of other potentially pathological conditions, such as autoimmune diseases. Twenty-seven children with CU had blood work done resulting in the identification of autoantibodies in five children, two of whom had associated autoimmune thyroid disease and required appropriate treatment.

Talking about the limitations of this study, we highlight the fact that this was a retrospective study based on the analysis of information collected through the review of clinical files, and the data obtained were therefore limited by the information registered. Inadvertently, urticaria episodes that had not yet fulfilled the criteria for classification as CU may have been wrongly classified as AU. Although, this was not proven in those referred for specialized consultations. However, among the others, we cannot state this with certainty. However, we know that in the pediatric age AU is more frequent, and it would be expected that in cases of CU there would be more ED visits with recurrence of episodes, therefore an accurate classification of CU may have occurred.

Nevertheless, we emphasize the importance of this study in a pediatric population for a better understanding of this topic in Portugal, taking into account that visits to the ED do not represent the whole proportion of cases of urticaria, as many do not resort to medical care and others are observed and treated in primary health care.

Conclusion

This study provided a detailed characterization of children diagnosed with urticaria seen at a pediatric ED.

The most frequent causes identified were infections, although drugs and food were frequently implicated, deserving further investigation. It is also noteworthy that although it was possible to confirm a drug or food etiology

as the cause of urticaria in only 18.8 and 28.3% of cases, respectively, the diagnosis of exclusion represents an added value. The patient should be referred to an allergy specialist in order to clarify a suspected food and/or drug allergy in AU, possible etiologies in the case of CU, optimize the therapeutic strategy in order to obtain total symptom control, and minimize the direct and indirect costs associated with this pathology.

The different forms of clinical presentation of urticaria make it a condition of increasing importance, both due to the progressive number of cases and the need for an adequate clinical and laboratory study/diagnosis and new therapeutic approaches. The importance of differential diagnosis is also highlighted, particularly in the exclusion of potentially fatal conditions, such as anaphylaxis in patients with a sudden onset of urticaria.

The different forms of clinical presentation of urticaria make it a pathology of increasing importance, either because of the progressive number of cases, or due to the need for further study and clinical-laboratory diagnosis and knowledge of new therapeutic approaches.

In the case of such a frequent entity, it would be expected to have solid studies, assessing incidence, prevalence, etiology, treatment and evolution, which are fundamental to facilitate the diagnosis and standardize its approach, which are strategies of extreme importance for a more suitable clinical practice.

The true epidemiological impact of urticaria at a national level, particularly in the pediatric age group, however, still remains to be determined.

This study aims to provide a way to improve knowledge of this entity and outline the best strategies for approach and guidance of urticaria episodes in ED and the importance of an accurate referral when appropriate.

References

- Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The international EAACI/GA(2)LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2022; 77(3):734-766. <https://doi.org/10.1111/all.15090>
- Schaefer P. Acute and chronic urticaria: evaluation and treatment. *Am Fam Physician*. 2017;95(11):717-724.
- Guo C, Saltoun C. Urticaria and angioedema. *Allergy Asthma Proc*. 2019;40(6):437-440. <https://doi.org/10.2500/aap.2019.40.4266>
- Pier J, Bingemann TA. Urticaria, angioedema, and anaphylaxis. *Pediatr Rev*. 2020;41(6):283-292. <https://doi.org/10.1542/pir.2019-0056>
- Kanani A, Betschel SD, Warrington R. Urticaria and angioedema. *Allergy Asthma Clin Immunol*. 2018;14(Suppl 2): 59. <https://doi.org/10.1186/s13223-018-0288-z>
- Caffarelli C, Duse M, Martelli A, Calvani M, Cardinale F, Chiappini E, et al. Urticaria in childhood. *Acta Biomed*. 2020;91(11-S):e2020013.
- Rios M, Silva R, Cunha L, Gomes E, Falcão H. Urticária crónica numa população pediátrica. *Nascer Crescer*. 2012;XXI:80-85.
- Talarico V, Marseglia GL, Lanari M, Esposito S, Masi S, De Filippo M, et al. Pediatric urticaria in the emergency department: epidemiological characteristics and predictive factors for its persistence in children. *Eur Ann Allergy Clin Immunol*. 2021;53(2):80-85. <https://doi.org/10.23822/EurAnnACI.1764-1489.148>
- Techasatian L, Phungoen P, Chaiyarit J, Uppala R. Etiological and predictive factors of pediatric urticaria in an emergency context. *BMC Pediatr*. 2021;21(1):92. <https://doi.org/10.1186/s12887-021-02553-y>
- Santa C, Valente CL, Mesquita M, Lopes J, Cardoso I, Barreira P, et al. Acute urticaria in children: from pediatric emergency department to allergology consultation at a central hospital. *Eur Ann Allergy Clin Immunol*. 2022;54(4):168-174. <https://doi.org/10.23822/EurAnnACI.1764-1489.204>
- Marques-Mejias MA, Tomas-Perez M, Vila-Nadal G, Quirce S. Acute urticaria in the pediatric emergency department: management and possible triggers. *Ann Allergy Asthma Immunol*. 2020;124(4):396-397. <https://doi.org/10.1016/j.anaai.2020.01.007>
- Notejane M, Defaz V, Cantarán V, Dall'Orso P. Urticaria y anafilaxia en un Departamento de Emergencia Pediátrica de referencia en Uruguay: estudio clínico y epidemiológico. *Arch Pediatr Urug*. 2018;89(5):311-319.
- Chambel M, Antunes J, Prates S. O mundo da urticária, com e sem alergia. *Rev Port Clínica Geral*. 2010;27:1-11. <https://doi.org/10.32385/rpimgf.v27i1.10824>
- Miles LM, Gabrielli S, Le M, Netchiporouk E, Baum S, Greenberger S, et al. Clinical characteristics, management, and natural history of chronic inducible urticaria in a pediatric cohort. *Int Arch Allergy Immunol*. 2021;182(8):757-764. <https://doi.org/10.1159/000514757>
- Napolitano M, Megna M, Costa C, Balato N, Patruno C. Chronic inducible urticarias in children. *J Allergy Clin Immunol Pract*. 2018;6(4):1391-1393. <https://doi.org/10.1016/j.jaip.2017.12.021>
- Fricke J, Avila G, Keller T, Weller K, Lau S, Maurer M, et al. Prevalence of chronic urticaria in children and adults across the globe: systematic review with meta-analysis. *Allergy*. 2020;75(2):423-432. <https://doi.org/10.1111/all.14037>
- Balp MM, Weller K, Carboni V, Chirilov A, Papavassilis C, Severin T, et al. Prevalence and clinical characteristics of chronic spontaneous urticaria in pediatric patients. *Pediatr Allergy Immunol*. 2018;29(6):630-636. <https://doi.org/10.1111/pai.12910>
- Sabroe RA. Acute urticaria. *Immunol Allergy Clin North Am*. 2014;34(1):11-21. <https://doi.org/10.1016/j.iac.2013.07.010>
- Lee SJ, Ha EK, Jee HM, Lee KS, Lee SW, Kim MA, et al. Prevalence and risk factors of urticaria with a focus on chronic urticaria in children. *Allergy Asthma Immunol Res*. 2017; 9(3):212-219. <https://doi.org/10.4168/aaair.2017.9.3.212>
- Minasi D, Manti S, Chiera F, Licari A, Marseglia GL. Acute urticaria in the infant. *Pediatr Allergy Immunol*. 2020;31(Suppl 26): 49-51. <https://doi.org/10.1111/pai.13350>
- Cetinkaya PG, Soyer O, Esenboga S, Sahiner UM, Teksam O, Sekerel BE. Predictive factors for progression to chronicity or recurrence after the first attack of acute urticaria in pre-school-age children. *Allergol Immunopathol (Madr)*. 2019;47(5): 484-490. <https://doi.org/10.1016/j.aller.2018.12.010>
- Costa C, Goncalo M, GPEU - Português de Estudos de Urticária. [Letter to the editor. Urticaria in the emergency room: recommendations for diagnostic and therapeutic approach]. *Acta Med Port*. 2017;30(4):347-349.
- Tsakok T, Du Toit G, Flohr C. Pediatric urticaria. *Immunol Allergy Clin North Am*. 2014;34(1):117-139. <https://doi.org/10.1016/j.iac.2013.09.008>
- Güvenir H, Dibek Misirtlioglu E, Vezir E, Toyran M, Ginis T, Civelek E, et al. Nonsteroidal anti-inflammatory drug hypersensitivity among children. *Allergy Asthma Proc*. 2015;36(5): 386-393. <https://doi.org/10.2500/aap.2015.36.3858>