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REVIEW ARTICLE

Chronic urticaria in children: epidemiology, diagnosis, and management

Urticaria crónica en niños: epidemiología, diagnóstico y manejo

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Abstract Pediatric urticaria is a common skin disorder affecting 15-20% of children at some point in their lives, with prevalence and causes varying by geographic region. It primarily occurs in older children and is triggered by food allergies, medications, insect bites, viral infections, or other factors. In its chronic form, characterized by recurrent wheals and itching persisting for more than six weeks, it significantly impacts the quality of life of children and their families due to symptom recurrence and management challenges. While in countries like Spain and Germany, it ranks among the leading allergic diseases, data in Latin America is limited. In Ecuador, 57% of cases have an idiopathic etiology, and medications are the most frequent trigger, with an average age of 7.7 years for the first episode. This review analyzes the clinical and epidemiological evidence of chronic pediatric urticaria, focusing on its prevalence in Latin America, to guide early diagnosis strategies and effective management in pediatrics.

Keywords chronic urticaria, children, diagnosis, treatment, quality of life.

Resumen La urticaria infantil es un trastorno cutáneo frecuente que afecta entre el 15 y 20 % de los niños en algún momento de su vida, con una prevalencia y causas que varían según la región geográfica. Se presenta principalmente en niños mayores, desencadenada por alergias a alimentos, medicamentos, picaduras de insectos, infecciones virales u otros factores. En su forma crónica, caracterizada por habones y prurito recurrente que persisten más de seis semanas, impacta considerablemente la calidad de vida de los niños y sus familias debido a la recurrencia de los síntomas y los desafíos en su manejo. Mientras que en países como España y Alemania es una de las principales enfermedades alérgicas, en América Latina los datos son limitados; en Ecuador, el 57 % de los casos tiene etiología idiopática y los medicamentos son el desencadenante más frecuente, con una edad promedio del primer episodio de 7,7 años. Esta revisión analiza la evidencia clínica y epidemiológica de la urticaria crónica infantil, enfocándose en su prevalencia en América Latina, para orientar estrategias de diagnóstico temprano y manejo efectivo en pediatría.

Palabras clave urticaria crónica, niños, diagnóstico, tratamiento, calidad de vida.

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PUBLIS EDITORIAL

Introduction

The prevalence of chronic urticaria ranges from 0.05% to 3%, depending on the population studied, although some studies report figures as high as 5%. Its annual incidence is estimated at 1.4%, affecting 5-15% of individuals at some point. It is most commonly observed between the third and sixth decades, peaking around 40 years old. The condition is more prevalent in women, possibly due to its association with autoimmune characteristics in 35-40% of cases (Ensina et al., 2022).

The prevalence of chronic urticaria in children is lower than in adults, ranging from 0.1 to 0.3%, with a predominance in males. Approximately 40% of patients with chronic urticaria experience angioedema, with this manifestation being the main symptom in 10% of cases (Zamitiz-Hernández et al., 2021).

Chronic spontaneous urticaria, also known as idiopathic or simply chronic urticaria, has an estimated prevalence of 0.5% to 1% in the general population (Coronado et al., 2021). Spain ranks fourth among allergic diseases after rhinitis, asthma, and drug allergies. In Germany, its prevalence reaches 8.8% among all forms of urticaria. While the Argentine Guide for Urticaria and Angioedema states that up to 20% of the population may experience urticaria at some point, there is no updated data on the specific prevalence of chronic urticaria in Latin America.

In Ecuador, a study determined that 57% of chronic urticaria cases are of idiopathic etiology, and 12% are associated with vasculitic urticaria. The etiology seems to vary depending on the region studied (Chérrez-Ojeda et al., 2017). The Ecuadorian Society of Allergy, Asthma, and Immunology (SEAAI) reported a study on chronic urticaria conducted between 2016 and 2018 in a population of 17,082 participants (9,287 children aged 7-8 years and 7,795 adolescents aged 16-17 years). This study analyzed the relationship between urticaria prevalence and exposure to polluted air. The average age of the first episode was 7.7 years, with at least one episode of urticaria reported in 3.3% of respondents (3.6% in children and 2.8% in adolescents).

Chronic urticaria was present in 2.1% of children and 1.1% of adolescents. The most common triggers were medications in children and food in adolescents (Álvaro, 2019). This study aimed to analyze the clinical and epidemiological evidence of pediatric chronic urticaria, focusing on its prevalence in Latin America, to guide strategies for early diagnosis and effective management in pediatrics.

Definition of urticaria

Urticaria is a skin disorder that primarily manifests through the appearance of welts or hives, characterized by intense itching. These lesions can vary in size, from a few millimeters to large areas of skin, and can occur anywhere on the body without a specific location (Méndez et al., 2018).

It is a common condition that affects a significant percentage of the population at some point. Studies estimate that between 15 and 25% of people will experience at least one episode of urticaria. This disorder can have various causes, including allergic reactions, stress, infections, and autoim-mune conditions. Its prevalence is higher in adults than children and occurs more frequently in women, especially between the third and fifth decades of life (Hurtado et al., 2022).

Urticaria is classified into two primary forms: acute and chronic. Acute urticaria, which is self-limiting and lasts less than 6 weeks, is common. On the other hand, chronic urticaria, which persists for 6 weeks or more, is further subdivided into three categories: inducible chronic urticaria, vasculitic urticaria, and chronic spontaneous urticaria. Although less common, chronic urticaria is more complex to treat, and its prevalence has been increasing in recent years (Zuberbier et al., 2018).

Prevalence of urticaria

The prevalence of urticaria ranges from 0.05 to 3%, depending on the studied population, although some studies report prevalences of up to 5%. Its annual incidence is estimated at 1.4% and is calculated to affect 5-15% of the popu-lation at some point in their life. Additionally, 35-40% of cases have an autoimmune origin (Ensina et al., 2022).

The prevalence of urticaria in children may vary depending on the population and geographical region (Peck et al., 2021). Globally, chronic urticaria affects a significant percentage of the pediatric population. Epidemiological studies suggest that it represents approximately 1% to 3% of all urticaria cases in this group, significantly impacting the quality of life of affected children and their families (Zamitiz-Hernández et al., 2021).

Identifying specific prevalence in the pediatric population is usually based on clinical data and surveys conducted in community and hospital settings. However, the variability in the clinical presentation of chronic urticaria and the challenges in determining its underlying cause make it difficult to establish its prevalence with precision (Barzilai et al., 2023). When chronic urticaria is suspected in a child, it is crucial

to seek evaluation by a healthcare professional. An accurate diagnosis and a personalized treatment plan are essential to improve the quality of life for affected children and their families (Álvaro, 2019).

Characteristics of childhood urticaria

The epidemiology of childhood urticaria encompasses the study of its frequency, distribution, and factors associated with its presence in the pediatric population. This disorder is relatively common in children, although its prevalence varies depending on the population and geographic region. It is estimated that between 15 and 20% of children experience some episode of urticaria during their childhood (Zuberbier et al., 2018). It can manifest at any stage, from infancy to adolescence, though it is more common in older children.

In Spain, urticaria ranks fourth among allergic diseases, after rhinitis, asthma, and drug allergies. In Germany, the prevalence reaches 8.8% of all forms of urticaria. According to the Argentine Guide for Urticaria and Angioedema, 20% of the population may experience urticaria at some point. However, there is no current data on the specific prevalence or incidence in Latin America. In Ecuador, it has been reported that 57% of urticaria cases have an idiopathic etiology, and 12% correspond to vasculitic urticaria, with etiological variations depending on the geographic region (Chérrez-Ojeda et al., 2017).

In 2020, the Ecuadorian Society of Allergy, Asthma, and Immunology (SEAAI) examined children aged 7 to 8 years and adolescents aged 16 to 17 years, finding that the average age of the first urticaria episode was 7.7 years. At least one episode of urticaria was reported in 3.3% of participants (3.6% in children and 2.8% in adolescents). Medications were identified as the primary cause of urticaria in these groups, although triggers have not yet been fully defined (Álvaro, 2019).

Allergies to food, medications, insect stings, viral infections, and, in some cases, non-allergic factors can cause childhood urticaria. A correlation with certain infections has been observed sporadically (Caffarelli et al., 2019). This disorder, particularly in its chronic form, can significantly impact the quality of life of the child and their family due to the recurrence of symptoms and the need for prolonged management.

Etiology and triggers of chronic urticaria

The etiology of urticaria in children is typically multifactorial, with several elements capable of triggering this condition. Knowledge about the role of viruses, bacteria, or parasites in developing urticaria is limited. However, after eradicating these parasites, some studies have documented improvements in pediatric patients with urticaria and parasitosis (López et al., 2020).

Among the most studied bacteria is Helicobacter pylori. The protein components of this bacterium can activate mast cells in vitro, inducing the release of histamine, TNF-alpha, IL-3, IFN-gamma, and LTB4. Studies in children are scarce, but a systematic review suggests that the remission of urticaria is significantly higher after treatment for the bacteria than those who did not receive eradication therapy. Other agents identified as causal in a small proportion of cases include Blastocystis hominis, Giardia lamblia, and Dientamoeba fragilis (Barros et al., 2023).

Viral infections, such as the common cold or gastrointestinal infections, can trigger urticaria in children. Current evidence is limited and based on isolated observations. However, there is enough justification to continue researching the role of viruses, bacteria, and parasites in the induction and exacerbation of chronic urticaria. The potential association between infections and urticaria suggests the need for additional studies to explore this relationship and its clinical implications (Álvaro, 2019).

Antibiotics, especially amoxicillin, are a widespread practice for treating various diseases. Despite its benefits, this therapeutic choice carries risks, with allergic reactions, particularly urticaria, being a common reason for health consultations in several countries, including Spain, Argentina, and Colombia (Sánchez-Caraballo et al., 2023).

Common causes and risk factors associated with urticaria in the pediatric population include food allergies, medications, insect stings (such as from bees, wasps, or mosquitoes), and exposure to environmental allergens like pollen, dust mites, or animal hair (Brehler et al., 2023). Some children may experience urticaria due to physical stimuli such as cold, heat, pressure, or sun exposure.

Emotional stress and psychological factors can also trigger or exacerbate urticaria episodes in some children. Another factor would be genetic predisposition to developing urticaria, mainly if there is a family history of allergies or skin conditions. Chronic urticaria is often the result of idiopathic causes and autoimmune disorders, and this condition may last from months to years, sometimes resolving without identifying the cause (Kolkhir et al., 2022).

Clinical manifestations and diagnosis in children

Urticaria in children refers to a skin condition characterized by the appearance of raised and itchy hives, known as welts. These rashes tend to move across the body, reaching their peak between eight and twelve hours. Generally, within the first 24 hours, the skin returns to normal (Coronado et al., 2021). Chronic urticaria can be associated with allergic conditions such as asthma, allergic rhinitis, and autoimmune

disorders (Criado et al., 2015).

Chronic urticaria can last for months or years and sometimes disappears without an apparent cause. The potential identifiable causes of chronic urticaria are similar to those of acute urticaria; however, in most cases, a specific cause cannot be determined, which is referred to as idiopathic urticaria. Some cases of chronic urticaria with no identifiable cause are the result of an autoimmune reaction, the exact source of which is undetectable. It is essential to do everything possible to identify the cause, and eliminating the trigger is the most effective treatment (Kolkhir et al., 2022).

There are two types of chronic urticaria (Figure 1): spontaneous chronic urticaria and inducible chronic urticaria. Spontaneous chronic urticaria appears spontaneously without an identifiable cause through clinical history. Inducible chronic urticaria is triggered by specific stimuli, such as symptomatic dermographism, heat, cold, pressure, water, or vibration (Guevara-Saldaña et al., 2017).

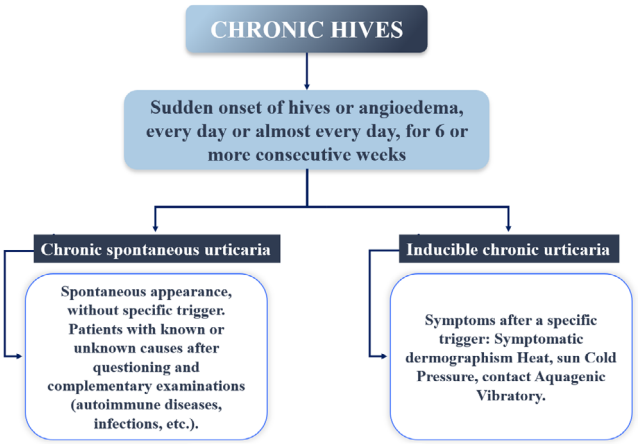

Figure 1. Classification of chronic urticaria (Zuberbier, 2018).

The global prevalence of chronic urticaria in the pediatric population is 1.38%, with approximately 60% of these cases corresponding to chronic spontaneous urticaria and the remaining 40% to inducible chronic urticaria (Azkur et al., 2016). Unlike acute urticaria, chronic urticaria can affect the individual's quality of life due to the recurrent and prolonged nature of the symptoms. There is no definitive test for diagnosing urticaria, so evaluation depends on the medical history and physical examination.

Anamnesis

The medical history of the current illness should include detailed information about individual episodes of urticaria, including the distribution, size, and appearance of the lesions, frequency of occurrence, duration of each lesion, and previous episodes. Activities and exposures immediately before, during, and within the last 24 hours of the urticaria's appearance should be recorded (Chérrez-Ojeda et al., 2017).

The doctor should specifically inquire about recent physical activity, exposure to potential allergens, insects, or animals, new soaps or detergents, new foods, recent infections, or recent episodes of stress. Additionally, the time of onset of urticaria upon contact with any possible trigger should be asked about. Some associated symptoms include itching, rhinorrhea, facial and tongue edema, and dyspnea, which may accompany the hives on the skin (Kolkhir et al., 2022).

Physical examination

The skin examination reveals the presence and distribution of urticaria lesions. There may be skin ulcers, hyperpigmentation, small papules, and jaundice if there is any comorbidity. Urticarial lesions appear as firm, well-defined elevations involving the dermis. These swellings are typically red and vary in size, from the size of a pinhead to covering large areas; some lesions can be extensive (Schoepke et al., 2013).

Smaller lesions may be confluent and may be absent during the consultation. Exposure to vibration (using a tuning fork), heat (using a tuning fork under warm water), cold (using a stethoscope or tuning fork), water, or pressure (light scratching of the affected area with a fingernail) can be employed to reproduce the urticaria (Chérrez-Ojeda et al., 2017).

Most chronic urticaria cases are idiopathic, and their most common cause is an autoimmune disorder leading to clinical manifestations. Urticarial vasculitis is often associated with connective tissue diseases, mainly systemic lupus erythematosus or Sjögren's syndrome. Urticaria accompanied by signs of cutaneous vasculitis should be considered if the urticaria is more painful than itchy, lasts more than 48 hours, does not resolve with pressure, or is associated with vesicles or purpura (Caffarelli et al., 2019).

Complementary studies

Complementary studies are unnecessary for a single episode of urticaria unless signs and symptoms suggest a specific disorder, such as an infection. Unusual, recurrent, or persistent cases require further evaluation. Allergy and laboratory tests should be conducted, including a complete blood count, biochemistry, liver function, and thyroid-stimulating hormone (TSH) levels (Kayiran & Akdeniz, 2019).

Signs and symptoms guide towards more specific tests, such as for autoimmune disorders and abnormalities in liver serology screening tests, eggs, and parasites in cases of eosinophilia, cryoglobulin, elevated creatinine, and thyroid

antibodies in cases of abnormal TSH levels. A skin biopsy is necessary if there are doubts about the diagnosis or if plaques persist for more than 48 hours (to exclude urticarial vasculitis) (Kolkhir et al., 2022).

Pathophysiology

Once mast cells are activated, histamine, bradykinin, kallikrein, and other vasoactive substances are released in the superficial dermis, causing intradermal edema and venous vasodilation. Occasionally, leukocytic infiltration occurs, and subsequently, other mediators such as platelet-activating factors, cytokines, leukotrienes, and prostaglandins cause neurosensory activation, vasodilation, and blood extravasation (Lima et al., 2023).

The exact mechanisms by which mast cells are activated, and cause hives in chronic spontaneous urticaria are not fully understood. Between 30 and 50% of patients have IgG autoantibodies directed against IgE or its high-affinity receptor. In the remaining cases, the stimulus for mast cell activation is unknown (Méndez et al., 2018; Kolkhir et al., 2022).

Basophils also play a role in the pathogenesis of chronic spontaneous urticaria. In patients with high disease activity, peripheral basopenia may be observed due to the migration of these cells to the skin. Basophils in chronic spontaneous urticaria have functional abnormalities that contribute to the development of this condition (Yanase et al., 2023).

Treatment

The goal of chronic urticaria treatment is to control the disease until the symptoms disappear and to identify the causes. Drugs or foods that may be potential triggers should be suspended. Treatment is indicated based on severity; first-line drugs are non-sedating antihistamines, and trigger factors should be avoided, especially in inducible chronic urticaria (Bauer et al., 2021).

Some causes are complex to avoid because treatment primarily relies on the use of antihistamines (Méndez et al., 2018; Caffarelli et al., 2019; Kolkhir et al., 2022), and second-generation antihistamines like cetirizine, levocetirizine, loratadine, desloratadine, rupatadine, fexofenadine, ebastine, and bilastine are preferred due to their lower risk of side effects, once-daily dosing, and reduced sedative effects.

These antihistamines are usually effective and act quickly, but their use should be consistent to achieve optimal results. If the response to the standard dose is insufficient, it is recommended to gradually increase the dose up to four times the usual dose (Zuberbier et al., 2018; Caffarelli et al., 2019; Kolkhir et al., 2022). Although the simultaneous use of different antihistamines is not recommended, switching to another antihistamine may be considered if the first one is ineffective. High doses of antihistamines are not safe in children, so caution should be exercised in this population.

Systemic corticosteroids like prednisone are indicated when symptoms are severe, but prolonged use is not recommended. Topical corticosteroids or antihistamines are not effective (Kolkhir et al., 2022).

As a third-line treatment alternative, the addition of an anti-IgE monoclonal antibody may be considered. Omalizumab is a medication that has demonstrated safety and efficacy in treating spontaneous and induced chronic urticaria. The recommended dose is 300 mg every 4 weeks, regardless of IgE levels in the body. Patients with induced chronic urticaria often do not respond to antihistamines or other common medications. Omalizumab can suppress specific allergic reactions and alleviate symptoms, but its use in children is limited (Caffarelli et al., 2019; Kolkhir et al., 2022).

Another therapeutic option is cyclosporine A, which has a moderate effect on mediator release. Its side effects are more pronounced than those of omalizumab, so it is used only in patients with severe chronic urticaria who do not respond to other treatments (Zuberbier et al., 2018; Caffarelli et al., 2019; Kolkhir et al., 2022; Azkur et al., 2016). Montelukast was previously used, but its efficacy is significantly lower. Patients with angioedema affecting the buccopharynx or airways should receive subcutaneous epinephrine and be hospitalized. Upon discharge, they should be educated on the use of self-injectable epinephrine.

Topical corticosteroids and antihistamines are not effective, and the etiology of concomitant systemic symptoms should be evaluated (Kolkhir et al., 2022; Sánchez-Borges et al., 2014). The purpose of pharmacological treatment is to manage symptoms, considering that urticaria tends to resolve naturally. The therapeutic approach is applied progressively, increasing in complexity (La-Forgia et al., 2023). Other therapeutic approaches may be necessary in more severe cases based on medical evaluation. Taking baths or showers with cold water, avoiding scratching, and wearing loose clothing are recommended to alleviate symptoms.

Management of chronic urticaria in children requires a comprehensive approach and collaboration with healthcare professionals to ensure effective treatment and the well-being of the affected child. Actions to consider include avoiding triggers, measures to relieve itching, and using medications, starting with first-line drugs (Chang et al., 2021). Understanding parents' pathology, collaboration, and attitude is essential for reasonable disease control and proper treatment adherence and follow-up.

Psychosocial evaluation and management are important; considering the influence of these factors and providing emotional support if stress or anxiety contribute to symptoms is crucial in resolving the condition. An elimination diet followed by reintroduction under medical supervision

can be used to identify potential triggers (Donnelly et al., 2023).

Patient and family education is necessary, providing information about the nature of urticaria, potential triggers, and management measures. Regular medical follow-up is also necessary to establish a plan for evaluating the response to treatment, adjusting medication as needed, and addressing any changes in symptoms (Caffarelli et al., 2019; Azkur et al., 2016; La-Forgia et al., 2023; Lopez et al., 2020).

Conclusions

Most of the health center workers were overweight, and a significant group was obese. In these cases, the risk of developing cardiovascular diseases and other non-communicable diseases is directly correlated with waist circumference, and over three-quarters of the participants had central obesity, confirmed by the waist-hip ratio. A considerable percentage of the individuals were classified as sedentary. The workers had iron-related conditions. High risks of chronic noncommunicable diseases were identified based on blood sugar, cholesterol, and triglyceride results. A small part of the sample showed a very high risk, presenting alterations in at least two of the biochemical indicators evaluated. The risk of chronic diseases could be increased due to the regular consumption of foods with high energy density, such as products rich in sugars, fried foods, fats, and meats. Among the habits considered to be risky, frequent cigarette consumption stood out as a significant factor that increases the probability of developing degenerative diseases.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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