

A prospective study of urticaria in children at a tertiary care hospital

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Abstract:

Introduction: Acute urticaria (AU) is a common manifestation with the relatively infrequent occurrence of chronic urticaria (CU) in childhood. Pediatric urticaria has specific features and remains poorly understood. **Methodology:** A prospective study was conducted in 100 patients below the age of 18 years with diagnosis of urticaria from 2014 to 2016. Patients were evaluated taking a detailed history, examination, and basic laboratory investigations. **Results:** Out of hundred children, males were 56 and females 44. Male to female ratio was 1.2:1. Youngest was 7 months male, oldest was 17 years male child and mean age was 7.1 years. Out of 100 cases, 89% presented with acute urticaria and 11% were chronic urticaria. In acute urticaria an underlying cause was present in 59.55 % (53) whereas 40.44 % (36) were idiopathic. Infection was the most common factor (75.47%). Family history was present in five cases. 71% patients presented with first episode whereas 29% gave a history of recurrence. All children were treated with non-sedative antihistamines along with avoiding underlying triggering factors. **Conclusion:** Acute urticaria is a common manifestation seen in our study. Triggering factors in urticaria were dominated by infections followed idiopathic in our study. 16.85% of acute urticaria evolved into recurrent disease and progressed into chronic form due to incomplete treatment and follow-up were observed in our study.

Key words: Urticaria, children, causative factors and treatment.

Introduction: Urticaria is a heterogenous group of mast cell mediated diseases characterized by itchy wheals (hives), angioedema or both. Urticaria of less than 6 weeks is classified as acute urticaria (AU) and longer than 6 weeks duration is classified as chronic urticaria (CU).^[1] Pediatric urticaria has specific features and remains poorly understood. Childhood urticaria management is currently suggested to be the same as in adults.^[2] However, there are pediatric-specific features that must be considered while eliciting triggers and pharmacological therapy.

Acute urticaria is a common manifestation with relatively infrequent occurrence of chronic urticaria in childhood.^[3]

Material and methods: Predesigned and pretested proforma were filled after taking informed consent. Privacy and confidentiality were maintained. The clinically diagnosed cases of urticaria (Itchy, blanchable urticarial wheals with or without angioedema lasting for less than 24 hours) were taken for the study. Detailed history and thorough physical examination were carried out in each patient. The physical examination should focus on conditions that might precipitate urticaria or could be potentially life-threatening and include the following^[4].

- Angioedema of the lips, tongue, or larynx.
- Individual urticarial lesions that are painful, long-lasting (>24 h), or ecchymotic or that leave residual hyperpigmentation or ecchymosis upon resolution are suggestive of urticarial vasculitis,
- Systemic signs or symptoms,
- Scleral icterus, hepatic enlargement, or tenderness,
- Thyromegaly,
- Pneumonia or bronchospasm(asthma) and
- Cutaneous evidence of bacterial or fungal infection.

Information was recorded using semi structured questionnaire guidelines by using local vernacular language. Family history was also noted. Routine investigations like CBP, AEC, IgE level, CRP, CUE, blood urea and sugar were performed in each case at the time of diagnosis. Thyroid function test was done in chronic urticaria cases. Patients were classified as acute urticaria (< 6 weeks duration) and chronic urticaria (> 6 weeks duration). Assessment of disease activity (UAS) in urticaria is based on number of wheals and severity of pruritus. (Mild - <20 wheals/24h and mild pruritus but not troublesome, Moderate - 20-50/24h and moderate pruritus with troublesome but does not interfere with daily normal activity and Severe - >50/24h or large confluent area of wheals and severe pruritus with troublesome and interfere with daily normal activity or sleep). All cases were treated according to the age with non-sedative antihistamines (Levocetirizine: 2–5 years- 1.25 mg twice a day; ≥6 years-5 mg once a day) along with identifying and eliminating triggering factors. All children were followed up biweekly till 12 weeks.

Inclusion criteria: All clinically diagnosed cases of urticaria in children up to the age of 18 years.

Exclusion criteria: Cases above 18 years of age.

Results: Out of hundred children, males were 56 and females 44. Male to female ratio was 1.2:1(chart 1). 52% of cases seen between the age group of 1 to 6 years, 28% between 7 to 12 years and 20% seen between the age group of 13 to 18 years (chart 2). Youngest was 7 months old male infant, oldest was 17 years old male child and mean age was 7.1 years. 71% patients presented with first episode whereas 29% gave a history of two or more episodes (chart 3). Isolated urticaria were seen in 85%, angioedema in 6% and both in 9% (chart 4). Children presented within 24 hours of onset had mild (figure 1) disease (38%) without angioedema, within 24 to 48 hours of onset had moderate (figure 2) disease (58%) with or without angioedema and children presented after 48 hours of onset had severe (figure 3) disease (4%) with angioedema (chart 5). Family history was present in five cases. Out of 100 cases, 89% presented with acute urticaria and 11% were chronic urticaria (chart 6). Out of 89 cases of AU an underlying cause was seen in 59.55% (53) whereas idiopathic in 40.44% (36) (chart 7). Out of 53 cases of AU 75.47% were infections (figure 4), 18.86% food allergies and 5.66% are drug allergies (figure 5) are observed as triggering factors (chart 8). In 11 cases of CU, 7 cases are chronic spontaneous urticaria (CSU) (figure 6), 2 cases are chronic physical urticaria with dermographism (image 7a,b), aquagenic (figure 8) and cholinergic are each one (chart 9).

All cases were treated according to the age with non-sedative antihistamines (Levocetirizine: 2–5 years- 1.25 mg twice a day; ≥ 6 years-5 mg once a day) along with underlying triggering factors. Mild cases are symptom free within 1 to 2 hours, moderate cases in 2 to 6 hours and severe cases in 6 to 12 hours with treatment. Moderate to severe disease with angioedema were treated with 0.5 mg/kg/d of prednisolone for 3 to 5 days along with non-sedative antihistamines. All cases improved clinically with usual dose except two cases of chronic urticaria where we have given up to 10 mg of levocetirizine.

All children were followed up every two weeks and assessed based on urticaria activity score (UAS) till 12 weeks. 78.65 % (70 cases) of AU were under regular treatment with follow up biweekly till 12 weeks and does not developed recurrence. 16.85 % (15 cases) of AU had atopy (based on clinical and raised eosinophilia, IgE antibodies) were under irregular treatment and follow up, developed recurrences subsequently progressed into chronic urticaria. All CU cases were treated with non-sedative antihistamines with regular follow-up.

Discussion: There is little published information on the prevalence, diagnosis, or management of urticaria in children. Accurate diagnosis is an essential prerequisite to a successful management approach. Urticaria is defined by the presence of wheals and/or angioedema.^[2] A wheal comprises a central swelling, pruritus or burning sensation, disappearing within a maximum of 24 hours without residual lesion.

Angioedema is a condition defined by non-dependent, non-pitting, transient edema lasting up to seven days due to the accumulation of vasoactive substances. These substances increase vascular permeability, resulting in swelling in the deep dermal, submucosal, and subcutaneous tissues of the face, lips, neck, extremities, and gastrointestinal (GI) system.^[5]

Angioedema is characterized by swelling of the lower dermis and subcutis associated with a tingling sensation or pain, its resolution taking up to 72 hours. The gold standard for measuring disease activity in spontaneous urticaria is the urticaria activity score (UAS).^[6] The therapeutic goal of acute urticaria is to control and prevent the development of urticarial lesions until the condition resolve by itself. The aim of treatment in children with spontaneous chronic urticaria (SCU) is to stop the recurrences of urticarial lesions by eliminating triggers or by the prophylactic use of non-sedating antihistamines.

Urticaria is classified into four main types.^[2] The classification is based on the precipitating factors and duration as (i) spontaneous acute urticaria, (ii) spontaneous chronic urticaria, (iii) physical urticaria and (iv) other urticarias. These different types display distinct underlying etiologies, involving specific management approaches.

More than 50% cases were between the age group of 1 to 6 years, more than 70% cases presented with first episode and 58% of cases reached to health care provider between 24 to 48 hours as observed in our study. Spontaneous acute urticaria affects 15-20% of the general population at some time during their lifetime.^[1] Spontaneous acute urticaria lasts less than 6 weeks and is the most common type of urticaria in children.^[2] As observed in our study also, 89% presented as AU. In our study an underlying cause was seen 59% of AU cases, in those two third cases were triggered by infections. Acute urticaria is most often a benign, self-limited skin disease. It usually occurs independently, but it may contribute to the more serious clinical manifestations of anaphylaxis: angioedema and anaphylactic shock.

Chronic urticaria (CU) affects 2-4% of individuals over their lifetime.^[7] But in our study CU was observed in 11% of the cases. The high prevalence of CU in our study could be due to

- 1) Changing of lifestyle.
- 2) Failure to identify triggering factors.
- 3) Irregular and incomplete treatment due to loss of follow up.
- 4) Small and limited period of study.

The etiologies of both acute and chronic urticaria are numerous. The etiologic agent is more likely to be identified in acute urticaria (40-60%) than in chronic urticaria (10-20%).^[8] In adults

where urticaria and angioedema coexists in 50 % of cases.^[9] But in children isolated urticaria were seen in 85%, angioedema in 6% and both in 9% in our study.

Aquagenic urticaria is a rare form of physical urticaria, appeared while taking a bath or a shower, in the rain, or in a swimming pool, as observed one case in our study. Well-defined pin head to small pea-sized wheals surrounded by variable sized erythema were provoked by contact with water on the face, neck, and trunk, regardless of its temperature or source. Cholinergic urticaria is a physical urticaria that is caused by sweating as observed one case in our study. It is sometimes referred to as heat bumps, as the rash appears as very small (1-4mm) wheals surrounded by bright red flares.

Diagnosis:

Laboratory studies may be helpful, as follows: Acute urticaria (<6 week) - Laboratory studies generally are not indicated. Chronic or recurrent urticaria (>6 week) - Basic laboratory studies should include complete blood count (CBC), erythrocyte sedimentation rate (ESR), thyroid-stimulating hormone (TSH), and antinuclear antibody (ANA).^[10]

Urticaria may be confused with a variety of other dermatologic diseases that are similar in appearance and are pruritic including atopic dermatitis, maculopapular drug eruptions, contact dermatitis, insect bites, erythema multiforme, pityriasis rosea, urticarial vasculitis, and others. Usually, the experienced clinician can distinguish urticaria from its mimickers owing to its distinctive appearance, intensely pruritic nature, and complete blanching with pressure.^[11]

Children with urticaria usually rub their skin due to itch in comparison to children with atopic dermatitis that scratch their skin until it bleeds.

Management

Acute urticaria may rarely progress to life-threatening angioedema or anaphylactic shock in a very short period, although anaphylactic shock is usually of rapid onset with acute urticarial rash in 20% of cases or no urticaria or angioedema.^[12] Any child with severe, sudden onset of urticarial rash along with angioedema, anaphylactic shock should be ruled out by history and examination (Difficulty in breathing, Wheezing). Prehospital measures may include the following when there is concern for anaphylactic shock:

- If associated angioedema is present, IM epinephrine
- If associated bronchospasm is present, nebulized albuterol
- Other measures may be appropriate, such as continuous ECG, blood pressure and pulse oximetry monitoring; administering intravenous crystalloids if the patient is hypotensive; and administering oxygen.

- Diphenhydramine or hydroxyzine, if available

Management of urticaria is focused on treating the symptoms and typically is not altered by underlying etiology. The mainstay is avoidance of further exposure to the antigen causing urticaria. Pharmacologic treatment options include the following:

Antihistamines, primarily those that block H1 receptors with low sedating activity, such as fexofenadine, loratadine, desloratadine, cetirizine, and levocetirizine are first-line therapy.^(11, 13) These are preferred over diphenhydramine and hydroxyzine; H2 antihistamines, such as cimetidine, famotidine, and ranitidine, may have a role when used in combination with H1 antihistamines, although the benefit is unclear.^[14]

Childhood urticaria management is currently the same as in adults.^[2] It consists of two essential steps;

- (i) Identification and elimination of eliciting triggers or underlying causes and
- (ii) treatment aimed at providing symptomatic relief.

In our study, all children with mild to moderate urticaria responded well to daily treatment with levocetirizine, and only severe cases required a short course (3-5 days) of 0.5 mg/kg prednisone to control symptoms. So early diagnosis and initiation of treatment with non-sedative antihistamines, minimizes the unnecessary use of steroids and its complications.

Continuous treatment with levocetirizine till 12 weeks significantly reduced exacerbations of acute urticaria as well as progression to chronic urticaria as observed in our study. Because once mast cell activates, the activity remains for minimum of 12 weeks. H1 oral antihistamines are the most preferred drugs to induce symptom relief. 2nd generation antihistamines are preferred over older 1st generation antihistamine molecules. Cetirizine and its active enantiomer, levocetirizine, have been most extensively studied for childhood urticaria.^[15]

Avoidance or elimination of urticarial triggers, underlying causes, is the only potentially curative therapy. Comprehensive anamnesis and physical examination are the keys for identification of relevant eliciting factors. Patient tailored diagnostic tests may also be useful for identification of eliciting triggers.

Infections are common triggering factors observed in our study. Wedi et al.^[16] has suggested that in children recurrent upper respiratory infection, pharyngitis, tonsillitis, and sinusitis with streptococci and staphylococci is associated with CU, and remission of urticarial symptoms has been noted with antibiotic therapy as noted in our study also.

In view of the marked adverse effects on the quality of life, ability to play, and school attendance, treatment is necessary in nearly all children with chronic spontaneous urticaria. CU negatively affects school performance. First-generation antihistamines, although effective, are no longer recommended for the management of children with chronic spontaneous urticaria. Second-generation antihistamines are the treatment of choice.^[15,17,18]

When to suspect food allergy⁽¹⁹⁾

- In individuals presenting with anaphylaxis or any combination of symptoms that occur within minutes to hours of ingesting food, especially in young children and/or if symptoms have followed the ingestion of a specific food on more than 1 occasion
- In infants, young children, and selected older children diagnosed with certain disorders, such as moderate to severe AD, Eosinophilic esophagitis, enterocolitis, enteropathy, and allergic proctocolitis
- In adults diagnosed with Eosinophilic esophagitis

Prognosis in acute urticaria: Excellent, most cases resolved within days only with antihistamines. It causes discomfort, but it does not cause mortality, unless it is associated with angioedema involving the upper airways which was not observed in our study. Morbidity depends on the severity and duration. Atopy is the most significant predictor of duration of AU. Continuous exposure to triggers becomes chronic.

Prognosis in acute urticaria: The prognosis in chronic urticaria is more guarded and depends on the comorbid disease causing the urticaria as well as the response to therapy.

According to the current international EACCI/GA2LEN/EDF/WAO guidelines on urticaria,^[11] physical urticaria is defined as a special group of urticaria subtypes, where wheals and/or angioedema are elicited by external physical stimuli. Physical urticaria needs to be distinguished from both spontaneous urticaria and other inducible urticaria types, such as aquagenic urticaria or cholinergic urticaria, where wheal formation is not induced by a physical stimulus. Physical urticarias usually have a chronic course, but children can be free of symptoms for weeks or months when the physical stimulus is avoidable and avoided. This is a clear-cut difference to chronic spontaneous urticaria. One point of confusion in the past has been between physical urticaria and cholinergic urticaria. Cholinergic urticaria symptoms can be elicited through a hot shower or bath as seen in our study also. The underlying mechanism in cholinergic urticaria, however, is not the external stimulus but the increase in body core temperature; cholinergic urticaria can also be elicited by exercise or emotional distress and is, therefore, included in the urticaria subgroup "other inducible urticarias." Acute and chronic urticaria in children can result

in severely impaired quality of life from pruritus and associated sleeplessness, as well as anxiety and depression to whole family.

Key concepts in urticaria management in children^[18]

- Avoidance/elimination of underlying causes and/or eliciting triggers is important.
- Second-generation H1-antihistamines are the mainstay of pharmacological treatment aimed at providing symptomatic relief. Up-dosing has not been validated in children. In our study, all CU cases responded with usual dose except in two cases required double dose to control lesions. First-generation H1-antihistamines should be avoided, mostly due to relevant side-effects.
- Difficult cases may require other therapeutic interventions, the risk–benefit ratio being carefully analyzed as there is hardly any evidence supporting it in children.
- Corticosteroids should be avoided whenever possible and strictly used for short periods only (3–7 days), given the unacceptable side-effects from long-term use.

Conclusion: The proper diagnosis and early treatment of urticaria and angioedema is very important to avoid recurrences and to improve quality of life. Although there have recently been important advances in the elucidation of the pathogenesis, allowing the implementation of innovative diagnostic and therapeutic procedures for patients suffering urticaria, the basic mechanisms remain elusive. Second-generation nonsedating antihistamines at usual or increased doses are presently recommended as first-line therapy for patients with acute and chronic spontaneous urticaria and angioedema.

Acute urticaria is a common manifestation seen in our study. Triggering factors in urticaria were dominated by infections followed idiopathic in our study. 16.85% of acute urticaria evolved into recurrent disease and progressed into chronic form due to incomplete treatment and follow-up were observed in our study.

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