



A clinico-epidemiological study on urticaria cases in various tertiary care hospitals affiliated to a medical college in Mangalore, India

Nitin Joseph, Akriti Suman¹, Siddhika Dangayach¹, Khushboo Sahni¹, Piyush Chaturvedi¹, N. N. Ramachandran¹

Abstract:

BACKGROUND: Urticaria affects one in every five persons in the population.

OBJECTIVES: This study was done to study the risk factors, clinical presentation, and management practices among patients with urticaria.

METHODS: Information from the medical case records of confirmed cases of urticaria at a government and private tertiary care hospital over the recent 4 years were recorded in a semi-structured pro forma.

RESULTS: Mean age of 115 patients was 31.2 ± 20.7 years. Majority of patients (69, 60%) had acute urticaria. The most common risk factors of urticaria in this study were allergy to food substances (27, 23.5%) and allergy to medications (18, 15.6%), followed by insect bites (16, 13.9%). Family history of urticaria was present in 8 (7%) patients. The most common symptom in urticaria was pruritus (68, 59.1%) and the most common sign was hives (40, 34.8%). Lesions were present all over the body in 52 (45.2%) and were bilateral in distribution in 59 (51.3%) patients. Sixty-eight (59.1%) and 69 (60%) urticaria patients were prescribed nonsedating and second-generation antihistamine (sgAH) drugs, respectively. Among chronic urticaria (CU) cases, 35 (76.1%) each received nonsedating and sgAH. Systemic steroids and topical steroid creams were prescribed in 21 (18.3%) and 7 (6.1%) urticaria patients, respectively. Mean duration of application of the topical steroid creams was 10 ± 4.8 days. Leukotriene antagonists were used in the management of greater proportion of patients (54.5%) with dermatographism in comparison to 16.1% without dermatographism ($P < 0.001$).

CONCLUSION: The study reported few important risk factors and certain common clinical presentation in urticaria. Second-generation nonsedating type of antihistamine drugs was the most preferred drug for the management of urticaria.

Keywords:

Acute urticaria, chronic urticaria, clinical presentation, management, risk factors

Introduction

Urticaria is a common dermatological morbidity characterized by the presence of pruritus and wheals with or without angioedema.^[1] Experience of at least one episode of urticaria among general

population is reported by approximately one in five individuals.^[2] It is classified as acute or chronic depending on its duration whether within 6 weeks or otherwise.^[3,4] Etiologically acute urticaria has been found to be triggered by allergens, medications, infections, food substances, and additives,^[5,6] whereas most cases of chronic urticaria (CU) have no external causes.^[7] CU are mostly not

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Associate Professor,
¹MBBS Students,
Department of Community
Medicine, Kasturba
Medical College,
Mangalore, Manipal
Academy of Higher
Education, Manipal,
Karnataka, India

Address for correspondence:

Dr. Nitin Joseph,
Department of Community
Medicine, Kasturba
Medical College, Light
House Hill Road,
Mangalore, Manipal
Academy of Higher
Education, Manipal,
Karnataka, India.
E-mail: drnitinjoseph@gmail.com

related to any specific trigger or inducible agent. About half of the patients with this condition are therefore of the Chronic Idiopathic Urticaria variety. Known causes of CU include circulating autoantibodies in about 30-50% patients. Infections, worm infestations and rarely hypersensitivity reaction to food additives, colouring agents and taste intensifiers feature among the other risk factors of CU.

Moreover, due to its self-limiting course and short duration, in acute urticaria, diagnostic tests are generally not recommended among patients as per the current guidelines. Only in situations, wherein risk factors need to be identified, diagnostic procedures are recommended.^[8] This can further help in modifying treatment approach and for framing suitable preventive strategies.^[8]

Most CU patients on the contrary do not benefit by an extensive workup involved in discovering its cause.^[9] CU is characterized by a diverse and heterogeneous presentation.^[3] Between 0.5% and 5% of the world's population suffer from CUs.^[4] Patients with CU are known to suffer from urticaria symptoms for as long as 3–5 years.^[10] CU due to the presence of intractable pruritus and its long duration is known to adversely affect the quality of life of the affected.^[11,12] The health-care costs in the management of CU are also substantial.^[4,9] The disease causes 20%–30% decrease in job performance, thereby significantly increasing the indirect health-care cost as well.^[13] Urticaria was identified as a risk factor for depression among adolescents too.^[14]

Management in urticaria has been found to vary across different geographical regions.^[9] Treatment remains a challenge to doctors because there has been no well-defined treatment recommendation.^[4] Very few research studies have been done in the field of acute urticaria as most previous studies have been done on CUs only. The knowledge of the clinico-epidemiological and medication usage in CUs in Asian population is also minimal.^[1] Therefore, this study was done to study the risk factors, clinical presentation, and management practices among patients with urticaria in an urban area in South India.

Methods

This was a record-based study done in the month of February 2018 in a government and private tertiary care hospital in Mangalore. Information from the medical case records of confirmed cases of urticaria at these hospitals over the recent 4 years (January 2015–2018) were recorded in a semi-structured pro forma. The pro forma was content validated by subject experts. It contained items on demographic, clinical manifestations,

investigations, associated comorbidities, and therapeutic data of patients.

The study protocol was approved by the Institutional Ethics Committee. The permission to obtain the relevant information from medical records was obtained from the medical superintendents of the respective hospitals. Records which were grossly incomplete were excluded from the study.

The data were entered and analyzed using the Statistical Package for the Social Sciences software package (SPSS Inc., Chicago, IL, USA) version 17. Data were presented in categories and percentages. Chi-square test was used to test association. $P < 0.05$ was taken as statistically significant association.

Results

Out of 115 patients, 72 (62.6%) were from the private hospital and rest from the government hospital.

Mean age of the patients was 31.2 ± 20.7 years [Table 1]. Out of the 115 patients, 69 (60%) had acute urticaria and the rest 46 (40%) had CU.

Table 1: Sociodemographic distribution of study participants

Characteristics	n (%)
Age group (years)	
0-10	27 (23.5)
11-20	15 (13.1)
21-30	18 (15.6)
31-40	18 (15.6)
41-50	17 (14.8)
51-60	10 (8.7)
61-70	6 (5.2)
71-80	4 (3.5)
Gender	
Male	47 (40.9)
Female	68 (59.1)
Marital status	
Unmarried	54 (47.0)
Married	61 (53.0)
Occupational status (n=102)	
Semi-professional	3 (2.9)
Skilled	5 (4.9)
Semi-skilled	12 (11.8)
Unskilled	6 (5.9)
Retired	7 (6.9)
Homemaker	43 (42.1)
Student	26 (25.5)
Place of residence	
Urban	72 (62.6)
Rural	43 (37.4)
Total	115 (100.0)

Among CU patients, 7 (15.2%) were aged ≤ 20 years, 16 (34.8%) were aged 21–40 years, 18 (39.1%) were aged 41–60 years, and 5 (10.9%) were aged >60 years. Fourteen (30.4%) were males and 32 (69.6%) were females.

As many as 27 (23.5%) patients had a history of allergy to food substances. Among them, allergy to vegetarian, nonvegetarian, and both types of foods was reported by 18, 3, and 6 patients, respectively.

Family history of urticaria was present in 8 (7%) patients [Table 2].

Of the total patients, 10 (8.7%) were smokers, 9 (7.8%) were tobacco chewers, and 9 (7.8%) were alcoholics. Among CU patients, 4 (8.7%) were smokers.

The median duration of urticaria among patients was 9 days (interquartile range [IQR]: 3, 456).

The most common symptom in urticaria was pruritus 68 (59.1%). Lesions were present all over the body in 52 (45.2%) patients [Table 3].

The most common sign in urticaria was hives 40 (34.8%) [Table 3].

The most common comorbidities in CU patients were allergic rhinitis (6, 13%), rhinorrhea (5, 10.9%), and anxiety (4, 8.7%). The various symptoms reported among patients of CU were pruritus (17, 37%), redness of the skin (12, 26.1%), breathlessness (3, 6.5%), and watering of the eyes in one patient. The various signs reported among them were dermatographism (11, 23.9%), hives (9, 19.6%), erythema (5, 10.9%), wheal (4, 8.7%), polymorphic lesions (3, 6.5%), and papular lesions (3, 6.5%). Signs such as urticarial vasculitis, flare, and scaly lesions were present in one patient each.

All the patients with urticaria were prescribed at least one variety of antihistamine drugs. Among them, 68 (59.1%) were prescribed nonsedating type of antihistamine drugs and 69 (60%) were prescribed second-generation antihistamine (sgAH) drugs. Sedating type of antihistamine drugs was given in 51 (44.3%) patients [Table 4].

Combination of sgAH like fexofenadine with first-generation (fg) hydroxyzine was given in 4 patients while sg ketotifen with fg diphenhydramine in one patient each. Combination of two sgAH drugs, namely fexofenadine and cetirizine, was observed in five patients and fexofenadine with olopatadine in one patient.

Among CU patients, 35 (76.1%) each received nonsedating and sgAH drugs. Combination of sgAH like fexofenadine with cetirizine was seen in two patients and fexofenadine

Table 2: Distribution of risk factors of urticaria among patients (n=115)

Risk factors	n (%)
Medications	18 (15.6)
Insect bites	16 (13.9)
Pollen grains	8 (7.0)
Physical agents	
Dust	6 (5.2)
Heat	4 (3.5)
Food substances (multiple responses)	
Pulses	13 (11.3)
Vegetables	10 (8.7)
Fruits	6 (5.2)
Cereals	6 (5.2)
Seafoods	5 (4.3)
Spices	3 (2.6)
Other food substances*	6 (5.2)
Family history of urticaria	8 (7.0)

*Other food substances were egg 2, chicken 1, mutton 1, milk 1, and cashew nut 1. Medications were amoxicillin 2, amoxicillin-clavulanic acid 1, cefotaxime 2, gentamicin 2, ofloxacin 2, sodium fusidate cream 1, povidone-iodine solution 1, paracetamol 3, pantoprazole 1, domperidone 1, ondansetron 1, and dicyclomine in 1 patient. Pulses comprise soybean 5, peanut 3, bengal gram 2, green pea 1, tur dal 1, and chickpea 1. Vegetables comprise okra 3, coriander leaves 2, chenopodium album 1, drumstick 1, cabbage 1, mustard seeds 1, and mushroom 1. Fruits comprise banana 3, apple 1, pineapple 1, and raspberry 1. Cereals comprise rice 5 and maize 1. Seafoods comprise prawns 2, shellfish 2, and jellyfish 1. Spices comprise pepper 1, cinnamon 1, and cumin 1

with olopatadine in 1 patient. In two patients, combination of chlorpheniramine maleate and pheniramine was given.

Oral steroids were prescribed in 21 (18.3%) urticaria patients. It was taken for a median duration of 3 days (IQR: 2, 9.25) and mean duration of 4.8 ± 3.7 days.

Three patients (6.5%) with CU were treated with systemic steroids. Of which, one patient was treated with both prednisolone and hydroxyzine.

Topical steroid creams were prescribed in 7 (6.1%) urticaria patients. Mean duration of application of the same was 10 ± 4.8 days.

Leukotriene antagonists were used in the management of 13 (28.3%) CU patients. Among the total patients, dermatographism was present in 22 and among 7 patients with CU. Twelve (54.5%) out of the 22 patients with dermatographism were managed using leukotriene antagonists in comparison to 15 (16.1%) out of 93 without dermatographism ($\chi^2 = 14.6$, $P < 0.001$). Emergency like situation as a consequence of urticaria was found in seven patients. Two of which were managed by adrenaline injections and five using hydrocortisone injections.

Discussion

In this study, majority of the cases of urticaria (23.5%) were aged ≤ 10 years in comparison to the age group of 21–30 years reported in a study done in Korea.^[15]

Table 3: Clinical features of urticaria among patients (n=115)

Characteristics	n (%)
Duration of urticaria	
<1 week	51 (44.4)
1-6 weeks	18 (15.6)
6 weeks-1 year	18 (15.6)
≥ 1 year	28 (24.4)
Symptoms	
Pruritus	68 (59.1)
Redness of the skin	34 (29.6)
Breathlessness	11 (9.6)
Vomiting	3 (2.6)
Others*	4 (3.5)
Signs	
Hives	40 (34.8)
Erythema	32 (27.8)
Polymorphic lesions	27 (23.5)
Dermographism	22 (19.1)
Wheal	20 (17.4)
Papules	16 (13.9)
Macules	9 (7.8)
Angioedema	9 (7.8)
Swelling of limbs	6 (5.2)
Periorbital fascial edema	5 (4.3)
Flare	4 (3.5)
Anaphylactic shock	4 (3.5)
Swelling of the lips	2 (1.7)
Others**	4 (3.5)
Body parts involved (multiple responses)	
All over the body	52 (45.2)
Forearm	39 (33.9)
Face	21 (18.3)
Lower limbs	16 (13.9)
Trunk	9 (7.8)
Others***	2 (1.7)
Side of the body involved	
Bilaterally	59 (51.3)
Left side	31 (27.0)
Right side	25 (21.7)
Comorbidities	
Rhinorrhea	32 (27.8)
Allergic rhinitis	21 (18.3)
Rhinobronchial atopy	20 (17.4)
Diabetes mellitus	19 (16.5)
Sinusitis	15 (13.0)
Anxiety	7 (6.1)
Contact dermatitis	5 (4.3)
Conjunctivitis	5 (4.3)
Asthma	4 (3.5)
Atopic dermatitis	4 (3.5)
Hypothyroidism	4 (3.5)
HTN	4 (3.5)
URTI	3 (2.6)
Fungal infection	3 (2.6)
Other comorbidities****	21 (18.3)

Table 3: Contd...

Characteristics	n (%)
Investigations (multiple responses)	
IgE assay	36 (31.3)
Eosinophil count	29 (25.2)
Erythrocyte sedimentation rate	26 (22.6)
Skin prick test	22 (19.1)
Skin biopsy	18 (15.6)
Liver function tests	8 (7.0)
Patch test	2 (1.7)
Antinuclear antibody test	1 (0.9)
Allergy test	1 (0.9)

*Dryness of the skin 1, watering of the eyes 1, numbness of the hands 1, burning sensation of the skin 1; **Urticarial vasculitis 1, facial puffiness 1, scaly lesions 1, hyperpigmented plaques 1; ***Neck 1, dorsum of the hand 1; ****Maxillary polyp 2, COPD 2, psychiatric illness 2, acute tonsillitis 2, bile stones 1, UTI 1, gastroenteritis 1, gastritis 1, *Helicobacter pylori* infection 1, renal cyst 1, ovarian cyst 1, angina 1, hypogonadism 1, cholangitis 1, hyperthyroidism 1, mesenteric lymphadenitis 1, pyoderma 1, neurofibromatosis 1. HTN=Hypertension, URTI=Upper respiratory tract infection, IgE=Immunoglobulin E, UTI=Urinary tract infection

Table 4: Medications used in the management of urticaria among patients (n=115)

Type of medication	n (%)
Nonsedating antihistamine drugs	
Fexofenadine	38 (33.0)
Cetirizine	27 (23.5)
Olopatadine	7 (6.1)
Azelastine hydrochloride	1 (0.9)
Loratidine	1 (0.9)
Sedating antihistamine drugs	
Hydroxyzine	20 (17.4)
Chlorpheniramine maleate	18 (15.6)
Pheniramine	15 (13.0)
Ketotifen	1 (0.9)
Leukotriene antagonists	
Montelukast	27 (23.5)
Systemic steroids	
Prednisolone	12 (10.4)
Budesonide	7 (6.1)
Deflazacort	1 (0.9)
Mometasone furoate	1 (0.9)
Topical ointments	
Calamine lotion	41 (35.6)
Fusidic acid cream	14 (12.2)
<i>Aloe vera</i> cream	4 (3.5)
Betamethasone cream	4 (3.5)
Mupirocin cream	3 (2.6)
Permethrin cream	2 (1.7)
Fluticasone cream	2 (1.7)
Clobetazole cream	1 (0.9)
Clotrimazole cream	1 (0.9)
Petroleum jelly	1 (0.9)

Among the CU patients, majority (39.1%) were aged 41–60 years. In other studies, a greater proportion of CU patients were seen in the age interval <20 years^[3] or >65 years.^[2] The observations of this study thus support the late onset of CU among patients.

Contd...

More than half of the patients with urticaria and 69.6% patients with CU were females in this study. Similarly, in other studies done among CU patients, females outnumbered males.^[1,9,16,17] On the contrary, a study done in Taiwan reported a higher proportion of CU among males.^[3]

In this study, the duration of urticaria among most cases was <1 week. In a study done in Korea, duration of urticaria was <1 week among 3.4%, 1–6 weeks among 17.9%, 6 weeks–3 months among 9.4%, 3–6 months among 21.4%, 6 months–1 year among 12%, 1–2 years among 11.1%, and 2 or more years among 24.8% patients.^[15]

In a study done in Israel, 15.6% patients with CU were smokers which were similar to our observations. The former study also reported that smokers were significantly more prone to develop CU.^[17] On the contrary, a study done in Italy reported that smoking was associated with a significantly reduced risk of chronic spontaneous urticaria (CSU).^[16]

In this study, the most common cause of urticaria was allergy to food substances, followed by allergy to medications and insect bites. In other studies, infections,^[18] food additives,^[19] stress,^[15,20] food,^[15] alcohol,^[20] medication,^[15,20] sunshine,^[15] heat,^[15,20] cold,^[15] metal touch,^[15,21] usage of personal hygiene/makeup products,^[21] and exposure to pollen^[15] have been reported as risk factors.

The most common comorbidities seen in this study among urticaria patients were rhinorrhea, followed by allergic rhinitis and rhinobronchial atopy. Among CU patients, in particular, allergic rhinitis, rhinorrhea, and anxiety were the most common morbidities reported. In other studies, common morbidities in CU were allergic rhinitis,^[1,9] common cold,^[2] asthma,^[9] atopic dermatitis,^[9] obesity,^[16,17,22] diabetes mellitus,^[17,22] hyperlipidemia,^[17,22] coeliac disease,^[23] hypertension,^[17] chronic renal failure,^[24] gout,^[24] anxiety,^[9,16] depression,^[9] dissociative and somatoform disorders,^[16] gastrointestinal disease,^[1] *Helicobacter pylori* infection,^[25] and malignancies.^[3,16] A study done in Israel also observed that CU patients have significantly increased prevalence of comorbidities as reflected by Charlson's comorbidity index.^[17]

In a study done in Korea, wheals were present in 86.3%, dermatographism in 30.7%, and angioedema in 48.6% urticaria cases.^[15] These findings were much more than our observations.

The most common symptom reported among CU patients was pruritus and the most common sign was dermatographism in this study. Another study done

among CSU patients reported wheals among 24% and angioedema among 25%, and the remaining 51% suffered both these symptoms.^[26] The presence of other physical urticarias, dermatographia, and neutrophil cell infiltrate on skin biopsy in a previous study was found to be associated with CUs which were more difficult to control.^[4]

The distribution of lesions in this study was seen most commonly all over the body. In a study done in Korea, distribution of lesions was on the extremities in 35.5%, over the trunk in 35.2%, and over the head in 29.3% urticaria patients.^[15]

In this study, erythrocyte sedimentation rate (ESR) was recommended as an investigative procedure in 22.6% patients. ESR may be raised in urticarial vasculitis and is raised always in autoinflammatory syndromes.^[20] Complete blood count, C-reactive protein, and ESR are important investigations for the diagnosis of underlying infections.^[8]

In this study, immunoglobulin E (IgE) assay was recommended in 31.3% and skin prick test in 19.1% patients. Only history suggestive of relevant sensitizations to Type I allergens and presence of very strong symptoms should prompt skin prick testing and specific IgE assay.^[8]

Skin patch test was done in 1.7% patients in this study. This test is done when the exogenous agent is not clear from the patient's history. Finally, if still the cause is not clear, specific IgE assay can be helpful.^[27]

Regarding management, the first step in management of acute urticaria is to remove the offending factor immediately. Underlying infections should be treated with appropriate antibiotics.^[28] Later, the patients are treated with licensed dosage of antihistamines given once in a day.^[26] In this study also, all patients with urticaria were treated with at least one antihistamine drug. The most frequently prescribed antihistamine drug in this study was fexofenadine followed by cetirizine. Another study done in Netherlands reported levocetirizine (71%), desloratadine (56%), fexofenadine (23%), clemastine (20%), and hydroxyzine (15%) as the most common drugs used in urticaria management.^[26]

In this study, sgAH drugs were the most commonly used antihistamines. The use of fg antihistamine (fgAH) drugs is discouraged since these antihistamines have serious side effects such as sedation.^[7] In addition, these drugs result in impaired cognition and speech disorganization among elderly patients.^[7]

In this study, 59.1% and 44.3% patients were prescribed nonsedating and sedating types of antihistamine drugs. A study done in Korea reported that 69.5% and 49.7%

urticaria patients were prescribed nonsedating and sedating antihistamine drugs, respectively.^[1] The latter study also reported that patients were found to receive nonsedating antihistamines for a significantly longer duration than sedating antihistamines.^[1]

Among CU patients on antihistamine drugs, the present study observed that 76.1% and 23.9% received nonsedating and sedating types, respectively. In other studies done in the USA, nonsedating antihistamines were used by 64%^[9] and 72%^[13] and sedating type by 7.9%^[9] and 46%^[13] CU patients, respectively. From the above observations, it can be inferred that nonsedating antihistamines were the most preferred antihistamines used even for the management of CU.

This was in accordance to the recommended practice of prescribing sg, nonsedating H₁ antihistamines as first-line therapy in CUs.^[29] If the follow-up urticaria control test shows that the disease is still uncontrolled, then the second-line therapy would be to up dose the standard dosing of these drugs upto four times as per requirement. If the disease is still uncontrolled, then the third-line treatment would be to add-on omalizumab or a maximum of 10 days of montelukast or cyclosporine.^[29]

This study observed that in few patients, combination of antihistamine drugs was used for the management of urticaria. Furthermore, standard urticaria management guidelines do not recommend to combine antihistamines as it has no additional benefits.^[7,30]

Leukotriene antagonists such as montelukast were prescribed in about a quarter of patients in this study. In a study done in the USA, montelukast in the management of CU patients was used in 24.1% patients compared to 28.3% in the present study.^[9] Combinations of nonsedating with sedating antihistamines at night or the addition of antileukotrienes have been reported to be useful in the management of resistant cases of urticaria.^[4,9,20,29] Moreover, 54.5% patients with dermatographism were managed with leukotriene antagonists in this study. Previous studies have observed that, in patients with dermatographia, the use of first- or sgAH or leukotriene receptor-blocking medication was associated with significantly better hive control.^[4]

In this study, 18.3% cases were managed using oral steroids. Oral corticosteroids are given in short courses for severe types of acute urticaria or angioedema affecting the mouth. However, in patients with urticarial vasculitis or delayed pressure urticaria, prolonged course is advised.^[20]

In this study, systemic steroids along with antihistamine drugs were used for management in only 6.5% patients

with CU. On the contrary, in the study done in Korea, majority of the patients with CU (69.9%), received combination of antihistamines and systemic steroids.^[1] In other studies done among CU patients, systemic steroids were used in the management of 53.7%^[9] and 84.3%^[3] patients.

Emergency like situation as a consequence of urticaria was seen in few cases, and majority were managed using hydrocortisone injections followed by adrenaline. Adrenaline injections are used in life-threatening conditions such as anaphylaxis and severe laryngeal angioedema but need to be used with caution in ischemic heart disease and hypertension.^[20]

In this study, seven cases of urticaria were managed using topical steroid creams. The routine use of these preparations, however, is not recommended.^[20]

In a study done in Korea, mean day for systemic corticosteroids prescribed was for 17.7 ± 42.3 days, which was more than our observations.^[1]

Conclusion

This study reported few important risk factors and clinical manifestations in urticaria. Advice regarding avoidance of the identified physical or dietary trigger in this study would be helpful for most patients with urticaria.

Second-generation nonsedating type of antihistamine drugs was observed to be the most preferred drug for the management of urticaria. However, the use of fgAH drugs and combining antihistamine drugs for the management of urticaria was observed in few patients. Thus, the development of recommended treatment guidelines may be needed, to support professionals in the management of urticaria.

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Conflicts of interest

There are no conflicts of interest.

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