

Urticaria: clinical profile, laboratory evaluation, serum IgE evaluation and its significance

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Abstract

Background: Urticaria is a recurrent pruritic skin disease characterised by wheals and or angioedema. The recurrent nature of urticaria, pruritus and wheals impacts negatively on the quality of life of patients. Prevalence studies, type, trigger factors and patient related factors including serum IgE vary depending on site of study. These factors were not documented in our patients. The aim of this study is to determine the clinical characteristics of our urticaria patients and determine the proportion of urticaria patients who have elevated Sr IgE, Eosinophilia, Basophilia, Hepatitis B and C virus seropositivity. Also, to correlate elevated Sr IgE with

age, gender, presence of atopy, dermatographism, type of urticaria, raised eosinophil count and resolution with anti-histamines.

Methods: A retrospective case review was conducted on 43 patients who attended the dermatology outpatient clinic from January 2017 to December 2018. The sociodemographic and clinical parameters of patients was documented using a questionnaire. Investigation results (Sr IgE levels, Eosinophil and Basophil counts, Hepatitis B and C virus seropositivity, stool ova and parasite) were extracted from cases records. Data was analyzed using SPSS version 22. Univariate descriptive statistics such as means, medians, frequencies and proportions are presented.

Results: Prevalence of urticaria was 4.2% and the mean age of the patients was 40.6±15.6 years. Patients were made up 62.8% males and 37.2% females. A history of atopy was noted in 34.9%, urticaria was acute and chronic in 4.7% and 95.3% respectively. Angioedema was present in 44.2% and absent in 53.5%. Majority of the patients (67.4%) were treated with anti-histamines. Serum IgE was elevated in 43.8%, Eosinophilia in 27.30%, Basophilia in 0%, hepatitis B seropositivity in 10%, hepatitis C seropositivity in 0% and a positive stool ova/parasite test in 2.3%.

Conclusions: Urticaria is more prevalent in males. Prevalence is more in those over 40 years of age and prevalence increases with age. Atopy and angioedema is demonstrable in some patients. Basophilia is low in urticaria. Eosinophilia and a raised serum IgE is found in some patients. Parasitology is low in urticaria.

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Introduction

Urticaria is a recurrent pruritic skin disease characterised by wheals and or angioedema.¹ Urticaria can be acute or chronic depending on if symptoms last less than or more than 6 weeks.¹ Chronic urticaria can be classified as spontaneous (CSU), with no identifiable trigger, or inducible (CINDU), with physical triggers like heat, sunlight, cold.¹ The recurrent nature of urticaria, pruritus and wheals impacts negatively on the quality of life of patients.¹⁻³

The prevalence of urticaria in the general population ranges from 0.5% to 1%.^{1,4} Country based prevalence of urticaria varies from 0.69% to 6.8%.⁵⁻⁸ Urticaria occurs in all age groups but it is more prevalent in individuals aged 20-45 years.^{2,4,9-11} Epidemiological studies show urticaria to be more prevalent in females although the mean age at diagnosis is similar in both genders.^{2,10-12} The mean duration of urticaria ranges from 1-5 years but can be longer in those whom in addition to having urticaria have angioedema, physical urticaria or a positive auto reactivity test.^{2,4,13-15}

Studies show CSU to be more prevalent than CIND with 67% CSU reported by Parisi *et al.* in Argentina.^{2,16,17} Physical triggers identified in CIND include cold (13.4%) and dermatographism (24.8%).¹⁶ The workup in the diagnosis of urticaria includes the estimation of serum IgE (Sr IgE).^{13,18} The Serum (Sr) IgE is elevated in 9%-95% of patients who have urticaria irrespective of age.^{6,9,11-14,18-20} An elevated Sr IgE is associated with increased

intensity and frequency of pruritus, increased wheal score, systemic symptoms, chronicity of urticaria, resistance to treatment, family history of atopy, longer duration of disease and other autoimmune diseases.^{3,10,13,18}

The pathogenesis of urticaria is not completely understood but autoantibodies against IgE receptors with consequent mast cell activation and degranulation is said to be the pathway to symptomatology.^{13,21-23} In a large proportion of patients triggers are not identifiable.¹⁴ In the few patients where triggers have been identified, these triggers include alcohol, Hepatitis B Virus and Hepatitis C Virus infection,^{2,24} drugs (non-steroidal anti-inflammatory drug) and stress.¹⁴ Food has not been found to trigger urticaria despite patients giving a history of food as a trigger.²⁵

Clinically, patients present with pruritus, wheals with or without angioedema.¹ These symptoms can occur spontaneously or be induced by physical factors.²⁶ Angioedema is reported in 0.12% to 39% of urticaria patients,^{1,6,15} in 16.2% of patients with CSU and in 15.3% of those who have CSU and concomitant CindU.¹⁴ Dermographism (a form of physical urticaria), is demonstrable in 0.12% of patients.^{1,6} In our cohort of urticaria patients, the prevalence of a positive Sr IgE is not known. The relationship of a positive Sr IgE to clinical characteristics (age, gender, presence of atopy, dermatographism, type of urticaria, raised eosinophil count, resolution with anti-histamines) is not known. Which of one of these patients will benefit from an anti-IgE biologic agent is not known. So, the aim of this study is to determine the clinical characteristics of urticaria patients (age, gender, spontaneous, inducible, chronicity, prevalence of dermatographism, presence of atopy, angioedema and response to anti-histamines) and determine the proportion of urticaria patients who have elevated Sr IgE, Eosinophilia, Basophilia, Hepatitis B and C virus seropositivity). Also, to correlate elevated Sr IgE with age, gender, presence of atopy, dermatographism, type of urticaria, raised eosinophil count and resolution with anti-histamines.

Methods

This was a cross sectional retrospective review conducted at the outpatient skin clinic of the Lagos State University Teaching Hospital. Case records of 43 newly diagnosed, treatment naïve urticaria patients who attended the clinic from January 2017 to December 2018. They were reviewed following ethical approval by the ethics review body of the hospital. Case records with incomplete documentation were excluded from further analysis.

A questionnaire designed for the study was used to document the relevant sociodemographic parameters (age, gender, duration of the disease) and clinical (chronicity, angioedema, atopy, spontaneous, inducible, dermatographism, response to antihistamine, Sr IgE elevation, Eosinophilia, Basophilia, Hepatitis B and C virus seropositivity) information. Any patient with serum IgE ≥ 100 IU/mL was regarded as having an elevated serum IgE.²⁷ Eosinophil count $\geq 6\%$ and basophil count $\geq 3\%$ was regarded as raised (based on hospital laboratory reference values). Statistical analysis was done using SPSS version 22. Univariate descriptive statistics such as means, medians, frequencies and proportions are presented. Associations between variables were assessed using the chi-square test while differences in means were tested using the t-test or Analysis of variance. Multivariable regression methods were used according to the nature of the outcome variable. Level of significance for all tests was set at 95%.

Results

Forty three (43) patients out of the 1,016 new patients seen over the study period were diagnosed to have urticaria, giving a prevalence of 4.2%. The mean age of the patients was 40.6 ± 15.6 years. Patients were 62.8% males and 37.2% females (M:F, 2:1). Marital status was single in 44.2%, married in 53.5% and widowed in 2.3%. Level of education was tertiary, secondary, primary and no formal education in 62.8%, 25.6%, 7.0% and 4.7% of the cases respectively. Smoking history was present in 7.0%, absent in 88.4%, no response in 4.7%. A history of atopy was noted in 34.9%, absent in 65.1%. Urticaria was acute and chronic in 4.7% and 95.3% respectively. Angioedema was present in 44.2% and absent in 53.5% (Table 1).

The majority of the patients (67.4%) were treated with a combination of anti-histamines and prednisolone followed by antihistamines only (32.6%, Figure 1).

Table 1. Clinical parameters of patients with urticaria.

Variables	n = 43	%
Age group		
< 20	3	7.0
20 – 29	9	20.9
30 – 39	11	25.6
≥ 40	20	46.5
Duration of clinic attendance (weeks)		
< 6	14	32.6
6 – 12	13	30.2
13 – 36	3	7.0
>36	10	23.3
Dermographism		
Yes	19	44.2
No	24	55.8
Duration of urticaria		
< 6 weeks	2	4.7
> 6 weeks	41	95.3
Type of Urticaria		
Spontaneous	28	65.1
Inducible	15	34.9
Resolution with antihistamine		
Yes	30	69.8
No	5	11.6
No response	8	18.6

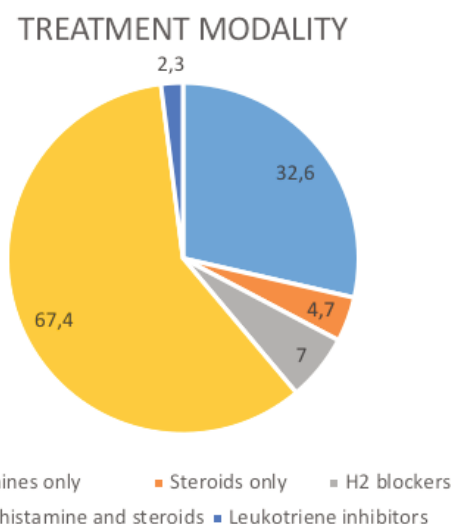


Figure 1. Treatment modality.

Laboratory investigation results of Sr IgE, raised Eosinophil and Basophil counts, hepatitis screen (HBV and HCV) and stool ova/parasite is shown in Figure 2. Sr IgE, was assessed in 16 patients and was elevated in almost half the patients, no patient was positive for HCV and a positive stool ova/parasite test was recorded in only one patient.

Clinical and sociodemographic factors associated with a high serum IgE could not be determined because of the small number of serum IgE positive patients; seven (7) out of sixteen (16).

Discussion

Urticaria though an uncommon presentation in dermatology clinics affects the quality of life of patients mostly due to the associated pruritus and frequent recurrence.^{2,3,15} The prevalence of urticaria in this study is higher than what was reported in Taiwan but comparable to what has reported in Nigeria and Korea.⁵⁻⁸ Prevalence studies of urticaria show its prevalence to vary from country to country.^{5,6,8} In this study, the prevalence of urticaria increased with increasing age, occurring mostly in those aged forty years and above. Urticaria appears to be uncommon in the young. Urticaria is an allergen driven condition.¹³

The relationship between an older age and allergies is not known. Other studies of urticaria show a similar age group affection especially affection of the over forties and increased prevalence in this age group as this study.^{6,14} Unlike our study, Raciborski in Poland reported the same prevalence of urticaria irrespective of age.¹¹ The mean age of our patients is higher than what is documented in China and India but is in keeping with what has been documented in the United Kingdom, Korea and Argentina.^{2,10,13,15,17,19,28}

Twice as many men had urticaria compared to women. This is contrary to the findings from other studies where more females had urticaria.^{2,12,19,29} The reason for this difference in gender affection between our study and that of others is not known. The duration of urticaria in almost all the patients was over 6 weeks making chronic urticaria the most common form of urticaria. Most studies of urticaria in consonance with this study report more of chronic urticaria.^{2,13} Acute urticarias usually has an identifiable cause (drugs, food) and management of this cause leads to resolution making chronic urticaria more prevalent than acute urticaria.

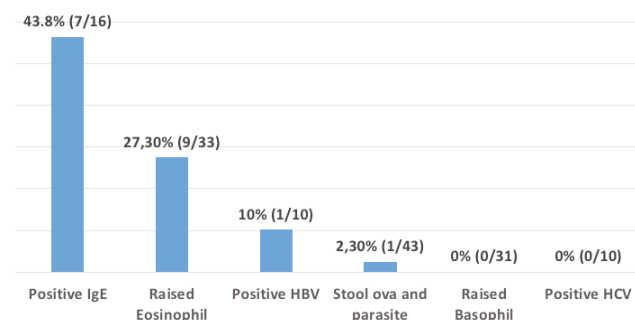


Figure 2. Proportion of patients with positive IgE, raised eosinophil, positive HBV, raised basophil, positive HCV and presence of ova/parasite in stool.

Dermographism, a clinical examination done to demonstrate physical urticaria was demonstrated in less than half of the patients. Thus, physical urticaria was not the most common form of urticaria in this study. The percentage of patients with a positive dermographism is however higher than that reported by Sanchez *et al.* and Seo *et al.*^{6,16} These two studies may have had a lower percentage as they studied more patients than we did.

The majority of the patients had spontaneous urticaria. Inducible urticaria was found in a few patients. As already written, dermographism, was not positive in majority of the patients in keeping with the low percentage of inducible (physical urticaria). Like our study, in Argentina, Parisi *et al.* had a low percentage of their patients having physical urticaria.¹⁷ This was however different from the study by Sanchez *et al.* who reported more inducible than spontaneous urticaria.¹⁶ However, spontaneous urticaria is reported by most authors as the more prevalent form of urticaria like in our study.^{2,16,17}

Resolution of lesions with antihistamine was recorded in most of the patients. In the pathogenesis of urticaria, histamine plays a major role.¹ Typically, antihistamines are the cornerstone of urticaria treatment.^{30,31} Non-resolution of lesions with antihistamine is one of the poor prognostic factors of urticaria.³⁰ Level of education was tertiary in over half of the patients. This would have made explaining the disease easier and hopefully helped with drug adherence, identification and avoidance of triggers.

A smoking history was not present in almost all the patients. Smoking is not a common habit in Nigeria. We were unable to find a relationship of smoking with urticaria in other studies.^{10,16,18}

A history of atopy was present in a third of the patients. One of the associations of urticaria is atopy.¹³ Atopy like urticaria is an IgE driven disease, sometimes having the same triggers. Atopy results in chronicity and poor resolution of urticaria.¹³ Angioedema another IgE driven disease was recorded in almost half the patients. A co-occurrence of angioedema and urticaria though uncommon is well known.³ The occurrence of angioedema in an urticaria patient portends a more severe disease and a long duration of disease.^{3,4} Angioedema occurring in a similar proportion of their urticaria patients as ours was reported by Curto-Barredo *et al.* and Choi *et al.*^{14,15} However, in Korea, angioedema was reported in a fewer patients compared to our study.⁶

Different drugs were used in the treatment of urticaria in the clinic with antihistamines either used alone or in combination with other medications. Majority of the patients were treated with a combination of anti-histamines and prednisolone followed by anti-histamines only. In the guidelines for urticaria management, anti-histamines are recommended either alone or in combination with other drugs.^{30,31} Usually, in the acute phase of treatment, prednisolone is used in combination with antihistamines and then patients are maintained on antihistamines. Lee *et al.* reported a similar treatment protocol like ours but had a higher use of antihistamines only.²⁸

Urticaria is an IgE driven disease and several triggers are identified.²² Also identified is hepatitis, pathogens as strongyloides stercoralis, or helicobacter pylori to mention a few.^{24,32} In the laboratory evaluation of urticaria, serum IgE levels, complete blood counts (hypereosinophilia, basophilia), hepatitis screen (HBV and HCV) and stool ova/parasite tests are done.²

Sr IgE, was raised in almost half the patients in whom it was done. An elevated Sr IgE is associated with increased intensity and frequency of pruritus, increased wheal score, systemic symptoms, chronicity of urticaria, resistance to treatment, family history of atopy, longer duration of disease and other autoimmune diseases.^{10,18} Also, in resistant disease, a raised serum IgE identifies

the patient in whom biologics can be used.¹⁹ The percentage of patients with a raised serum IgE in this study is in keeping with that in literature.^{9,14,15} Serum IgE is elevated in 9-95% of urticaria irrespective of age.^{9,20}

Blood eosinophilia is a marker of urticaria patients but high levels are not recorded in routine clinic attendance.³³ In most outpatient clinics, urticaria patients present with a history, lesions having resolved. Thus, leading to the low number of patients with raised eosinophils in routine clinical evaluations. Blood eosinophilia was recorded in less than a third of our patients. In a study of dermatology patients with eosinophilia, urticaria patients were found to account for a large percentage of the eosinophilia.³⁴ Altrichter *et al.* reported similar to our study, a low prevalence of eosinophilia in patients who do not have an active disease.³³ They adduced this low positivity rate to recruitment of eosinophils into the skin during active disease and immunologic destruction in the blood.³³

Blood basophilia was not recorded in any of the patients in keeping with documented low basophil count in studies of urticaria patients.^{35,36} Basophil count is said to be low in urticaria due to a consumption effect during urticaria pathogenesis and in the urticaria lesions (wheals).³⁶

Hepatitis screen was positive in only one patient and this was hepatitis B virus. No patient was positive to hepatitis C virus. Hepatitis C virus disease is known to present cutaneously as urticaria.²⁴ Only a quarter of the patients had a hepatitis screen. It is difficult to draw conclusions and make recommendations based on this study on the role of hepatitis in urticaria in Nigerian patients. In a review article on hepatitis and urticaria by Kolkhir *et al.*, hepatitis B and C were present in urticaria patients and this is contrary to the lack of positivity to hepatitis C in our study.²⁴ In China following a large population study of urticaria, like our study, a low positive screen for hepatitis was found this was hepatitis B virus.² From these studies, it appears hepatitis B and not hepatitis C is more important in urticaria. Only one patient had a positive stool ova/parasite test. Intestinal helminths are reported to cause urticaria but prevalence studies are few.^{32,37,38} In the few studies, positivity rates for helminths like our study is low.^{32,37,38}

Relating patient factors to a raised Sr IgE in this study could not statistically be achieved because serum IgE was raised in only a few patients (7) in whom serum IgE was assessed. A raised serum IgE in urticaria is associated with a positive family history of atopy, pruritus, chronicity, prolonged use of antihistamines, increased disease activity and severity.^{10,13,16,18}

In conclusion, urticaria is more prevalent in males. Prevalence is predominant in those over 40 years and prevalence increases with age. Atopy and angioedema is demonstrable in some patients. Basophilia is low in urticaria. Eosinophilia and a raised Sr IgE is found in some patients. Parasitology is low in urticaria patients.

There were some limitations to this study. The retrospective nature of the study limited the information which could be retrieved from case records like the urticaria activity score. The number of patients was also few despite this being a two year study. Furthermore, patients were financially responsible for their investigations and treatment. The result of this was the inability of some patients to conduct requested investigations for financial reasons.

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