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Serum Total IgE in Assessing Disease Severity among Patients with Chronic Spontaneous Urticaria

*Azzad MAK[1], Rahman R[2], Naser MA[3], Ullah MF[4], Ahmed NF[5], Haque ATMR[6]

Abstract

Immunoglobulin E (IgE) and its high-affinity receptor, FcεRI, play key roles in the pathogenesis of chronic spontaneous urticaria (CSU). Emerging evidence suggests that total serum IgE may serve as a useful biomarker for assessing disease activity, identifying disease endotypes, and predicting treatment responses in patients with CSU. A cross-sectional study was carried out in the Department of Dermatology & Venereology of Bangladesh Medical University (BMU), Dhaka, Bangladesh, between January and December of 2025, to evaluate the role of serum total IgE levels in assessing disease severity among patients with chronic spontaneous urticaria (CSU). A total of 83 patients with CSU were included in the study. Total serum IgE levels and disease severity were assessed. The majority (48.2%) of the patients belonged to age 21-30 years with female patients were predominant 46 (55.4%) The median total serum IgE levels was 92.0 (65.0-215.0) IU/mL. The prevalence of elevated IgE levels (>100 IU/mL) was 45.8% among patients. The median disease duration differed significantly in mild (6.5 months), moderate (12.0 months) and severe disease (32.0 months) (p<0.001). There was a significant positive correlation between chronic urticaria severity score vs disease duration (r=0.775; p=0.001), while total serum IgE vs. disease duration (r=0.695; p=0.001) and chronic urticaria severity score vs total serum IgE (r=0.688; p=0.001). The elevated total serum IgE levels were significantly associated with a higher disease severity and duration.

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Introduction

Urticaria is a mast cell–driven inflammatory disorder characterized by the occurrence of transient wheals (hives), angioedema, or both, typically in the absence of systemic symptoms. The condition results from mast cell degranulation, which may occur spontaneously or be triggered by a variety of endogenous and exogenous factors.[1] Urticaria is classified according to duration into acute urticaria, lasting less than six weeks, and chronic urticaria, persisting for six weeks or longer. Chronic urticaria may be further categorized as chronic spontaneous urticaria (CSU), in which no identifiable trigger is found, or chronic inducible urticaria, which is provoked by specific and reproducible stimuli.[2] The prevalence of urticaria in the general population has been estimated to range from 0.5% to 1.8%, affecting individuals of all ages but occurring more frequently in adults. Women are affected approximately twice as often as men, and the disease may persist for months or years, substantially impairing quality of life and causing considerable physical and psychological burden.[3] The characteristic clinical manifestation of urticaria is the development of wheals (hives), which

1. *Dr. Mohammad Abul Kalam Azzad, Associate Professor, Department of Dermatology & Venereology, Bangladesh Medical University (BMU), Dhaka-1000.
2. Dr. Reefaat Rahman, Associate Professor, Department of Obstetrics & Gynaecology, Bangladesh Medical University (BMU), Dhaka-1000.
3. Dr. Mohammad Abu Naser, Medical Officer, Department of Dermatology & Venereology, Bangladesh Medical University (BMU), Dhaka-1000.
4. Dr. Muhammad Foyez Ullah, Medical Officer, Department of Dermatology & Venereology, Bangladesh Medical University (BMU), Dhaka-1000.
5. Dr. Nur Faysal Ahmed, Associate Professor, Department of Medicine, Mugda Medical College & Hospital, Dhaka-1214.
6. Dr. Abu Taher Mohammod Rezaul Haque, Assistant Professor, Department of Dermatology & Venereology, Bangladesh Medical University (BMU), Dhaka-1000.

Address of Correspondence:
Email: abunaser1973@gmail.com

are transient, erythematous or pale, edematous skin lesions accompanied by intense pruritus. These wheals vary in size and shape and typically resolve within a few hours, often reappearing at different anatomical sites. Lesions may occur anywhere on the body, including the face, trunk, extremities, and mucosal surfaces.[4,5] The etiology of chronic urticaria (CU) is complex and multifactorial, involving interactions among immunological, genetic, and environmental factors. In many patients, no identifiable cause can be established, and the condition is therefore classified as idiopathic chronic urticaria. Nevertheless, several potential triggers and associated risk factors have been recognized, including autoimmune mechanisms, viral and bacterial infections, physical stimuli, medications such as non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, and angiotensin-converting enzyme (ACE) inhibitors, as well as psychological factors including emotional stress and anxiety.[6]

The recurrent and unpredictable nature of chronic spontaneous urticaria (CSU) can substantially impair patients' quality of life and negatively affect work productivity, social functioning, and daily activities. Recent international guidelines recommend non-sedating, second-generation H1-antihistamines as the first-line treatment for patients with CSU.[2,7] For patients who remain symptomatic despite treatment with approved doses of H1-antihistamines, anti-immunoglobulin E (IgE) therapy with omalizumab is recommended as an effective second-line option. More than half of antihistamine-refractory patients may benefit from omalizumab, a widely used monoclonal antibody that controls symptoms by binding to circulating free IgE.[8] Immunoglobulin E plays a central role in the initiation and persistence of allergic inflammation. Its high-affinity receptor, FcεRI, is expressed on various immune and structural cells, including tissue mast cells, circulating basophils, airway smooth muscle cells, and antigen-presenting cells. The interaction between IgE and FcεRI promotes cellular activation and the release of inflammatory mediators that contribute to the pathogenesis of allergic diseases, including CSU.[9]

Although chronic urticaria (CU) is not typically considered an IgE-mediated allergic disease, elevated serum IgE levels have been reported in a subset of patients, particularly those with concomitant atopic conditions or identifiable allergic triggers. Similar observations have been made in atopic dermatitis (AD), where serum IgE levels are frequently elevated but do not consistently correlate with disease severity. Patients with mild AD may exhibit markedly increased IgE concentrations, whereas those with severe disease may present with only modest elevations or even normal IgE levels. Consequently, total serum IgE is not regarded as a reliable biomarker for assessing disease severity. Nevertheless, the measurement of total and allergen-specific IgE can provide valuable information regarding an individual's atopic status, including sensitization to environmental or food allergens, thereby facilitating the identification of potential triggers and guiding allergen avoidance strategies or adjunctive therapeutic interventions.[10] Omalizumab has demonstrated significant efficacy in controlling symptoms in patients with severe CSU who are refractory to antihistamine therapy. The therapeutic effect of omalizumab is primarily mediated through its binding to circulating free IgE, thereby reducing IgE-mediated activation of mast cells and basophils. Given the central role of free IgE in the mechanism of action of anti-IgE therapy, the development of reliable methods for measuring serum free IgE is of considerable clinical importance. Such methods may facilitate treatment monitoring and optimize the clinical application of anti-IgE therapy in patients with

CSU.[8] Therefore, the primary objective of this study was to evaluate the predictive role of serum total IgE levels in assessing disease severity among patients with chronic spontaneous urticaria (CSU).

Methods

This cross-sectional study was carried out in the Department of Dermatology & Venereology of Bangladesh Medical University (BMU), Dhaka, Bangladesh, between January and December of 2025. A total of 83 patients adults aged 20–50 years, of both sexes, diagnosed with CSU were included in the study. Informed written consents were obtained from the patients before enrollment in this study. Exclusion criteria included acute urticaria, urticarial vasculitis, other non-CU subtypes, inducible urticaria unrelated to CSU, isolated angioedema, systemic diseases affecting assessment, pregnant or lactating women and individuals with a history of malignancies or with AD and use of immunosuppressive drugs, psychoactive therapy, biologics, or systemic corticosteroids within two weeks prior to enrollment. History taking including age, sex, onset, course, duration of the CU, associated disorders, and history of medications. To exclude the presence of associated dermatological problems. Local examination for assessing the severity of urticaria using the urticaria total severity score. The urticaria total severity score is determined by adding the scores of six parameters listed in Table-I. These parameters include the number of wheals, size of wheals, pruritus intensity, duration of symptoms, frequency of wheal occurrence, and the frequency of antihistamine use. Each parameter is scored from 0 to 3. Disease severity is categorized as follows: clear (0), mild (1–6), moderate (7–12), or severe (13–18). Total serum IgE was measured by a Chemilumnescenco Immunoassay method. Notably, while the upper normal limit of total serum IgE is 100 U/mL, we will consider only levels above 100 U/mL to be significantly elevated, thereby excluding “borderline” antibody elevations.

Table-I: Urticaria total severity score

Parameters	Scores			
	0	**1**	**2**	**3**
Number of wheals	None	≤1	11-50	>50
Size of wheals	None	<1 cm	1-3 cm	>3 cm
Intensity of pruritus	None	Mild	Moderate	Severe
Duration of persistence of symptoms	None	<1 hour	1-12 hours	>12 hours
Frequency of appearance	None	<Once or once a week	2-3 times a week	Daily/almost daily
Frequency of antihistamine use	None	<Once or once a week	2-3 times a week	Daily/almost daily

All the relevant collected data was compiled on a master chart first and then statistical analysis was done by using Statistical Packages for Social Sciences (SPSS, version 23 for Windows) (SPSS Inc, Chicago, IL, USA). Mann-Whitney test, unpaired t-test and Kruskal-Wallis test were employed for comparison. Besides, Spearman’s correlation coefficient test was used. Significant value of ‘p’ was decided to be at a level of 0.05 in two tailed tests. This study was approved by the Institutional Review Board of Bangladesh Medical University (BMU), Dhaka, Bangladesh.

Results

In this study, out of 83 patients with chronic spontaneous urticaria, the majority (48.2%) belonged to the 21–30 years age group; the mean age was 31.9±6.6 years. There were 37 (44.6%) were male and 46 (55.4%) were female. The median total serum IgE levels was 92.0 (65.0–215.0) IU/mL. The prevalence of elevated IgE levels (>100 IU/mL) was

45.8% among patients and median duration of disease was 14.0 (7.0–30.0) months (Table-II). Majority (39.8%) patients was found severe chronic urticarial disease. The mean chronic urticaria severity score was 10.3±3.7 with range of 6–18 (Table-III). The median disease duration was significantly higher in high IgE levels 30.0 (17.5–38.5) months compared with normal IgE levels 8.0 (5.0–12.5) months. The mean chronic urticaria severity score was significantly higher in high IgE levels 13.3±2.6 compared with normal IgE levels 7.7±2.4 (Table-IV). The median disease duration differed significantly among mild (6.5 months), moderate (12.0 months) and severe disease (32.0 months) (p<0.001) (Table-V). Significant positive correlations were observed between chronic urticaria severity score and disease duration (r=0.775; p=0.001), total serum IgE and disease duration (r=0.695; p=0.001), and chronic urticaria severity score and total serum IgE (r=0.688; p=0.001) (Table-VI).

Table-II: Baseline characteristics of the study patients (n=83)

Variables	Frequency	Parentage
Age group (in years)		
21–30	40	48.2
31–40	33	39.8
41–50	10	12.0
Mean±SD	31.9±6.6	
Range (min-max)	23.0-48.0	
Sex		
Male	37	44.6
Female	46	55.4
Total serum IgE (IU/mL)		
Normal	45	54.2
High	38	45.8
Median (IQR)	92.0 (65.0-215.0)	
Duration of disease (in months)		
≤12	39	47.0
13–24	16	19.3
25–36	17	20.5
>36	11	13.3
Median (IQR)	14.0 (7.0-30.0)	

Table-III: Chronic urticaria severity of the study patients (n=83)

Variables	Frequency	Parentage
Number of wheals		
None	0	0.0
<10	40	48.2
11-50	15	18.1
>50	28	33.7
Size of wheals		
None	0	0.0
<1 cm	48	57.8
1-3 cm	26	31.3
>3 cm	9	10.8
Intensity of pruritus		
None	0	0.0
Mild	36	43.4
Moderate	34	41.0
Severe	13	15.7
Duration of persistence of symptoms		
None	0	0.0
<1 hour	47	56.6
1-12 hours	23	27.7
>12 hours	13	15.7
Frequency of appearance		
None	0	0.0
Once/week	54	65.1
2-3/week	22	26.5
Daily	7	8.4
Frequency of antihistamine use		
None	0	0.0
Once/week	27	32.5
2-3/week	16	19.3
Daily	40	48.2
Chronic urticaria severity score		
Mild	20	24.1
Moderate	30	36.1
Severe	33	39.8
Mean±SD	10.3 ±3.7	
Range (min-max)	6.0-18.0	

Table-IV: Association between serum IgE level with duration of disease and chronic urticaria severity score (n=83)

Variables	Total serum IgE				p-value
	High (n=38)		Normal (n=45)		
	Frequency	Percentage	Frequency	Percentage	
Duration of disease (in months)					
≤12	5	13.2	34	75.6	
13-24	9	23.7	7	15.6	
25-36	14	36.8	3	6.7	
>36	10	26.3	1	2.2	
Median (IQR)	30.0 (17.5-38.5)		8.0 (5.0-12.5)		[a]0.001
Chronic urticaria severity score					
Mild	2	5.3	18	40.0	
Moderate	8	21.1	22	48.9	
Severe	28	73.7	5	11.1	
Mean±SD	13.3±2.6		7.7±2.4		[b]0.001
Range (min-max)	6.0-18.0		6.0-15.0		

[a]p-value reached from Mann-Whitney test; [b]p-value reached from unpaired t-test.

Table-V: Association between chronic urticaria severity score and duration of disease (n=83)

Duration of disease (in months)	Chronic urticaria severity score						p-value
	Mild (n=20)		Moderate (n=30)		Severe (n=33)		
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	
≤12	20	100.0	16	53.3	3	9.1	
13–24	-	-	10	33.3	6	18.2	
25–36	-	-	3	10.0	14	42.4	
>36	-	-	1	3.3	10	30.3	
Median (IQR)	6.5 (4.3-10.0)		12.0 (6.0-18.0)		32.0 (22.5-40.5)		0.001

p-value reached from Kruskal-Wallis test.

Table-VI: Spearman's correlation coefficient between different variables

Variables	r	p-value
Chronic urticaria severity score vs. total serum IgE	0.688	0.001
Chronic urticaria severity score vs. duration of disease	0.775	0.001
Total serum IgE vs. duration of disease	0.695	0.001

Discussion

CSU is a prevalent allergic dermatologic condition characterized by the spontaneous emergence of pruritic wheals (hives), angioedema, or both, persisting for more than 6 weeks. The pathophysiology of CSU is thought to involve autoimmune mechanisms, particularly the presence of autoantibodies targeting IgE or its high-affinity receptors on mast cells and basophils, leading to histamine release.[1] In this study, the majority (48.2%) patients belonged to age 21–30 years with mean age was 31.9±6.6 years. Farouk et al.[1] reported that the mean age was 31.6±8.4 years. Kuna *et al.*[11] obtained

that out of 41 CSU patients the mean age was found 42.9±16.2 years.

In the present study, out of 83 patients, 37(44.6%) were male and 46(55.4%) were female. Farouk et al. discovered that there were 37(38.1%) males and 60(61.9%) females. Kuna *et al.*[11] revealed that 41 CSU patients (32 were women and 9 were men). Wang *et al.*[12], that encompassed 12 hospitals and included 1,715 outpatients (198 with autoimmune urticaria and 1,517 with CU), reported a female predominance among patients older than 20 years.

In this study observed that the median total serum IgE levels was 92.0 (65.0-215.0) IU/mL. The prevalence of elevated IgE levels (>100 IU/mL) was 45.8% among patients. Farouk *et al.*[1] demonstrated that the total serum IgE levels ranged between 32 and 942 IU/mL, with a mean score of 200 IU/mL. The prevalence of elevated IgE levels (>150 IU/mL) was 50.5% among patients. Kuna *et al.*[11] described that the mean total IgE was found 203.1±396.7 IU/L.

In the present study, the majority (39.8%) of the patients had severe chronic urticarial disease. The mean chronic urticaria severity score was 10.3±3.7 with range from 6-18. Farouk *et al*.[1] obtained that the CSU disease total severity score ranged between 6 and 18, with a mean score of 9.6, including 30 patients (30.9%) with mild severity, 43 patients (44.3%) with moderate severity, and 24 patients (24.7%) with severe disease. Egyptian cohort reported by Shebiny *et al.,*[13] where 40.5% of patients exhibited fewer than 10 lesions. However, Dias *et al*.[14] emphasized that wheal count and pruritus intensity alone may be insufficient to comprehensively assess disease activity or monitor therapeutic response in CSU.

In this current study, the median disease duration was significantly higher in high IgE levels 30.0 (17.5-38.5) months compared with normal IgE levels 8.0 (5.0-12.5) months. The mean chronic urticaria severity score was significantly higher in high IgE levels 13.3±2.6 compared with normal IgE levels 7.7±2.4. In a study conducted by Farouk *et al*.[1] had observed that the mean disease duration was significantly higher in patients with high IgE levels (26.3 months), compared to patients with normal IgE levels (17.9 months, *P* <0.001). Similarly, the mean CU severity score was significantly higher in patients with high IgE levels (11.1 IU/mL), compared to patients with normal IgE levels (6.4 IU/mL) (p<0.001). These variations may reflect the smaller sample size of our cohort relative to those in the studies by Gao *et al.*[15] (302 patients) and Altrichter *et al*.[8] (926 patients), limiting the generalizability of these specific findings. Kessel *et al.*[16] reported significantly higher rates of elevated IgE levels in patients who had their CSU for more than 25 months compared with those with shorter disease duration (40% vs. 23%).

In this study, the median disease duration differed significantly in mild (6.5 months), moderate (12.0 months) and severe disease (32.0 months) (p<0.001). Farouk *et al.*[1] reported that the mean disease duration differed significantly in mild (11.8 months), moderate (23.3 months), and severe disease (33.2 months) (p<0.001).

In the present study, there was a significant positive correlation between chronic urticaria severity score and disease duration (r=0.775; p=0.001), between total serum IgE and disease duration (r=0.695) and chronic urticaria severity score and total serum IgE (r=0.688; p=0.001). In a study conducted by Farouk *et al.*[1] described that there were significant positive correlations between total serum IgE levels and disease severity (r=0.663; p=0.001) and disease duration (r=0.518; p=0.001). Further, there was a

significant positive correlation between disease severity and disease duration (r=0.761). Jang et al.[8] obtained that the correlation coefficients between serum free and total IgE levels were higher in the high serum IgE group (IgE >100 IU/mL, rho=0.85, p<0.001) than in the low serum IgE group (IgE <100 IU/mL, rho=0.38, p=0.08). Significantly higher serum free/total IgE levels were noted in CSU patients than in HCs with a positive correlation between the 2 values (rho=0.87, p<0.001). These results are in agreement with the findings of Kessel *et al.*[16], who also reported elevated IgE levels in patients with more severe and long-standing CSU.

This study has several limitations. Although the current sample size is relatively small , further validation in a larger population would be valuable to enable more robust statistical comparisons among different CU subtypes. Additionally, the study was conducted at a single center, which may limit the generalizability of the findings. Other potentially influential factors, such as comorbidities and treatment regimens, were not comprehensively evaluated and may have affected the results.

Conclusion

To conclude, elevated total serum IgE levels were significantly associated with a higher disease severity and duration. Increasing disease duration is significantly associated with greater disease severity in chronic urticaria. There was a significant positive correlation between chronic urticaria severity score vs disease duration, total serum IgE vs disease duration and chronic urticaria severity score vs total serum IgE. Our findings of elevated IgE levels in patients with CSU support the concept that CSU may be considered an immune-mediated disorder. Furthermore, serum IgE levels may serve as a useful biomarker for evaluating patients with CSU, as they appear to be associated with both disease severity and duration. Therefore, assessment of IgE levels could contribute to improved disease monitoring and may help guide clinical management strategies.

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