
ORIGINAL ARTICLE

Correlation of Total IgE Level with Chronic Spontaneous Urticaria Severity**Katkanit Thammakumpee, M.D.¹, Vorapot Sapsirisavat, M.D.², Kanyarat Thammakumpee, M.D.³**¹Department of Internal Medicine, Faculty of Medicine, Burapha University, Chonburi, Thailand²Department of Preventive Medicine and Family Medicine, Faculty of Medicine, Burapha University, Chonburi, Thailand.³Department of Ophthalmology, Faculty of Medicine, Burapha University, Chonburi, Thailand**Received:** June 27, 2026 **Revised:** August 24, 2026 **Accepted:** September 9, 2026

ABSTRACT

BACKGROUND: Immunoglobulin E (IgE) contributes to the pathophysiology of chronic spontaneous urticaria (CSU), the occurrence of urticaria for more than 6 weeks. High total IgE levels may be associated with increased disease severity. Research within the Thai population remains limited.

OBJECTIVES: This study was done to evaluate the correlation between total IgE levels and CSU severity.

METHODS: A cross-sectional study of adults (aged >15 years) with a diagnosis of CSU was conducted. Demographic data and disease severity using the Urticaria Activity Score for 7 days (UAS7) were recorded. Total IgE levels and biological parameters were measured and their correlations were evaluated.

RESULTS: A total of 100 clinical datasets (52 patients) were analyzed in this study. The median UAS7 score was 6 (interquartile range, 0–16), and the median total IgE level was 94.8 IU/mL (interquartile range, 43.2–196.8). Total IgE levels showed a positive but non-significant correlation with UAS7 (correlation coefficient (r) = 0.090, p = 0.37). Weak correlations were observed between UAS7 and white blood cell count (r = 0.111, p = 0.27) and D-dimer levels (r = 0.054, p = 0.60).

CONCLUSION: Total IgE, WBC, and D-dimer levels were not significantly correlated with CSU disease severity in this cohort. These findings do not support the routine use of total IgE as a direct indicator of disease activity.

KEYWORDS: chronic spontaneous urticaria, Immunoglobulin, Immunoglobulin E, disease severity

INTRODUCTION

Chronic spontaneous urticaria (CSU) is a common condition characterized by the presence of wheals, angioedema, or both for more than six weeks without an identifiable cause.¹ The global prevalence of CSU ranges from 0.1% in the United States of America (USA) to 2.7% in China. A systematic review and meta-analysis reported a higher prevalence of CSU among women compared to men (1.3% vs. 0.8%) and a higher prevalence in the pediatric population (0–19 years) than in adults (1.4% vs. 0.9%).^{2–4} The recurrent and unpredictable nature of these symptoms significantly impacts patients' quality of life.¹

Type I autoimmune CSU, immunoglobulin E (IgE) mediated, and type IIb autoimmune CSU (immunoglobulin G-mediated) are considered to be involved in the pathogenesis of most CSU cases. Both mechanisms lead to the activation and degranulation of skin mast cells, the recruitment of key effector cells, and the subsequent formation of wheals. In many CSU patients, IgE and its high-affinity receptor are involved in this mast cell activation.⁵ Consequently, current urticaria treatment guidelines recommend the use of omalizumab, a targeted anti-IgE antibody, as the primary biologic therapy for patients who do not respond effectively to second-generation antihistamine therapy.¹

Elevated total serum IgE levels in CSU were first documented over four decades ago.⁶ Total IgE levels below 100 IU/mL are generally regarded as being within the normal range.⁷ High total IgE levels may be associated with increased disease severity, longer disease duration, and a greater likelihood of responding to omalizumab treatment for patients with CSU.⁸ Nevertheless, serum IgE levels are influenced by multiple determinants—including age, sex, genetic background, and environmental exposure—

which can lead to significant variations across different populations.^{9–11}

Research exploring the relationship between total IgE levels and CSU severity specifically within the Thai population remains limited. Accordingly, the primary objective of our study was to evaluate the correlation between total IgE levels and disease severity among Thai patients diagnosed with CSU.

METHODS

This cross-sectional study was conducted from October 2025 to April 2026 at the Department of Internal Medicine, Burapha University, Thailand. Fifty-two adults (aged >15 years) with a diagnosis of CSU were included. Patients were excluded if they presented with physical urticaria, nonallergic food hypersensitivity (food intolerance), or chronic infections. Physical urticaria and nonallergic food hypersensitivity were excluded because they are non-IgE-mediated conditions that could confound the clinical assessment of CSU severity (UAS7), whereas chronic infections were excluded due to their potential to alter total serum IgE levels independently.

The presence of nonallergic food hypersensitivity and chronic infections was determined based on medical history, physical examination, and review of the electronic medical records. This study did not exclude patients who had received previous treatment for CSU. Information regarding prior and current treatments was collected for all participants. Most participants were not receiving medications known to affect total serum IgE levels. Participants receiving medications that might influence total serum IgE levels were instructed to discontinue these medications before blood collection.

This study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Burapha University Institutional Review Board, Chonburi (IRB1-125/2568). All participants provided

informed consent prior to inclusion, and their privacy was protected. The purpose of the study and the examination process were clearly explained to all participants.

Study Population and Sample Size

The study population comprised patients diagnosed with CSU who attended the Internal Medicine Outpatient Clinic at Burapha University Hospital between October 1, 2025 and April 30, 2026. The study sample consisted of 100 datasets with CSU that met the eligibility criteria and agreed to participate in the study during the study period. The sample size was calculated for correlation analysis according to the method described by Hulley et al.¹² Based on a previously reported correlation coefficient ($r=0.30$) between total serum IgE levels and disease severity in patients with chronic urticaria reported by Kessel et al.¹³, with a two-sided significance level of 0.05 ($Z\alpha=1.96$) and a statistical power of 80% ($Z\beta=0.8416$), the minimum required sample size was calculated using the following formula: $N=[(Z\alpha+Z\beta)/C]^2+3$ where $C=0.5 \times \ln[(1+r)/(1-r)]=0.3095$. To account for potential data incompleteness or exclusion criteria (15%), the sample size was adjusted to 100 datasets. Eligible patients were consecutively recruited until the target sample size was achieved. A total of 100 datasets were obtained from 52 participants, with some participants contributing data from more than one study visit.

Data collection and disease severity assessment

Upon enrollment, demographic data and medical history, including history of familial atopy (allergic rhinitis, atopic dermatitis, asthma, urticaria, and food allergy), as well as previous and current medications for CSU, were recorded. Disease severity was evaluated using the Urticaria Activity Score for 7 days (UAS7). For newly diagnosed

patients, UAS7 was assessed before the initiation of treatment. For patients with an established diagnosis of CSU, UAS7 was assessed at the study visit during routine follow-up while receiving treatment. This distinction between treatment-naïve and treated patients was intentionally maintained to transparently account for the confounding effects of concurrent medications on clinical severity. The UAS7 is calculated as the sum of the daily Urticaria Activity Scores (UAS) recorded over seven consecutive days. Each daily score is the sum of the itch severity score (0=none, 1=mild, 2=moderate, 3=intense) and the wheal score (0=none, 1=<20 wheals/24 h, 2=20–50 wheals/24 h, 3=>50 wheals/24 h). When wheals were confluent and individual lesions could not be reliably counted, they were classified as "large confluent areas of wheals" according to the International Guideline, corresponding to a wheal score of 3. No participant presented with isolated angioedema or concomitant angioedema during the study.¹ The resulting UAS7 scores range from a minimum of 0 to a maximum of 42.¹⁴ Blood samples for laboratory analyses were collected at the same study visit at which UAS7 was assessed.

Blood collection and analysis: Venous blood samples were collected and analyzed. We obtained data for the following laboratory parameters: total serum IgE levels, complete blood count (CBC) with differential, plasma D-dimer levels, erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP) levels.

Statistical analyses

Normally distributed continuous data were presented as mean±standard deviation (SD), while non-normally distributed continuous data were expressed as median and interquartile range (IQR). Categorical variables were reported as frequencies and percentages.

Scatterplots were used to illustrate the

relationships between total IgE levels and UAS7. Correlations between variables were assessed using Pearson's or Spearman's correlation coefficients (r), as appropriate. Statistical significance was defined as $p<0.05$, and 95% confidence intervals (CIs) were calculated where appropriate. Statistical analyses were performed using STATA version 18.0 (StataCorp LLC, College Station, TX, USA).

RESULTS

Demographic data

A total of 52 patients with CSU were enrolled,

including 12 males (23.1%) and 40 females (76.9%). While the study involved 52 individual participants, a total of 100 clinical datasets were analyzed. A family history of allergic rhinitis was the most prevalent condition, reported by 29 patients (55.0%). Other atopic conditions were less frequent, including a history of asthma (7.7%), urticaria (3.8%), and food allergy (1.9%); notably, no cases of atopic dermatitis were reported. Detailed demographic data are summarized (Table 1.)

Table 1 Demographic Characteristics of the Study Population (N=52)

	Number (%) or mean±SD
Age (years), mean±SD,	43.0±16.9
Female, number of subjects n (%)	40 (76.9)
Family history, number of subjects n (%)	
Allergic rhinitis	29 (55)
Asthma	4 (7.7)
Urticaria	2 (3.8)
Food allergy	1 (1.9)
Atopic dermatitis	0 (0.0)

Biological parameters

The clinical laboratory results and disease activity scores for the study population are summarized in Table 2. The cohort exhibited a median UAS7 score of 6 (IQR, 0–16) and a median total serum IgE level of 94.8 IU/mL (IQR, 43.2–196.8). Hematological analysis revealed a median hemoglobin level of 13.3 g/dL (IQR, 12.7–14.1),

a median white blood cell (WBC) count of 6,685 cells/mm³ (IQR, 5,620–7,915), and a median platelet count of 257,000 cells/mm³ (IQR, 223,000–336,500). Regarding inflammatory markers, median ESR was 15 mm/hr (IQR, 5–23) and the median CRP level was 1.83 mg/L (IQR, 0.71–3.65). The median D-dimer level was 0.23 ng/mL (IQR, 0.16–0.40).

Table 2 UAS7 and Biological Data of the Study Population

Parameter	N studies	Median (IQR)
Disease severity		
UAS7	100	6 (0-16)
Biological parameters		
Total IgE (IU/mL)	100	94.8 (43.2-196.8)
Complete blood count	100	
Hemoglobin (g/dL)		13.3 (12.7-14.05)
White blood cell (cells/mm ³)		6,685 (5,620-7,915)
Platelet count (cells/mm ³)		257,000 (223,000-336,500)
ESR (mm/hr)	99	15 (5-23)
CRP (mg/L)	97	1.83 (0.71-3.65)
D-dimer (ng/mL)	100	0.23 (0.16-0.40)

Abbreviations: IQR, Interquartile Range; UAS7, Urticaria Activity Score for 7 days; IgE, Immunoglobulin E; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

Correlation between total IgE levels, disease severity, and clinical parameters

Scatter plots (Figure 1) illustrate the correlation between total serum IgE levels and UAS7 scores, revealing substantial variability and the presence of several outliers. The curve suggested a non-linear pattern. Correlation analysis further demonstrated negligible and statistically non-significant relationships between UAS7 and biological parameters (Table 3). Total IgE levels showed a positive but non-significant correlation with UAS7 ($r=0.090$, $p=0.37$). Similarly, weak correlations were observed between UAS7 and

WBC ($r=0.111$, $p=0.27$), as well as D-dimer levels ($r=0.054$, $p=0.60$). Inflammatory markers, including ESR and CRP, demonstrated non-significant negative correlations with UAS7 ($r=-0.121$, $p=0.23$ and $r=-0.044$, $p=0.67$, respectively). In addition, no significant associations were found between UAS7 and age ($r=0.080$, $p=0.43$) or sex ($r=-0.105$, $p=0.30$).

Overall, these findings indicate that neither total IgE levels nor routine laboratory parameters were significantly correlated with disease activity in this patient cohort.

Table 3 Correlation between UAS7 and Clinical Variables (N=100)

Variables	Correlation Coefficient	P-value
UAS7	1.000	1.00
Total IgE	0.090	0.37
White blood cell count	0.111	0.27
D-dimer	0.054	0.60
ESR	-0.121	0.23
CRP	-0.044	0.67
Age	0.080	0.43
Female sex	-0.105	0.30

Abbreviations: UAS7, Urticaria Activity Score over 7 days; IgE, Immunoglobulin E; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

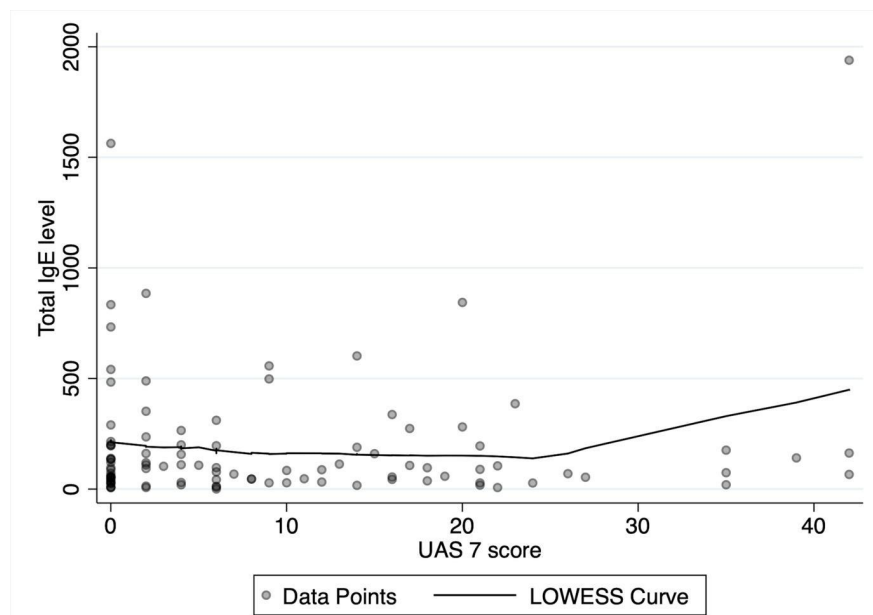


Figure 1 Correlation between Total IgE Levels and UAS7 Scores

DISCUSSION

This study found that CSU severity (as measured by UAS7) positively correlates with total IgE, WBC count, and D-dimer levels, although these findings did not reach statistical significance: $r=0.090$ ($p=0.37$), $r=0.111$ ($p=0.27$), and $r=0.054$ ($p=0.60$), respectively. Total IgE levels play a crucial role in the activation and degranulation of mast cells in CSU patients.⁵ Beyond its key role in the pathogenesis of CSU and its function as a therapeutic target, IgE levels are frequently investigated for their potential to correlate with disease severity and treatment response. While total IgE levels above 100 IU/mL are generally considered elevated,⁷ it is well-established that mean levels vary significantly based on age, sex, genetic background, and environmental exposure.⁹⁻¹¹ In clinical studies of CSU, median or mean total IgE levels are most commonly reported between 100 and 300 IU/mL (63.0% of studies).⁸ Conversely, several studies have identified subpopulations of CSU patients with low or very low IgE levels.¹⁵⁻¹⁹ Taken together, these data suggest

that while CSU can present with a wide range of IgE concentrations, elevated levels remain the more prevalent clinical finding. Despite its established role, evidence regarding the predictive value of IgE remains inconsistent. Kessel et al. demonstrated that elevated total IgE levels significantly correlate with both the severity and duration of the condition,¹³ whereas Hasan reported that high total IgE levels do not necessarily correlate with the clinical severity of chronic urticaria.²⁰ Mean total IgE serum levels have often been studied in patients with CSU and have been proposed as a biomarker of disease activity; however, results remain contradictory.^{13,21} The discrepancy with Kessel et al. may stem from several factors: our cohort was skewed toward mild disease severity (median UAS7=6), total IgE naturally varies by demographic and environmental factors, and our population exhibited marked IgE heterogeneity, including low-IgE endotypes without IgE-driven pathology.

D-dimer is a sensitive marker for cross-linked fibrin degradation, coagulation activation, and

fibrinolysis. Elevated D-dimer levels in CSU patients suggest that the coagulation cascade plays a significant role in the disease's pathogenesis. Specifically, the activation of this cascade and the subsequent generation of thrombin may trigger mast cell degranulation, leading to urticarial symptoms.^{22,23} Previous studies have established a correlation between D-dimer levels and CSU severity, demonstrating: 1) higher D-dimer plasma levels in CSU patients compared to healthy controls, 2) elevated D-dimer levels in patients with more active disease, and 3) a return to normal D-dimer levels during clinical remission.^{24,25} These findings suggest that measuring D-dimer levels could be added to clinical tools, such as UAS7, to evaluate severity. However, further research is required to fully elucidate the relationship between D-dimer levels, autoimmunity, and treatment response. Given the cross-sectional correlation design, a single-point UAS7 score cannot predict treatment escalation. Furthermore, because no statistically significant correlations were identified, routine screening of total IgE in all CSU patients may not be cost-effective. Clinically, total IgE measurement should be reserved for specific indications, such as predicting treatment response prior to anti-IgE (omalizumab) therapy or evaluating concomitant atopic conditions.

WBCs, or leukocytes, serve as fundamental mediators of the human immune system by facilitating both innate and humoral immune responses. While reference intervals for WBC counts and relative percentages vary by patient age and hospital population, leukocytosis—generally defined in adults as a WBC count exceeding 11,000 cells/mm³—is a frequent laboratory finding secondary to infection, systemic inflammation, allergic reactions, malignancy, or hereditary disorders. Consequently, a comprehensive evaluation of the WBC differential is essential for

identifying underlying etiologies.²⁶ Our study of the relationship between total WBC counts and urticaria severity indicated that, despite observable numerical trends, such correlations did not reach statistical significance.

Consequently, elevated levels of total IgE, WBC count, and D-dimer should be interpreted as part of a broader diagnostic framework rather than isolated predictors of disease severity. The primary strength of this study lies in its focus on the Thai population, a group for which research regarding CSU biomarkers remains limited. However, several significant limitations must be acknowledged. First, the predominantly low disease severity among participants (median UAS7=6) limited the feasibility of subgroup analyses across severity categories (e.g., mild, moderate, severe) due to imbalanced category distributions. Second, over half of the cohort (55%) had a family history of allergic rhinitis, a condition known to independently influence total IgE levels, which may complicate the interpretation of IgE's specific relationship to urticaria severity. Additionally, the chronic, recurrent nature of CSU and the effect of standard non-biologic treatments, which can significantly reduce UAS7 scores while total IgE levels remain unchanged, introduce major temporal confounders that limit the interpretation of our one-time correlation. Furthermore, the variation in follow-up visits per patient (ranging from 1 to 5) precluded balanced intra-individual longitudinal evaluations; nevertheless, overall analysis consistently demonstrated no statistically significant correlation between total IgE and UAS7. Another limitation of this study is that autoimmune endotyping of CSU was not performed. Future studies involving larger cohorts with a broader range of chronic urticaria severity are warranted to more effectively evaluate the correlation between urticaria severity

and specific biomarkers. Furthermore, such studies should consider selecting a population without comorbidities that influence total IgE levels.

Conclusion: Our findings demonstrate that total IgE, WBC, and D-dimer levels were not significantly correlated with CSU disease severity as measured by UAS7 in this cohort. Therefore, routine measurement of these biological markers as standalone predictors of disease severity is not supported by our data. Given the study's limitations regarding the predominantly mild disease severity

and atopic comorbidities among participants, further research in broader clinical spectrums is warranted to evaluate the utility of these biological markers in clinical practice.

CONFLICTS OF INTEREST: The authors declare that they have no conflict of interest

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ORIGINAL ARTICLE

การศึกษาความสัมพันธ์ระหว่างระดับอิมมูโนโกลบูลินอีและความรุนแรงในผู้ป่วยลมพิษเรื้อรัง

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บทคัดย่อ

ที่มาของปัญหา: อิมมูโนโกลบูลินอี (Immunoglobulin E; IgE) เป็นหนึ่งในปัจจัยสำคัญที่เกี่ยวข้องกับ พยาธิกำเนิดของโรคลมพิษเรื้อรังชนิดเกิดขึ้นเอง (chronic spontaneous urticaria; CSU) หรือลมพิษ ที่เป็นต่อเนื่องมากกว่า 6 สัปดาห์ โดยมีรายงานว่าระดับ IgE รวม (total IgE) ที่สูงอาจสัมพันธ์กับกิจกรรมของโรคและความรุนแรงของอาการที่เพิ่มขึ้น อย่างไรก็ตาม หลักฐานเชิงประจักษ์เกี่ยวกับ ความสัมพันธ์ดังกล่าวในประเทศไทยยังมีจำกัด

วัตถุประสงค์: เพื่อประเมินความสัมพันธ์ระหว่างระดับ IgE และความรุนแรงของโรค CSU

วิธีการศึกษา: การศึกษาแบบภาคตัดขวางกลุ่มตัวอย่างในผู้ป่วยโรค CSU ที่อายุมากกว่า 15 ปี ได้มีการบันทึกข้อมูลพื้นฐานและประเมินความรุนแรงของโรคโดยใช้ Urticaria Activity Score over 7 days (UAS7) รวมทั้งตรวจระดับ IgE และผลตรวจทางห้องปฏิบัติการ และวิเคราะห์ความสัมพันธ์ระหว่างตัวแปรดังกล่าว

ผลการศึกษา: ข้อมูล 100 ชุดจากผู้ป่วย 52 ราย ถูกนำมาวิเคราะห์ ค่ามัธยฐานของ UAS7 เท่ากับ 6 (พิสัยระหว่างควอไทล์ 0–16) และค่ามัธยฐานของระดับ IgE เท่ากับ 94.8 IU/mL (พิสัยระหว่างควอไทล์ 43.2–196.8) ระดับ IgE มีความสัมพันธ์เชิงบวกกับ UAS7 (ค่าสัมประสิทธิ์สหสัมพันธ์ (r) = 0.090, p = 0.37) และยังพบความสัมพันธ์ระหว่าง UAS7 กับจำนวนเม็ดเลือดขาว (r = 0.111, p = 0.27) และระดับ D-dimer (r = 0.054, p = 0.60)

สรุป: ระดับ total IgE, WBC และ D-dimer ไม่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับความรุนแรงของโรค CSU ในกลุ่มตัวอย่างนี้ ผลการศึกษาดังกล่าวไม่สนับสนุนการใช้ระดับ total IgE เพื่อประเมินความรุนแรง ของโรค CSU

คำสำคัญ: โรคลมพิษเรื้อรังชนิดเกิดขึ้นเอง, อิมมูโนโกลบูลิน, อิมมูโนโกลบูลินอี, ความรุนแรงของโรค