



## Original Research

# Sleep Disturbance and Psychological Stress: Two Interconnected Conditions in Chronic Spontaneous Urticaria

Pinar Ozdemir Cetinkaya, Birgul Ozkesici Kurt, Ayberk Aktaran, Asli Aksu, Ilknur Kivanc Altunay

Department of Dermatology and Venereology, University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Türkiye

### Abstract

**Objectives:** Chronic spontaneous urticaria (CSU) is a common disease characterized by wheals and/or angioedema. Since it is a chronic, itch-related disease, it may substantially affect the psychological status and quality of sleep. In this study, it was aimed to evaluate the impact of CSU on depression, anxiety, stress, and quality of sleep, as well as their relation to disease-specific factors.

**Methods:** This prospective case-control study included 86 patients with CSU and 86 controls. The sociodemographic and clinical characteristics of the patients, such as scores of urticaria activity score (UAS7) and chronic urticaria quality of life questionnaire (CU-Q2oL), were recorded. Depression, Anxiety, and Stress Scales-21 (DASS-21), Pittsburgh Sleep Quality Index (PSQI), and Dermatology Life Quality Index (DLQI) were used to evaluate their psychological status, quality of sleep, and life.

**Results:** Of 172 participants, the patient group comprised 86 patients with CSU, and the control group comprised 86 age and sex-matched volunteers. Of 86 patients with CSU, 60 (69.8%) were females and 26 (30.2%) males with a median age of 34.5 years. In the patients with CSU, the median scores (interquartile range) for depression, anxiety, and stress, according to DASS-21, were 6 (8), 5 (6.25) and 6 (7), respectively. Additionally, the median scores of PSQI and DLQI were 7 (5) and 5.5 (11), respectively. The median scores for depression, anxiety, and stress according to DASS-21, the median scores of PSQI and DLQI were statistically significantly higher in the patient group than in the control group. According to the PSQI classification, 68 (79.1%) patients had poor sleep quality, while 18 (20.9%) patients had good sleep quality. When the patient group was examined in two groups, those with good and poor sleep quality, UAS7, depression, anxiety, stress, and DLQI/CU-Q2oL scores were statistically significantly higher in the patients with poor sleep quality than in the patients with good sleep quality.

**Conclusion:** Treatment of urticaria is typically symptomatic and aims to reduce the symptoms of itching and wheals. However, clinicians can contribute to the well-being of patients if they are aware of psychological comorbidities and sleep disturbances.

**Keywords:** Anxiety, depression, sleep, stress, urticaria

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Urticaria is a mast-cell-driven disease characterized by wheals, angioedema, or both. The wheals are typically itchy and have a central swelling surrounded by a halo of reflex erythema that usually resolves within 24 hours. If symptoms and signs of urticaria persist for more than 6

weeks with no identifiable triggers, it is classified as chronic spontaneous urticaria (CSU).<sup>[1]</sup>

Although the natural course of CSU is not well-known, it is a common disease that may continue for many years.<sup>[2,3]</sup> Given that CSU is a chronic, itch-related disease, many

**Address for correspondence:** Pinar Ozdemir Cetinkaya, MD. Department of Dermatology and Venereology, University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Türkiye

**Phone:** +90 506 338 84 50 **E-mail:** pinarozdemir44@gmail.com

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studies have reported that patients with CSU were prone to have psychiatric comorbidities and poor quality of life (QoL).<sup>[4-6]</sup> In a current meta-analysis by Huang et al.,<sup>[7]</sup> it was found that patients with CSU had approximately 6-fold increased risk for anxiety and depression compared to the control group.

Sleep disturbance and QoL in chronic inflammatory skin diseases such as psoriasis and atopic dermatitis were well-studied, and there are also several studies evaluating the quality of sleep in chronic urticaria (CU).<sup>[8-12]</sup> In the literature, it was reported that a great number of patients with CSU had poor sleep quality, and the quality of sleep was affected by the severity of the disease and the degree of itching.<sup>[10-12]</sup> Furthermore, previous studies found that sleep disturbance and itching were associated with greater levels of depression, anxiety, and stress.<sup>[4,13,14]</sup> In light of all these findings, addressing sleep quality in the management of CU may be crucial. Understanding the complex interplay between disease severity, psychological state, and sleep quality could provide valuable insights for holistic approaches to managing CU patients' overall well-being.

In our study, we aimed to evaluate the presence of anxiety, depression, and stress and quality of sleep in patients with CSU and compare the presence and/or level of these conditions with the control group. Besides, we further evaluated the relationship between sleep disturbance and psychological state in the patients with CSU, as well as the impact of disease severity on these factors.

## Methods

This is a prospective, case-control study. It was carried out between June 1, 2023, and January 1, 2024, with 86 patients admitted to the dermatology outpatient clinic and 86 controls. The institutional ethics committee has given approval for the study (16/05/2023, no:3935). Detailed information about the study was given to all the participants, and an informed consent form was signed by them. The study followed the rules of the latest version of the 'Helsinki Declaration' and 'Guidelines for Good Clinical Practice'.

The patient group consisted of 86 patients over 18 years of age with the diagnosis of CSU. The diagnosis of CSU was made clinically with history and dermatological examination based on the criteria defined in the international EAACI/GA<sup>2</sup>LEN/EuroGuiDerm/APAAACI guideline by the dermatologists conducting the study.<sup>[1]</sup> The demographic and clinical features of the patients, such as duration of disease, accompanying angioedema and allergic diseases, and medications, were recorded. Disease activity and QoL in the patient group were measured by Urticaria Activity Score 7 (UAS7) and Chronic Urticaria Quality of Life

Questionnaire (CU-Q2oL). The control group comprised 86 volunteers over 18 years old with no dermatological and psychiatric diseases. The patient and control groups were asked to fill out Depression, Anxiety and Stress Scales-21 (DASS-21), Pittsburgh Sleep Quality Index (PSQI), and Dermatology Life Quality Index (DLQI) to evaluate their psychological status, quality of sleep and QoL.

CSU disease activity was assessed with UAS7, which is a 4-point Likert scale self-evaluation test, on 7 consecutive days. The key findings of urticaria (pruritus and wheals) are scored between 0-3 points for each day. The total score can vary between 0-42 points. Disease activity is classified in 5 sections according to the UAS7 score: UAS7=0, no urticaria; UAS7=1-6, well-regulated; CSU; UAS7=7-15, mild activity CSU; UAS7=16-27, moderate activity CSU; UAS7=28-42, severe activity CSU.<sup>[15]</sup>

The validated Turkish version of CU-Q2oL was used to reveal the QoL of the patients with CSU.<sup>[16]</sup> CU-Q2oL is a 23-item disease-specific questionnaire with a 5-point Likert scale. Out of 23 questions, 6 questions are designed to assess sleep characteristics and mental status. The total score can vary between 0-100 points. Higher scores indicate poor QoL.<sup>[17]</sup>

The quality of life of the study groups was assessed by the validated Turkish version of the DLQI.<sup>[18]</sup> DLQI is a 10-item self-reported questionnaire with a 4-point Likert scale (0-3 points). The score of DLQI varies between 0-30. As the score gets higher, the QoL gets worse, and scores >10 indicate that the QoL is moderately or severely affected.<sup>[19]</sup>

The validated Turkish version of DASS-21 was used to evaluate the psychological status of the patient and control groups.<sup>[20]</sup> DASS-21 is a self-rating questionnaire consisting of 21 items scored with a 4-point Likert scale (0-3 points). DASS-21 evaluates 3 dimensions of depression, anxiety and stress separately, with 7 questions for each. There are 5 categories according to the scores of 3 dimensions. For depression, the scores are as follows: 0-4=none, 5-6=mild, 7-10=moderate, 11-13=severe, ≥14=extremely severe. For anxiety, the scores are as follows: 0-3=none, 4-5=mild, 6-7=moderate, 8-9=severe, ≥10=extremely severe. For stress, the scores are as follows: 0-7=none, 8-9=mild, 10-12=moderate, 13-16=severe, and ≥17=extremely severe.<sup>[21]</sup>

The validated Turkish version of the PSQI was used to evaluate the sleep quality of the patient and control groups.<sup>[22]</sup> It is a self-assessment tool consisting of 7 components with a combination of questions with a 4-point Likert scale (0-3 points) and open-ended questions. The seven components of PSQI are subjective sleep quality, latency, duration and disturbances of sleep, habitual sleep

efficiency, history of drugs to sleep and dysfunction during daytime. The global score of the scale is obtained by summing the scores of 7 components and varies between 0 and 21.<sup>[23]</sup> Higher global scores indicate poor sleep quality, and the suggested cut-off value for the global score is  $\geq 5$  to identify poor sleepers.<sup>[24]</sup>

### Statistical Analysis

All analyses were carried out using IBM SPSS Statistics for Windows, Version 20.00 (Armonk, New York, USA: IBM Corp), and a p-value less than 0.05 was accepted for statistical significance. The Shapiro–Wilk test was employed to check the normality distribution of the variables. Continuous variables were presented as median and interquartile range (IQR). Categorical variables were presented as frequencies (n) and percentages (%). Independent samples were compared with the Mann-Whitney U test and the Kruskal-Wallis test. The Dunn's Test was used for pairwise comparisons. Categorical variables were compared by Pearson's chi-square and Fisher's exact test. The Spearman correlation test was used to analyze correlations between non-parametric continuous variables. The power of the correlations was defined as follows: very weak:  $r < 0.2$ ; weak:  $r = 0.2-0.39$ ; moderate:  $r = 0.4-0.59$ ; strong:  $r = 0.6-0.8$ ; very strong:  $r > 0.8$ .

### Results

A total of 172 participants were included in this study. The patient group consisted of 86 patients with CSU, and the control group consisted and 86 age- and sex-matched volunteers without dermatological or psychiatric diseases ( $p = 0.780$ ,  $p = 0.742$ , respectively). Of 86 patients with CSU, 60 (69.8%) were females and 26 (30.2%) were males. The ages of the patients were between 18 to 64 years, and the median age was 34.5 (IQR=19) years. The median duration of the disease was 36 months (IQR=60). Thirty-seven patients (43%) had accompanying angioedema, and the median duration of angioedema was 24 months (IQR=36). The demographic and clinical characteristics of patients with CSU are presented in Table 1.

The median depression, anxiety and stress scores of the DASS-21 were statistically significantly higher in the patient group than in the control group ( $p = 0.019$ ,  $p = 0.001$ ,  $p = 0.036$ , respectively). According to PSQI, the median global score of the patient group was statistically significantly higher than the scores of the control group ( $p < 0.001$ ). The median DLQI scores of the patient group were statistically significantly higher than the scores of the control group ( $p < 0.001$ ). Comparison of DASS-21, PSQI and DLQI scores between the patient and control groups are shown in Table 2.

**Table 1.** The demographic and clinical characteristics of patients with CSU

	Patient group (n=86)
Sex (n/%)	
Female	60 (69.8)
Male	26 (30.2)
Age [Median, (IQR), years]	34.5 (19)
Duration of disease [Median, (IQR), months]	36 (60)
Angioedema (n/%)	
Absent	49 (57)
Present	37 (43)
Duration of angioedema [Median, (IQR), months]	24 (36)
Accompanying allergic diseases (n/%)	
Allergic asthma	18 (20.9)
Allergic rhinitis	22 (25.6)
Allergic conjunctivitis	13 (15.1)
Allergic contact dermatitis	5 (5.8)
Previous treatments (n/%)	
H1-antihistamines (the standard dose or up to 4 times the standard dose)	86 (100)
Systemic corticosteroids	53 (61.6)
Cyclosporine	4 (4.7)
Leukotriene receptor antagonist	8 (9.3)
Adrenaline	3 (3.5)
Current treatments (n/%)	
Only H1-antihistamines (the standard dose or up to 4 times the standard dose)	31 (36)
Omalizumab, all	55 (64)
Omalizumab 300 mg	49 (57)
Omalizumab 450 mg	4 (4.7)
Omalizumab 600 mg	2 (2.3)
Need for additional H1-antihistamines in addition to omalizumab	31 (36)
UAS7 [Median, (IQR)]	12 (18)
UAS7 classification	
Urticaria-free	11 (12.8)
Well-controlled	11 (12.8)
Mild activity	27 (31.4)
Moderate activity	21 (24.4)
Severe activity	16 (18.6)
CU-Q2oL [Median, (IQR)]	30.43 (34.24)

IQR: Interquartile range; CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; UAS7: Urticaria Activity Score 7. Data were expressed as median and IQR in continuous variables and n (%) in categorical variables.

When the patient group was examined in two groups, those with good and poor sleep quality, UAS7 scores, depression, anxiety, and stress scores according to DASS-21 and DLQI and CU-Q2oL scores were statistically significantly higher in the patients with poor sleep quality than in the patients with good sleep quality ( $p = 0.006$ ,  $p < 0.001$ ,  $p = 0.002$ ,  $p < 0.001$ ,  $p < 0.001$ ,  $p < 0.001$ , respectively) (Table 3).

**Table 2.** Comparison of DASS-21, PSQI, and DLQI scores between the patient and control group

	Patient group (n=86)	Control group (n=86)	p
DASS-21 [Median, (IQR)]			
Depression	6 (8)	4 (5)	0.019*
Anxiety	5 (6.25)	3 (4.25)	0.001*
Stress	6 (7)	6 (4)	0.036*
DASS-21 Classification (n/%)			
Depression			
Absent	36 (41.9)	48 (55.8)	0.067
Present	50 (58.1)	38 (44.2)	
None	36 (41.9)	48 (55.8)	
Mild	11 (12.8)	16 (18.6)	
Moderate	22 (25.6)	18 (20.9)	
Severe	7 (8.1)	3 (3.5)	
Extremely severe	10 (11.6)	1 (1.2)	
Anxiety			
Absent	35 (40.7)	52 (60.5)	0.010*
Present	51 (59.3)	34 (39.5)	
None	35 (40.7)	52 (60.5)	
Mild	10 (11.6)	13 (15.1)	
Moderate	16 (18.6)	12 (14)	
Severe	9 (10.5)	4 (4.7)	
Extremely severe	16 (18.6)	5 (5.8)	
Stress			
Absent	49 (57)	68 (79.1)	0.002*
Present	37 (43)	18 (20.9)	
None	49 (57)	68 (79.1)	
Mild	9 (10.5)	8 (9.3)	
Moderate	10 (11.6)	7 (8.1)	
Severe	12 (14)	2 (2.3)	
Extremely severe	6 (7)	1 (1.2)	
PSQI [Median, (IQR)]	7 (5)	5 (4.5)	<0.001*
PSQI classification (n/%)			
Poor sleep quality	68 (79.1)	47 (54.7)	0.001*
Good sleep quality	18 (20.9)	39 (45.3)	
DLQI [Median, (IQR)]	5.5 (11)	1 (2)	<0.001*
DLQI classification (n/%)			
Severely affected	31 (36)	4 (4.7)	<0.001*
Mildly-Moderately affected	55 (64)	82 (95.3)	

CI: Confidence Interval; DASS-21: Depression, Anxiety and Stress Scales-21; DLQI: Dermatology Life Quality Index; IQR: Interquartile range; PSQI: Pittsburgh Sleep Quality Index; Data were expressed as median (IQR) in continuous variables and n (%) in categorical variables. Independent samples were compared with the Mann-Whitney U and Chi-Square tests. If one or more cells had an expected count of less than 5, the Fisher's Exact test was used. \*p<0.05.

There were statistically significant positive correlations between UAS7, CU-Q2oL, dimensions of DASS-21, PSQI and DLQI scores in the patient group ( $p<0.05$ ) (Table 4). When the patient group was divided into 3 classes: those using only H1-antihistamines, those using only 300 mg omalizumab, and those using high-dose-omalizumab and/or needing antihistamines in addition to standard/high-dose omalizumab, no significant difference

was found regarding the median CU-Q2oL, dimensions of DASS-21, PSQI and DLQI scores ( $p=0.089$ ,  $p=0.192$ ,  $p=0.175$ ,  $p=0.790$ ,  $p=0.074$ ,  $p=0.060$ , respectively). The median UAS7 scores of groups using only H1-antihistamines, using only 300 mg omalizumab, and using high dose-omalizumab and/or needing antihistamines in addition to standard/high-dose omalizumab were 16 (IQR=19), 7.5 (IQR=16.5), 15 (IQR=16.5), respectively.

**Table 3.** UAS7, DASS-21, DLQI, and CU-Q2oL scores in patients with poor sleep quality and good sleep quality

Patients with CSU (n=86)	Good sleep quality group (n=18)	Poor sleep quality group (n=68)	p
DASS-21 [Median, (IQR)]			
Depression	1.5 (6)	7 (7.75)	<0.001*
Anxiety	2 (6)	6 (7)	0.002*
Stress	2 (7.25)	7 (9)	<0.001*
DASS-21 Classification (n/%)			
Depression			
Absent	11 (61.1)	25 (36.8)	0.063
Present	7 (38.9)	43 (63.2)	
Anxiety			
Absent	12 (66.7)	23 (33.8)	0.012*
Present	6 (33.3)	45 (66.2)	
Stress			
Absent	14 (77.8)	35 (51.5)	0.045*
Present	4 (22.2)	33 (48.5)	
UAS7 [Median, (IQR)]	7 (12.5)	15.5 (17)	0.006*
DLQI [Median, (IQR)]	1.5 (2.5)	9 (11.75)	<0.001*
CU-Q2oL [Median, (IQR)]	17.39 (23.91)	40.21 (33.29)	<0.001*

CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; CSU: Chronic spontaneous urticaria; DASS-21: Depression, Anxiety and Stress Scales-21; DLQI: Dermatology Life Quality Index; IQR: Interquartile range; UAS7: Urticaria Activity Score-7. Data were expressed as median (IQR) in continuous variables and n (%) in categorical variables. Independent samples were compared with the Mann-Whitney U and Chi-Square tests. \*p<0.05.

**Table 4.** Correlation of UAS7, CU-Q2oL, DASS-21, PSQI, and DLQI scores in the patient group

	UAS7	CU-Q2oL	DASS-21 Depression	DASS-21 Anxiety	DASS-21 Stress	PSQI	DLQI
UAS7	r=1	r=0.610 p<0.001*	r=0.382 p<0.001*	r=0.406 p<0.001*	r=0.348 p=0.001*	r=0.321 p=0.003*	r=0.658 p<0.001*
CU-Q2oL	r=0.610 p<0.001*	r=1	r=0.562 p<0.001*	r=0.529 p<0.001*	r=0.540 p<0.001*	r=0.538 p<0.001*	r=0.836 p<0.001*
DASS-21 Depression	r=0.382 p<0.001*	r=0.562 p<0.001*	r=1	r=0.768 p<0.001*	r=0.777 p<0.001*	r=0.516 p<0.001*	r=0.495 p<0.001*
DASS-21 Anxiety	r=0.406 p<0.001*	r=0.529 p<0.001*	r=0.768 p<0.001*	r=1	r=0.702 p<0.001*	r=0.474 p<0.001*	r=0.504 p<0.001*
DASS-21 Stress	r=0.348 p=0.001*	r=0.540 p<0.001*	r=0.777 p<0.001*	r=0.702 p<0.001*	r=1	r=0.449 p<0.001*	r=0.490 p<0.001*
PSQI	r=0.321 p=0.003*	r=0.538 p<0.001*	r=0.516 p<0.001*	r=0.474 p<0.001*	r=0.449 p<0.001*	r=1	r=0.489 p<0.001*
DLQI	r=0.658 p<0.001*	r=0.836 p<0.001*	r=0.495 p<0.001*	r=0.504 p<0.001*	r=0.490 p<0.001*	r=0.489 p<0.001*	r=1

CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; DASS-21: Depression, Anxiety and Stress Scales-21; DLQI: Dermatology Life Quality Index; PSQI: Pittsburgh Sleep Quality Index; UAS7: Urticaria Activity Score. The Spearman's correlation test was used. r=correlation coefficient \*p<0.05.

There was a statistically significant difference in UAS7 score in these 3 treatment groups (p=0.023). Those using high dose-omalizumab and/or needing antihistamines in addition to standard/high-dose omalizumab had statistically significantly higher median UAS7 scores compared to those using only 300 mg omalizumab (p=0.020). Those using only H1-antihistamines had statistically

significantly higher median UAS7 scores compared to those using only 300 mg omalizumab (p=0.013). There was no statistically significant difference in UAS7 score between those using only H1-antihistamines and those using high-dose-omalizumab and/or needing antihistamines in addition to standard/high-dose omalizumab (p=0.904).

## Discussion

Chronic spontaneous urticaria is a debilitating disease due to the sudden appearance of itchy wheals and its unpredictable course and duration.<sup>[2,25]</sup> Beyond being a skin disease, patients with CSU frequently exhibit psychiatric comorbidities and sleep disorders.<sup>[4,26-29]</sup> Actually, the relationship between psychiatric problems and urticaria is bidirectional. While several studies suggested that psychiatric problems, especially stress, may contribute to the etiopathogenesis of urticaria, other studies have reported that patients with CSU are at risk of developing psychiatric comorbidities.<sup>[7,30-34]</sup> Besides, patients with CSU frequently experience sleep disturbance.<sup>[28,29]</sup> Itching is thought to be the leading cause of low sleep quality in patients with CSU.<sup>[4]</sup> Several studies also suggest a relationship between sleep disturbance and mental disorders. Sleep disturbance was shown to be associated with an increased risk of depression.<sup>[35]</sup> In summary, urticaria is a disease that may interfere with patients' sleep, psychosocial well-being and daily activities. Consequently, it has a significant impact on QoL.<sup>[36,37]</sup>

In this study, one of our aims was to evaluate the relationship between disease severity, depression, anxiety, stress and sleep quality in patients with CSU. While scores of depression, anxiety, stress and sleep quality were significantly higher in patients with CSU than in the control group, DASS-21, PSQI, CU-Q2oL and UAS7 scores were significantly correlated. This indicates the complex relationship between psychological status, sleep quality, QoL and disease severity in CSU.

In the literature, there are studies evaluating the psychosocial status and sleep quality of patients with CU separately, as well as a few studies evaluating these factors altogether. Huang et al.<sup>[4]</sup> investigated whether depression and anxiety in CSU were mediated by itching and sleep disturbance in 393 patients and reported that itching and sleep disturbance mediated 95.7% of CSU's effect on anxiety and 116.7% on depression. Abdel-Meguid et al.<sup>[29]</sup> evaluated 25 patients with CSU and 25 controls in terms of psychosocial well-being and sleep quality and reported that all 25 patients were poor sleepers (PSQI>5), 72% of the patients were found to have depression and 92% had anxiety. Anxiety, depression, and sleep quality scores showed a significant positive correlation. DLQI and PSQI scores were positively correlated with UAS7 scores, but Hospital Anxiety Depression Scale scores were not correlated with UAS7. Sánchez-Díaz et al.<sup>[10]</sup> conducted a cross-sectional study with 75 CSU patients to assess the impact of sleep quality on the QoL and emotional status of these patients, and they found that 78.67% (59/75) of the patients had poor quality of sleep. Furthermore, these patients with poor sleep quality had inadequate disease control, worse QoL according

to DLQI/CU-Q2oL, and higher anxiety/depression scores. In our case-control study, 58.1%, 59.3%, and 43% of the patients with CSU had symptoms of depression, anxiety, and stress, respectively, and 79.1% of the patients had poor sleep quality. Moreover, UAS7, depression, anxiety, stress and QoL scores were significantly higher in group of patients who had poor sleep quality. Although the percentages of the prevalence of depression, anxiety, and sleep quality vary due to the different methods of the studies, the sample size, and the scales used, all of the studies reached the same conclusion that sleep quality was impaired in CSU and was associated with accompanying psychiatric comorbidities. Even if reducing the wheals and itching is the main treatment goal in the management of patients with CSU, it may not always be sufficient for the overall well-being of the patients. Therefore, accompanying sleep disturbances and psychiatric comorbidities should be kept in mind in all patients with CSU.

While most of the studies in the literature evaluated the anxiety-depression-sleep relationship, this study also investigated the levels of stress in CSU. Patients often report a history of significant life stressors before the onset of urticarial plaques. Growing knowledge suggests that the complex interactions between stress, neuropeptides, neurokinins and inflammatory mediators have a role in the etiopathogenesis of CU.<sup>[38]</sup> Moreover, the key cells in urticaria etiopathogenesis, mast cells, can respond to stress-related proinflammatory processes and neuropeptides via degranulation of histamine and other inflammatory mediators.<sup>[39]</sup> Varghese et al.<sup>[40]</sup> compared the stress scores and inflammatory marker levels of 45 patients with CU and 45 controls and observed significantly higher stress scores and systemic inflammation markers in patients with CU. Similar to previous research, in this study, it was found that patients with CSU had higher stress scores and 2.85-fold increased risk for stress compared to the control group. Ultimately, insomnia secondary to CU may result from stress which can disrupt the circadian rhythm of cortisol secretion.<sup>[41]</sup>

This study had also other noteworthy findings. Depression, anxiety, stress, sleep quality, QoL, and disease severity were found to be significantly correlated. In the literature, there were also studies showing the correlation of these factors. Choi et al.<sup>[26]</sup> conducted a comparative study that included 79 patients with CU and 39 patients with persistent asthma. They reported that the prevalence of depression and anxiety based on the Hospital Anxiety Depression Scale were 48.1% and 38%; only depression was significantly more prevalent in patients with chronic urticaria. Additionally, anxiety, depression, and stress were negatively correlated with QoL. Another noteworthy finding of the study was that scores of depression were not associated with the severity of disease,

but instead, they were associated with the severity of sleep difficulty. Tawil et al.<sup>[27]</sup> evaluated the QoL and psychological well-being of 264 patients with CU and found moderate correlations between DLQI/CU-Q2oL, the psychological distress scores, and the urticaria control test. These findings further indicated that when the disease was more severe, distress was more profound, and the QoL was worse. Ates et al.<sup>[12]</sup> carried out a case-control study (21 patients with CSU vs. 19 healthy controls) to assess the relationships between QoL, sleep problems, and sleep quality and reported that CU–Q2oL total score was positively correlated with sleep latency and PSQI–C1 (subjective sleep quality) score. With all these findings, it may be suggested that psychosocial status, sleep quality and disease severity are interconnected in the course of CSU and these factors together affect the QoL of the patients. Furthermore, these intertwined relationships may explain how CU can significantly impact the QoL as much as moderate-to-severe psoriasis, atopic dermatitis, and even severe coronary artery disease.<sup>[36,37,42]</sup>

Our study had a strength compared to studies in the literature that it divided the patients with CSU into treatment groups as those using only H1-antihistamines, those using only 300 mg omalizumab, and those using high-dose-omalizumab and/or needing antihistamines in addition to standard/high dose omalizumab. Patients with CSU were compared according to these 3 treatment groups, and it was found that CSU severity was significantly less in patients using only 300 mg omalizumab, and psychological status, QoL and sleep quality were better than in the other treatment groups despite an insignificant difference. With these findings, it may be suggested that patients who received treatment and had lower UAS7 scores were still prone to psychosocial problems, and clinicians should be aware of this issue in the management of CSU.

Our study has several limitations. Although the design of the study was prospective, it was a case-control study that had limited ability to make inferences about causal relationships. Second, the psychological status and sleep quality of the study population were measured by self-reported questionnaires that were generally used in clinical practice. Still, the patients and controls did not undergo psychiatric evaluation by the clinicians.

## Conclusion

Treatment of urticaria is typically symptomatic and aims to reduce the symptoms of itching and wheals. However, clinicians can contribute to the well-being of patients if they are aware of psychological comorbidities and sleep disturbance related to CSU and address these conditions in the treatment schedule.

## Disclosures

**Ethics Committee Approval:** This study was approved by the Sisli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (date: 16.05.2023, number: 3935).

**Peer-review:** Externally peer-reviewed.

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