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Sıkıntıya dayanma düzeyi kronik spontan ürtikerin şiddeti ile ilişkili olabilir mi?

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#### Abstract

**Background and Design:** Chronic spontaneous urticaria (CSU) is a common disease characterized by erythematous and itchy wheals, angioedema, or both that last for >6 weeks. Its etiology is not yet fully determined. This study aimed to analyze the distress tolerance (DT) levels of patients with CSU and correlations between DT and clinical parameters and other psychological symptoms.

**Materials and Methods:** Fifty-two patients with CSU without any concomitant diseases were included in the study. The control group included 50 healthy volunteers with similar baseline demographics but without physical or psychiatric diseases. The urticaria activity score 7 (UAS7) was used to determine the disease severity in the patient group. In both groups, Sociodemographic and Clinical Data Form, Distress Tolerance Scale (DTS), Beck Depression Inventory (BDI), and state and trait anxiety inventory were used. Statistical differences in psychiatric scale scores were found between the patient and control groups, and a correlation was found between UAS7 and scale scores in the patient group.

**Results:** No differences in sociodemographic variables were found between the patient and control groups. The DTS and subgroup score analysis revealed statistically significant differences between the patient and control groups. The DTS-total scores (p<0.001), DTS tolerance subdimension scores (p<0.001), DTS self-efficacy subdimension scores (p=0.002), and DTS regulation subdimension scores (p=0.02) were statistically lower in the patient group than in the control group. The BDI (p<0.01) and anxiety scores (state, p<0.001; trait, p=0.002) were also higher in the patient group than in the control group. Furthermore, a positive correlation was found between UAS7 scores and all scale scores. **Conclusion:** Psychological disorders are prevalent in patients with CSU and exhibit an interaction with the prognosis. Although the interaction is well-known, no clear multidisciplinary approach has been established for patients with CSU. In this study, DT was significantly reduced in patients with CSU could be addressed in psychotherapy and might be a beneficial criterion not only for the treatment but also for disease severity.

Keywords: Anxiety, chronic urticaria, depression, distress tolerance

### Öz

Amaç: Kronik spontan ürtiker (KSÜ) eritemli, kaşıntılı kabarıklıklar, anjiyoödem ya da her ikisinin birlikte altı haftadan uzun görülmesiyle karakterize ve sık karşılaşılan bir hastalıktır. Etiyolojisi tam olarak aydınlatılmamıştır. Bu çalışmada KSÜ hastalarının sıkıntıya dayanma tolerans (DT) düzeylerini ve bunun klinik parametreler ve diğer ruhsal semptomlarla ilişkisini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Çalışmaya eşlik eden başka herhangi bir hastalığı olmayan toplam 52 KSÜ hastası ve benzer sosyo-demografik özellikleri olan 50 sağlıklı kişi dahil edildi. Hasta grubunda hastalık şiddetini değerlendirmede ürtiker aktivite skoru 7 (ÜAS7) kullanıldı. Her iki grup da Sosyo-demografik ve Klinik Bilgi Formu, Sıkıntıya Dayanma Ölçeği (SDÖ), Beck Depresyon Ölçeği (BDÖ), Durumluk ve Sürekli Kaygı Puanları ile değerlendirildi. Hasta ve kontrol grubunda kullanılan psikiyatrik ölçekler arasında istatistiksel farklılık olup olmadığı ve hasta grubunda ÜAS7 ile ölçekler arasındaki korelasyon varlığı incelendi.

Bulgular: Hasta ve kontrol grupları arasında sosyo-demografik açıdan fark bulunmamaktaydı. Sıkıntıya dayanma ölçeği total ve alt ölçek puanlamalarında hasta ve kontrol grubu arasında istatistiksel olarak anlamlı farklılıklar vardı. SDÖ total, tolerans, öz yeterlilik puanı ve SDÖ

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regülasyon puanlarının tamamı hasta grubunda istatistiksel olarak daha düşük bulundu (sırasıyla; p<0,001, p<0,001, p=0,002, p=0,02). Hasta grubunda BDÖ (p<0,01) ve anksiyete puanları (durumluk p<0,001 ve sürekli p=0,002) da kontrol grubuna göre anlamlı olarak yüksekti. Ayrıca UAS7 ile diğer tüm ölçekler arasında pozitif korelasyon vardı.

**Sonuç:** Psikolojik bozukluklar KSÜ hastalarında sık görülür ve hastalık seyri ile karşılıklı bir etkileşime sahiptir. Bu etkileşim iyi bilinmesine rağmen KSÜ hastalarına multidisipliner açıdan nasıl yaklaşılacağı net değildir. Çalışmamızda, sıkıntıya dayanma eşiğinin KSÜ hastalarında büyük ölçüde azaldığını, hastalık şiddeti ile ruhsal semptomlar arasında pozitif korelasyon olabileceğini belirledik. Sonuç olarak, sıkıntıya DT'nin KSÜ hastalarında psikoterapide ele alınabileceğini ve yalnızca tedavi açısından değil, hastalık şiddeti yönünden de yararlı bir ölçüt olabileceğini düşünüyoruz.

Anahtar Kelimeler: Anksiyete, kronik ürtiker, depresyon, sıkıntıya dayanma

### Introduction

Urticaria is a cutaneous vascular reaction induced by immunological or non-immunological mechanisms. Chronic urticaria (CU) is characterized by recurrent episodes of transient wheals, frequently associated with angioedema that present daily or at least twice a week for over 6 weeks. Approximately 15-20% of individuals develop at least one episode of urticaria in their lives. CU is classified as chronic spontaneous urticaria (CSU), which presents without an identifiable provoking factor, and chronic inducible urticaria, which presents due to various stimuli<sup>14</sup>.

Although several factors such as drugs, nutrients, infections, allergens, malignancies, and other dermatological diseases could be responsible for the etiology of CU, the cause remains unclear in approximately 50% of the cases<sup>5</sup>. Similar to several dermatological diseases, there could be significant psychiatric morbidities in 35-60% of CU cases<sup>6,7-10</sup>. CU negatively affects the quality of life of the patients and could lead to psychiatric problems. Similar to other skin diseases, psychiatric morbidities are among the most important indicators of the prognosis and general well-being of patients with CSU<sup>11</sup>. Anxiety disorders, somatoform disorder, and depression are the most frequently reported psychiatric disorders in patients with CU<sup>12,13</sup>. Despite its well-known association with psychiatric disorders, whether the psychiatric problems in patients with CSU are the causes or outcomes of severe disease and prognosis is unclear.

Distress tolerance (DT) could be described as the ability to endure negative psychological conditions. Although distress is considered an emotional state, cognitive or physical processes could lead to distress<sup>14</sup>. DT was reported to be associated with all emotional states and indicates the controllability of these situations<sup>15</sup>. Leyro et al.<sup>16</sup> described DT as the capacity to withstand actual or perceived negative affections and obstructive mental and/or physical events. When DT is low, individuals may experience higher psychiatric and psychosomatic symptoms. DT is important in the etiopathology of mental diseases, and it could be one of the factors that should be improved in psychotherapy and that it determines the response to treatment<sup>17</sup>. The description of the psychiatric symptoms and determination of the correlation between symptoms and disease prognosis could be important for patients with CSU. Certain studies have reported that there may be a correlation between several psychological disorders such as anxiety disorders, obsessive-compulsive disorder, personality disorders, and eating disorders and DT<sup>18-20</sup>.

Thus, in this study, we aimed to analyze the DT levels of patients with CSU and the correlations between DT and clinical parameters and other psychological symptoms.

### **Materials and Methods**

A total of 102 participants divided into two study groups were included. Group 1 included 52 patients with CSU, and group 2 included 50 healthy volunteers who applied to the study centers for a general health examination. During data collection, the authors strictly applied the inclusion criteria. Furthermore, 50 healthy individuals who met the study criteria and matched the baseline properties of the patient group (e.g., age and sex) were included in the control group. The socio-demographics of the participants are presented in Table 1.

Between June 2018 and January 2020, 52 patients aged 18-65 years who were diagnosed with CSU in the dermatology outpatient clinic of Fethi Sekin City Hospital were included. The exclusion criteria were as follows: Pregnancy, concomitant dermatological or systemic disease, or known psychiatric pathology and psychiatric treatment history. The inclusion criteria were as follows: No history of psychiatric disease and no previous psychiatric treatment. The control group included 50 healthy individuals having similar demographics.

Beck Depression Inventory (BDI), sociodemographic and clinical data form, Distress Tolerance Scale (DTS), and State and Trait Anxiety Scores (STAI) were administered to the patient and control groups. Urticaria activity score (UAS) was applied only in the patient group. The control group included healthy individuals aged 18-65 years without any psychiatric disorder, concomitant disease that would mask/affect skin lesions, a history of medical treatment within the last 3 months, or neurological and systemic disease.

The study protocol was approved by the Firat University Non-Interventional Research Ethics Committee (approval number: 05, date: 15.02.2018). Verbal and written consent from the participants was obtained.

#### Scales

BDI was developed by Aaron T. Beck. It is a 21-item multiple-choice selfreport inventory, a common psychometric test employed to measure the severity of depression.

**Sociodemographic and clinical data form:** The questionnaire was developed by the authors to record the sociodemographic parameters of the participants, such as age, sex, marital status, education, occupation, residential status, and family size. It also includes information about disease duration and presence of stress factors at disease onset.

**DTS:** This scale aims to determine the stress endurance of the patient based on individual variations. DTS includes three subscales: DTS-1, tolerance to emotional distress (DTS tolerance); DTS-2, subjective evaluation of distress and awareness (DTS self-efficacy); and DTS-3, regulation efforts to reduce distress (DTS regulation). The scale was developed by Simons and Gaher<sup>14</sup> and was validated by Sargin et al.<sup>21</sup> for the Turkish language.



**STAI:** This scoring system was developed by Spielberger et al.<sup>22</sup> and validated by Öner and Le Compte<sup>23</sup>. It includes 40 items to determine the self-perceptions of patients. It has two subscales: STAI-1 (state anxiety scores) evaluates the current state of anxiety and STAI-2 (trait anxiety scores) evaluates relatively stable aspects of "anxiety proneness," including general states of calmness and security.

**UAS7:** The UAS is calculated to determine disease severity. The test is applied daily and includes the number of wheals and itching severity<sup>24</sup>.

#### **Statistical Analysis**

Data entry and analysis were conducted using IBM SPSS Statistics version 20 software (IBM Corp., Armonk, NY, USA). The demographics of the study population were analyzed with the chi-square test. The normal distribution of data was determined, and the resulting data were analyzed with parametric tests. Two groups of dependent and two groups of independent data were analyzed by Student's t-test. Analysis of variance was conducted in cases with more than two variables. Correlations between the variables were tested with Pearson correlation analysis. The statistical significance was determined as p=0.05.

### Results

**STAI-1:** The STAI-1 test results were significantly (p<0.001) higher in the patient group (mean: 40.9, SD: 1.32) than in the control group (mean: 32.1, SD: 1.13). When the control group was excluded from the analysis, no significant differences were found between the patients based on sex (p=0.081), marital status (p=0.24), education level (p=0.12), place of residence (p=0.051), income level (p=0.36), occupation (p=0.66), and age at disease onset (p=0.11). On the contrary, a weak positive correlation was found between STAI-1 and disease duration (r=0.311, p=0.025).

**STAI-2:** Similar to STAI-1, the findings were significantly higher in the patient group (mean: 46.4, SD: 1.51) than in the control group (mean: 41.0, SD: 1.10).

**BDI:** The mean score was 5.4 (SD: 0.70) in the control group, and it was significantly higher in the patient group (mean: 14.3, SD: 1.16, p<0.01). When the control group was excluded from the analysis, a statistically significant difference was observed based on sex (p<0.01).

In the BDI test, a statistical difference in sex was found (mean BDI: 10.4, SD: 1.19), where male participants scored higher than female participants (18.9; SD: 1.69). Furthermore, the correlation between disease duration and BDI scale scores was weak, significant, and positive (p=0.010; r=0.350).

**DTS-1:** The mean DTS-1 score was 35.4 (SD: 0.89) in the control group, and it was significantly lower in the patient group (mean: 27.7, SD: 1.22, p<0.001). When the control group was excluded from the analysis, no statistically significant differences were found in sex (p=0.81), marital status (p=0.21), education level (p=0.57), place of residence (p=0.94), income level (p=0.27), occupation (p=0.50), age at disease onset (p=0.32), and disease duration (p=0.67).

**DTS-2:** The DTS-2 scores of the patient group were significantly lower (mean: 7.5; SD: 0.44) than the control group (mean: 9.4; SD: 0.65; p=0.002).

**DTS-3:** The mean DTS-3 score was 11.7 (SD: 0.28) in the control group, and the mean score was significantly lower in the patient group (mean: 11.1; SD: 0.33; p=0.20).

**DTS-total:** The total DTS score was 56.8 (SD: 1.29) in the control group, and it was significantly lower in the patient group (46.3, SD: 1.71, p<0.001). When the control group was excluded from the analysis, a significant correlation was found between sex and the DTS-T-score (p=0.014). The mean DTS-T score was 41.9 (SE: 2.02) in men and 51.5 (SE: 2.44) in women. Furthermore, a negative, weak, and significant correlation was found between disease duration and total DTF score (p=0.017; r=-0.311).

**UAS 7:** The mean UAS7 score was 27.5±9.6 (minimum: 6; maximum: 42) in the patient group, and a positive correlation was found between all scale and subscale scores and UAS7 (Table 2).

The results of comparing the psychometric values are presented in Table 3.

### Discussion

The treatment satisfaction of dermatology patients with psychiatric symptoms is low. Physicians spent more time with these patients, which could in turn lead to burnout symptoms in physicians<sup>25</sup>. Although psychiatric symptoms are common, studies should investigate possible

Table 1. Socio-demographic characteristics of the patients and controls							
	CSU, n=52	Control, n=50	t/x²	р			
Age	38.5±11.8	36±12.1	1.051	0.296			
Sex	Female: 28% (53.8)	Female: 25	0.151	0.608			
	Male: 24% (46.2)	Male: 25	0.151	0.098			
UAS	27.5±9.6; min.: 6; max.: 42 UAS <6 (3%) UAS >28 (29.5%)	-	-	-			
Age at disease onset	4 18 <% (7.7) 6 18-25% (11.5) 32 26-40% (61.5) 10 >41% (19.3)	-	-	-			
Duration of disease years	5.3±6.5	-	-	-			
Family history	Positive: 4	-	-	-			
	Negative: 48	-	-	-			

CSU: Chronic spontaneous urticaria, UAS: Urticaria activity score, min.: Minimum, max.: Maximum



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approaches to these patient groups, and psychiatric support methods that should be adopted in treatment are important. DT has not been examined in patients with CSU. In the present study, the total and subscale DT scores were low in patients with CSU and correlated with disease severity. Since DT levels could be low in patients with CSU, an approach that considers DT levels could be beneficial for these patients. Psychiatric comorbidity and psychiatric drug use are more common in patients with CU than in the general population, and anxiety, depression, and somatoform disorders are prevalent<sup>6</sup>. Literature data on factors associated with the psychiatric comorbidity of CSU are insufficient. Despite studies on the correlation between psychiatric disorders and CU<sup>6,11-13</sup>, the benefits of a multidisciplinary approach (allergists, dermatologists, and psychiatrists) are still unclear. The low DT level determined in this study and the correlation between DT scale score and disease severity (UAS7) in patients with CSU could be an important target for a multidisciplinary approach in the treatment of CSU.

Although the low total DT and subscale scores in patients with CSU in the present study could be expected, the correlation between the scale scores and disease severity (UAS) suggested that patients with severe disease should be monitored closely for psychiatric symptoms. Previous studies have shown that stress may play a role in CSU onset<sup>2632</sup>. The correlation found in the present study shows that disease severity may also be affected by distress level and other psychiatric symptoms. Therefore, psychiatric evaluation is important for patients with CSU.

CSU could induce psychiatric disorders, leading to psychiatric comorbidities until recent years<sup>26</sup>. Inflammation observed in CSU and peripheral proinflammatory cytokines could affect the brain without crossing the blood-brain barrier. Proinflammatory cytokines may lead to the development of psychiatric disorders because of their effect on serotonin and dopamine pathways<sup>11,27</sup>. Given the bidirectional interaction between the brain and the immune system<sup>28</sup>, stress and psychological state may also influence the exacerbation of CSU. Complex interactions between stress, skin, and the nervous system may play a role in the etiology of CSU. The elevated psychological stress level that has been closely related to CSU could be attributed to the instability of this neuro-immune-cutaneous circle<sup>29</sup>. Choi et

al.30 confirmed that patients with CU frequently develop psychiatric conditions, such as depression and anxiety. Moreover, stress was associated with pruritus severity and urticarial activity<sup>30</sup>. Psychotropic drugs (e.g., antidepressants and benzodiazepines) could have a positive effect on CSU treatment<sup>11,31</sup>. Psychotherapy methods reduce stress and psychiatric symptoms. Thus, further research is required to determine the effect of psychotherapy on CSU treatment. In this study, both BDI and STAI scores were significantly higher in the patient group. However, DT was low in patients with CSU and was associated with disease severity. In the study, depression scores and DTS-total scores were significantly higher in men. The difference could be due to personal traits such as age, sex, place of residence, and coping style<sup>11</sup>. Thus, CSU specialists should adopt the biopsychosocial model in their approaches. Previous studies conducted by Chu et al.<sup>6</sup> and Zabolinejad et al.<sup>32</sup> have reported that patients with CSU and at risk of developing a psychiatric disorder and anxiety scores were associated with CSU severity, similar to our findings, and the decrease in DTS could be one of the causes of the psychiatric disorders commonly observed in patients with CSU. In the present study, correlations were determined between disease duration and DTS-T, STAI-1, and depression scores. This supported the hypothesis of a reciprocal correlation between CSU and psychological factors. Furthermore, the correlations between DT and disease duration and psychological symptoms supported our hypothesis that the former could be an inductive and maintaining factor to consider.

#### **Study Limitations**

This study has some limitations. First, since the study data included selfreported scales, the findings could have been affected by unpredicted factors. Second, in the subscale analysis, sociodemographic factors such as marriage and unemployment could affect the findings, and these effects could be determined in future studies with larger patient groups. Third, a cross-sectional methodology was adopted in the study, which limited the study data. Fourth, patients who did not have a psychiatric disease history and did not receive any psychiatric treatment were included in the study. Fifth, a detailed diagnostic psychiatric disorders were the cause or consequence of CSU. Thus, adequate psychiatric interventions could contribute to the treatment

Table 2. Correlation between disease severity UAS and scale scores								
	DTS-total	DTS-1 tolerance	DTS-2 self-efficacy	<b>DTS-3</b> regulation	BDI	STAI-1	STAI-2	
UAS	r=-0.561 p<0.001	r=-0.532 p<0.001	r=-0.383 p=0.005	r=-0.414 p=0.002	r=0.613 p<0.001	r=0.359 p=0.009	r =0.568 p<0.001	
BDI: Beck depression inventory, DTS: Distress tolerance scale, STAI-1: State anxiety scores, STAI-2: Trait anxiety scores, UAS: Urticaira activity score								

Table 3. Comparison of psychometric values between groups							
	Cr. urticaria, n=52	Control, n=50	t	р			
DTS-total	46.3±12.3	56.8±9.15	-4.887	<0.001			
DTS-1 tolerance	35.4±8.8	27.7±6.3	-5.037	<0.001			
DTS-2 self-efficacy	7.55±3.17	9.46±2.80	-3.203	0.002			
DTS-3 regulation	11.01±2.45	11.74±2.02	-1.623	0.02			
BDI	14.34±8.39	5.48±5	6.446	<0.01			
STAI-1	40.94±9.54	32.16±8.05	5.014	<0.001			
STAI-2	46.48±10.82	41.02±8.44	2.834	0.002			

BDI: Beck depression inventory, DTS: Distress tolerance scale, STAI-1: State anxiety scores; STAI-2: Trait anxiety scores, <sup>a</sup>Student's t-test



of the disease. Psychiatric evaluation of DT, which was considered an etiological factor in psychiatric disorders, and enforcing DT with psychotherapy methods in patients with CSU could be important in the treatment and could contribute to the treatment and follow-up of patients with CSU.

# Conclusion

The result of the present study based on the DT levels revealed that patients with CSU could have low DT levels, which could be associated with disease severity and duration and other psychiatric symptoms such as anxiety and depression. Therefore, it may be important to consider psychiatric attributes and adopt a multidisciplinary approach in the general management and treatment of patients with CSU.

### Ethics

Ethics Committee Approval: The study protocol was approved by the Firat University Non-Interventional Research Ethics Committee (approval number: 05, date: 15.02.2018).

Informed Consent: Verbal and written consent from the participants was obtained.

Peer-review: Externally and internally peer-reviewed.

#### Authorship Contributions

Concept: N.G.G., M.G.G., S.Ö., Design: N.G.G., M.G.G., S.Ö., Data Collection or Processing: N.G.G., S.Ö., Analysis or Interpretation: N.G.G., M.G.G., S.Ö., Literature Search: N.G.G., M.G.G., S.Ö., Writing: N.G.G., M.G.G.

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