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The impact of COVID-19 pandemic on the management of patients with chronic urticaria: An observational two-center study from Turkey

Yasemin Erdem[1] | Algün Polat Ekinci[2] | Ilknur Kivanc Altunay[1] | Onur Sivaz[1] | Sena Inal[1] | Mehmet Onur Gokalp[2] | Gizem Pehlivan[2] | Esen Özkaya[2]

[1]Sisli Hamidiye Etfal Training and Research Hospital, Department of Dermatology, Health Science University, Istanbul, Turkey

[2]Istanbul Faculty of Medicine, Department of Dermatology and Venereology, Istanbul University, Istanbul, Turkey

Correspondence
Yasemin Erdem, Health Science University, Sisli Hamidiye Etfal Training and Research Hospital, Halaskargazi Cad, Etfak Sok. 34371, Sisli, Istanbul, Turkey.
Email: erdemyasemin1@gmail.com

Abstract

The Coronavirus Disease 2019 (COVID-19) outbreak significantly affected the clinical practice in hospitals and the management of many diseases. The aim of this study was to evaluate the effect of pandemic-related factors on the severity and course of chronic urticaria (CU). A total of 194 CU patients who were on regular follow-up, were enrolled in the study. The disease activity was assessed by means of the weekly urticaria activity score (UAS7) and urticaria control test (UCT). Patients were divided into two subgroups according to their disease aggravation as "aggravated" and "non-aggravated". Two groups were compared in terms of demographic, clinical, COVID-19-associated parameters, and parameters related with the effect of COVID-19 pandemic on CU management. The omalizumab use was statistically higher (P = .017), and the systemic corticosteroid use was statistically lower (P = .025) in the "aggravated" group. Adherence to quarantine was significantly lower in the "aggravated" group (P = .027). 173 patients (89.2%) were unable to contact a dermatologist during the pandemic. Among 186 patients who received treatment for CU before the pandemic, 48 (25.8%) did not continue the existing treatment during the pandemic. CU aggravated in one patient with COVID-19 and remained stable in the other. This study showed that CU patients, especially those on omalizumab therapy, had difficulties in attending medical care and even in the maintenance of their existing therapies during the pandemic. Creating novel follow-up and treatment models as well as the increased use of teledermatology might be beneficial in the management of this life-disturbing condition.

KEYWORDS
chronic urticaria, COVID-19, management, omalizumab, pandemic, UAS7, UCT

1 | INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) is a pandemic that started in China, in late December 2019 and spread all over the world. In line with the recommendations of the World Health Organization (WHO), in order to combat the pandemic, rules affecting the social life, the educational system, and the health care system have been introduced.[1] COVID-19 pandemic also affected clinical practice in hospitals. The vast majority of hospitals changed their policy, which prioritized the fight against the pandemic. Accordingly, several

hospitals were declared as pandemic hospitals. Elective procedures have been postponed, and outpatient services were closed. As a result, patients' access to health care centers was decreased, and the follow-up and treatment of chronic diseases became a problem.

Chronic urticaria (CU) is one of the common skin diseases which is characterized by wheals, angioedema, or both, for more than 6 weeks.[2] The disease is of idiopathic nature in most of the cases, although infections, stress, drugs, and other factors might play a role in the etiology. Treatment is usually initiated with systemic antihistamines in standard or high dose, and continued with the addition of leukotriene antagonists, or alternative drugs such as doxepin, or omalizumab in unresponsive cases, according to treatment algorithms.[2-4] During the extraordinary pandemic conditions, procedures for the disease follow-up, management, and treatment have been updated, and guidelines have been published.[5-9] The aim of this study was to evaluate the effect of pandemic-related factors on the severity and course of the disease in a series of patients with CU.

2 | MATERIALS AND METHODS

This prospective, observational study was conducted on 194 patients with CU in the allergy units of two dermatology departments. Systemic diseases including malignancies, focal and systemic infections, and food and drugs as triggering factors were ruled out. Patients with regular follow-up within the last year were enrolled in the study, excluding those with chronic inducible urticaria only.

Detailed demographic (gender, age, marital status) and clinical (presence of concomitant disease, accompanying angioedema, duration of urticaria, drugs used for the treatment of urticaria, disease activity) parameters were recorded. Each patient was asked questions that were indicated in Table 2, for the evaluation of the effects of the pandemic on the disease.

The disease activity was assessed by means of the weekly urticaria activity score (UAS7) and urticaria control test (UCT).[10,11] Both were evaluated before (before March 11, 2020) and during the pandemic (after June 1, 2020). The rationale on determining these dates was based on the report of the first case of COVID-19 on March 11, 2020, and the onset of a "new normalization" on June 1, 2020 in Turkey.[12] After the first case of COVID-19 was reported in Turkey on March 11, 2020, several hospitals have been turned to pandemic centers, whereas non-emergency routine health services and outpatient clinics stopped working. As of 1 June, according to a "new normalization" process, the outpatient clinics were opened, and the routine health services restarted.

COVID-19 diagnosis was confirmed by the presence of a positive polymerase chain reaction (PCR) test result for coronavirus. The patients with COVID-19 diagnosis were questioned in detail about COVID-19 symptoms, treatment, and the course of their urticaria during the COVID-19 management.

The "disease aggravation" was defined using the UAS7 score. Accordingly, a UAS7 score ≤ 6 before the pandemic and a UAS7 score ≥ 7 during the pandemic, and a minimum increase in UAS7 by 7 points during the pandemic was accepted as "aggravated" disease. Patients were divided into two subgroups according to their disease aggravation as "aggravated" and "non-aggravated". The above-mentioned demographic and clinical parameters were compared between these two groups. Furthermore, these two groups were compared in terms of COVID-19 associated parameters listed in Table 2 (the working status during the pandemic, the adherence to quarantine, the use of self-protective equipment against the COVID-19 infection, the presence of COVID-19 positive individuals in their close environment, the history of contact to a COVID-19 positive individual, the presence of COVID-19-like symptoms such as fever, fatigue, cough, dyspnoea, sore throat, and headache, a PCR test performed for the suspicion of COVID-19, and the diagnosis of COVID-19 with a positive PCR test result) and parameters related with the effect of COVID-19 pandemic on CU management (continuation of the existing treatment for urticaria, availability of patient's own or any other dermatologist for contacting during the pandemic).

UAS is widely used for measuring the disease activity of CU. The daily UAS is a sum of the daily intensity of itch (no itch = 0 points; mild itch = 1 point; moderate itch = 2 points; severe itch = 3 points) and number of wheals (no wheals = 0 points; 1-20 wheals = 1 point; 21-50 wheels = 2 points; >50 wheals = 3 points), giving a range of 0 to 6 points per day. Weekly UAS (UAS7) which ranges from 0 to 42 is calculated by adding the scores of 7 consecutive days (10). UAS7 score ranges reflect different levels of disease activity, that is, symptom free (0 points), minimal (1-6 points), mild (7-15 points), moderate (16-27 points), and severe (28-42 points).[10]

The UCT consists of four questions that are rated between 0 and 4 points. The total UCT score is calculated by summing up the points for all questions and ranges between 0 and 16. Low points indicate high disease activity and poor disease control. Scores between 0 and 11 were defined as "poor disease control", scores ≥12 as "good disease control".[11]

The study was approved by the local ethics committee at the Şişli Hamidiye Etfal Training and Research Hospital (approval number: 2020/1618) and conducted in accordance with the Declaration of Helsinki.

2.1 | Statistical analysis

Statistical analyses were performed using SPSS software version 15 (SPSS Inc., Chicago, Illinois, USA). The descriptive statistics comprised the mean, SD, minimum and maximum scores for the numerical variables, and numbers and percentages for the categorical variables. The comparison of the independent variables in both groups was performed using the Student *t* test when there was a normal distribution and the Mann-Whitney *U* test when there was no normal distribution. The comparison was performed using the Kruskal-Wallis test when there were more than two groups.

3 | RESULTS

This study consisted of overall 194 CU patients including 133 (68.6%) females and 61 (31.4%) males. The male: female ratio was 1:2.2. The median age was 40 years (age range: 10-76 years). There was no statistically significant difference between patients with "aggravated" and "non-aggravated" disease regarding the demographic and clinical parameters with an exception of the drugs used for the treatment of CU (Table 1). The omalizumab use was statistically higher ($P < .05$) and the systemic corticosteroid use was statistically lower ($P < .05$) in the "aggravated" group in comparison to the "non-aggravated" group (Table 1). Although statistically not significant, the combined use of antihistamine and montelukast was more common in the "aggravated" group. The share of antihistamine use was similar in both groups.

Table 2 shows a detailed comparison of COVID-19-associated parameters and the parameters related with the effect of COVID-19 pandemic on CU management between the "aggravated" and the "non-aggravated" groups. Adherence to quarantine was significantly lower in the "aggravated" group ($P < .05$). Although statistically not significant, the presence of COVID-19-like symptoms was more frequently associated with CU aggravation. Other parameters were similar between the two groups.

Table 3 shows a detailed comparison of parameters related with the effect of COVID-19 pandemic on the two groups. Among 186 patients who received treatment for CU before the pandemic, 48 (25.8%) did not continue the existing treatment during the pandemic, and this was statistically similar between the "aggravated" and the "non-aggravated" groups. 173 patients (89.2%) were unable to contact their own or any other dermatologist during the pandemic (Table 3).

Table 4 shows a detailed evaluation of the disease severity. The mean UAS7 was 7.5 ± 10.2 before the pandemic, and 8.5 ± 11.2 during the pandemic (Table 4). The difference was statistically not significant. The mean UCT score during the pandemic was found as 11.0 ± 3.7.

Two patients (1%) were diagnosed with COVID-19. The clinical features of these patients were summarized in Table 5.

TABLE 1 The demographic and clinical findings of patients with chronic urticaria in relation to their disease aggravation

Demographic and clinical findings	Total (n = 194)	"Aggravated" group (n = 38)	"Non-aggravated" group (n = 156)	*P*-value
Gender				
Female, n (%)	133 (68.6)	29 (76.3)	104 (66.7)	.340
Male, n (%)	61 (31.4)	9 (23.7)	52 (33.3)	
Age				
Median, year (range)	40 (10–76)	41.5 (20-65)	40 (10-76)	.702
Mean, year (SD)	39.5 (±13.1)	40.24 (±11.8)	39.3 (±13.4)	
Marital status				
Married, n (%)	135 (69.6)	22 (57.9)	113 (72.4)	.121
Single, n (%)	59 (30.4)	16 (42.1)	43 (27.6)	
Concomitant disease, n (%)[a]	76 (39.2)	16 (42.1)	60 (38.5)	.820
Diabetes mellitus, n (%)	15 (7.7)	4 (10.5)	11 (7.1)	.488
Hypertension, n (%)	22 (11.3)	4 (10.5)	18 (11.5)	.859
Thyroid disease, n (%)	11 (5.7)	1 (2.6)	10 (6.4)	.326
Asthma bronchiale, n (%)	9 (4.6)	4 (10.5)	5 (3.2)	.075
Allergic rhinoconjunctivitis, n (%)	9 (4.6)	1 (2.6)	8 (5.1)	.484
Accompanying angioedema, n (%)	64 (33.0)	9 (23.7)	55 (35.3)	.243
Duration of urticaria				
Median, month (range)	30.0 (6-480)	36.0 (9-240)	27.0 (6–480)	.262
Mean, month (SD)	50.5 (±61.9)	58.5 (±62.8)	48.6 (±61.7)	
Drugs used for the treatment of urticaria				
Systemic antihistamine, n (%)	140 (72.2)	24 (63.2)	116 (74.4)	.238
Omalizumab, n (%)	34 (17.5)	12 (31.6)	22 (14.1)	**.017**
Antihistamine-montelukast, n (%)	5 (2.6)	3 (7.9)	2 (1.3)	.052
Systemic corticosteroid, n (%)[b]	9 (8.6)	0 (0)	9 (13.4)	**.025**

[a]Some patients had more than one concomitant disease.
[b]Systemic corticosteroids have only been used for a short time in acute exacerbations.
Note: Statistically significant *P*-values are highlighted in bold. Categorical variables were compared using chi square test and non-parametric continuous variables were compared using Mann-Whitney *U* test. $P < .05$ was accepted as statistical significant
Abbreviation: SD, standart deviation.

TABLE 2 The comparison of pandemic-related factors between two groups of patients with chronic urticaria

COVID-19-associated parameters	Total (n = 194)	Aggravated group (n = 38)	Non-aggravated group (n = 156)	*P*-value
Working status during the pandemic				
None, n (%)	140 (72.2)	29 (76.3)	111 (71.2)	.405
At home, n (%)	15 (7.7)	4 (5.7)	11 (7.1)	
At the workplace, n (%)	39 (20.1)	5 (17.5)	34 (21.8)	
Adherence to quarantine, n (%)	184 (94.8)	33 (86.8)	151 (96.8)	**.027**
Patients using self-protective equipment, n (%)	192 (99)	38 (100)	154 (98.7)	.483
Patients who had COVID-19 positive individuals in their close environment, n (%)	39 (20.1)	8 (21.1)	31 (19.9)	.871
Patients with history of contact to a COVID-19 positive individual, n (%)	8 (4.1)	3 (7.9)	5 (3.2)	.229
Patients with COVID-19-like symptoms, n (%)	20 (10.3)	7 (18.4)	13 (8.3)	.078
Patients underwent a PCR test for COVID-19, n (%)	14 (7.2)	3 (7.9)	11 (7.1)	.740
Patients with a positive PCR test and a definite diagnosis of COVID-19, n (%)	2 (1.0)	1 (2.6)	1 (0.6)	.354

Note: A statistically significant *P*-value is highlighted in bold. Categorical variables were compared using chi square test and non-parametric continuous variables were compared using Mann Whitney U test. $P < .05$ was accepted as statistical significant.

TABLE 3 The comparison of parameters related with the effect of the COVID-19 pandemic on chronic urticaria (CU) management between two groups

Parameters related with the effect of the COVID-19 pandemic on CU management	Total (n = 194)	Aggravated group (n = 38)	Non-aggravated group (n = 156)	*P*-value
Patients who continued their existing treatment for urticaria during the pandemic, n (%)	138/186[a] (74.2)	27/38 (71.1)	111/148 (75.0)	.620
Patients who did not continue their existing treatment during the pandemic, n (%)	48/186[a] (25.8)	11/38 (28.9)	37/148 (23.0)	.620
Antihistamine, n (%)	31/140 (22.1)	6/24 (25.0)	25/116 (21.6)	
Omalizumab, n (%)	15/34 (44.1)	5/12 (41.7)	10/22 (45.5)	
Antihistamine-montelucast, n (%)	0/0 (0)	0 (0)	0 (0)	
Systemic corticosteroid, n (%)	2/9 (22.2)	0 (0)	2/9 (22.2)	
Patients receiving a new treatment, n (%)	5/194 (2.6)	0 (0)	5/156 (3.2)	.568
Patients whose own or another dermatologist was available to be contacted during the pandemic, n (%)	21/194 (10.8)	3/38 (7.9)	18/156 (11.5)	.771
Patients who were unable to contact their own or another dermatologist during the pandemic, n (%)[b]	173/194 (89.2)	35/38 (92.1)	138/156 (88.5)	.771
• because dermatology outpatient clinics were closed, n (%)	88/194 (45.4)	9/38 (23.7)	79/156 (50.6)	
• because of the fear of COVID-19 contamination from hospital, n (%)	58/194 (29.9)	17/38 (44.7)	41/156 (26.3)	
• other causes, n (%)	34/194 (17.5)	13/38 (34.2)	21/156 (13.5)	

[a]Of 194 patients 186 were receiving therapy for CU before the pandemic.
[b]Patients expressed more than one reason to explain why they were unable to contact a dermatologist.
Note: Categorical variables were compared using chi square test.

4 | DISCUSSION

CU is a disease which is characterized by aggravations and remissions during its course.[14] In this study, CU aggravated in 38 (19.5%) of 194 patients during the COVID-19 pandemic.

There were some differences between the "aggravated" and "non-aggravated" groups in this study. Interestingly, the use of omalizumab was significantly higher in the "aggravated" group. Omalizumab, as a novel treatment option, is known to be an effective and safe agent in the treatment of moderate to severe CU that is

TABLE 4 The evaluation of the urticarial disease activity by using the weekly urticaria activity score (UAS7) and urticaria control test (UCT) scores before and during the COVID-19 pandemic

Disease activity	Before the pandemic	During the pandemic
UAS7 score		
Range	0-42	0-42
Mean (SD)	7.52 (±10.2)	8.54 (±11.2)
Aggravated group UAS7 score		
Range	0-6	7-42
Mean (SD)	2.3 (±2.2)	20.8 (±11.1)
Disease activity according to UAS7		
Symptom free, n (%)	67 (34.5)	71 (36.6)
Minimal, n (%)	63 (32.5)	48 (24.7)
Mild, n (%)	32 (16.5)	35 (18.0)
Moderate, n (%)	14 (7.2)	19 (9.8)
Severe, n (%)	18 (9.3)	21 (10.8)
Patient groups according to UAS7		
UAS7 0–6, n (%)	130	129
UAS7 ≥ 7, n (%)	64	65
UCT score		
Range	NA	0-16
Mean (SD)	NA	11.0 (±3.6)
Disease control by UCT score		
Good disease control UCT ≥12, n (%)	NA	87 (44.8)
Poor disease control UCT <12, n (%)	NA	107 (55.2)

Note: UAS7: 0 points = symptom free, 1-6 points = minimal, 7-15 points = mild, 16-27 points = moderate, 28-42 points = severe.
Abbreviations: NA, not applicable; SD, standart deviation.

resistant to H1-antihistamine treatment.[2,15] It is usually administered as a single subcutaneous injection every 28 days which means regular hospital visits for patients to reach the dermatologist, to obtain the drug, and to get the injection. Any failure in these steps may result in interruption or discontinuation of treatment. In accordance with that, 15 (44.1%) of 34 patients who were on omalizumab therapy before the pandemic in this study, could not continue their treatment during the pandemic due to life-threatening pandemic conditions. Only 10.8% of patients were able to contact their own or another dermatologist while 89.2% of patients were not. The main reasons were "closing of the outpatient clinics" and "fear of COVID-19 contamination" as reported by 50.9% and 33.5% of patients, respectively. Recently, it was recommended by study groups to continue omalizumab as home treatment during the pandemic.[8,9] The main concern on the administration of omalizumab at home is the risk of anaphylaxis, however, this risk was reported to be very low (0.1%) in asthma bronchiale patients who received omalizumab.[16] On the other hand, CU patients receiving omalizumab treatment, were not reported to have anaphylaxis in the pivotal study, and only several suspicious cases of anaphylaxis were reported.[17] In the light of these data, administration of omalizumab at home in appropriate patients with CU was reported as safe, and home treatment was recommended after the fourth administration.[17]

Postponing the appointments for non-urgent examinations, extending the intervals between the appointments, and increased use of teledermatology would be other preventive measures against the spread of the COVID-19 in and from hospitals. Teledermatology comes to the forefront as a preferable method in the pandemic period to protect both patients and physicians.[18]

The use of systemic corticosteroids was significantly lower in the "aggravated" group. Systemic corticosteroids are fast acting and highly effective in urticaria. However, they are only recommended for short-term use to suppress the urticaria attacks in those with a poor response to antihistamines, in order to avoid long-term side effects. In this series, the higher use of systemic corticosteroids in the "non-aggravated" group seems to be related with a rapid symptom control, thus preventing disease aggravation. Low-dose systemic corticosteroid therapy, on the other hand, was thought to have an inhibitory effect on the inflammatory cytokine storm caused by the COVID-19, however, it may increase the risk of prolonged viral replication as well.[19] Therefore, low dose and short-term use of systemic corticosteroids may be recommended only in selected cases of urticaria patients during the COVID-19 pandemic.[19]

Adherence to quarantine (includes social distancing, work from home, travel restrictions, and stay-at-home over the weekend) was significantly lower in the "aggravated" group. Consequently, COVID-19-like symptoms were higher in this group although statistically not significant. One explanation might be that these patients had in fact COVID-19, but did not admit to the hospital because of the mildness of the symptoms so that no coronavirus test was performed. Another explanation might be that a test was performed and the result was false-negative. Up to 20%-67% false-negative results were reported in coronavirus PCR testing due to the timing and quality of the tests performed.[20] Moreover, the presence of COVID-19-like symptoms might have resulted from other viral or bacterial upper respiratory tract infections leading to an exacerbation of CU. Infections are well-known causes of acute urticaria,[21] whereas they might trigger or exacerbate CU as well.[21] However, it is usually difficult to make a clear interpretation on this issue because urticaria might have various triggering factors.

Behaviors in daily life, medical practices, and dermatology practices were hugely affected by the pandemic process.[22,23] There is limited evidence on the safety of the immunomodulatory, immunosuppressive drugs, and biologics used in the treatment of skin diseases during the COVID-19 pandemic. Several reports and guidelines were published on treatment, management, and follow-up of skin diseases during the COVID-19 pandemic,[24,25] including urticaria[5-9] with special concern on this issue. General recommendations were that patients should be made aware of the social distancing, and hand hygiene,[5,8] and of the necessity of lessening the face-to-face visits, and postponing appointments unless there are emergency

TABLE 5 The demographic and clinical findings of patients with chronic idiopathic urticaria diagnosed with COVID-19 in our cohort and in the literature

Study/Author	Age, gender	Concomitant disease	Drug used for the treatment of urticaria, duration	Drug used for the treatment of COVID-19	COVID-19 diagnostic tools	Hospitalization due to COVID-19	Urticaria severity due to COVID-19, UAS7 scores before/during COVID-19, change in %	Non-urticarial cutaneous manifestation
Present cohort, Patient 1	55 year-old, female	No	Loratadine 10 mg/day, 2 years	Hydroxychloroquine 400 mg twice on day 1, followed by 400 mg/day for 4 days Enoxaparine sodium 4000 IU/day subcutaneously for 7 days	Positive PCR test and chest CT findings	Yes, 7 days	Remained stable, UAS7 = 0/0	Chilblains on lower legs
Present cohort, Patient 2	37 year-old, female	Asthma bronchiale	Cetirizine 10 mg/day, 2 years	Hydroxychloroquine 400 mg twice on day 1, followed by 400 mg/day for 4 days	Positive PCR test	No, at-home treatment	Exacerbated, UAS7 = 6/20, increased to 3.3-fold	Chilblains on fingers
Criado et al[13]	57 year-old, female	No	Bilastine 80 mg/day, not defined	Amoxicillin-clavulanate for 7 days	Positive PCR test and chest CT findings	No, at-home treatment	Exacerbated, UAS7 = 6/42 increased to 7-fold	Not defined

Abbreviations: CT, computed tomography; PCR, polymerase chain reaction; UAS7, weekly urticaria activity score.

situations, as well as the preference of teledermatology or phone triage rather than face-to-face visits.[5,6,8] Further recommendations included avoidance of the triggering factors and learning of the stress coping methods. The benefit/risk ratio should be considered for each patient to select an appropriate treatment, especially for those whose treatment will be initiated at the pandemic-era. Non-sedative H1-antihistamines with their good efficacy and reliability profile,[2] are usually the preferred treatment of choice. The use of non-sedative H1-antihistamines generally do not require close surveillance or hospital conditions, thus rendering them as patient-friendly for CU in the COVID-19 pandemic era. Accordingly, the percentage of patients using non-sedative H1-antihistamines was higher in our cohort. For patients unresponsive to H1-antihistamines, the Dermatoallergy Working Group of Turkish Society of the Dermatology recommended the use of omalizumab rather than systemic immunosuppressants.[8] Immunosuppressant drugs which were initiated for CU before the pandemic were not discontinued, however, patients were recommended to strictly obey the social distancing rules. The British Society of Allergy and Clinical Immunology (BSACI) recommended to postpone the initiation of omalizumab in new patients with CU until the pandemic restrictions are removed.[9] For patients who were already on omalizumab therapy and who had a stable course of urticaria, extended dose intervals or temporary drug discontinuation were recommended.[8] The BSACI on the other hand, recommended to educate appropriate patients with CU about the self-administration of omalizumab at home after the second dose of the drug, so that they would be able to administrate the third dose and then subsequent doses at home during the pandemic period.[9]

There is no evidence that omalizumab has an immunosuppressant effect. Randomized controlled studies showed that omalizumab did not increase the risk of infection in the study group when compared with the placebo group.[26] Moreover, omalizumab was shown to promote the induction of interferon-α (IFN-α) production in plasmacytoid dendritic cells by IgE blockage, thereby reducing the susceptibility to viral respiratory tract infections.[27] Indeed, it was reported that omalizumab significantly reduced seasonal viral respiratory infections in children with asthma.[28] In light of these data, discontinuation of omalizumab was not recommended in patients who were already using this drug at the time when the pandemic started.[8]

For patients with a definite diagnosis of COVID-19, on the other hand, it was recommended to discontinue any immunosuppressant therapies, whereas glucocorticoids should be tapered off.[8] There is no clear data on the use of omalizumab in COVID-19-positive patients. In a recent case report, omalizumab was initiated for a CU patient who had COVID-19 disease.[13] This patient was reported to have COVID-19-related symptoms for 16 days. The patient received omalizumab after COVID-19-related symptoms had regressed, and CU completely subsided within 72 hours of omalizumab therapy.[13] Another patient with allergic asthma bronchiale was reported to have COVID-19 disease while he was under omalizumab therapy.[29] This patient was reported to have COVID-19-related symptoms for 20 days, and a second PCR test at the 17th day of the disease was negative. The authors asserted that the use of omalizumab might have

a protective effect on COVID-19 progression in this patient.[29] More data are needed to evaluate the impact of omalizumab therapy on the course of COVID-19 more properly.

Various cutaneous manifestations as well as systemic findings were reported during the course of COVID-19. Cutaneous findings accompanied in 0.2%-20.4% of patients.[30] New-onset urticaria was reported in 16% of COVID-19 patients in a study,[31] and in case reports.[32,33] COVID-19 might lead to the development of new-onset urticaria or exacerbation of pre-existing urticaria through activation of the mast cells and basophils directly or indirectly by the virus.[26]

There are limited number of reports on the course of CU in patients with COVID-19 in the literature.[13] One patient was reported to have exacerbation of CU following the diagnosis of COVID-19.[13] Two patients in our study group were diagnosed with COVID-19 disease. Exacerbation of urticaria was observed following the diagnosis of COVID-19 infection in one patient, whereas the severity of urticaria did not change in the other patient. Like other viral infections, COVID-19 might also be expected to cause exacerbations of CU. However, there might be several other triggering factors of CU such as drugs, or even psychogenic stress. Drugs for COVID-19 treatment such as chloroquine, hydroxychloroquine, lopinavir/ritonavir and other antiretroviral agents, and intravenous immunoglobulin treatment were reported to cause urticaria as well.[34] All these factors need to be considered when evaluating patients with exacerbations of CU during COVID-19 disease.

The major limitation of this study was its small cohort size. However, the cohort consisted of registered CU patients who were on regular follow-up, which allowed us to provide data on their pre-pandemic clinical situation. This might be regarded as a strong aspect of this study.

5 | CONCLUSION

This study showed that CU was significantly aggravated in patients who were on omalizumab therapy. Patients had less access to health care services, leading to impaired maintenance of omalizumab therapy as the major negative impact of the pandemic on CU. Creating novel follow-up and treatment models as well as the increased use of tele-dermatology might be beneficial in the management of this life-disturbing condition.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Yasemin Erdem: Design of study, statistical analysis, writing of original draft, critical editing. **Algün Polat Ekinci**: Design of study, critical editing. **İlknur Kıvanç Altunay**: Design of study. **Onur Sivaz**: Data collection. **Sena İnal**: Data collection. **Mehmet Onur Gokalp**: Data collection. **Gizem Pehlivan**: Data collection. **Esen Özkaya**: Design of study, writing of original draft, critical editing.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Yasemin Erdem https://orcid.org/0000-0002-6597-2957
Algün Polat Ekinci https://orcid.org/0000-0003-4056-8402
Ilknur Kivanc Altunay https://orcid.org/0000-0002-1354-7123
Onur Sivaz https://orcid.org/0000-0002-7606-9587
Sena Inal https://orcid.org/0000-0001-8840-4015
Mehmet Onur Gokalp https://orcid.org/0000-0001-5617-1229
Gizem Pehlivan https://orcid.org/0000-0002-5906-3976
Esen Özkaya https://orcid.org/0000-0002-9585-9509

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