

# Cutaneous Findings of COVID-19 Infection Related with Length of Hospital Stay: A Prospective, Multicenter Study

## COVID-19 Enfeksiyonunun Hastanede Yatış Süresiyle İlişkili Kutanöz Bulguları: Prospektif, Çok Merkezli Çalışma

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**ABSTRACT Objective:** Coronavirus disease-2019 (COVID-19) was declared a pandemic in March 2020. As the number of cases increased, the infection emerged as a multi-systemic disease. Respiratory, cardiac, hepatic, urinary, circulatory, gastrointestinal systems and finally skin may be the target organs of COVID-19. The aim of this study was to evaluate the cutaneous signs of COVID-19 and their effect on the patients' prognosis. **Material and Methods:** A total of 192 hospitalized COVID-19 cases, between May 2021 to July 2021 were included in the study. The length of stay (LoS) of the patients were recorded. Hospitalization and discharge decisions and all treatments of the patients were determined at the discretion of the treating physician according to the pandemic guidelines of the Ministry of Health. Fever, fatigue, cough, dyspnea, myalgia, anosmia, and headache were considered COVID-19 symptoms. **Results:** Dermatological manifestations were seen in 10 cases. LoS in the group with dermatological findings was shorter than the group without dermatological findings and the difference was statistically significant between the groups. Discharge of the patients was the endpoint of the study. **Conclusion:** Our multicenter study suggests that patients with cutaneous findings usually do not have classical symptoms for COVID-19 and have a shorter LoS.

**Keywords:** COVID-19; dermatology; length of stay; pandemics; prognosis

**ÖZET Amaç:** Koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)], Mart 2020 tarihinde pandemi ilan edildi. Vaka sayısı arttıkça enfeksiyon multisistemik bir hastalık olarak gözlemlenmeye başlandı. Solunum, kardiyak, hepatit, renal, vasküler, gastrointestinal sistemler ve son olarak deri, COVID-19'un hedef organları olabilmektedir. Bu çalışmanın amacı, COVID-19'un kutanöz belirtilerini ve bunların hasta prognozu üzerindeki etkisini değerlendirmektir. **Gereç ve Yöntemler:** Mayıs-Temmuz 2021 tarihleri arasında hastanede yatan toplam 192 COVID-19 vakası çalışmaya dâhil edildi. Hastaların, hastanede kalış süreleri [length of stay (LoS)] kaydedildi. Hastaların yatış ve taburculuk kararları ve tüm tedavileri, Sağlık Bakanlığının pandemi kılavuzlarına göre tedaviyi yapan hekimin inisiyatifinde belirlendi. Ateş, yorgunluk, öksürük, nefes darlığı, miyalji, anosmi ve baş ağrısı, COVID-19 semptomları olarak kabul edildi. **Bulgular:** On olguda dermatolojik bulgular görüldü. Dermatolojik bulgusu olan gruptaki LoS, dermatolojik bulgusu olmayan gruba göre daha kısaydı ve gruplar arasındaki fark istatistiksel olarak anlamlıydı. Hastaların taburcu edilmesi çalışmanın bitiş noktasıydı. **Sonuç:** Çok merkezli çalışmamız, kutanöz bulguları olan hastaların genellikle COVID-19 için klasik semptomlarının olmadığını ve daha kısa bir LoS'a sahip olduğunu göstermektedir.

**Anahtar Kelimeler:** COVID-19; dermatoloji; yatış süresi; pandemik; prognoz

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Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was firstly reported as an etiological agent causing a new respiratory system disease [coronavirus disease-2019 (COVID-19)] in Wuhan, China, in December 2019.<sup>1</sup> It has been declared a pandemic by the World Health Organization in March 2020.<sup>2</sup> With the rapid increase of patients worldwide, the clinical spectrum of the disease is better understood and studied. The most common symptoms are fever, fatigue, cough, dyspnea, myalgia, anosmia, and headache.<sup>3</sup> In early reports, cutaneous lesions are not mentioned in clinical signs of COVID-19. But recently skin manifestations have been categorized as erythematous rash, chilblain-like lesions, urticaria, vesicular lesions and vascular lesions.<sup>4</sup> Lately, symmetrical flexural and intertriginous exanthema, purpuric rash, erythema multiforme-like rash and Kawasaki-like disease/multisystemic inflammatory syndrome in children, mottling, Sweet syndrome-like, pustular eruptions and androgenetic alopecia are suggested as other cutaneous manifestations of COVID-19.<sup>5,6</sup> The incidence of cutaneous findings varied in different countries.<sup>1,5,7</sup>

As the pandemic escalates, health systems are challenged. Determining the factors affecting the length of stay (LoS) of patients with COVID-19 can have a critical role in determining the prognosis, and the correct use of resources such as beds, staff and equipment.<sup>8</sup>

## MATERIAL AND METHODS

### STUDY DESIGN AND PATIENTS

A total of 192 consecutive hospitalized COVID-19 cases, from 4 centers in different cities among Turkey between May 2021 to July 2021 were included in this prospective study. The study was conducted in 1 tertiary and 3 secondary care hospitals. Those under the age of 18, pregnant and with prior history of dermatologic disease were excluded. All the patients with skin involvement, and COVID-19 infection were examined by trained dermatologists involved in the study.

Hospitalization and discharge decisions and all treatments of the patients were determined at the discretion of the treating physician according to the pandemic guidelines of the Ministry of Health. Fever,

fatigue, cough, dyspnea, myalgia, anosmia, and headache were considered COVID-19 symptoms. The criteria for patient discharge were considered in case of the absence of fever for at least 2 days, substantial improvement in both lungs on thorax computed tomography (CT), clinical remission of respiratory symptoms, and 2 throat-swab samples negative for viral RNA obtained at least 24 hours apart. Demographic characteristics, COVID-19 symptoms, comorbid diseases, smoking habit, oxygen saturation, C-reactive protein (CRP), thorax CT, polymerase chain reaction (PCR) for SARS-CoV-2, dermatological findings and the length of hospital stay were recorded. Discharge of the patients was the endpoint of the study.

### ETHICS

The study was authorized by an ethics committee (İstinye University Clinical Research Ethics Committee, 2/2020.K-037, May 21, 2020) and the Ministry of Health. The study was conducted according to the principles of the Declaration of Helsinki. Informed consent form was obtained from all participants.

### STATISTICAL ANALYSIS

Statistical analysis was made using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Chi-square ( $\chi^2$ ) test and Fischer's exact test were used for the comparison of categorical data. Mann-Whitney U test was used to analyze quantitative data and the Wilcoxon test was used to analyze repetitive measurements. Data were expressed as median [interquartile range (IQR)] and percent (%) where appropriate.  $p < 0.05$  was considered statistically significant.

Post-hoc power analysis using G\*Power (Heinrich Heine University Düsseldorf, Germany) 3.1 revealed we had 64% power detecting decrease in length of hospital stay days from  $12.14 \pm 4.54$  to 8.7 in a 10 patient group with cutaneous findings, 182 patient control group with  $\alpha$  error probability of 0.05.

## RESULTS

A total of 192 laboratory testing (PCR) confirmed COVID-19 positive and hospitalized patients (124

TABLE 1: Demographic characteristics.						
Variables		Unit of measure	Cutaneous finding (+)	Cutaneous finding (-)	p value	Total
Age		Median	41	45	0.461	45
		IQR	(32.50-48.75)	(33-54)		(33-54)
Gender	Female	n	6	62	0.17	68
		%	60	34.1		35.4
	Male	n	4	120		124
		%	40	65.9		64.6
Smoking		n	3	49	0.831	52
		%	30	26.9		27.1
Comorbidity		n	2	35	0.952	37
		%	20	19.2		19.3

IQR: Interquartile range.

male, 68 female), with median age of 45 (IQR 33-54) were included in the study (Table 1). Dermatological findings were reported in 10 (5.21%) cases; urticaria (n=4, 40%), maculopapular eruption (n=4, 40%) and zona zoster (n=2, 20%) (Figure 1, Figure 2, Figure 3) (Table 1). All the cutaneous manifestations were observed on the onset of the hospitalization.

Hypertension (14.6%), diabetes mellitus (5.7%), chronic obstructive pulmonary disease (4.7%) and chronic renal failure (4.2%) were the comorbidities.

In the group with dermatological findings, 2 (20%) patients; in the group without dermatological findings, 35 (19.2%) patients had a history of comorbidity and the difference between groups was not significant (p=0.952).

A total of 52 (27.1%) patients had a history of smoking and there was no significant difference between the 2 groups (p=0.831) (Table 2). Oxygen saturation was monitored as median 96 (IQR 95-97) at admission, while those with dermatological findings had a median of 97.5 (IQR 96-98) and those without dermatological findings were observed as 96 (IQR 95-97) and the difference between groups was not significant (p=0.139) (Table 2).

The median CRP checked at the time of admission was 2.08 (IQR 0.41-7.88), while in the group with dermatological findings was 2.08 (IQR 0.37-7.93) in the group without dermatological findings.



FIGURE 1: A 27 year old female patient, urticarial lesions.



FIGURE 2: A 32 year old female patient, erythematous, maculopapular eruption on her trunk.



**FIGURE 3:** A 48 year old male patient, grouped vesicles due to herpes zoster on his thoracic dermatomal area.

2.07 (IQR 0.84-3.10) and the difference between groups was not significant ( $p=0.626$ ) (Table 2).

Thorax CT showed findings compatible with COVID-19 in 128 (67%) patients. Eight (80%) patients were in the group with dermatological findings, and 120 (66.3%) patients were in the group without dermatological findings, and the difference between groups was not significant ( $p=0.50$ ) (Table 2).

In the group with dermatological findings, 2 (20%) patients; in the group without dermatological findings, 132 (72.5 %) patients had COVID-19 symptoms and there was a significant difference (Table 1) between 2 groups ( $p=0.002$ ) (Table 2).

The median LoS was 12 (IQR 9-14) days. The median LoS was 12 (IQR 9-15) days in the group

without dermatological findings and 8.5 (IQR 6-12) days in the group with dermatological findings (Figure 4). LoS in the group with dermatological findings was significantly shorter than the group without dermatological findings and the difference was statistically significant between the groups ( $p=0.008$ ) (Table 2).

None of the 192 patients died or were taken to the intensive care unit.

## DISCUSSION

In history, skin involvement has taken an important place in most of the devastating plagues. Black death, measles, smallpox, and yellow fever are the main examples. There are many articles published about clinical symptoms but we think that dermatologic involvement is still not sufficiently prominent.

Cutaneous manifestations related to COVID-19 are emerging every day. The incidence of skin lesions during COVID-19 infection was reported between 0.2% and 29%, in the published literature.<sup>9,10</sup> Skin findings related to COVID-19 were evaluated in 6 subgroups; maculopapular eruption, urticaria, chilblain-like acral pattern, vesicular lesions, livedo reticularis-livedo racemosa like pattern, and purpuric vasculitic pattern.<sup>11</sup> Maculopapular exanthema reported as the most common cutaneous manifestation found in 15.9% of COVID-19 patients.<sup>9</sup>

**TABLE 2:** Clinical findings.

Variables	Unit of measure	Cutaneous finding (+)	Cutaneous finding (-)	p value	Total
Symptomatic	n	2	132	0.002	134
	%	20.0	72.5		
CT	n	8	120	0.5	128
	%	80.0	66.3		
PCR	n	10	163	0.602	173
	%	100	89.6		
CRP	Median	2.08	2.07	0.626	2.08
	IQR	(0.37-7.93)	(0.84-3.10)		
SpO <sub>2</sub>	Median	97.5	96	0.139	96
	IQR	(96-98)	(95-97)		
Length of hospital stay (days)	Median	8.5	12	0.008	12
	IQR	(6-12)	(9-15)		

CT: Computed tomography; PCR: Polymerase chain reaction; CRP: C-reactive protein; IQR: Interquartile range.

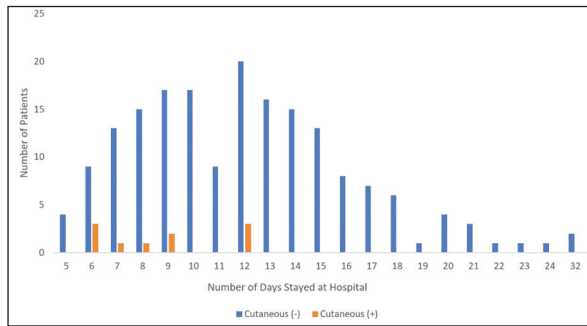


FIGURE 4: Distribution of the patients by the length of stay hospital.

Most of the patients with skin findings in our study were asymptomatic in terms of COVID-19 infection.

In our study, maculopapular eruption was one of the most common dermatological findings which was seen in 40% of the patients. One of these patients had lesions after hydroxychloroquine use.

Urticaria is reported as a dermatological finding of COVID-19. It has been suggested that, in viral infections, immunoglobulin M and immunoglobulin G may cross react with mast cell immunoglobulin E, in a study.<sup>12</sup> According to a study from China, urticarial lesions were observed in 1.2% of non-severe patients and in 1.7% of severe patients but the difference was statistically significant.<sup>13</sup> According to Dastoli et al., non-drug urticaria might be associated with systemic eosinophilia, and possibly to a better prognosis of the disease.<sup>14</sup> In our study, we found urticaria in 4 (40%) patients. None of these patients had a history of a new drug in the last 15 days.

Herpes zoster has also been reported as one of the skin symptoms of COVID-19.<sup>15</sup> COVID-19 infection is associated with a reduction in lymphocytes, monocytes, and eosinophils. Lymphopenia may be a triggering factor for herpes virus family recurrences.<sup>16</sup> In our study, 2 (20%) patients had classical zona zoster lesions; monomorphic grouped vesicles with central umbilication and located on the dermatomes. In a study from Spain, it was suggested that vesicular lesions may be an indicator for COVID-19 infection.<sup>10</sup>

LoS is an important parameter for mortality and morbidity of COVID-19 infection, which has a cru-

cial role in estimating the hospital bed capacity for the sustainability of healthcare services.<sup>8</sup> The median duration of LoS has been reported in studies as 10-13 days.<sup>17,18</sup> It has been reported longer (19-21 days) in far east countries than in the United States and European countries.<sup>17,19,20</sup> It may be associated with several factors such as time of period after symptom onset, disease severity, age, regional health practice policies.<sup>8,17</sup> Thai et al. reported that elderly patients and cases identified as domestically had longer LoS.<sup>17</sup> In another study, Wu et al. stated that longer hospitalization is associated with having fever, bilateral pneumonia, shorter duration from symptom onset to admission and diabetes.<sup>21</sup>

## CONCLUSION

Our multicenter study suggests that patients with cutaneous findings usually do not have classical symptoms for COVID-19 and have a shorter LoS. Our findings might be helpful to predict a short hospital stay in case of cutaneous presentations.

### Source of Finance

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

**Idea/Concept:** Aslı Tatlıparmak, Zehra Aşiran Serdar; **Design:** Aslı Tatlıparmak, Selda Pelin Kartal; **Control/Supervision:** Zehra Aşiran Serdar, Selda Pelin Kartal; **Data Collection and/or Processing:** Aslı Tatlıparmak, Gökçen Çelik, Fatmanur Hacineciipoğlu; **Analysis and/or Interpretation:** Şirin Yurtlu Temel, Gizem Kocabaş Yenipazar; **Literature Review:** İnci Serdar; **Writing the Article:** Aslı Tatlıparmak, Ali Cankut Tatlıparmak; **Critical Review:** Zehra Aşiran Serdar, Selda Pelin Kartal.



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