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RESEARCH ARTICLE/KLİNİK ÇALIŞMA

FLORA 2023;28(3):449-455 • doi: 10.5578/flora.20239715

Evaluation of Clinical and Laboratory Findings of COVID-19 Patients with Dermatological Involvements: A Single-Center Retrospective Cross-Sectional Study

Dermatolojik Tutulumu Olan COVID-19 Hastalarının Klinik ve Laboratuvar Bulgularının Değerlendirilmesi: Tek Merkezli Retrospektif Kesitsel Bir Çalışma

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Cite this article as: *Kaya Ö, Alkan S, Keskinkaya Z, Çinpolat YH, Işık Mermutlu S, Oğuz Kılıç S. Evaluation of clinical and laboratory findings of COVID-19 patients with dermatological involvements: A single-center retrospective cross-sectional study. FLORA 2023;28(3):449-455.*

ABSTRACT

Introduction: *Cutaneous manifestations of the coronavirus disease-2019 (COVID-19) are increasingly reported, with their incidence and pathophysiological mechanisms yet to be clarified. The aim of this study was to evaluate COVID-19 patients presenting with dermatological involvement.*

Materials and Methods: *COVID-19 patients with dermatological involvements followed up in a single tertiary center between August 2020 and August 2021 were assessed in terms of demographic characteristics, clinical and laboratory findings, and treatment methods.*

Results: *A total of 65 patients (female:male ratio= 0.4:1, mean age= 59.7 ± 18.2 years) were evaluated. The dermatological involvements due to COVID-19 were maculopapular rash (n= 49, 75.4%), urticaria (n= 9, 13.8%), herpes zoster (HZ) (n= 6, 9.2%), and pernio (n= 1, 1.5%). In COVID-19 patients with dermatological involvements pulmonary involvement rate was 96.9%. The most common accompanying symptoms were anosmia (n= 47, 72.3%) and ageusia (n= 43, 66.2%), The mean time between the first COVID-19 symptom and the onset of dermatological involvement was 3.3 ± 1.2 days, and the mean time to regression of the lesions was 3.2 ± 1.8 days.*

Conclusion: *Anosmia, ageusia, and pulmonary involvement were common findings especially in patients with maculopapular rash and HZ, probably due to increased inflammation and cytokine storm. The assessment of anosmia and ageusia, especially in patients presenting with maculopapular rash and HZ, may help early recognition of COVID-19 cases. In addition, it should be predicted that individuals with this combination may have a higher risk of pulmonary involvement and disease severity and necessary precautions should be taken during the early stages.*

Key Words: *COVID-19; Herpes zoster; Maculopapular rash; Ageusia; Anosmia*

Received/Geliş Tarihi: 03/01/2023 - Accepted/Kabul Ediliş Tarihi: 10/02/2023

Available Online Date: 20.09.2023

ÖZ

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Giriş: *Koronavirüs hastalığı-2019 (COVID-19)'un deri belirtileri, insidansları ve patofizyolojik mekanizmaları henüz açıklığa kavuşturulmamış olmakla birlikte giderek daha fazla rapor edilmektedir. Bu çalışmanın amacı dermatolojik tutulum ile başvuran COVID-19 hastalarını değerlendirmektir.*

Materyal ve Metod: *Ağustos 2020 ve Ağustos 2021 tarihleri arasında üçüncü basamak bir merkezde takip edilen dermatolojik tutulumu olan COVID-19 hastaları demografik özellikler, klinik ve laboratuvar bulguları ve tedavi yöntemleri açısından değerlendirildi.*

Bulgular: *Toplam 65 hasta (kadın:erkek oranı= 0.4:1, ortalama yaş= 59.7 ± 18.2 yıl) değerlendirildi. COVID-19'a bağlı dermatolojik tutulumlar makülopapüler döküntü (n= 49, %75.4), ürtiker (n= 9, %13.8), herpes zoster (HZ) (n= 6, %9.2) ve pernio idi (n= 1, %1.5). Dermatolojik tutulumu olan COVID-19 hastalarında eşlik eden semptomların başında koku kaybı (n= 47, %72.3) ve tat kaybı (n= 43, %66.2) olup, akciğer tutulum oranı %96.9 olarak bulundu. İlk COVID-19 semptomu ile dermatolojik tutulum başlangıcı arasındaki ortalama süre 3.3 ± 1.2; lezyonların gerileme süresi ortalama 3.2 ± 1.8 gündü.*

Sonuç: *Muhtemelen artmış inflamasyon ve sitokin fırtınasına bağlı olarak tat kaybı, koku kaybı ve pulmoner tutulum özellikle makülopapüler döküntü ve HZ'li hastalarda sık görülen bulgulardı. Özellikle makülopapüler döküntü ve HZ ile başvuran hastalarda tat kaybı ve koku kaybının değerlendirilmesi, COVID-19 vakalarının erken tanınmasına yardımcı olabilir. Ayrıca bu birlikteliğe sahip kişilerde akciğer tutulumunun ve hastalık şiddetinin daha yüksek olacağı öngörülmeli ve erken dönemde gerekli önlemler alınmalıdır.*

Anahtar Kelimeler: *COVID-19; Herpes zoster; Makülopapüler döküntü; Tat kaybı; Koku kaybı*

INTRODUCTION

The coronavirus disease-2019 (COVID-19) has rapidly spread worldwide since December 2019. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the causative agent of COVID-19, enters the host cell via binding to angiotensin-converting enzyme 2 (ACE2) receptors using its spike (S) proteins. Although it is primarily a respiratory tract infection, it may affect multiple organ systems harboring ACE2 receptors, including the skin[1].

Cutaneous manifestations associated with COVID-19 are increasingly reported, with their incidence and pathophysiological mechanisms still to be clarified. In light of the case reports and studies, dermatological involvements in COVID-19 were classified into five main categories: maculopapular, urticarial, vesicular, chilblain-like, and livedo/necrosis. In addition, reactive dermatological involvements such as erythema multiforme, a multisystem inflammatory syndrome in children (MIS-C), and multisystem inflammatory syndrome in adults (MIS-A) have been reported[2,3].

The objective of this study was to assess demographic and clinical characteristics, laboratory findings, and treatment methods in COVID-19 patients with dermatological involvement.

MATERIALS and METHODS

This study is a retrospective cross-sectional study evaluating 65 patients with dermatological involvement due to COVID-19 in a tertiary healthcare facility between August 2020 and August 2021. The study excluded patients who tested negative for SARS-CoV-2 through polymerase chain reaction (PCR) testing, those who developed dermatological involvement more than one month after the diagnosis of COVID-19, and individuals younger than 18 years of age.

Age, gender, comorbidities, and smoking status were recorded using the patients' information in the hospital registry system. Additionally, the study recorded the accompanying symptoms experienced

by the patients during the course of COVID-19, the presence and extent of pulmonary involvement observed in computed tomography (CT) scans, and any abnormal laboratory findings.

In addition, the type of dermatological involvement, the onset of dermatological involvement following the first COVID-19 symptom, the duration of the rash, and treatments for dermatological involvement were recorded.

Hemoglobin levels, leukocyte, and platelet counts, as well as leukocyte differentiation, were measured using the photometric method, impedance method, and light scattering technique on the Mindray BC 6800 automatic complete blood count analyzer (Mindray Bio-Medical Electronics, Shenzhen, China). Prothrombin time (PT), fibrinogen, and D-dimer levels were measured using the ACL TOP 500 coagulation autoanalyzer (Instrumentation Laboratory, Bedford, MA) to evaluate the coagulation and fibrinolysis cascades. Erythrocyte sedimentation rate (ESR) was measured with the Vision C ESR analyzer (YHLO Biotech, Shenzhen, China) using the modified Westergren method. Serum procalcitonin and ferritin levels as inflammation-related parameters were measured using the electrochemiluminescent immunoassay method on a Cobas e601 immunology analyzer (Roche Diagnostics, Mannheim, Germany). C-reactive protein (CRP) was quantified on IMMAGE 800 nephelometer (Beckman Coulter, Miami, FL). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), creatinine (Cr), uric acid, albumin, magnesium (Mg), and calcium (Ca) were measured by using colorimetric methods on Cobas c702 autoanalyzer (Roche Diagnostics, Mannheim, Germany).

This study was conducted with the approval of Çanakkale Onsekiz Mart University, Faculty of Medicine Clinical Research Ethics Committee (Approval no: 2022/14-11, Date: 16.11.2022).

RESULTS

Sixty-five patients with dermatological involvement due to COVID-19 were included in the study. The female-to-male ratio was 0.4:1. The mean age of the patients was 58.3 ± 17.6 years. The medical history, demographic and clinical characteristics of patients are in Table 1.

The most common dermatological involvement was maculopapular rash (n= 49, 75.4%). The maculopapular rash was followed by urticaria (n= 9, 13.8%), herpes zoster (HZ) (n= 6, 9.2%), and pernio (n= 1, 1.5%), respectively. Reactive dermatological involvement was not observed in any of the patients. In all patients, dermatological involvement started following at least one COVID-19 symptom. The mean duration between the onset of initial COVID-19 symptoms and the appearance of dermatological involvement was 3.3 ± 1.3 days.

Clinical patterns of skin manifestations during COVID-19 infection in the patients:

-Maculopapular rash: Maculopapular exanthemas mainly involve the trunk and extremities. Some patients are reported mild pruritus. Eleven patients received oral antihistamine therapy, while four were managed with short-term systemic corticosteroids. Maculopapular rash completely resolved within a mean duration of 2.7 ± 0.6 days.

-Urticaria: All urticarial lesions were located on the trunk and extremities. All patients received second-generation antihistamines (sg-AH). Since the lesions were generalized in two patients, short-term systemic corticosteroids were added to the treatment. Urticarial lesions completely resolved within a mean duration of 2.8 ± 0.4 days.

-Herpes zoster: HS lesions were on the face (including HZ ophthalmicus), on the hips/buttocks or inguinal region in one patient, and in the truncal area in four other patients. Bilateral involvement was present in one patient with a truncal lesion and was unilateral in all other patients. All patients received standard-dose systemic valacyclovir therapy. Vesicular lesions completely resolved within a mean duration of 8.3 ± 1.6 days.

-Pernio (Chilblain): An 80-year-old patient presented with pernio-like lesions in the acral region. The lesions spontaneously resolved in approximately four days without requiring any treatment.

Table 1. Demographic characteristics and clinical findings of COVID-19 patients with dermatological involvement

	MPR n= 49 (75.4%)	Urticaria n= 9 (13.8%)	HZ n= 6 (9.2%)	Pernio n= 1 (1.5%)	Total n= 65 (100%)
Gender, n (%)					
Female	14 (28.6)	3	3 (50)	0	20 (30.8)
Age (year), mean ± SD	59.1 ± 17.8	45.7 ± 13.9	63.8 ± 13.1	80	58.3 ± 17.6
Smoking, n (%)	3 (6.1)	0	1 (16.7)	0	4 (6.2)
Comorbidity, n (%)					
Hypertension	3 (6.1)	0	0	0	3 (4.6)
Diabetes mellitus	3 (6.1)	0	0	0	3 (4.6)
Fever, n (%)	13 (26.5)	3 (33.3)	6 (100)	1 (100)	23 (35.4)
Myalgia, n (%)	13 (26.5)	4 (44.4)	3 (50)	0	20 (30.8)
Dyspnea, n (%)	15 (30.6)	2 (22.2)	0	1 (100)	18 (27.7)
Sore throat n (%)	9 (18.4)	3 (23.1)	1 (16.7)	0	13 (20)
Rhinorrhea and/or nasal congestion, n (%)	9 (18.4)	1 (11.1)	5 (83.3)	0	15 (23.1)
Diarrhea, n (%)	6 (12.2)	0	2 (33.3)	0	8 (12.3)
Nausea/vomiting, n (%)	5 (10.2)	1 (11.1)	0	0	6 (9.2)
Anosmia, n (%)	37 (75.5)	3 (33.3)	6 (100)	1 (100)	47 (72.3)
Ageusia, n (%)	36 (73.5)	2 (22.2)	5 (83.3)	0	43 (66.2)
Pulmonary involvement on CT, n (%)	47 (95.9)	9 (100)	6 (100)	1 (100)	63 (96.9)
≥50%	5 (10.6)	1 (11.1)	0	1 (100)	7 (11.1)
<50%	42 (89.4)	8 (88.9)	6 (100)	0	56 (88.9)
Time to DI onset (day), mean ± SD	3.3 ± 1.2	2.6 ± 0.7	4.7 ± 2.0	3	3.3 ± 1.3
Time to DI resolution (day), mean ± SD	2.7 ± 0.6	2.8 ± 0.4	8.3 ± 1.6	4	3.2 ± 1.8

MPE: Maculopapular rash, HZ: Herpes zoster, SD: Standard deviation, CT: Computed tomography, DI: Dermatological involvement.

The most prominent laboratory abnormalities detected in patients were elevations in the median range of eosinophil count (0.96 10x3/µL), CRP (2.6 mg/L), and ferritin (266.0 mL/ng). The laboratory findings are summarized in Table 2.

DISCUSSION

Maculopapular rash may present during viral infections. It is one of the most frequently documented dermatological manifestations of COVID-19. The pathogenesis of the maculopapular rash observed during COVID-19 is attributed to two main factors: the presence of ACE2 receptors on keratinocytes, which facilitate the entry of SARS-CoV-2, and the activation of T lymphocytes triggering a severe immune response and cytokine storm[4,5].

Contrary to initial expectations, ACE2 receptors are primarily found in a limited percentage (~1-2%) of lung cells with low pulmonary expression. However, it is believed that the release of IFN during hyperinflammation and cytokine storm can upregulate the expression of ACE2 receptors in the lungs. This increase in ACE2 receptor availability is associated with pulmonary involvement and the development of acute respiratory distress syndrome (ARDS) observed during the second and third phases of COVID-19, respectively[6-8]. In our study, we observed an increased rate of pulmonary involvement (95.9%) in patients with maculopapular rash, which is likely attributed to the heightened immune response mentioned earlier.

Table 2. Laboratory findings of COVID-19 patients with dermatological involvement

	MPR	Urticaria	HZ	Pernio	Total
CBC parameters					
WBC (4.5-11 10^3/μL) median (range)	8.10 (3.10-17.50)	4.77 (3.88-23.10)	6.50 (6.30-9.10)	7.19	7.3 (3.1-23.1)
LYM (1.5-4 10^3/μL) mean ± SD	1.43 ± 0.69	1.47 ± 0.74	1.17 ± 0.58	1.53	1.41 ± 0.68
PLT (150-400 10^3/μL) mean ± SD	234.4 ± 64.4	265.9 ± 90.4	258.8±60.0	134.0	239.5 ± 68.9
MON (0.2-0.95 10^3/μL) median (range)	1.20 (0.23-11.20)	0.52 (0.30-0.74)	1.30 (0.80-1.88)	0.99	1.10 (0.23-11.20)
EO (0.02-0.5 10^3/μL) median (range)	1.02 (0.25-2.10)	0.66 (0-1.03)	0.39 (0.23-0.87)	0.66	0.96 (0-2.10)
BASO (0-0.15 10^3/μL) median (range)	0.26 (0-0.90)	0 (0-0)	0.10 (0.10-0.14)	0.12	0.20 (0-0.90)
HGB (11.7-15.5 g/dL) mean ± SD	13.7 ± 1.9	13.3 ± 1.0	14.7 ± 1.9	12.9	13.3 ± 1.0
Inflammation parameters					
ESR (0-20 mm/hr), median (range)	30.0 (11.0-99.0)	25.0 (19.0-101.0)	33.5 (12.0-64.0)	24.0	27.0 (11.0-101.0)
CRP (0-0.5 mg/L), median (range)	2.4 (0.4-29.8)	3.4 (0.4-24.2)	3.0 (0.2-11.0)	12.9	2.6 (0.2-29.8)
Procalcitonin (0-0.5 ng/mL) median (range)	0.7 (0.1-40.0)	0.5 (0.1-1.3)	14.3 (13.8-14.9)	0.3	0.7 (0.1-40.0)
Ferritin (13-150 mL/ng), median (range)	401.0 (82.0-980.0)	102.0 (78.0-595.0)	200.0 (102.0.0-298.0)	633.0	266.0 (78.0-980.0)
Coagulation parameters					
PT (0.8-1.2 s), mean ± SD	0.91 ± 0.36	1.02 ± 0.32	0.53 ± 0.29	0.05	0.90 ± 0.37
Fibrinogen (200-400 mg/L), mean ± SD	460.1 ± 191.9	392.0 ± 139.9	349.8 ± 71.0	455.0	440.4 ± 178.4
D-dimer (0-500 μg/L), median (range)	227.0 (28.0-2066)	412.0 (286.0-1221)	257.0 (145.0-570.0)	440.0	276.0 (28.0-2066)
Other biochemical parameters					
ALT (5-33 U/L), median (range)	22.0 (5.4-123.2)	25.4 (15.3-75.9)	14.9 (10.0-25.5)	31.9	22.5 (5.4-123.2)
AST (5-32 U/L), median (range)	26.5 (10.2-216.9	27.8 (14.1-66.0)	20.2 (11.1-63.0)	27.8	26.1 (10.2-216.9)
GGT (5-36 U/L), median (range)	28.0 (7.0-147.0)	27.0 (19.0-75.0)	13.0 (10.0-52.0)	21.0	27.0 (7.0-147.0)
LDH (135-225 U/L), median (range)	193.0 (76.0-980.0)	170.7 (111.5-796.0)	94.2 (77.7-185.6)	79.0	170.7 (76.0-980.0)
ALP (40-129 U/L), median (range)	69.3 (29.0-200.0)	47.0 (29.0-241.0)	92.7 (75.0-114.0)	77.0	69.8 (29.0-241.0)
Cr (0.7-1.2 mg/dL), median (range)	0.60 (0.10-1.78)	0.30 (0.20-0.99)	0.38 (0.12-0.63)	0.29	0.48 (0.10-1.78)
Albumin (3.5-5.5 g/dL), mean ± SD	3.65 ± 0.50	3.70 ± 0.42	3.72 ± 0.25	2.48	3.64 ± 0.49
Ca (8.8-10.2mg/dL), mean ± SD	8.76 ± 0.56	8.72 ± 0.53	8.93 ± 0.53	8.86	8.77 ± 0.54
Mg (1.6-2.4mg/dL), mean ± SD	1.98 ± 0.54	1.98 ± 0.11	2.07 ± 0.21	1.99	1.99 ± 0.46
Vit D (20-150 ng/mL), median (range)	33.0 (13.0-81.0)	35 (19.0-63.0)	34.0 (22.0-76.0)	76.0	33.5 (13.0-81.0)

Reference values and units for laboratory parameters are provided in brackets. MPR: Maculopapular rash, SD: Standard deviation, CBC: Complete blood count, WBC: White blood cells, LYM: Lymphocyte, PLT: Platelet, MON: Monocyte, EO: Eosinophil, BASO: Basophil, HGB: Hemoglobin, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, PT: Prothrombin time, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase, LDH: Lactate dehydrogenase, ALP: Alkaline phosphatase, Cr: Creatinine, Mg: Magnesium, Ca: Calcium, Vit: Vitamin, HZ: Herpes zoster.

Anosmia and ageusia were the leading symptoms in our COVID-19 patients presenting with maculopapular rash. In a study evaluating 500 COVID-19 patients, the rates of anosmia and ageusia were reported as 44% and 43%, respectively[9]. These rates were nearly two times higher in our series [anosmia (75.5%) and ageusia (73.5%)]. Anosmia and ageusia associated with COVID-19 have a pathogenesis similar to maculopapular rash: Elevated levels of ACE2 receptor expression in the olfactory epithelium (OE) and buccal mucosa, especially in the tongue, and increased inflammation mediated by tumor necrosis factor-alpha (TNF-α) in these regions[10-12]. Therefore, it is not surprising that high rates of anosmia and ageusia are seen in COVID-19 patients with a maculopapular rash.

Herpes zoster occurs due to the reactivation of dormant varicella-zoster virus (VZV) infection due to advanced age, immune suppression, and psychological stress. The development of HZ after COVID-19 has been reported in many case reports. It is thought that VZV reactivation may occur due to a decrease in absolute lymphocyte count, especially CD3+ CD8+ lymphocytes, and functional impairment of CD4 + T cells during COVID-19[13-15]. In this study, 83% of the HZ patients (five out of six HZ patients) had lymphopenia. Cytokines released as a compensatory response to the low lymphocyte count can result in increased inflammation and the development of a cytokine storm[15]. As mentioned above, increased inflammatory response and cytokine storm are responsible for developing anosmia, ageusia, and pulmonary involvement in COVID-19 patients[6-8]. Similarly, all patients with HZ had pulmonary involvement, anosmia, and 83.3% had ageusia. Lymphopenia, responsible for developing HZ in COVID-19 patients, may indirectly increase the risk of pulmonary involvement, anosmia, and ageusia.

Both SARS-CoV-2 and anti-COVID-19 drugs have been identified as new triggering factors for urticaria[16]. In this study, the triggering factor for all patients was determined to be SARS-CoV-2, as none of the patients had a history of drug use prior to the development of the lesions. As in our study, urticarial lesions typically spread to the trunk or limbs and usually begin at the same time as other symptoms of COVID-19[17]. While sg-AH treatment is generally sufficient; short-term systemic corticosteroids may be required in some patients[16]. The patients in the study were controlled with sg-AH, and none needed systemic corticosteroids. None of the patients had a history of urticaria, and no patient had a repeat urticaria attack. Pernio associated with COVID-19 is a rare manifestation that occurs in elderly patients with multiple comorbidities and abnormal coagulation parameters[18]. In the current study, pernio was detected in only one patient in this study. The patient diagnosed with pernio was 80 years old, had abnormal coagulation parameters, and, had more than 50% pulmonary involvement on CT. However, contrary to the literature, the patient did not have any comorbidities.

The limited number of patients was the primary constraint of the study, while the exclusion of suspicious cases with negative PCR tests was its main strength.

CONCLUSION

In conclusion, our study revealed that COVID-19 can lead to various dermatological manifestations, which may serve as an initial indication of the disease in certain patients[18]. Notably, we observed a significant occurrence of pulmonary involvement, anosmia, and ageusia in COVID-19 patients who also presented with maculopapular rash and HZ. In this context, it is crucial to evaluate anosmia and ageusia in all patients presenting with maculopapular rash and herpes zoster. These associations strongly suggest a probable diagnosis of COVID-19, and therefore, a PCR test should be conducted. Prompt isolation of these patients is essential to minimize the risk of transmission. Furthermore, since these patients may experience a cytokine storm leading to pulmonary involvement and increased disease severity, early precautions should be implemented to manage their condition effectively.

ETHICS COMMITTEE APPROVAL

This study was approved by the Çanakkale Onsekiz Mart University Clinical Research Ethics Committee (Decision no: Decision no: 2022/14-11, Date: 16.11.2022).

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: ÖK, SA

Analysis/Interpretation: All of authors

Data Collection or Processing: All of authors

Writing: ÖK, ZK

Review and Correction: All of authors

Final Approval: All of authors

REFERENCES

1. *Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty 2020;9:45. https://doi.org/10.1186/s40249-020-00662-x*
2. *Genovese G, Moltrasio C, Berti E, Marzano AV. Skin manifestations associated with COVID-19: Current knowledge and future perspectives. Dermatology 2021;237:1-12. https://doi.org/10.1159/000512932*
3. *Drenovska K, Schmidt E, Vassileva S. COVID-19 pandemic and the skin. Int J Dermatol 2020;59:1312-9. https://doi.org/10.1111/ijd.15189*
4. *Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, et al. SARS-CoV-2 and viral sepsis: Observations and hypotheses. Lancet 2020;395:1517-20. https://doi.org/10.1016/S0140-6736(20)30920-X*
5. *Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. J Med Virol 2020;92:424-32. https://doi.org/10.1002/jmv.25685*
6. *Nicastri E, Petrosillo N, Ascoli Bartoli T, Lepore L, Mondi A, Palmieri F, et al. National Institute for the infectious diseases "L. Spallanzani", IRCCS. Recommendations for COVID-19 clinical management. Infect Dis Rep 2020;12:8543. https://doi.org/10.4081/idr.2020.8543*
7. *Aboudounya MM, Heads RJ. COVID-19 and Toll-Like Receptor 4 (TLR4): SARS-CoV-2 may bind and activate TLR4 to increase ACE2 expression, facilitating entry and causing hyperinflammation. Mediators Inflamm 2021;2021:8874339. https://doi.org/10.1155/2021/8874339*
8. *Ziegler CGK, Allon SJ, Nyquist SK, Mbano IM, Miao VN, Tzouanas CN, et al. SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues. Cell 2020;181:1016-35. https://doi.org/10.1016/j.cell.2020.04.035*
9. *Al-Rawi NH, Sammouda AR, AlRahin EA, Ali FAA, Arayedh GSA, Daryanavard HA, et al. Prevalence of anosmia or ageusia in patients with COVID-19 among United Arab Emirates population. Int Dent J 2022;72:249-56. https://doi.org/10.1016/j.identj.2021.05.006*
10. *Meng X, Deng Y, Dai Z, Meng Z. COVID-19 and anosmia: A review based on up-to-date knowledge. Am J Otolaryngol 2020;41:102581. https://doi.org/10.1016/j.amjoto.2020.102581*
11. *Vaira LA, Salzano G, Fois AG, Piombino P, De Riu G. Potential pathogenesis of ageusia and anosmia in COVID-19 patients. Int Forum Allergy Rhinol 2020;10:1103-4. https://doi.org/10.1002/alr.22593*
12. *Najafloo R, Majidi J, Asghari A, Aleemardani M, Kamrava SK, Simorgh S, et al. Mechanism of anosmia caused by symptoms of COVID-19 and emerging treatments. ACS Chem Neurosci 2021;12:3795-805. https://doi.org/10.1021/acschemneuro.1c00477*
13. *Algaadi SA. Herpes zoster and COVID-19 infection: A coincidence or a causal relationship? Infection 2022;50:289-93. https://doi.org/10.1007/s15010-021-01714-6*
14. *Saati A, Al-Husayni F, Malibari AA, Bogari AA, Alharbi M. Herpes zoster co-infection in an immunocompetent patient with COVID-19. Cureus 2020;12:e8998. https://doi.org/10.7759/cureus.8998*
15. *Fathi N, Rezaei N. Lymphopenia in COVID-19: Therapeutic opportunities. Cell Biol Int 2020;44:1792-7. https://doi.org/10.1002/cbin.11403*
16. *Martora F, Villani A, Fabbrocini G, Battista T. COVID-19 and cutaneous manifestations: A review of the published literature (published online ahead of print, 2022 Nov 7). J Cosmet Dermatol 2023;22:4-10. https://doi.org/10.1111/jocd.15477*
17. *Galvan-Casas C, Catala A, Carretero G, Rodriguez-Jimenez P. Classification of the cutaneous manifestations of COVID-19: A rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol 2020;183:71-7. https://doi.org/10.1111/bjd.19163*
18. *Seque CA, Enokihara MMSES, Porro AM, Tomimori J. Skin manifestations associated with COVID-19. An Bras Dermatol 2022;97:75-88. https://doi.org/10.1016/j.abd.2021.08.002*

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