



Research Article

Mucocutaneous Manifestations of COVID-19 among Iraqi Patients in Al Diwaniyah Province, Iraq: Case Series Study

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A B S T R A C T

Background: The relatively wide distribution of ACE2 receptors all over body tissues suggests the possibility of clinical manifestations other than that of the respiratory tract. The usual incubation period is about 14 days which is often followed by the usual respiratory symptoms and constitutional signs. Globally, additional novel manifestations, including dermatological ones have been reported.

Aim: To characterise the skin manifestations in patients with COVID-19 in Al Diwaniyah Province, mid-Euphrates region of Iraq.

Method: The present case series study included 54 patients with COVID-19 and a variety of skin manifestations. Those patients visited the dermatology unit at Al Diwaniyah teaching hospital, Al Diwaniyah province, Iraq during the period of the study. The study started in July 2020 and ended in June 2021.

Results: The most common features were those of morbilliform eruptions accounting for 18.5% of cases followed by urticarial lesions accounting for 13.0% of cases for followed by ecchymotic pruritic lesion (11.1%). Other features such as oral ulceration and vesicular lesions were also seen in 9.3% of cases. All the body was involved in 29.6% followed by tongue and lip involvement. Morbilliform eruption was the most common diagnosis followed by acute urticaria, herpes simplex, leukocytoclastic vasculitis and then by a variety of other skin manifestations.

Conclusion: Skin manifestations in association with COVID-19 were highly variable with onset and duration which could be due to infection, drug reaction or immune mechanisms.

Keywords: Skin Lesion, COVID-19, Morbilliform Eruption, Urticarial Lesion

Introduction

In December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in China, Wuhan

city and from there it has rapidly spread around the globe.^{1,2} The virus is well known to be associated with respiratory manifestations.^{3,4} The disease was considered a pandemic

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in March 2020 by the World Health Organization (WHO) because of its high infectivity rate and relatively high mortality among immune-compromised individuals and elderly population.^{5,6} By August 2020, more than 20 million patients with SARS-CoV-2 infection were registered and more than 750,000 patients have died because of its related complications in more than 200 countries and regions all over the world.⁷

The virus is a single-stranded RNA, positive sense, enveloped novel virus belonging to the genus Betacoronavirus.⁸ In humans, the receptor that mediates cellular entry of the virus is the angiotensin-converting enzyme (ACE2).^{9,10} The virus is known to attack the respiratory tract via this receptor; however, this receptor has been also identified in other tissues of the body such as the gastrointestinal tract and the skin.¹¹ Highest expression of ACE2 has been linked to thyroid, heart, testis, small intestine, and adipose tissue and low expression of the receptor has been linked to brain, bone marrow, blood, spleen and muscle tissues.¹¹ On the other hand, medium receptor expression has been linked to the adrenal gland, liver, colon, lung and urinary bladder.¹¹ Expression of ACE2 receptors by skin tissue and the possibility of being a target for SARS-CoV-2 infection have been studied by Xue X et al.¹² The expression of these receptors in keratinocytes was the highest followed by other skin cellular components such as melanocytes, fibroblasts and sweat gland cells.¹² The relatively wide distribution of ACE2 receptors all over body tissues suggests the possibility of clinical manifestations other than that of the respiratory tract because of the involvement of dermatological tissues.⁷ Because of its spread by respiratory droplets, SARS-CoV-2 has a relatively high infectious rate. The usual incubation period is about 14 days which is often followed by the usual respiratory symptoms and constitutional signs.⁷ Globally, additional novel manifestations, including dermatological ones have been reported.¹³ Initial reports have identified 0.2% of patients to have skin manifestations.¹⁴ However, later reports have identified higher rates of skin manifestations reaching figures such as 20.4%.¹³ Later reports highlight the documentation of skin manifestations in relation to COVID-19 in all age groups including paediatric age groups with various prevalence rates.⁷ The diagnosis and treatment of these skin manifestations may aid in improving the quality of life as well as the prognosis of the disease.

There is little published data from Iraq dealing with skin manifestations of COVID-19 in patients and this was the primary justification of planning and conduction of the current study aiming at characterisation of skin manifestation in association with COVID-19 in Al Diwaniyah Province, mid-Euphrates region of Iraq.

Materials and Method

The present case series study included 54 patients with

COVID-19 and a variety of skin manifestations. The patients who visited the dermatology unit at Al Diwaniyah teaching hospital, Al Diwaniyah province, Iraq during the period of the study were included. The study started in July 2020 and ended in June 2021. A questionnaire form was prepared and included information about age, gender, severity and duration of COVID-19, duration of disease, duration of skin manifestations, character of lesion, site of lesion, diagnosis and treatment.

The main inclusion criteria included patients with COVID-19 diagnosed by pcr and ct scan, aged 16 years or old .

The main exclusion criteria included patients with history of current infectious dermatological diseases, patients with history of taking drugs induced skin rash for 2 weeks before infection with COVID-19.

The study was approved by the ethics committee of the College of Medicine, University of Al-Qadisiyah, and verbal consent was obtained from all participants.

The statistical analysis was done with the aid of Statistical Package for Social Sciences (SPSS) version 16 (IBM, Chicago, USA) and Microsoft Office Excel 2007. Quantitative data were expressed as range, standard deviation and mean; while, qualitative data were expressed as percentage and number. Independent samples t-test was used to evaluate the difference in mean of quantitative variables between different patient's groups; where chi-square test was used to compare variation in proportions of qualitative variables between patient's groups. The cutoff value labelling significance was chosen at $p \leq 0.05$ and the cutoff level labelling high significance was chosen at $p \leq 0.01$.

Results

The current study included 54 patients with COVID-19 and skin manifestations. The demographic characteristics of those patients are shown in Table 1. The mean age of all patients was 43.92 ± 17.33 years with a range of 16 to 93 years and there was no significant difference in mean age between male and female patients ($p = 0.587$). The mean duration of disease was 13.35 ± 7.76 days and it ranged from 3 to 30 days and there was no significant difference in the mean duration of disease between male and female patients ($p = 0.202$). The frequency distribution of patients according to the severity of disease is also shown in Table 1.

The frequency distribution of enrolled COVID-19 patients according to features of skin lesions is shown in Table 2. The most common features were those of morbilliform eruptions accounting for 18.5% of cases followed by urticarial lesions accounting for 13.0% of cases and then ecchymotic pruritic lesion (11.1%). Other features such as oral ulceration and vesicular lesions were also seen in 9.3% of cases. In addition, a variety of dermatological manifestations were also reported in various proportions as shown in Table 2.

Table 1. Demographic Characteristics of Patients with COVID-19 enrolled in the Current Study

Characteristic	Total (n = 54)	Male (n = 30)	Female (n = 24)	p
Age				
Mean ± SD	43.92 ± 17.33	42.76 ± 18.39	45.45 ± 16.13	0.587 I
Range	16-93	16-93	16-70	NS
Duration				
Mean ± SD	13.35 ± 7.76	12.14 ± 7.32	14.95 ± 8.20	0.202 I
Range	3-30	3-30	5-30	NS
Severity				
Mild, n (%)	21 (38.9)	11 (36.7)	10 (41.7)	-
Moderate, n (%)	22 (40.7)	11 (36.7)	11 (45.8)	
Severe, n (%)	7 (13.0)	4 (13.3)	3 (12.5)	
Critical, n (%)	4 (7.4)	4 (13.3)	0 (0.0)	

n: number of cases; SD: standard deviation; I: independent sample t-test; NS: not significant at $p > 0.05$.

Table 2. Frequency Distribution of enrolled COVID-19 Patients according to Features of Skin Lesions

Features	Number of Cases	Percentage
Morbilliform eruption	10	18.5
Urticarial lesion	7	13.0
Echymotic pruritic lesion	6	11.1
Oral ulceration	5	9.3
Vesicular lesion	5	9.3
Acne form (folliculitis)	4	7.4
Annular erythematous lesion	3	5.6
Erythema multiforme	3	5.6
Multiple erythematous papules	3	5.6
Acral erythema	1	1.9
Erosive empiginized lesions	1	1.9
Erythematous ulceration	1	1.9
Monpmorphic pustule	1	1.9
Multiple round pale plaques with fine scales	1	1.9
Purpuric lesion	1	1.9
Strawberry tongue	1	1.9
Xanthomatous eruption	1	1.9

Table 4. Frequency Distribution of enrolled COVID-19 Patients according to Diagnosis of Lesions

Site	Number of Cases	Percentage
All body	16	29.6
Tongue and lip	8	14.8
Upper limb + trunk	5	9.3
Lower limb + upper limb	5	9.3
Lower limb	4	7.4
Chest	3	5.6

Lower limb + trunk	3	5.6
Trunk	3	5.6
Palm and sole	2	3.7
Toes	2	3.7
Upper limb	1	1.9
Lower upper limb + trunk	1	1.9
Neck and trunk	1	1.9

Table 3. Frequency Distribution of enrolled COVID-19 Patients according to Site of Lesions

Diagnosis	Number of Cases	Percentage
Morbilliform eruption	10	18.5
Acute urticarial	7	13.0
Herpes simplex	7	13.0
Leukocytoclastic vasculitis (LCV)	7	13.0
Folliculitis	5	9.3
Erythema multiforme	3	5.6
Erythema annulare centrifugum	3	5.6
Post covid chicken pox like lesion	3	5.6
Pityriasis rosea like lesion	2	3.7
Pseudochilblain	3	5.6
Drug eruption	1	1.9
Herpes zoster	1	1.9
Miliaria	1	1.9
Strawberry tongue	1	1.9

The frequency distribution of enrolled COVID-19 patients according to the site of lesions is shown in Table 3. All the body was involved in 29.6% followed by tongue and lip involvement. Other parts of the body such as extremities and trunk were involved in various combinations and in various proportions as shown in Table 3.

The frequency distribution of enrolled COVID-19 patients according to the diagnosis of lesions is shown in Table 4. Morbilliform eruption was the most common followed by acute urticaria, herpes simplex, leukocytoclastic vasculitis and then followed by a variety of skin manifestations as shown in Table 4.

Discussion

A global health issue is the pandemic of COVID-19 which continues to spread rapidly. The clinical manifestations in association with the disease needs further research

work in order to be well characterized despite the growing bulk of data with this regard including its dermatological manifestations.⁷ SARS-CoV-2 has been associated with a variety of skin lesions. In the past, a number of respiratory viruses have been associated with rare dermatological manifestations¹⁵; however, these lesions are not characteristic of Coronavirus family.¹⁶

In the current study, morbilliform lesions were seen in 18.5% of patients respectively. Among the most frequent skin manifestations seen in association with COVID-19 are maculopapular lesions and these are frequently due to drug reactions or viral infections.¹⁷ In one study, the prevalence rate was 47%.¹⁸ In the current study also, urticarial lesions were seen in 13.0% of patients. Several previous authors have reported urticarial lesions in association with COVID-19.¹⁹ Lesions affecting the toes have been seen in 2 cases in the current study. Erythematous lesions affecting the toes of patients, frequently termed as (COVID toes) have been described to affect a number of COVID-19 patients and some have linked them to an autoimmune pathogenesis.²⁰ In addition, vesicular lesions have been described in 9.3% of cases in the current study. Herpes simplex is one of the common viruses to be associated with such lesions in addition to a number of other viruses¹⁵ and these lesions are commonly associated with heat exposure, medications, contact dermatitis and autoimmune pathogenesis.⁷

In general skin manifestations in association with COVID-19 can be grouped into two major kinds: exanthems and vascular lesions.⁷ Skin manifestations and their identifications in relation to COVID-19 may help physicians in the future to diagnose and treat new cases of sCOVID-19. Exanthems appear in the form of urticarial, maculopapular and vesicular rashes and the most frequent among these by far are the maculopapular rashes. The onset and the duration of these rashes in different studies are variable. Vesicular eruptions are also of variable onset. These manifestations are often seen after the systemic manifestations but in rare cases, they may precede the systemic features.⁷

Vascular lesions in association with SARS-CoV-2 infections can be in the form of livedoid, petechiae/ purpura or chilblain lesions⁷ and these were reported in the current study. The pathogenesis of skin lesions in association

with COVID-19 can be attributed to drug reactions or overproduction of cytokines.^{21,22} Other mechanisms may involve thrombogenic vasculopathy.^{23,24}

Conclusion

Skin manifestations in association with COVID-19 are highly variable with variable onset and duration and can be due to infection, drug reaction or immune mechanisms.

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