

RESEARCH PAPER

Incidence and Characterization of Skin Lesions Among Hospitalized Patients with COVID-19 infection: An Observational Cohort Study from Iraq

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Abstract

Background and objectives: A wide arrays of skin lesions occurred in the setting of COVID-19 infection. We aimed to estimate the incidence and types of skin lesions among hospitalized patients with COVID-19 infection.

Methods: We conducted an observational cohort study on 369 hospitalized patients with COVID-19 infection at Basra Teaching Hospital for 3 months. We studied the incidence and types of skin lesions.

Results: Among 369 hospitalized patients, skin lesions were developed in (5%). Of those who developed skin lesions, 33% were asymptomatic. Skin lesions were more frequent in young females (83.3%). The most frequent type of skin lesion was maculopapular (44.3%) which occurred exclusively in the medical ward and half of them in asymptomatic patients. For pustular lesions, all were female, diabetic, in the ICU, in symptomatic patients with the highest levels of serum C-reactive proteins. Pseudo-chilblain lesions were reported only in younger female and half of patients were asymptomatic. Urticarial lesions were reported in the younger patients, two-thirds were symptomatic and in the ICU. Purpuric lesions were reported in the older patient who developed acute kidney injury. Extremities were the most common distribution of skin lesions in (38.8%). The mean latency period for development of skin lesions was (8.6 ± 9.1), the shortest for urticarial lesions and the longest for purpuric lesions.

Conclusions: Different types of skin lesions were reported in patients with COVID-19 and may be the sole manifestations of the disease.

Keywords: COVID-19, skin lesions, Pseudo-chilblain.

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Introduction

A wide range of skin lesions was reported in patients with COVID-19 infection.¹⁻³ The frequency of skin lesions was reported from 0.2-20% from different studies mainly from Europe and China.⁴⁻⁶ The association of skin lesions with the severity of the illness was unclear.⁷ Maculopapular skin lesions involving the trunk were the most common cutaneous manifestations of COVID-19 infection^{1,2,5,8,8}

Pseudo-chilblain lesions (COVID toes) was reported in the absence of cold exposure or underlying diseases associated with chilblain lesions.^{1-3,10-17} The cutaneous manifestations may occurred before, at the time or after the onset of COVID-19 symptoms.^{5,10,11,18-20} The objective of the study was to estimate the incidence of skin lesions among hospitalized patients with COVID-19 infection, to estimate the frequency of skin lesions' types and assess the risk factors for the development of these skin lesions. The purpose of the study was to estimate the incidence of AKI in hospitalized patients with COVID-19 infection in Basrah, Iraq.

Methods

Study design, setting and participants

This was a single center observational cohort study conducted on patients with PCR confirmed COVID-19 infection who were hospitalized at Basra Teaching Hospital from March 1, 2020, to June 1, 2020. The study was approved by the Institutional Review Board of the University of Basra and Basra Health Directorate. Data were obtained from medical records of patients hospitalized at both medical ward and intensive care unit. Direct examination was performed after wearing full PPE protections and for some cases, photos were sent for characterization of the skin lesions' types. Patients with recent skin lesions were included in this study. Any preexisting skin diseases were excluded from the study. All patients with COVID-19 infection, whether symptomatic or asymptomatic, were hospitalized in the isolation wards according to the Basra Health Directorate guidelines. Asymptomatic patients were discovered by contact tracing. Patients' demographics, medical history of chronic diseases, dermatologic diseases and bed location were obtained. Skin lesions' type, distribution, symptoms, latency period and duration were documented. Type of skin lesions were characterized into: Maculopapular, petechial, pseudo-chilblain, pustular, urticarial and purpuric lesions. Distribution of skin lesions were determined according to the affected sites into: Generalized, facial, truncal, inguinal, extremities, palmar and toes. Regarding symptoms of skin lesions, they were either asymptomatic or symptomatic (itching or pain). Acute kidney injury was defined as increased in serum creatinine by 0.3 mg/dL from the baseline within 48 hours or 1.5 times increased in serum creatinine from baseline within 7 days according to KDIGO guideline by the help of nephrologist.²¹ Inflammatory markers such as

serum ferritin and C-reactive proteins were sent. Skin biopsy was not done due to COVID-19 transmission precaution.

Outcomes

The outcome of the study was to study the incidence and types of skin lesions in patients with COVID-19.

Statistics

Baseline demographics, clinical and laboratory characteristics of the overall patients and clinical characteristics of skin lesions were described using mean $\pm$ SD for continuous variables and numbers (percentages) for categorical variables. Comparative analyses between patients who developed skin lesions from those who didn't were performed using χ^2 test or Fischer's Exact test for categorical variables and independent sample t-test for continuous variables. Demographics, clinical and laboratory characteristics per types of skin lesions were analyzed using χ^2 test or Fischer's Exact test for categorical variables and one-way ANOVA for continuous variables. P values less than or equal to 0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 25.

Results

From March 1, 2020, to June 1, 2020, 372 patients were admitted to Basra Teaching Hospital with a diagnosis of COVID-19 infection that was confirmed by polymerase chain reaction. Of these, 369 patients were included in this study after exclusion of 3 patients with preexisting skin diseases. Overall, 18 of 369 patients (5%) developed skin lesion during their hospitalization (Figure-1). Five patients were in the ICU and 13 patients were in the medical ward.

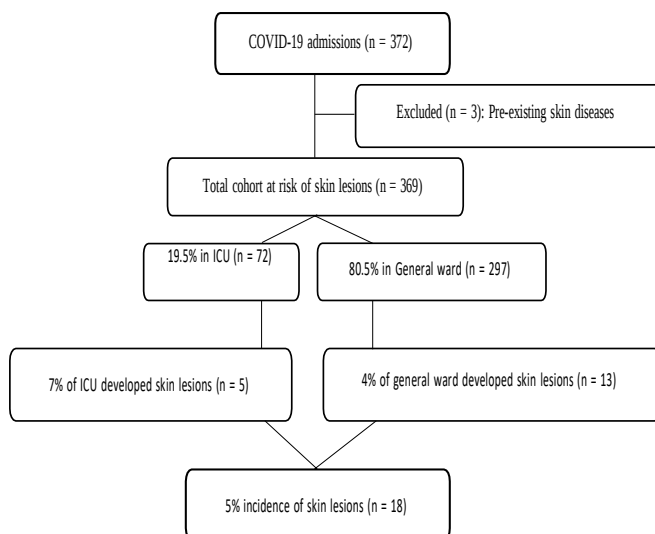


Figure 1. Flowchart illustrating the incidence of skin lesions among hospitalized patients with COVID-19 infection.

The baseline clinical characteristics of the patients were provided in Table-1. The mean age was 51 ± 14 SD, 62.1% were female, mean BMI was 28.5 ± 4.2 SD, 40.1% were hypertensive and 27.9% were diabetic, 19.5% were admitted in the ICU, 5% developed skin lesions, 17.3% developed acute kidney injury and 6.5% died. Mean serum CRP and serum ferritin were 38 ± 67 and 325 ± 490 respectively.

Table 1. Baseline demographic and clinical and laboratory characteristics.

Characteristics	Overall cohort (n = 369)
Age, years	51 ± 14
Female	229 (62.1)
Body mass index (kg/m ²)	28.5 ± 4.2
Hypertension	148 (40.1)
Diabetes	103 (27.9)
Acute kidney injury	64 (17.3)
Intensive care unit	72 (19.5)
Skin lesions	18 (4.9)
Death	24 (6.5)
Serum C-reactive protein, mg/dl	38 ± 67.6
Serum ferritin, ng/ml	325 ± 490

Values were expressed as mean $\pm$ SDs and n (%).

Table-2 showed the comparison of patients who developed skin lesions from those who didn't. The characteristics of patients who developed skin lesions were as follow: The mean age was 40 ± 19.6 SD, 83.3% were female, mean BMI was 28.7 ± 3.9 SD, 27.8% were hypertensive, 38.9% were diabetic, 27.8% were in the ICU, 5.6% developed AKI and none was died. The levels of inflammatory markers were non statistically different between the two groups: For CRP, for those with skin lesions vs no skin lesions (49 ± 72.7 vs 37 ± 67 ; $P = 0.470$) and for serum ferritin, for those with skin lesions vs no skin lesions (343.5 ± 407 vs 324 ± 494 ; $P = 0.870$).

Table 2. Baseline demographics, clinical and laboratory characteristics by skin lesion status.

Characteristics	Skin Lesions(n = 18)	No skin Lesions (351)	P value
Age, years	40 ± 19.6	51.6 ± 13.8	0.001
Female	15 (83.3)	214 (61)	0.079
Body mass index (kg/m ²)	28.7 ± 3.9	28.5 ± 4.2	0.804
Hypertension	5 (27.8)	143 (40.7)	0.331
Diabetes	7 (38.9)	96 (27.4)	0.290
Acute kidney injury	1 (5.6)	63 (18)	0.333
Intensive care unit	5 (27.8)	67 (19.1)	0.364
Death	0 (0.0)	24 (6.8)	0.619
Serum C-reactive protein, mg/dl	49 ± 72.7	37 ± 67	0.470
Serum ferritin, ng/ml	343.5 ± 407	324 ± 494	0.870

Values were expressed as mean ± SDs and n (%).

(Table-3), showed clinical characteristics of skin lesions. Thirty-three percent of patients who developed skin lesions were asymptomatic regarding COVID-19 presentations. The most common skin lesions were maculopapular in 44.3% with a mean duration was 5 ± 2.9 SD, 50% were itchy, 27.8% was painful and the most common site was the extremities in 38.8%. the mean time from symptoms in symptomatic patients to development of skin lesions was 8.6 days.

Table 3. Clinical characteristics of skin lesions.

Characteristics	Skin lesion cohort (n = 18)
Presenting symptoms	
Asymptomatic	6 (33)
Symptomatic	12 (67)
Type of skin lesions	
Maculopapular	8 (44.3)
Petechial	1 (5.6)
Pseudo-chilblain	2 (11.1)
Pustular	3 (16.7)
Urticarial	3 (16.7)
Purpuric	1 (5.6)
Latency period	8.6 ± 9.1
Distribution of skin lesions	
Generalized	2 (11.1)
Facial	2 (11.1)
Extremities	7 (38.8)
Truncal	1 (5.6)
Inguinal	3 (16.7)
Palmar	1 (5.6)
Toes	2 (11.1)
Symptoms of skin lesions	
No symptoms	4 (22.2)
Itching	9 (50)
Pain	5 (27.8)
Duration of skin lesions	5 ± 2.9

Values were expressed as mean ± SDs and n (%).

Demographics, clinical and laboratory characteristics by types of skin lesions were provided in (table-4). Pseudo-chilblain and urticarial lesions occurred in younger age group less than 30 years, all types of lesions were more frequent in female, BMI was comparable in all types of lesion, maculopapular lesions were more common in patients with hypertension and diabetes, all pustular lesions were in symptomatic patients, occurred in diabetic and in the ICU, 50% of maculopapular and pseudo-chilblain lesions occurred in asymptomatic patients, 87.5% of maculopapular lesions were itchy and 100% of pustular lesions were painful. Purpuric skin lesions showed longer duration and latency.

Table 4. Demographics, clinical and laboratory characteristics by types of skin lesions status.

Variables	Maculopapular (n = 8)	Petechial (n =1)	Pseudo-chilblain (n = 2)	Pustular (n =3)	Urticarial (n =3)	Purpuric (n = 1)	P value
Age, year	45.5 ± 19	52	25.5 ± 7.8	49.3 ± 10	16 ± 16.7	60	0.111
Female	6 (75)	1 (100)	2 (100)	3 (100)	2 (66.7)	1 (100)	0.791
Body mass index	28.4 ± 3	33	27.5 ± 2	31 ± 4.6	24 ± 5.7	33	0.239
Hypertension	3 (37.5)	0 (0)	0 (0)	1 (33.3)	0 (0)	1 (100)	0.377
Diabetes	3 (37.5)	0 (0)	0 (0)	3 (100)	0 (0)	1 (100)	0.072
Acute kidney injury	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0.003
Bed location							
Medical ward	8 (100)	1 (100)	2 (100)	0 (0)	1 (33.3)	1 (100)	0.012
Intensive care unit	0 (0)	0 (0)	0 (0)	3 (100)	2 (66.7)	0 (0)	0.012
Presentations							
Symptomatic	4 (50)	1 (100)	1 (50)	3 (100)	2 (66.7)	1 (100)	0.586
Asymptomatic	4 (50)	0 (0)	1 (50)	0 (0)	1 (33.3)	0 (0)	0.586
Skin lesions symptoms							
No symptoms	1 (12.5)	0 (0)	0 (0)	0 (0)	2 (66.7)	1 (100)	0.004
Itching	7 (87.5)	1 (100)	0 (0)	0 (0)	1 (33.3)	0 (0)	0.004
Pain	0 (0)	0 (0)	2 (100)	3 (100)	0 (0)	0 (0)	0.004
Latency, days	11 ± 9.7	6	3.5 ± 2	5 ± 1	2.3 ± 2.5	30	0.086
Duration, days	3.9 ± 1.6	4	5.5 ± 2	6.7 ± 2.9	3.7 ± 1.2	14	0.004
Serum C-reactive protein, mg/dl	16.5 ± 22	9	6 ± 4	156.7 ± 111.5	67.3 ± 76.5	60	0.057
Serum ferritin, ng/ml	136.4 ± 177	139	34 ± 33	687 ± 255.8	722 ± 713	685	0.085

Values were expressed as mean ± SDs and n (%).

Discussions

In the present study, the incidence of skin lesions was 5% among hospitalized patients with COVID-19 infection. Italian prospective study by Recalcati reported 20.4% incidence of skin lesions. The lower incidence in our study compared to Recalcati study was because in our country, the guideline of ministry of health at the time of study was to hospitalize all patients and contacts with PCR positive test to reduce the transmission of the virus so inclusion of asymptomatic patients reduces the incidence of skin lesions in our study.²² In binational, multicenter and prospective study recruited 678 patients from China and Italy; incidence of skin lesions was 7.8%. The mean age was higher than our study (55.9 vs 40 years) and less female than our study (40% vs 83%). The comparable incidence of skin lesions was due to similar denominators (the vast majority of hospitalized COVID-19 patients have mild disease in both studies).²³ In a Chinese study of 1099 patients hospitalized with COVID-19, only 0.2% developed new skin lesions. The mean age of patients were similar to our study (47 vs 40 years), less female (42 vs 83%) and the composite endpoint of the study was ICU admission, use of mechanical ventilation and mortality whereas the main aim of our study was incidence of new skin lesions.²⁴ The mean time from symptoms in symptomatic patients to development of skin lesions was 8.6 days, but 33% of patients developed skin lesions while asymptomatic. Recalcati et al. reported that 8 out of 18 developed skin lesions at time of The Medical Journal of Basrah University (2020); 38(2): 46-54 COVID-19, skin lesions, Pseudo-chilblain 10.33762/mjbu.2020.128833.1044 Page 51 COVID-19 diagnosis and 10 out of 18 after hospitalization.⁵ Manalo et al. reported 10 days from diagnosis of COVID-19 (25). Zhang et al. reported median of 19 days.²⁶ Jimenez, et al. reported latency of 10 days from symptoms and 3 days from hospitalization.²⁷ Hunt et al. reported skin lesions along with fever before diagnosis.²⁸ Mahe et al. reported skin lesions 4

days after fever.²⁹ Fernandez-Nieto et al. reported 6 days latency period from symptoms.¹⁶ Estébanez et al. reported latency of 13 days from diagnosis.³⁰ Henry et al. reported skin lesion development 2 days before respiratory symptoms.³¹ Najarian et al. reported 1 day latency period from onset of symptoms.⁸ Kolivras, et al reported 3 days latency from respiratory symptoms.³² Marzano et al. reported 3 days latency.³³ The most frequent skin lesions in the present study were maculopapular in 44.3% (8 out of 18 patients). Pseudo-chilblain skin lesions were most frequent in a study by Duong et al. (49.3%), by Fernandez-Nieto et al. (72%), by Freeman et al. (63%), by de Masson, et al. from France case series by Landa et al. with 6 patients had pseudo chilblain lesions, case series by Piccolo et al. with 63 patients had pseudo-chilblain lesions.^{10,18,34-37} The higher frequency in some of these reports may reflect media attention to pseudo chilblain lesions and the health care provider suggested this type of skin lesions even without laboratory confirmation whereas in our study, all pseudo-chilblain lesions (11.1%) were in laboratory-confirmed cases. In these studies, after restriction to laboratory-confirmed cases, the most frequent skin lesions were maculopapular which was similar to our study findings. Furthermore, Spanish case series reported half of laboratory-confirmed lesions as maculopapular, 19% pseudo-chilblain and 19% urticarial.³⁸ Pseudo-chilblain lesions developed in mild cases of COVID-19 in the aforementioned studies which was in agreement with our study where these lesions developed in mild cases and one of them was asymptomatic. Also, pseudo-chilblain lesions in our study were reported exclusively in younger than 40 years old patients and exclusively in female whereas the mean age in this study was 44.7 and 63% were female.³⁸ In our study, all pustular lesions and three-quarter of urticarial lesions were associated with severe disease in the ICU whereas in this study, 7% of pseudo-chilblain, 12% of vesicular, 16% of urticarial, 17% of

maculopapular and 41% of livedo/necrosis were reported in the ICU.³⁸ Moreover, pustular lesions were common in older age group and patients with the highest inflammatory markers (CRP). In the present study, 50% of skin lesion were itchy and 27.8% were painful. The symptoms of skin lesions according to these studies were as follows: itching in 67% and pain in 9% in a study by Galvan Casas et al., itching in 33.3% and pain in 50% in a study by Landa et al., itching in 36.3% and pain in 9% in a study by Marzano et al. itching in 27% and pain in 27% in a study by Picollo et al. and itching in 21.45 in a study by Recalcati et al.^{1,15,18-20,38} The most frequent involved site was extremities in 38.8%. In these studies, the most frequent involved sites were as follows: hands in 25% and feet in 55% in a study by Fernandez-Nieto et al., extremities in 100% in a study by Landa et al., trunk in 81.8% in a study by Marzano et al., feet in 86%, hand in 6% and both in 7% in a study by Picollo et al., trunk in a study by Recalcati and feet in 57% and hands in 28.5% in a study by Recalcati et al.^{5,15,16,18-20} No death was reported for those who developed skin lesions even in the 5 patients who were admitted on the ICU which indicate good patients' outcome in those who developed skin lesions. The Medical Journal of Basrah University (2020); 38(2): 46-54 COVID-19, skin lesions, Pseudo-chilblain 10.33762/mjbu.2020.128833.1044 Page 52 lesions whereas 3 deaths were reported in Spanish study.¹ The present study has some limitations. First, the study was performed at hospital, so we missed those who developed skin lesions in the community. Second, the pandemic is expanding, so we expect more cases if we extend the study time. Third, skin biopsy was not performed due to infection transmission precaution. In conclusion, different skin lesions were reported among patients with Covid-19 and up to 33% in asymptomatic patients. Maculopapular was the most frequent type and with pseudo chilblain, petechial and purpuric lesions were reported in mild cases while pustular and majority of urticarial lesions occurred in severe cases in the

ICU. Nevertheless, the outcome was good.

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