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Characteristics of Dermatological Manifestations in COVID-19 Patients

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Original Article

Summary

The COVID-19 pandemic outbreak is commonly presented with pulmonary manifestations. The skin lesions are recently regarded as common extra-pulmonary manifestations of the disease. This study aimed to characterize the cutaneous manifestations in COVID-19 patients and identifying the specific lesions and the underlying cause. This study was an observational cross sectional study implemented in the COVID-19 wards of Rozhawa Emergency hospital, outpatient clinics and COVID-19 wards of Rizgay Teaching hospital, outpatient clinics of Dermatology Teaching center and private clinics of Dermatology and Internal Medicine in Erbil city-Kurdistan region/Iraq through a period of six months from 1st of January to 30th of June, . on sample of 100 COVID-19 patients with skin manifestations. Results of the study showed that COVID-19 skin manifestations was mainly after the disease (54%). The common skin manifestation of COVID-19 disease was hair loss (29%), followed by; urticaria (17%), acne (10%) and skin erythema (10%). The onset of skin manifestations was related to age of patients and severity of COVID-19 disease. Types of skin manifestations were related to gender of patients, severity of COVID-19 disease and onset of skin manifestations. In conclusions: the common dermatological manifestations of COVID-19 disease were hair loss, urticaria, acne and skin erythema with predominance of late presentation. The types of skin lesions and the onset of presentation are affected by severity of COVID-19 disease.

Keywords: *COVID-19, Epidemiology, Pathogenesis, Presentations, Skin manifestations.*

1. INTRODUCTION

The coronavirus disease 19 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan city (China) at end of 2019 year leads to pandemic as declared by world health organization (WHO). The SARS-CoV-2 is RNA virus with many reported human variants (alpha, beta, gamma and delta variants) (1). The respiratory system the main target of SARS-CoV-2 and the COVID-19 disease is regarded as viral respiratory illness. Pathogenesis of COVID-19 diseases is composed of early phase (viral replication and tissue damage) and late phase (immune system trigger and cytokine storm). The virus was transmitted between humans through close contact and respiratory droplets (2). The COVID-19 disease recently is representing highly contagious public health problem with millions of deaths all over the world (3). The first reported case infected with COVID-19 in Iraq was at February 24th, 2020. At first 6 months of pandemic outbreak, low incidence rates of COVID-19 were recorded among Iraqi population due to different reasons specifically strict and national wide social distancing and closing borders (4). Nowadays, the infected Iraqi cases reached to the number of one million infected cases with COVID-19 disease and thousands of deaths (5). After recent use of COVID-19 vaccines, the global incidence and case fatality rate of COVID-19 diseases are obviously declined (6).

The COVID-19 disease in some cases is asymptomatic and in symptomatic cases, main symptoms are fever, cough and generalized fatigue , however, other symptoms like tiredness, nasal discharge, productive cough, haemoptysis, sore throat, vomiting, diarrhea and shortness of breath are also reported. Generally these symptoms appeared after about 5 days of incubation period (7-10). Disease duration is ranged between 6-41 days and median duration of 14 days depending on age of patients and their immunity status. These manifestations might be complicated by respiratory pneumonia, acute respiratory distress syndrome, acute renal disease, cardiac diseases and lastly death in severe form of disease. In addition to clinical presentation, the common diagnostic tool for COVID-19 disease is real-time quantitative polymerase chain reaction (rt-PCR), followed by x-ray, computerized tomography (CT) scan and other laboratory tests. The severity of COVID-19 diseases is classified into mild, moderate, severe and critical in regard to clinical features, CT scan findings, oxygen saturation, laboratory findings and organ failure (2,8,11-14).

Nowadays, the dermatological lesions are reported as potential clinical features of COVID-

19 disease. Common cutaneous lesions of COVID-19 disease are hair loss, maculopapular rash, vesicular changes, urticaria, livedo reticularis and chilblain lesions. The incidence rate of skin manifestations is ranging between 0.2% to 20.4% (15-19).

The skin involvement in COVID-19 disease is related to lesions of skin caused by the virus or related to aggravation of previous skin disease, or related to COVID-19 treatment in addition to skin diseases due to personal protective equipments especially among health care workers. These skin lesions are affecting all the body surfaces with more prevalent lesions in the trunk. Dermatological lesions accompanying COVID-19 disease might present earlier in course of COVID-19 disease before the classical symptoms and signs, or during the course of the disease or after the disease. This earlier presentation of skin manifestations is indicator for theory that they could be presenting feature of COVID-19 disease. These earlier skin features could be useful in recognizing COVID-19 disease carriers and helping in affecting the transmission cycle of the viral disease. The relationship between cutaneous features of COVID-19 disease and its severity is till now under research (20-23).

The diagnosis of COVID-19 disease skin manifestations is depending mainly on history and examination of skin of the body at specific sites like hands, abdomen, face, nails and mucosa for any lesion in addition to use of dermoscopy with high caution . Previous skin diseases might increase the risk and severity of COVID-19 disease (24,25).

Till now, no guidelines were established for treatment of skin lesions related to COVID-19 disease. Most of these lesions resolved spontaneously. The first step in treating these skin lesions is by reducing the effects on immunity like interleukin-17 inhibitors in addition to other options of lowering dose of traditional immunosuppressants. However, the corticosteroids treatment was not advised to be lowered or stopped (21, 26).

High incidence of COVID-19 disease in Kurdistan region associated with high morbidity and mortality rates (27) with scarcity of literatures discussing the dermatological manifestations of this disease urged us to conduct this study that aimed to characterize the cutaneous manifestations in COVID-19 patients and identifying the specific lesions and the underlying cause.

2. PATIENTS and METHODS

The present study was an observational cross sectional study implemented in the COVID-19 wards of Rozhawa Emergency hospital, outpatient clinics and COVID-19 wards of Rizgay Teaching hospital, outpatient clinics of Dermatology Teaching center and private clinics of Dermatology and Internal Medicine in Erbil city-Kurdistan region/Iraq through the period of six months from 1st of January to 30th of June, .. The studied population was all COVID-19 patients with dermatological manifestations attended to outpatient clinic. Inclusion criteria were COVID-19 patients from all age groups regardless of gender with obvious dermatological manifestations. Exclusion criteria were patients with previous dermatological diseases. The severe COVID-19 cases with skin manifestations were admitted to COVID-19 wards of the hospitals. The study ethics were implemented in regard to Helsinki Declaration by documented agreement of patients, approved by ethical committee in Kurdistan Board for Medical Specialties and management of COVID-19 patients with dermatological manifestations accordingly. A sample of one hundred COVID- 19 patients with skin manifestations was enrolled in present study. The selected patients included COVID-19 patients admitted to COVID-19 hospitals and those patients who were not admitted to hospitals and only represented to Dermatology center.

Information of patients was collected directly by researchers or from their records through a prepared questionnaire designed by the researchers according to previous literatures 21-24. Each selected patient was subjected to full history and examination by researchers including hair and nail examination. The questionnaire included demographic characteristics of COVID-19 patients skin manifestations (age, gender and severity of COVID-19 disease), treatment characteristics of COVID-19 patients skin manifestations (treated or not and type of treatment), Skin manifestations of COVID-19 patients (onset of presentation and types of skin manifestations). The patients enrolled in the study were previously tested positive by COVID-19-Reverse transcription polymerase chain reaction (RT-PCR) test or serology test. The confirmation of COVID-19 diagnosis was done according to the local guidelines implemented by Kurdistan Ministry of Health. Each patient included in this study was examined by the researchers after taking full history and dermatological disorders were diagnosed by Specialist in Dermatology according to history, clinical examination and dermoscopy. The COVID-19 severity was categorized by the researchers according to World

Health Organization (WHO) classification into mild (having symptoms and signs of COVID-19 disease like fever, sore throat, etc, without dyspnea and abnormal chest imaging), moderate (shortness of breath, abnormal chest imaging and SpO2 of ≥90%), severe (SpO2 of <90%, increased respiratory rate and signs of severe respiratory distress) and critical (acute respiratory distress syndrome, septic shock and sepsis) 28. In current study no cases were detected with critical severity. The patients' data were entered and interpreted statistically by SPSS program-26. Suitable statistical tests were implemented accordingly and p value of ≤0.05 considered significant

3. RESULTS

This study included one hundred COVID-19 patients with skin manifestations presented with mean age of (34.6 years) and range of 18-90 years; 37.5% of patients were in age group <30 years, 18.1% of them were in age group 1-77 years, 12% of them were in age group of less than 20 years, 17% of them were in age group 20-29 years, 35% of them were in age group 30-39 years, 21% of them were in age group 40-49 years and 15% of them were in age group of 50 years and more. Female COVID-19 patients with skin manifestations were more than males with female to male ratio of 1.5:1. Covid-19 severity of studied patients was classified into mild (67%), moderate (20%) and severe (13%). (Table 1). The treatment of COVID-19 patients with skin manifestations was received by 97% of them, while 3% of them did not receive treatment. The antibiotics were administered for 71% of COVID-19 patients with skin manifestations and dexamethasone for 20% of them. (Table 2).

The presentations of COVID-19 skin manifestations were initial (8%), during disease (38%) and after the disease (54%). The common skin manifestation of COVID-19 disease was hair loss (29%), followed by; urticaria (17%), acne (10%), skin erythema (10%), vasculitis (5%), Herpes zoster-like (5%), Pityriasis Rosea-like (4%), Maculopapular rash (4%), lichen planus (3%), etc. (Table 3).

There was a significant association between increased age of COVID-19 patients and skin manifestations during COVID-19 disease (p=0.009). No significant differences were observed between COVID-19 patients with different age groups regarding types of skin manifestations (p=0.09). (Table 4 and Figure 1).

No significant differences were observed between COVID-19 patients with different gender

groups regarding skin manifestations presentations (p=0.6). There was a significant association between female COVID-19 patients and hair loss, while male COVID-19 patients were significantly associated with Pityriasis Rosea-like skin lesions (p=0.001). (Table 5).

There was a significant association between severe COVID-19 disease and skin manifestations during COVID-19 disease (p=0.005). A significant association was observed between vasculitis and severe COVID-19 disease, while hair loss was significantly related to mild COVID-19 disease (p=0.001). (Table 6).

There was a highly significant association between initial presentation of skin disease and urticaria, while the vasuclitis was significantly related to during presentation and hair loss was significantly related to after presentation (p<0.001). (Table 7)

Table 1. General characteristics of COVID-19 patients with skin manifestations.

Variable		**No.**	**%**
Age (year)	<20	12	12.0
	20-29	17	17.0
	30-39	35	35.0
	40-49	21	21.0
	≥50	15	15.0
	Mean (SD)	34.6 (15.1)	-
Gender	Male	39	39.0
	Female	61	61.0
Severity of COVID-19 disease	Mild	67	67.0
	Moderate	20	20.0
	Severe	13	13.0
Total		**100**	**100.0**

Table 2. Treatment characteristics of COVID-19 patients with skin manifestations.

Variable		**No.**	**%**
Treatment	Yes	97	97.0
	No	3	3.0
Antibiotics	Yes	71	71.0
	No	29	29.0
Dexamethasone	Yes	20	20.0
	No	80	80.0
Total		**100**	**100.0**

Table 3. Skin manifestations of COVID-19 patients.

Variable	No.	%
Onset of skin manifestations		
Initial presentation	8	8.0
During	38	38.0
After	54	54.0
Type of skin manifestations		
Hair loss	29	29.0
Urticaria	17	17.0
Acne	10	10.0
Skin erythema	10	10.0
Vasculitis	5	5.0
Herpes zoster-like	5	5.0
Pityriasis Rosea-like	4	4.0
Maculopapular rash	4	4.0
Levodoreticularis	3	3.0
Lichen planus	3	3.0
Vascular eruption	2	2.0
Eczema	1	1.0
Purpuric rash	1	1.0
Seborrhic dermatitis	1	1.0
Chilplain	1	1.0
Drug eruption	1	1.0
Chicken pox-like	1	1.0
Others	2	2.0
Total	**100**	**100.0**

Table 4. Distribution of COVID-19 onset and types skin manifestations according to age of patients

Variable	Age groups				
	<20 y	**20-29 y**	**30-39 y**	**40-49 y**	**≥50 y**
Onset of skin manifestations*					
Initial	1 (8.3)	0	1 (2.9)	5 (23.8)	1 (6.7)
During	5 (41.7)	7 (41.2)	8 (22.9)	8 (38.1)	10 (66.7)
After	6 (50.0)	10 (58.8)	26 (74.3)	8 (38.1)	4 (26.6)
Types of skin manifestations**					
Hair loss	2 (16.7)	4 (23.5)	16 (45.7)	4 (19.0)	3 (20.0)
Urticaria	3 (25.0)	3 (16.7)	5 (14.3)	4 (19.0)	2 (13.3)
Acne	0	3 (16.7)	3 (8.6)	4 (19.0)	0
Skin erythema	3 (25.0)	2 (11.8)	3 (8.6)	1 (4.8)	1 (6.7)
Vasculitis	0	0	0	2 (9.5)	3 (20.0)
Herpes zoster-like	1 (8.3)	1 (5.9)	1 (2.9)	1 (4.8)	1 (6.7)
Pityriasis Rosea-like	1 (8.3)	1 (5.9)	1 (2.9)	1 (4.8)	0
Maculopapular rash	2 (16.7)	0	1 (2.9)	0	1 (6.7)
Levodoreticularis	0	1 (5.9)	0	2 (9.5)	0
Lichen planus	0	1 (5.9)	2 (5.7)	0	0
Vascular eruption	0	0	0	0	2 (13.3)
Eczema	0	0	0	0	1 (6.7)
Purpuric rash	0	0	1 (2.9)	0	0
Seborrhic dermatitis	0	1 (5.9)	0	0	0
Chilplain	0	0	0	1 (4.8)	0
Drug eruption	0	0	0	0	1 (6.7)
Chicken pox-like	0	0	0	1 (4.8)	0
Others	0	0	2 (5.7)	0	0

Values in the table presented as No. (%)
**P. value within Onset of skin manifestations = 0.009 Significant,*
***P. value within Skin manifestation types = 0.090 not significant.*

Table 5. Distribution of COVID-19 onset and types of skin manifestations according to gender

Variable	Gender			
	Male		Female	
	No.	%	No.	%
Onset of skin manifestations*				
Initial	2	5.1	6	9.8
During	16	41.0	22	36.1
After	21	53.8	33	54.1
Types of skin manifestations**				
Hair loss	2	5.1	27	44.3
Urticaria	7	17.9	10	16.4
Acne	3	7.7	7	11.5
Skin erythema	6	15.4	4	6.6
Vasculitis	4	10.3	1	1.6
Herpes zoster-like	3	7.7	2	3.3
Pityriasis Rosea-like	4	10.3	0	0.0
Maculopapular rash	4	10.3	0	0.0
Levodoreticularis	1	2.6	2	3.3
Lichen planus	3	7.7	0	0.0
Vascular eruption	0	0.0	2	3.3
Eczema	1	2.6	0	0.0
Purpuric rash	0	0.0	1	1.6
Seborrhic dermatitis	0	0.0	1	1.6
Chilplain	0	0.0	1	1.6
Drug eruption	0	0.0	1	1.6
Chicken pox-like	0	0.0	1	1.6
Others	1	2.6	1	1.6

**P. value within onset of skin manifestations = 0.600 not significant*
***P. value within type of skin manifestations 0.001 significant.*

Table 6. Distribution of onset and types of skin manifestations according to severity of COVID-19

Variable	COVID-19 severity					
	Mild		Moderate		Severe	
	No.	%	No.	%	No.	%
Onset of skin manifestations*						
Initial presentation	7	10.4	1	5.0	0	0.0
During	19	28.4	8	40.0	11	84.6
After	41	61.2	11	55.0	2	15.4
Types of skin manifestations**						
Hair loss	21	31.3	7	35.0	1	7.7
Urticaria	14	20.9	3	15.0	0	0.0
Acne	9	13.4	1	5.0	0	0.0
Skin erythema	4	6.0	3	15.0	3	23.1
Vasculitis	1	1.5	0	0.0	4	30.8
Herpes zoster-like	3	4.5	2	10.0	0	0.0
Pityriasis Rosea-like	4	6.0	0	0.0	0	0.0
Maculopapular rash	2	3.0	0	0.0	2	15.4
Levodoreticularis	1	1.5	1	5.0	1	7.7
Lichen planus	3	4.5	0	0.0	0	0.0
Vascular eruption	0	0.0	1	5.0	1	7.7
Eczema	1	1.5	0	0.0	0	0.0
Purpuric rash	0	0.0	1	5.0	0	0.0
Seborrhic dermatitis	0	0.0	1	5.0	0	0.0
Chilplain	0	0.0	0	0.0	1	7.7
Drug eruption	1	1.5	0	0.0	0	0.0
Chicken pox-like	1	1.5	0	0.0	0	0.0
Others	2	3.0	0	0.0	0	0.0

**P. value within onset of skin manifestations = 0.005 significant*
***P. value within type of skin manifestations = 0.001 significant.*

Table 7. Distribution of COVID-19 types of skin manifestations according to their onset

Types of skin manifestations	Onset of skin manifestations					
	Initial		During		After	
	No.	%	No.	%	No.	%
Hair loss	0	0.0	3	7.9	26	48.1
Urticaria	7	87.5	7	18.4	3	5.6
Acne	0	0.0	2	5.3	8	14.8
Skin erythema	0	0.0	7	18.4	3	5.6
Vasculitis	0	0.0	4	10.5	1	1.9
Herpes zoster-like	0	0.0	3	7.9	2	3.7
Pityriasis Rosea-like	0	0.0	0	0.0	4	7.4
Maculopapular rash	0	0.0	3	7.9	1	1.9
Levodoreticularis	1	12.5	2	5.3	0	0.0
Lichen planus	0	0.0	0	0.0	3	5.6
Vascular eruption	0	0.0	2	5.3	0	0.0
Eczema	0	0.0	0	0.0	1	1.9
Purpuric rash	0	0.0	1	2.6	0	0.0
Seborrhic dermatitis	0	0.0	1	2.6	0	0.0
Chilplain	0	0.0	1	2.6	0	0.0
Drug eruption	0	0.0	1	2.6	0	0.0
Chicken pox-like	0	0.0	1	2.6	0	0.0
Others	0	0.0	0	0.0	2	3.7

P. value<0.001 Significant

4. DISCUSSION

Physicians specifically the dermatologists must take in consideration the skin manifestations of COVID- 19 disease that could be helpful in earlier diagnosis of the disease or as predictor of severity and deterioration of the disease. Additionally, treatment of these cutaneous lesions is essential part in treatment of COVID-19 disease and preventing dermatological complications (29).

The present study showed that (54%) of skin manifestations were presented after COVID-19 disease, (38%) of manifestations presented during the disease and (8%) of them were presented initially. These findings are close to results of Sachdeva et al. (30) case reports and review of literatures study from different countries which revealed that (12.5%) of skin manifestations were presented in COVID-19 patients before pulmonary features, while (69.4%) of skin lesions were presented after respiratory symptoms. Our study found a significant association between increased age of patients and skin manifestations during COVID-19 disease (p=0.009). Similarly, Singh et al. (31) systematic review study in USA reported that onset and types of cutaneous lesions of COVID-19 disease are related to age of patients. Current study also found a significant association between severe COVID-19 disease and skin manifestations during COVID-19 disease (p=0.005). This finding is consistent with reports of Genovese et al. (32) study in Italy which stated that onset of skin lesions is related to severity of COVID-19 disease. However, some authors reported that skin lesions during severe COVID-19 disease might be related to hypercoagulability and reaction to drugs (33).

The current study showed that common skin manifestation of COVID-19 disease was hair loss (29%), followed by; urticaria (17%), acne (10%), skin erythema (10%), vasculitis (5%), Herpes zoster-like (5%), Pityriasis Rosea-like (4%), Maculopapular rash (4%), lichen planus (3%), etc. This finding is similar to results of Mieczkowska et al. (34) study in USA which reported many COVID-19 cases with hair loss especially after the resolving of the disease. A systematic review study conducted in Iran by Jamshidi et al. (22) on 47 articles included 1847 COVID-19 patients found that maculopapular rash was the main skin lesion of COVID-19 disease followed by chilblain-like and urticaria-like lesions and vascular lesions. Differences in proportions of skin lesions associated with COVID-19 disease might be related to differences in demographics of patients, severity

patterns of the disease and immunity status of patients in addition to differences in methodology between different studies. The original mechanism in developing skin lesions of COVID-19 disease is understood till now, however, some theories documented the effect of viral particles on cutaneous vessels activating cytokines, Langerhans cells and keratinocytes (35). Others reported the effect of microthromboses aggregation in developing livedo reticularis-like lesions (36) in addition to effect of other inflammatory markers during COVID-19 disease (37).

Current study reported a significant association between female COVID-19 patients and hair loss, while male COVID-19 patients were significantly associated with Pityriasis Rosea-like skin lesions (p=0.001). Consistently, Thuangtong et al. (38) retrospective chart review and telephone interviews study in Thailand on 93 patients with previous COVID-19 which found that hair loss was common cutaneous manifestation predominantly among females, on other hand, Veraldi et al. (39) study in Italy reported male gender COVID-19 patients with Pityriasis Rosea-like skin lesions. Our study showed a significant association between vasculitis and severe COVID-19 disease, while hair loss was significantly related to mild COVID-19 disease (p=0.001). This finding coincides with reports of McGonagle et al. (40) study in UK which stated that immune disturbances, hypercoagulability, complement activation and endothelial dysfunction in severe COVID-19 disease lead to vasculitis, while Starace et al. (41) multi-countries study revealed that severity of hair loss was affected by severity of COVID-19 disease. In present study, there was a highly significant association between initial presentation of skin disease and urticaria, while the vasculitis was significantly related to during presentation and hair loss was significantly related to after presentation (p<0.001). Recent American study by Pagali and Parikh reported severe urticarial rash as initial presentation of COVID-19 disease (42), while Reiff et al. (43) study in UK reported the vasculitis during acute COVID-19 disease course.

5. CONCLUSIONS

The common dermatological manifestations of COVID-19 disease were hair loss, urticaria, acne and skin erythema with predominance of late presentation. The types of skin lesions and the onset of presentation are affected by severity of COVID-19 disease. The onset of skin lesions presentation is different according to skin lesions types. This study recommended the importance of identifying the cutaneous manifestations in diagnosis and categorizing the COVID-19 disease.

Ethical Clearance: Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 of ethical principles for medical research involving human subjects. Data and privacy of patients were kept confidentially.

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