

Common Dermatological Complications of COVID 19: How Does it Affect the Skin?

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ABSTRACT

The novel corona virus disease of COVID-19 is associated with significant morbidity and mortality. It is primarily a respiratory virus, hence much of the attention has been focused on the respiratory and cardiovascular complications. Nevertheless, it affects other systems such as cutaneous, renal, neurological, and musculoskeletal. In this review, we will discuss the dermatological features and complications of COVID-19: The association of cutaneous signs and symptoms with COVID19 is being studied all over the world, primarily to see whether these dermatoses can aid in the early detection of SARSCoV2 infection. Dermatological manifestations in patients of all ages can range from erythematous rash, urticaria, livedo reticularis and acrocyanosis. Similarly, dermatologists who treat COVID-19 patients with biologics or immunomodulators for inflammatory dermatoses should exercise caution and follow precise guidelines when modifying the doses of these drugs. There are several types of skin findings described in association with COVID-19. This review includes common, rare, and occupational cutaneous exhibitions. During this pandemic, health care worker as well as public must apply strict infection control measures such as wearing personal protective equipment (PPE) for long periods, extensive hand washing and use of alcohol-based sanitizers, which lead to new skin manifestations, examples include contact dermatitis, contact irritant dermatitis, blisters, contact urticaria and secondary infections. It can also lead to exacerbation of many pre-existing dermatoses like eczema, psoriasis, and different variants of dermatitis. This has undoubtedly had significant impacts on compliance with such measures and subsequently time taken off work. It is important to distinguish that the dermatological conditions are not currently a criterion for diagnosis for COVID-19, although that might change as we have more emerging evidence. Whilst most of these dermatological findings are self-resolving focus should be on treating post-COVID-19 skin complications effectively. We think, recognition of these cutaneous features could aid the early diagnosis of COVID-19 and therefore control the epidemic, especially in areas where doing the conventional tests might be scarce or not even available.

KEYWORDS: SARS-CoV-2; Cutaneous; Rash; Occupational

INTRODUCTION

With over 125 million people infected with COVID-19 globally and more than 2.7 million deaths since the beginning of the pandemic [1], the World Health Organization (WHO) has recommended the implementation of public health measures, such as isolation of all individuals suspected of infection with this disease for a 14-day quarantine period, amongst others. Many governments have also introduced “social distancing” and “lock-

downs” of varying stringency of entire populations to mitigate the spread of COVID-19 [2-7].

The evolvement of COVID-19 virus has challenged health care professionals across the globe in an extraordinary way [8-10]. On review of the developing evidence, the COVID-19 virus has adverse effects on different body systems. Currently, the confirmed mechanism of action is hypothesized which could be an immune

Quick Response Code:



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Received: June 09, 2021 **Published:** June 15, 2021

How to cite this article: Abdulrahman H, Afify EM, Mohammed AS, Malik RA and Dergaa I. Common Dermatological Complications of COVID 19: How Does it Affect the Skin?. 2021- 3(3) OAJBS.ID.000294. DOI: [10.38125/OAJBS.000294](https://doi.org/10.38125/OAJBS.000294)

response to the virus, a direct viral involvement, microthrombus related changes or a vasculitis [11]. COVID-19 virus symptoms are variable, ranging from no symptoms to symptoms that are typically associated with acute viral infections such as coryza, cough, shortness of breath and fever [12]. Infrequently it can affect other systems, like cardiovascular, renal, central nervous system and cutaneous system [12]. Distinguishing skin manifestations relating to COVID-19 from other viral exanthems, and drug reactions can be challenging [13,14].

Cutaneous involvement during the COVID19 disease was reported to be 0.2 percent in China, where only two patients out of 1,099 with documented SARSCoV2 infection presented with a “skin rash” and no other symptoms [15]. In Italy, the recorded range of skin manifestations reached 20.4 percent, with 18 of 88 COVID19 patients having issues. They either had an erythematous rash (14 patients), extensive urticarial lesions (3 patients) or chickenpox like vesicles (1 patient). The lesions were asymptomatic or mildly pruritic, and they often affected the trunk. They emerged at the start of the infection or during hospitalization and healed within a few days [15]. Since no association with disease severity was discovered, a nonspecific character was assumed [16]. Skin involvement was registered in just 4.9 percent.

Five patients out of 103 of the patients in a French prospective study on the incidence and types of COVID19 associated cutaneous manifestations, manifested as an erythematous rash (two patients) and urticaria (two patients) [17]. Lesions occurred during the illness or prodromal period, mostly on the face and upper body, were pruritic and resolved within 24 hours to 6 days. The authors concluded that COVID19 cutaneous manifestations were rare and often nonspecific [16]. These preliminary findings were accompanied by an increasing array of individual reports and case studies. Despite dermatological presentations of COVID-19 being uncommon, a clinician’s awareness will contribute to prompt, correct diagnosis, and therefore effective disease management whether a patient is asymptomatic or weakly symptomatic [18]. No direct correlation with disease activity has been established yet [11]. However, cutaneous manifestation could be the only presenting symptoms of COVID-19. The reported cutaneous manifestations of COVID-19 are numerous, discrete, and sometimes perplexing.

Thus, the aim of this article is to highlight cutaneous manifestations. Despite being infrequent, it is crucial for clinicians and other health care workers to be aware of them, as this will lead to sooner and better diagnosis resulting in better containment of the pandemic.

METHODOLOGY

We searched PubMed and Google scholar databases for peer-reviewed, pre-print or published studies with the terms ‘dermatology’, ‘skin’, ‘COVID-19’ and ‘SARS-CoV-2’ from November 1, 2019, until May 25, 2020.

DISCUSSION

In this review, we will discuss the effect of COVID-19 on skin, and how the knowledge of it could help in fighting the pandemic. These manifestations are common, rare, and occupational.

Common Cutaneous Manifestations

We classified the reported skin manifestations from the most common to the least common:

- 1-Maculopapular rash
- 2-Urticaria
- 3-Chilblain
- 4-Vesicular rash
- 5-Livedo reticularis
- 6-Petechiae
- 7-Vasculitis

Maculopapular rash: In a comprehensive review done by Rahimi et al. [11] they found maculopapular rash to be the most common dermatological features of COVID-19, and it can occur with or without itching. It mostly affects females and those over 60 years old. They also concluded that whilst 35% of patients were asymptomatic it happens more during the active disease with the torso being the commonly affected part. In some cases, the rash appeared later during the disease course, with repeated COVID-19 PCR being negative hence pointing more towards drug hypersensitivity reaction. A case report published by Lin et al. [13] reported that maculopapular rash look like the measles rash, which supports the aetiology of viral exanthem. Patients reported pain, but no itching. Rash occurred on day 6 of COVID-19 classical symptoms sparing the face and the mucous membranes. Most of these rashes are self-limiting resolving within few days and did not correlate with disease activity [16].

Urticaria: Urticarial rashes incidence is estimated to be around 1% of the general population in the United States with similar prevalence in other countries. Elsner et al. [19] study of 84 patients reported that urticaria was found in 18.6 percent. It affected all ages, ranging from 2 months to 71 years, more than half of cases reported to be in females. It happens mainly during the active phase of the disease and affects all body parts. Lin et al. [13] reported that a 47-year-old female came up with an urticarial rash on her upper and lower limbs, it was very itchy and occurred on the fifth day from the laboratory confirmation of COVID-19. They also suggested that urticaria might precede the onset of COVID-19. An important point to bear in mind is that urticaria could be due to drug reaction. Additionally, urticaria can present as a prodromal symptom. From a case report in Scotland [20], the urticaria presented 2 days before the typical respiratory symptoms of COVID-19 and similar findings were found in a French study [21]. A case report of an 8-year-old girl [22] who presented with only an urticarial rash, no respiratory symptoms but positive for COVID 19 seems to be a recurring observation in children, one could think if all the children with rashes that do not respond to conventional measures should be offered PCR testing or at least antigen testing [3,5].

Chilblain (Pernio): Chilblain is a condition characterized by the development of cold-induced erythro-cyanotic skin lesions. It has been reported that chilblains occurred in 81 patients (18%) without any history of exposure to cold [11]. Patients in that group had some special characteristics which made it different from the others; it mostly presented in younger patients with a mean age of 31.7 years and in females. Interestingly, none of the cutaneous manifestations were reported in asymptomatic carriers except for chilblains [11]. It was also the only cutaneous manifestation that happened after a complete recovery. An article published by Lipsker et al. [23] found that chilblains can be a paraviral phenomenon i.e., it normally occurred in patients who are symptomatic or

with very few symptoms and the duration was 1-4 weeks post symptoms. Most of these patients tested negative for COVID-19 by nasopharyngeal swabs and have negative antibodies test. This might suggest a natural resistance to COVID-19.

In a systemic review done by Mirza et al. [24], the authors found it affected males and females equally and most of the lesions settled in 2-4 weeks without treatment. In Italy, these lesions were mainly observed in children [18], which is very interesting given that majority of children are normally asymptomatic carriers of the virus. This reiterates the fact that at times dermatological findings can be the only pointer towards COVID-19 diagnosis.

Vesicular lesions: The review done by Rahimi et al. [11] found that 13.5 percent of patients had a vesicular rash, mimicking chickenpox. According to the study conducted by Gottlieb et al. [25] vesicular lesions are mostly widespread disseminated papulovesicular rashes with itching like chicken pox and the rashes include small, fluid-filled blisters, often on an erythematous base. However, some patients presented with localized vesicular herpetiform lesions [25]. Vesicular rashes usually appear in the active phase of the disease [25]. On the other hand, other case series noted that the lesions appeared small and monomorphic as contrasting to the chickenpox rash with a hemorrhagic content. In most cases the vesicular rash came first before other symptoms. Mawhirt et al. [26] stated that there were an increased number of Varicella Zoster infections in patients with COVID-19 reported in Spain. However, is not clear if it was directly caused by the virus or the reactivation of the Varicella Zoster virus through the usual mechanism. Additionally, it has been reported that vesicular rashes and pseudo-chilblains to be more specific to COVID-19 infection compared to maculopapular and urticarial rashes which are less specific [27].

Livedo reticularis: This is a less common and asymptomatic manifestation with the same incidence between males and females, but it affects patients aged over 60 more. With unilateral presentation it can resolve spontaneously within a few hours in contrast to the bilateral presenting rash which commonly happens with autoimmune disease and needs treatment [26]. Although livedo reticularis is uncommon it is, associated with more severe disease, increased risk of massive systemic thromboembolic events, multi organ failure and greater mortality, up to 10 percent [25].

Another study [27] which presented two cases of livedo reticularis that appeared after presenting with COVID-19 symptoms. In the reported cases, deposition of C4c complement was found in the immunofluorescence studies. Livedo racemosa (LR) is a violaceous web or net-like patterning of the skin like livedo reticularis, the difference is livedo racemosa is more permanent, disseminates diffusely, and found in lower extremities [23]. There appears to be a direct correlation between certain dermatological findings and COVID-19 symptom severity [28]. Those with conditions such as pseudo-chilblains have less severe COVID-19 symptoms whereas those presenting with livedo reticularis or necrosis have more severe COVID-19 presentations [27,28].

Petechiae: It has been reported that petechial rashes are uncommon, so far in reported studies only 2 patients have been identified, one patient with petechiae who was initially misdiagnosed as dengue fever (in an endemic area) was then later discovered to have COVID-19. In this case the patient was also noted to be significantly thrombocytopenic [24]. Whilst an isolated petechial rash is uncommon, petechiae and purpura associated

with thrombocytopenia is more common, given that SARS-CoV-2 may cause thrombocytopenia by several mechanisms including bone marrow suppression, consumptive coagulopathy, immune-mediated platelet destruction, or cytokine release syndrome. Petechiae and purpura are associated with varying levels of thrombocytopenia as well as immune thrombocytopenic purpura (ITP) [24]. It may also signify maculopapular exanthem or purpuric vasculitis, retiform purpura denotes a more severe finding and associated with an increased mortality, in some cases it presented with peripheral livedo racemose [24]. Morphologically petechiae are small subdermal hemorrhages, while purpura are larger variants of this. Treatment options include immunoglobulin and medication called eltrombopag.

Cutaneous vasculitis: The major concern about cutaneous vasculitis as we all know is that it might develop quickly to systemic vasculitis, which has a high mortality and morbidity. COVID-19 associated cutaneous small vessel vasculitis (CSVV) can occur during the last part of active infection [24]. As expected, the pathophysiology is a combination of immune complex deposition in the small vessels, complement mediated inflammation, tissue destruction by either infection or medication. Cutaneous vasculitis is found to be associated with more severe COVID-19 infection, characterised by devastating microvascular injury syndrome and hyper-coagulable status [13]. It can present as palpable purpura, with or without non-blanching petechiae and in some cases other signs included urticaria, ulceration, haemorrhagic bullae, purpuric like lesions, erythematous urticaria-like papules with central purpura or hyperpigmentation. It commonly affects lower limbs or follows cranial caudal distribution. Some cases have been found to be medications induced vasculitis with patients having significant improvement after medication cessation and administration of systemic and topical steroid.

Rare Cutaneous Manifestations

They are other rare skin manifestations related to COVID-19 which are worth mentioning at the same time. The first rare, interesting condition affects children exclusively. COVID-19 typically presents with mild symptoms in children with many children being asymptomatic carriers [29]. Nonetheless, it been reported from different parts of the world the evolvement of this syndrome, which is labelled multisystem inflammatory syndrome in children (MIS-C) or paediatric multisystem inflammatory syndrome (PMIS). A study from the South Thames Retrieval Service, London, UK [23], reported that over a 10-day period they had a group of eight children with features of hyperinflammatory shock, similar signs of atypical Kawasaki disease shock syndrome or toxic shock syndrome whereas usually this service has 2 children per week with this. Half of the group had family contact of COVID-19, 2 tested positive for COVID-19 and the third child who unfortunately passed away tested positive in the autopsy examination. All the eight children needed PICU support and stayed in hospital between 3-7 days. This study formed the base for a national alert to make professionals caring for the Paediatrics population more vigilant. An observational cohort study done by Verdoni et al. [30] where they studied the incidence of Kawasaki virus before and after COVID-19 in Italy, reported a 30-fold increase in the incidence, with increased disease severity and evidence of immune response to the virus. Moreover, children who were diagnosed after the pandemic were older and found to have a higher rate of cardiac complications [30]. The rash that appeared was erythematous, polymorphic, and affected hands and feet. Other rare skin complications include

dactylitis, distal ischemia and necrosis. All of which point towards the thrombotic and vasculopathy effect of the COVID-19 virus.

Occupational Complications of COVID-19

This pandemic has placed unprecedented challenge on health care workers. COVID-19 is highly infectious; thus, infection control measures must be very strict to protect health care workers (HCWs) and control the spread of the infection. These measures including PPE (gloves, masks, goggles, face shields and isolation gown like hazmat suit) washing hands and using anti-septic products [31].

A cross sectional multi-centre study done by Jiang et al. [31] found that device-related pressure injury (DRPI) caused by PPE was 30.3% amongst HCWs. Commonly affected sites were hands, the nose bridge, cheeks, ears, and forehead. Moreover, the duration of wearing PPE (longer than 6 hours, 3, Wuhan study), sweating and type of PPE have significant impact on the prevalence of this injury and its severity. Whilst these skin lesions affect primarily HCWs, patients and their carers can also be affected [32]. PPE can result in erythema, maceration, fissuring, papules, and erosions, all of which are associated with pruritis, pain and might lead to a skin infection. HCWs who have a pre-existing skin condition are likely to have exacerbations. Prevention of PPE related injury will lead to better compliance of the HCWs and consequently more protection and well-being for them [33]. Suggested measures such as film dressing (although practicality can be an issue), barrier creams, using face shields instead of goggles, improving the PPE designs and material and education on proper PPE donning and doffing can counteract these conditions.

Occupational Dermatitis

It is well known that hand dermatitis is common in HCWs, overzealous hand washing, or alcohol-based sanitizers and other irritants are the primary culprits, that's why sometimes it called hand hygiene-related dermatitis. It includes irritant contact dermatitis and allergic contact dermatitis.

It has been reported that risk factors were females, frequency of hand wash, which directly related to number of working hours [26]. According to the American Academy of Dermatology, HCWs need to use petroleum-based emollients between hand washing, when not working and overnight to decrease the transdermal water loss [26]. It has been reported that the best preventative measures were using alcohol hand rub when hands are not visibly soiled as it causes less skin irritation and has great anti-septic properties. Washing with lukewarm water instead of hot water and applying barrier creams all help [13].

Delivery of Dermatological Care during the COVID-19 Pandemic

When this pandemic was declared by WHO back in March 2020, health systems around the world geared up to deal with it. Hospitals cancelled all routine booked appointments and elective admissions to focus the human, financial and logistic resources towards the pandemic and at the same time to control the spread of the outbreak [4-34]. Dermatological services were no different. Many Dermatology wards turned to COVID-19 wards with almost all the outpatients work done remotely but skin care requires close contact. However, like other aspects of our life during this pandemic people made good use of technology. Telemedicine and tele dermatology proved helpful.

In a systemic review by Elsner et al. [19], the authors studied the use of video consultations (store and forward images), concluding that the use of tele dermatology proved safe and effective. Tele dermatology is very suitable to the specialty given that it is an image dependent specialty. The challenging issues were use and acceptance by both public and insurance authorities, some might need further skin examination and diagnostic tools such as biopsy, dermatoscopy and patch testing [17]. Nevertheless, few of the dermatology emergencies such as malignancies vasculitis, need a timely manner intervention and perhaps face to face consultations. It looks likely that the use of tele dermatology will continue well after this pandemic pass, as it will certainly compensate for the loss of direct consultation numbers affected by social distancing and other infection control measures and procedures. More investment in infra-structures is needed to ensure the desired expansion of the service.

CONCLUSION

Patients with COVID-19 most commonly present with respiratory symptoms, but multiorgan involvement can occur, with multiple skin manifestations. The pathophysiology of COVID-19 skin involvement is still not clear, but different theories have been proposed and are under research such as immunological response, vasculopathy and thrombosis. The recognition of these conditions could help early diagnosis ensuring effective management hence helping to contain the pandemic and hopefully stop it. This point is more important in areas where the availability and the access for the COVID-19 PCR is limited by either economic reasons or facility access for testing.

ACKNOWLEDGEMENT

Open Access funding provided by the Qatar National Library. The authors wish to express their sincere gratitude to all participants for their efforts which helped in completion of this study.

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