

## Dermatological manifestations of Coronavirus Disease 2019 (COVID-19)

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*Sri Lanka Journal of Dermatology*, 2021, **22**: 1-4

### Abstract

The prevalence of dermatological manifestations among patients with COVID-19 has a wide variation from 0.2 - 20.4% in different countries. The commonly described manifestations are; maculopapular eruptions, urticarial lesions, pseudo-chilblains, vesicular eruptions and livedo or necrosis. There are several other manifestations described such as; enanthems, purpuric flexural lesions, Dengue-like rash, erythema multiforme-like lesions and vasculitis-like lesions. The study done in the National Hospital of Sri Lanka has revealed a prevalence of 1.7%. The survey among dermatologists island wide shows few cases with different cutaneous manifestations of COVID-19. It is important to be vigilant as the COVID-19 virus as well as the knowledge about it, is still evolving.

### Introduction

During the initial period of the COVID-19 pandemic in early months of 2020, data on dermatological manifestations of COVID-19 were scarce. Couple of months later, different dermatological manifestations of COVID-19 began to be reported. The virus spreading indicators are different among countries. Similarly, reported dermatological manifestations show variability among different countries. The frequency of the skin lesions associated with COVID-19 infection varies widely according to the series in different countries; in a Chinese study of 1099 positive cases, the incidence was only 0.2%, while in an Italian series of 88 patients it was 20.4%<sup>1</sup>. The cutaneous manifestations in relation to COVID-19 infection can be broadly classified into dermatological manifestation in active COVID-19 infection and post Covid period, and dermatological issues in relation to transmission preventive measures and vaccination.

The main pathogenic mechanisms of skin manifestations of COVID-19 are due to, immune dysregulation or hypersensitivity reactions, vasculitis, hypercoagulable states, vessel thrombosis or neogenesis and cytopathic effects of the virus<sup>2</sup>.

Different mechanisms are involved in producing different clinical presentations. Endothelial swelling with presence of SARS-CoV-2 viral particles in the endothelial cells produces chilblains or covid toes<sup>2</sup>. The cell mediated immune responses give rise to papulo-squamous and perifollicular papular lesions. Viremia leading to entry of virus in to the epidermal cells causing cytopathic effect brings up chickenpox like eruption and zosteriform blisters. The formation of microthrombi or immune complex deposition on the endothelium produces vasculopathy manifesting as livedoid pattern and Covid feet<sup>2</sup>.

Galván Casas *et al.* in their Spanish study with 375 patients have classified the skin lesions observed during COVID-19 infection into 5 types: maculopapular eruptions in 47%, urticarial lesions in 19%, acral areas of erythema with vesicles or pustules (pseudo-chilblain) in 19%, other vesicular eruptions in 9%, and livedo or necrosis in 6% of cases<sup>3</sup>. There are several other manifestations described by other researchers<sup>4</sup>. In these patients have developed enanthems, purpuric flexural lesions and Dengue-like rash. Erythema multiforme-like lesions and vasculitis-like lesions are also described. Dermatologists also have perceived an increased number of herpes zoster cases in COVID-19 patients<sup>4</sup>. In the Spanish study, both groups of patients with urticarial and maculopapular lesions showed very similar associated findings: both groups had received drugs more commonly than those with pseudo-chilblain or vesicular lesions; lasted for a shorter period (6.8 days for urticarial and 8.6 for maculopapular); usually appeared at the same time than the rest of the symptoms and associated with more severe disease. Itching was seen in 92% of urticarial lesions and 57% of maulo-popular lesions<sup>3</sup>.

Erythematous maculo-papular eruptions present with varying degree of scaling sometimes associated with purpura. A few cases showed infiltrated papules in the extremities, mostly dorsum of the hands, that appears as pseudo-vesicular.

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The urticarial lesions are mostly distributed in the trunk or can be disperse. A few lesions occur in the palms.

The pseudo-chilblain lesions (or the Covid toes) which is considered as a specific manifestation of COVID-19, appear as purpuric, itchy and painful areas over fingers, toes, hands and feet in an asymmetrical distribution. Usually young patients are affected, and may last around 12 days. These appear later in the course of the disease and sometimes in the post infection period. Can be associated with less severe disease.

Another specific manifestation associated with COVID-19 infection is the characteristic vesicular eruption (Figure 1). The individual lesion of this is similar to the chickenpox vesicle, starting on the trunk in contrast to chickenpox, and is not associated with high fever. The small monomorphic vesicles then spread to limbs and later can progress to haemorrhagic larger bullae. Itching can be a common symptom. This is commonly seen in middle aged patients and lasts for a mean of 10 days. The eruption may appear before other symptoms or may occur later. In these patients Covid severity is intermediate.



**Figure 1.** Vesicular eruption in a patient with positive PCR for COVID-19.

Livedo or retiform purpura and livedoid necrosis occur due to occlusive vascular disease including areas of truncal or acral ischemia. This occurs more in older patients with more severe disease and has a higher mortality. Anyway, in some series the severity had been variable including transient livedo, with some suffering COVID-19 that did not require hospitalization.

Enanthems in COVID-19 can occur 2 days before to 24 days after the onset of symptoms. These can be easily missed because of precautionary measures taken on patient examination<sup>5</sup>. They can manifest as, erythematous buccal lesions with macules and petechial lesions in hard palate, tongue, and lips.

These can progress to painful vesiculobullous lesions with ulceration. Further, painful inflammation of the tongue papilla with irregular ulcers on the tongue has been described as Covid tongue where tongue may be significantly swollen with loss of taste. This may be a direct effect of the virus or secondary infection with other organisms or immunologically mediated.

Studies analyzing severe cases of COVID-19 infection have demonstrated patients with androgenetic alopecia are prone to progress in to severe disease. This is postulated to be due to a regulatory effect on receptors for spike proteins. Interestingly these findings may pave way for novel knowledge on androgenetic alopecia<sup>6,7</sup>.

Acute telogen effluvium is a common occurrence in post COVID-19 patients. In contrast to other major illnesses, this occur sooner at a median of 1.5 months and resolution of most of the cases observed by two months. The factors such as hypoxia, inflammation, metabolic abnormalities, medications, and the need for mechanical ventilation could play a role in the development and severity of post Covid telogen effluvium.

Multi-system Inflammatory Syndrome in Children (MIS-C) occurs weeks after the COVID-19 infection in patients up to 20 years of age. Majority (81%) have skin manifestations. The skin manifestations are: edema with plantar and palmar redness; dry lips; purpuric or urticarial lesions, erythema multiforme etc. The syndrome appears to be similar to Kawasaki disease, which involves inflammation of blood vessels, and can lead to coronary artery aneurysms and permanent cardiac damage, if not treated. The syndrome is treated with intravenous IVIG, aspirin and steroids in severe cases in addition to supportive care.

The health care workers and also the general public can manifest lesions due to disease transmission preventive measures<sup>1,2</sup>. Free formaldehyde contained in the material used to produce the masks can induce contact dermatitis, which may extend even up to upper eye lids. Similarly, adhesives used in surgical mask contain a preservative, dibromodicyanobutane which may be the cause for contact dermatitis. Flexible aluminum or steel nose clip and the overlaying polyurethane foam are further allergens.

Post-inflammatory hyperpigmentation in areas where the mask presses on the skin like the nasal bridge, cheeks and chin can be a long-term consequences. This friction can lead to permanent scarring on the

nasal bridge. Protective hats may induce pruritus and folliculitis over the scalp and exacerbate seborrheic dermatitis.

Long-term use of protective gloves leads to maceration and erosions, possibly leading to contact dermatitis. Exaggerated hand washing with detergents/ disinfectants also can impair the hydro-lipid mantle of the skin surface and may be responsible for irritation and contact dermatitis.

To prevent these manifestations there are few measures the users can take. It is recommended to apply hand cream frequently, especially following hand washing and before wearing the Personal Protective Equipments (PPE). Frequent use of emollients, while using soap-free cleansers, use of alcohol-based cleansers or other antibacterial hand rubs, use of lukewarm water, use of paper towels to dry the hands instead of electric air dryers would be helpful. The anti-inflammatory topical medications under the supervision of a specialist is recommended.

There are so many post vaccination skin manifestations reported and vaccination can affect on pre-

existing dermatoses. Those issues are not discussed in this article.

The prevalence of dermatological manifestations among patients with COVID-19 has a wide variation from 0.2-20.4%. Hence a study was carried out by the author in July 2021 at the National Hospital of Sri Lanka (NHSL), Colombo. First part of the study included a descriptive cross-sectional study conducted among PCR positive COVID-19 patients in NHSL to identify their skin conditions. In order to ascertain an overall understanding of the country's situation a comprehensive questionnaire was circulated among the members of the Sri Lanka College of Dermatologists, to obtain information on the patients they have encountered.

Among the 476 patients who were individually screened at the NHSL only two patients had developed a novel skin manifestation in relation to the COVID-19 infection. Those were maculo-papular eruption and an area of thrombophlebitis on the leg. However, the information gathered with the questionnaire from the dermatologists revealed their experience which is summarized in the following table.

**Table**

<i>Novel dermatological manifestations (Number of patients)</i>	<i>Novel dermatological manifestations among the paediatric population (Number of patients)</i>	<i>Exacerbation of previously diagnosed dermatological conditions (Number of patients)</i>	<i>Medication and vaccine related dermatological manifestation (Number of patients)</i>
<ul style="list-style-type: none"> <li>• Acute urticaria (9)</li> <li>• Maculopapular eruptions (5)</li> <li>• Pityriasis rosea (4)</li> <li>• Vasculitic rash (2)</li> <li>• Exanthems (2)</li> <li>• Erythema multiforme (1)</li> <li>• Bullous lesions (1)</li> <li>• Contact dermatitis (1)</li> <li>• Dermatomyositis (1)</li> <li>• Covid toes (1)</li> <li>• Miliaria rubra (1)</li> <li>• Thrombophlebitis (1)</li> <li>• Maculopapular eruptions (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Kawasaki disease (2)</li> <li>• Pityriasis rosea (2)</li> <li>• Erythematous nodules (2)</li> <li>• Petechial lesions (1)</li> <li>• Vasculitic rash (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Psoriasis (11)</li> <li>• Eczema (7)</li> <li>• Chronic urticaria (2)</li> <li>• Contact dermatitis (1)</li> <li>• Tenia incognito (1)</li> <li>• Fungal infections – Dermatophytosis (1), Candidiasis (1)</li> <li>• Venous ulcers (1)</li> <li>• Chronic paronychia (1)</li> <li>• Acne rosacea (1)</li> <li>• Pemphigus vulgaris (1)</li> <li>• Lepra reaction (1)</li> <li>• Alopecia areata (1)</li> <li>• Bullous disorders (1)</li> <li>• Discoid lupus erythematosus</li> </ul>	<ul style="list-style-type: none"> <li>• Steroid induced acne (1)</li> <li>• Urticarial lesions following vaccination (1)</li> </ul>

## Conclusion

COVID-19 related dermatoses may present before, after or with other symptoms. Further studies are needed to precisely ascertain the features and pathophysiology behind different morphologies. Dermatological findings should not be overlooked and should prompt early involvement of dermatologists as appropriate. It is important to be vigilant on these as the COVID-19 virus as well as the knowledge about it, is still evolving.

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