

Dermatological manifestations among patients with COVID-19: The Sri Lankan experience

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Abstract

Background: Patients diagnosed with COVID-19 demonstrate a wide spectrum of cutaneous manifestations, some of which are at a high prevalence. These manifestations, of which some are unique, have been considered to occur due to COVID-19 infection and the associated inflammatory response. Furthermore, there are reports on exacerbation of previously diagnosed dermatoses and cutaneous side effects of medications and vaccines administered.

Methodology: The first phase of the study included a descriptive cross-sectional study conducted at the National Hospital of Sri Lanka (NHSL) among PCR-positive COVID patients to identify their skin conditions. Secondly, 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.

Results: Out of the patients at NHSL only 1.7% (n=8) had developed associated skin manifestations. Two (0.4%) developed novel conditions: thrombophlebitis and a maculopapular exanthem. Six (1.3%) patients had exacerbation of pre-existing conditions including eczema, psoriasis and discoid lupus erythematosus. The dermatologists revealed a wide variety of manifestations with the majority experiencing an exacerbation of pre-existing conditions and a few developing novel lesions including COVID-toes and Kawasaki-like diseases in children which are considered specific for COVID-19.

Conclusions: The study demonstrates a range of COVID-19-associated dermatoses. These can present before or with other COVID-19 symptoms. Further, studies are necessary to precisely determine the timing and pathophysiology of different manifestations. Dermatological findings are important and should prompt the early involvement of dermatologists as appropriate.

Keywords: COVID-19, Cutaneous Manifestations, Sri Lanka

Background

COVID-19 is considered a multisystem disorder. An increasing number of cases related to dermatological manifestations have been reported [1]. The published data describe a complex range of skin manifestations

associated with the infection [2]. The first patient was described in Thailand in early 2020 as having a petechial rash similar to dengue fever [3]. There is a wide variation in the prevalence of skin lesions associated with COVID-19 infection. A large-scale study

in China including 1099 COVID-19-positive cases had only 0.2% developing dermatological manifestations, while a series of 88 patients in Italy reported a high prevalence of skin manifestations of 20.4% [4].

As new information gathers, distinct cutaneous patterns are being linked to COVID-19. They develop at different stages in the disease course and are associated with unique durations, different degrees of severity, and prognosis [5]. Especially with ongoing vaccination programs and the emergence of new variants, the number of patients without typical symptoms of COVID-19 is increasing and certain dermatological manifestations may point towards an early diagnosis of COVID [2]. It is unclear whether the cutaneous manifestations of COVID-19 are a direct consequence of an aberrant immune response or due to the inherent pathogenesis of the disease itself [6]. These lesions are recognized less, due to the lack of routine dermatology consultations during the pandemic [2]. It remains to be determined whether COVID-19 infection can directly cause a worsening of pre-existing chronic inflammatory diseases such as psoriasis or atopic dermatitis. However, there exists a large body of evidence that shows exacerbations are due to the disruption of routine treatment of such skin conditions [7].

The drug regimens used for the treatment of COVID-19 patients could result in cutaneous adverse effects or aggravation of previous dermatological disorders [3]. Generalized pustular reaction and worsening of psoriasis due to hydroxychloroquine are widely reported [8]. The immune response against the virus may enhance drug allergy. The concomitant excessive production of proinflammatory cytokines may be a contributing factor [9]. The frequently linked medication-related dermatoses in COVID-19 are erythema-multiforme-like patterns, generalized pustular erythema and Stevens-Johnson Syndrome [10].

In some cases, skin manifestations may help identify asymptomatic COVID-19 carriers or in others, predict a more severe disease [10]. Chilblains are reported more frequently in younger

patients and seem to predict a milder disease. Fixed livedo reticularis and retiform purpura appear in older patients and tend to predict a worse prognosis [10].

The patterns of cutaneous manifestations can be classified into the following: exanthema (varicella-like eruption, papulovesicular, and morbilliform eruption), vascular (similar to chilblain, livedoid and purpuric lesions), urticarial and acral-papular eruptions [7,8,10-14]. Overall, vesicular lesions and pseudo-chilblain which is commonly recognized as “COVID toe” may represent the most characteristic skin manifestations of COVID-19 [2]. Maculopapular eruptions, urticaria and “COVID toe” (pernio-like lesions/ pseudo chilblains) are known as the most common mucocutaneous manifestations [15]. Out of the exanthema patterns, the “varicella-like” lesion is a specific and early skin manifestation and could signify useful evidence in asymptomatic or mildly symptomatic patients [16].

Dermatology’s outlook on the COVID-19 pandemic is multi-dimensional. It is important that clinicians are aware of the spectrum of COVID-19 skin manifestations, improving testing for the virus and clinical management [2]. While many countries have made scientific publications on dermatological manifestations, Sri Lanka has no documented evidence. This study was conducted to identify the prevalence, disease spectrum, and clinical behaviour, and to establish a link between dermatological manifestations and the severity of COVID-19.

Methodology

The study was conducted in two phases. The first consisted of a descriptive cross-sectional study conducted at the National Hospital of Sri Lanka (NHSL) with the approval of the Ethics Review Committee of NHSL, where patients with RT-PCR positivity were examined for the development of novel dermatological manifestations, exacerbation of existing conditions and medication-related skin conditions. To achieve these targets, 476 patients

were screened within a period of two weeks at the NHSL COVID treatment units. These patients were followed up at two and four weeks after the initial screening via phone calls by questioning whether they have noticed any change on their skin during the period. Out of 476, 468 follow-up calls were answered by the patient or a family member. If they responded positively, a physical visit was arranged to identify the development of the dermatological condition. In the second phase, to obtain a broader view of the country's situation, a questionnaire was circulated among all dermatologists who are members of the Sri Lankan College of Dermatologists. This includes dermatologists stationed all over the country, working at both government and private sector hospitals. Fifty-two (65%) responded out of eighty dermatologists.

Results

The study population at NHSL consisted of 476 RT-PCR-positive COVID-19 patients who were being treated in the hospital. The cohort consisted of 261 males with a male: female ratio of 1.2:1. During initial evaluation and follow-up for four weeks, eight patients (1.7%) reported skin manifestations and two patients (0.4%) developed novel dermatological manifestations. Out of the patients with new skin lesions, the first had thrombophlebitis in the left calf area which had developed during inward treatment for COVID-19. This had spontaneously subsided over a couple of days. The second patient developed a maculopapular exanthem towards the completion of fourteen days of COVID positivity. This patient complained of an itchy papular rash with ill-defined erythematous maculopapular eruption over both upper and lower extremities. The condition resolved over a couple of days with emollients and antihistamines.

Six patients (1.3%) had exacerbations of previously diagnosed dermatological conditions. Four of them (0.9%) experienced an exacerbation of eczema, mainly in the lower limbs and all of

them had discontinued their routine treatment due to a multitude of reasons after being diagnosed with COVID. All these patients were commenced on appropriate treatments. One case (0.2%) each with widespread discoid lupus erythematosus and psoriasis had mild exacerbations due to the stoppage of the immunosuppressive medication. Since the conditions were not disabling, treatment was re-commenced at the discharge from COVID treatment.

The expert opinion sought through dermatologists all over the country yielded many cases with a wide clinical variety. Acute urticaria was the commonest reported condition (n=9) with the majority (n=6) presenting after two weeks of the diagnosis of COVID and the other three developed while being treated at hospitals and intermediate COVID care centres. The condition had responded well to anti-histamines. The maculopapular eruption was another common lesion among patients (n=5). The majority have developed lesions during the early part of the illness. These were itchy lesions that were mostly in the extremities and associated with fever and cervical adenopathy in one case. Pityriasis rosea was seen among four patients. These patients have developed mildly itchy lesions with a scaly margin mainly involving the knees and forearms. Some did not have evidence of the classical herald patch. While the condition subsided with treatment, the lesions remained to a lesser degree during follow-up visits. A lesion similar to "COVID toes" that had developed 2-3 months after the diagnosis of COVID-19 was reported by one dermatologist. Diffused hair loss several months following the diagnosis of COVID was reported by one patient. The patient shown in Figure 01 presented with vesicular eruption mimicking varicella zoster infection within one week after being diagnosed to have COVID-19 infection. But in contrast to varicella zoster, there was no fever and the vesicles first appeared on the trunk and then spread to the limbs with only a few lesions on

the face. Tzanck smear was negative and lesions improved with supportive care. Other reported lesions included, exanthems (n=2), erythema multiforme (n=1), dermatomyositis (n=1), oropharyngeal candidiasis in a diabetic patient, miliaria rubra (n=1) and contact dermatitis due to face mask (n=1).

Dermatological manifestations have been reported among children who have tested positive as well. The “Kawasaki-like” disease, which is a well-known entity among children with COVID-19 had been reported by two dermatologists. Both of these children have developed periorbital swelling, conjunctival redness, blotchy erythema, tiny pustules over upper limbs and trunk, cervical lymphadenopathy, proximal muscle pain, nail fold telangiectasia and small joint swelling. Prior to the onset of fever one child had experienced acute urticaria as well. The same child went on to develop post-COVID multisystem inflammatory syndrome in children (MIS-C). Other lesions among the paediatric population included pityriasis rosea (n=2), erythematous nodules (n=2), petechial lesions (n=1) and vasculitic rashes (n=1).

The major proportion of patients diagnosed with COVID-19 that dermatologists have encountered was due to exacerbation of existing dermatological conditions. Exacerbation of psoriasis (n=10) was the commonest complaint among patients. Most of these exacerbations were due to withholding of routine medication, especially immunosuppressive treatment and not having access to regular treatment at intermediate centres and COVID home care. A few patients (n=3) with stable plaque psoriasis had gone on to develop severe erythrodermic psoriasis which has necessitated hospital admission and intensive treatment. There were no reports of overlapping cutaneous manifestations. The summary of the conditions developed with patient numbers is given in Table 1.

Medication usage and vaccination have also

contributed to dermatological manifestations. One patient had developed truncal acne after being treated by dexamethasone for severe COVID pneumonia and the other patient developed a large urticarial lesion on the back, 12 hours following the first dose of the AstraZeneca vaccine.

Discussion

This study highlighted the wide spectrum of cutaneous manifestations described concurrently or after the diagnosis of COVID-19 in other studies [7]. Cutaneous manifestations of COVID-19 were reported late in the course of the pandemic and there was a paucity of literature illustrating dermatological presentations [17].

The prevalence of dermatological manifestations among patients with COVID-19 had a wide variation from 0.2 - 20.4% [4]. Among the patients at NHSL, 1.7% had developed either a novel skin manifestation or has experienced an exacerbation of a previously diagnosed condition.

A systematic review on the topic revealed that around 12% of the cutaneous manifestations occur before other COVID-19 signs, highlighting their importance in assisting in the detection of the infection [18]. Despite this, most studies have been unable to identify a correlation between dermatological manifestations and disease severity or establish a temporal relationship with the disease [11,18,19]. The current study population did not reveal any convincing evidence to suggest a correlation, mainly due to the non-specificity of the symptoms and the low proportion of affected patients (1.7%).

In dermatological practice, immunosuppressants are used for the management of autoimmune and inflammatory diseases such as psoriasis, atopic dermatitis, systemic lupus erythematosus, and dermatomyositis among many other conditions [14]. With the onset of COVID, these immunosuppressants are best withheld while maintaining the delicate balance between treating COVID and keeping the dermatological condition

under control. This decision should be based on a multitude of factors and the involvement of a dermatologist is important to avoid unnecessary morbidity to the patient.

The commonest morphologies among PCR-confirmed patients in other studies included morbilliform, pernio-like, urticarial, macular erythematous, vesicular, papulosquamous, and retiform purpura-like lesions. Perno-like lesions were considered to be more COVID-19-specific than other dermatologic manifestations. Such propensity towards certain lesions was not seen in this study and a mixture of various and rather non-specific conditions were noted in the cohort of patients. This highlighted the importance of vigilantly identifying skin lesions and treating them appropriately. A limitation of the survey conducted among the dermatologists was that some of the cutaneous manifestations may have

been undetected or not referred to a dermatologist due to practical issues.

Conclusions

In conclusion, this study demonstrated a wide range of COVID-19-related dermatoses. These cutaneous manifestations can present before, concurrently or following other COVID-19 symptoms. Among the patients at NHSL, 1.7% had developed either a novel skin manifestation or experienced an exacerbation of a previously diagnosed condition. However, further studies are necessary to precisely determine the timing of cutaneous findings and to ascertain the pathophysiology behind different morphologies. It is important that dermatological findings should not be overlooked as signs of COVID-19 and should prompt the early involvement of dermatologists as appropriate.

Author Declaration

Author contributions: JA and VJM contributed to the conceptualization and design of the study. All authors contributed to the acquisition and analysis of data. JA and VJM contributed to the data interpretation and writing of the manuscript. All authors read and approved the final manuscript.

Conflicts of interest: The authors declare that they have no conflicts of interest concerning the research, authorship, and/or publication of this article.

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Table 1: Summary of dermatological manifestations from both phases of the study

Novel dermatological manifestations (Number of patients)	Novel dermatological manifestations among the paediatric population (Number of patients)	Exacerbation of previously diagnosed dermatological conditions (Number of patients)	Medication and vaccine-related dermatological manifestations (Number of patients)
- Acute urticaria (9) - Maculopapular eruptions (5) - Pityriasis rosea (4) - Vasculitic rash (2) - Exanthems (2) - Erythema multiforme (1) - Blistering lesions (1) - Contact dermatitis (1) - Dermatomyositis (1) - COVID toes (1) - Miliaria rubra (1) - Thrombophlebitis (1) - Maculopapular eruptions (1)	- Kawasaki disease(2) - Pityriasis rosea (2) - Erythematous nodules (2) - Petechial lesions (1) - Vasculitic rash (1)	- Psoriasis (11) - Eczema (7) - Chronic urticaria (2) - Contact dermatitis (1) - Tinea incognito (1) - Fungal infections – Dermatophytosis (1), Candidiasis (1) - Venous ulcers (1) - Chronic paronychia (1) - Acne rosacea (1) - Pemphigus vulgaris (1) - Lepra reaction (1) - Alopecia areata (1) - Bullous disorders (1) - Discoid lupus erythematosus (1)	- Steroid-induced acne (1) - Urticarial lesions following vaccination (1)



Figure 01: Vesicular eruption mimicking varicella zoster infection