

Cutaneous Manifestations Associated with COVID-19 Infection in a COVID-Designated Hospital in North Chennai – A Descriptive Cross-Sectional Study

Abstract

Background: Coronavirus disease 2019 (COVID-19) affects different organ systems, including the skin. There are reports on cutaneous manifestations of COVID-19 available in the literature. In this study, we have tried to describe the dermatological signs of COVID-19 in different categories of patients. **Materials and Methods:** A descriptive cross sectional study was conducted to describe various cutaneous manifestations of COVID-19 in different categories of reverse transcriptase polymerase chain reaction (RT-PCR)-positive COVID-19 patients in a COVID-designated tertiary care hospital. Approval was obtained from the Institutional Ethical Committee, and 5460 RT-PCR-confirmed COVID-19-positive patients were included under five categories. Investigators following a strict COVID protocol examined and documented the findings. Investigations and treatment were carried out as per the protocol, and the study was conducted for a period of 6 months. **Results:** Out of the 5460 patients studied, 1.9% patients had cutaneous manifestations. Vasculitis (24%) and maculo papular rash (19%) were the common findings. The incidence of vasculitis was 44.4%, 61%, and 6.6% in categories A, B, and C, respectively. Maculopapular rash and urticaria were the common findings in categories D and E, respectively. COVID digit was seen in only one case. Other manifestations such as acne, adverse drug reaction, erythroderma, and bullous disorders were also noted. **Conclusion:** Cutaneous manifestations because of vascular pathology were the most common association in severe COVID-19, which indicates that the presence of vasculitic skin signs correlated with disease severity and elevated d-dimer values. Urticaria and maculo-papular rash were transient and did not give any clue to the diagnosis or severity of the disease.

Keywords: COVID-19, cutaneous manifestation, vasculitis

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the respiratory pathogen severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a coronavirus, first reported in the Wuhan province of China in December 2019. COVID-19 not only caused pulmonary symptoms but also dermatological signs and symptoms.^[1]

SARS-CoV-2, the causative pathogen, is an RNA virus that chiefly establishes an infection after binding to ACE-2 receptors in the respiratory tract and starts replicating.^[2] Initial estimates have shown a 2% fatality rate, but it needs re-consideration once the prevalence of mild and asymptomatic cases is better defined.^[3]

Increasingly, varied cutaneous manifestations have been reported from many parts of

the world, suggesting a role for a proper cutaneous examination, documentation, and correlation of results, which may aid in better patient management.^[4,5] Vasculopathic cutaneous manifestations indicate that coagulation dysfunction may be devastating in severe COVID-19.^[6]

Although COVID-19-related dermatoses are being reported, categorization of patients and correlation of skin findings and disease severity in different categories are not available in the literature. We have correlated the different cutaneous manifestations with five categories of COVID.

Methods

In this descriptive cross-sectional study, after ethical committee approval, 5460 reverse-transcriptase polymerase chain

**Parimalam Kumar¹,
Guru Radha²,
Madhanchand
Muthukrishnan³,
Balakumaran
Chandrasekaran⁴,
Pravinkumar
Subbiah⁵,
Jagan Raman⁶**

¹Prof & Head Department of Dermatology, Madras Medical College, Chennai, Tamil Nadu, India, ²Assistant Surgeon, Govt Leprosy Training Centre, Arangandanallur, Thirukkoilur, ³Consultant, Madhans Derma Clinic, Madurai, ⁴Senior Resident, Department of Dermatology Sri Balaji Medical College, Chennai, ⁵Assistant Surgeon, Govt Headquarters Hospital, Manapara, ⁶Assistant Prof, Department of Dermatology Indira Medical College, Thiruvallur

Address for correspondence:

Dr. Parimalam Kumar,
No 4, East Ellaiamman Koil
Street, Dr. Radhakrishnan
Nagar, Thiruottiyur,
Chennai - 600 019, Tamil Nadu,
India.
E-mail: drparimalam@gmail.
com

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reaction (RT-PCR)-confirmed COVID-19-positive patients registered under Government Stanley Hospital for a period of 6 months from July 2020 who fulfilled criteria of being RT-PCR-positive were included. Investigators with full protective gear examined COVID-19-positive patients and included them under the following five categories:

Category A – Moderate to severe cases treated in a COVID-designated hospital.

Category B – Mild cases with the co-morbidity treated in a corona treatment center.

Category C – Mild cases with no co-morbidity treated in a corona care center.

Category D – COVID-19 outpatients kept on home quarantine.

Category E – Patients attending dermatology out- and in-patient care who subsequently become COVID-19-positive.

Thorough general, systemic and dermatological examination was performed. Skin manifestations occurring 5 days before and within 15 days of taking swab were noted. Investigations including CT chest, serum D-dimer, IL-6, and serum ferritin were performed in all patients under categories A and B. All patients were treated according to the COVID protocol. Data were analyzed with appropriate statistical tools.

Results

Out of the 5460 patients, two-third were men. The various clinical presentations in different categories are given in Figures 1 and 2. Vascular manifestations were common in categories A, B, C and non-vascular lesions in categories C and D. Vascular lesions such as purpura, petechiae, and ecchymoses were the most common findings [25 (24%)], followed by maculo-papular rash [20 (19.2%)]. There was only one COVID digit observed in this study. These vascular manifestations were observed in categories A, B, and C. Out of the 18 patients under category A, 13 had co-morbidities. On classifying the disease based on severity, ten had severe illness and eight had moderate disease. Cutaneous manifestation of vasculitis was found in five of them, and one had COVID digit. Severity of vascular manifestations correlated with d-dimer values; higher the value, more severe was the manifestation. Of the ten severe COVID-19 cases, all of them had co-morbidities and three succumbed to the illness. Among the non-vascular manifestations, urticaria and pruritus were transient.

Discussion

A descriptive study of cutaneous manifestations in COVID-19-positive patients is quite a challenge. In this study, the same set of investigators studied all the 5460 COVID-19-positive patients and documented the results.

Table 1^[4,6-8] shows a comparison of salient features of this study with four main studies from different parts of the world. There is a lack of documentation on pathognomonic or specific skin lesion diagnostic of COVID-19. Out of the varied clinical manifestations, nearly one-fourth were related to vascular pathology, followed by a maculo-papular rash. For convenience, we have broadly classified the cutaneous manifestations seen in moderate to severe cases of COVID-19 as vasculitic and non-vasculitic lesions. COVID digit, purpura, petechiae, ecchymoses, and livedoid pattern were included under vasculitic lesions. The non-vasculitic lesions includes emergency conditions such as adverse cutaneous drug reaction and erythroderma, and non-emergency conditions such as maculo-papular, and urticarial lesions.

Vasculitic manifestation

Vasculopathy in COVID-19 infection is a cutaneous eruption secondary to systemic coagulopathic consequences.

COVID toes/digits

COVID toes^[9] are vasculopathy lesions that present as erythematous to violaceous papules usually over the fingers and toes following exposure to cold. Generally, self-resolving however, recurrence is possible with repeated cold exposure. They are most likely because of Type I interferon-mediated complement activation and resultant micro-angiopathy.

We had one case of finger involvement in a patient with severe COVID-19 infection with raised inflammatory markers. With treatment, there was complete healing of the digit.

Livedoid pattern

Livedo refers to a vascular reaction pattern that manifests as “mottling” of the skin, with a net-like/reticular discoloration of the skin on the trunk and extremities, and it presents usually with tender purpuric macules or papules and the borders are angulated or retiform.^[5,10] It usually heals with ivory scars, but if persistent, leads to ischemia and necrosis.

Petechiae, purpura, and ecchymosis

Petechiae, purpura, and ecchymosis may be cutaneous eruptions secondary to systemic vascular consequences caused by COVID-19 infection or drug-induced.^[11-13] In our patients, these vascular lesions occurred within 3 days of onset of the febrile illness. Most of them are because of disease activity itself, but five cases gave a history of OTC drug intake before the onset of purpura, which suggests that they could be drug-induced. In four cases, purpura was transient, raising a doubt whether they are because of disease or drug.

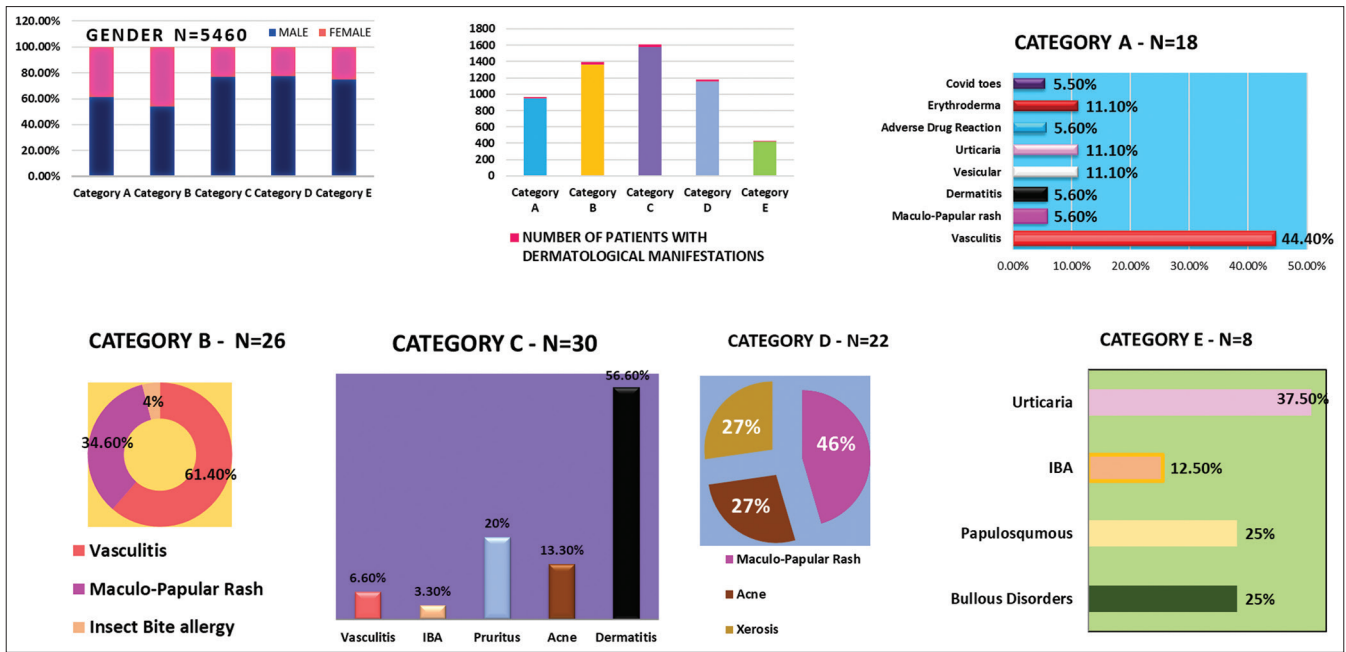


Figure 1: Gender distribution and clinical manifestations in COVID-19



Figure 2: Cutaneous manifestations of COVID-19 patients in Category A: (a) COVID digit, (b) Vasculitic papules, (c) Purpura, (d) Ecchymosis, (e) Maculo-papular rash, (f) Urticaria, (g) Vesicular eruption, and (h) Drug reaction

Non-vasculitic manifestations

Non-vasculitic skin manifestations including erythema multiforme-like lesions have been documented.^[14]

Maculo-papular rash

According to some authors, maculo-papular rash^[7,8] was the most common cutaneous manifestation in COVID-19,

Table 1: Comparison of salient features of COVID manifestations with other studies

Author	Schwartz et al. ^[6]	Freeman et al. ^[7]	Galvan Casas ^[4]	Jindal et al. ^[8]	Current study
Type of study	Prospective	Prospective	Prospective	Meta-Analysis	Prospective
N	88	716	NA	NA	5460
Skin findings	18 [20.4%]	171 (23.88%)	375	458	104 (1.90%)
Categorization	No	No	No	No	Yes
COVID digits	-	-	-	-	0.9%
Vasculitic	-	19.4%	19%	15.1%	24%
Livedo	-	-	6%	4.4%	-
Vesicular	5%	11%	9%	15.3%	1.9%
Maculo-papular	78%	22%	47%	42.5%	19.2%
Urticaria	17%	16%	19%	17.9%	4.8%
Dermatitis	-	-	-	-	17.3%
Mortality	NA	NA	NA	NA	2.8%

which can be because of an immune response to viral antigens. Our patients had rashes from day 5 of fever to day 7. None developed beyond 10 days of onset of COVID symptoms. In those in whom the maculo-papular rash was secondary to a drug reaction, a rash appeared 2 days following drug intake and 1 day after the first symptom of COVID infection. The drugs implicated in our study were ivermectin and azithromycin, whereas azithromycin, lopinavir/ritonavir, and less commonly anti-malarials such as hydroxychloroquine was reported by Suchonwanit et al.^[18] One patient had a purpuric component, which might indicate “bleed into the rash” in those having thrombocytopenia. One of our patients with drug rash had peripheral eosinophilia. All these patients had fever during their illness.

Dermatitis

Foo et al. have described contact dermatitis because of frequent washing.^[15] In our study, there was worsening of the existing eczematous lesion, which became more pruritic. Dermatitis was seen in patients of Category C who had seborrheic dermatitis-like presentation.

Urticarial lesions

Urticaria when associated with systemic eosinophilia may indicate better outcome of COVID-19.^[16] Urticarial lesions are manifestations occurring because of IgE-mediated immediate Type I hyper-sensitivity immune response to viral antigens or drug haptens. Hydroxychloroquine^[17,18] is used for COVID therapies, which could be attributed to the cause of urticaria in some cases. In Category A, among all our patients with urticaria, pallor was more marked.

Vesicular (Varicella-like) eruptions

Vesicles or bulla occur as an immune response to any viral antigens. Varicella-like eruptions have been documented in COVID-19.^[17] We observed four patients with vesicles. The first patient was immediately started on tab acyclovir. From the next case onward, we waited for the lesions to

evolve. Our second case had new blisters on subsequent days with central umbilication and was treated as Varicella. The third and fourth cases were observed, and they did not develop any new vesicles and the lesions healed on their own over 5 days. They were probably vesicular eruptions of the COVID-19 infection.

Emergency conditions

Adverse cutaneous drug eruption

According to Lee et al., one in five patients with stage 3 and 4 COVID-19 experiences ADR.^[19]

In our study, there were two patients one with mild reaction and the other with severe reaction which progressed to erythroderma. Both recovered without sequelae.

Cutaneous manifestations of COVID due vascular pathology were the most frequently observed skin lesions in our study. They were seen in Category A and B, particularly in patients with co-morbidities. Based on our findings, vascular cutaneous manifestations may give clues to suspicion in undiagnosed cases and severity of the disease in diagnosed cases requiring early initiation of therapy and close follow-up. Urticaria and maculo-papular rash were transient and did not give any clue to the diagnosis or severity of the disease.

COVID-19 infection was very much prevalent in those on immuno-suppressant therapy. However, on treatment, they recovered completely. Recognition of skin features, especially in patients with darker skin phototypes, is important in proper assessment of patients. Cutaneous manifestations due to vascular pathology were the most common finding in severe COVID-19, indicating the important role of vasculitis.

Other findings

Leg ulcers worsened and bled more easily. Worsening of psoriasis in two patients was because of withdrawal of methotrexate. Bullous pemphigoid took a psoriasisiform course in one patient.

Mortality

There were three deaths in Category A who had severe disease and who developed ecchymosis. Although ecchymosis was frequently observed in Category A and B, the associated co-morbidities and age of the patient were attributed to the course of illness and disease outcome.

Conclusion

Cutaneous manifestations were observed in 1.9% of COVID-19 patients. Vasculitic manifestations were the most common cutaneous findings that correlated with disease severity and D-dimer values. If a patient develops vasculitic lesions during the course of illness, it is worth re-assessing the severity of disease and repeat inflammatory markers.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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