



COVID-19 VACCINATION & SKIN MANIFESTATIONS IN THE INDIAN REGION

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ABSTRACT

This review has detailed the dangerous pandemic through which millions of people across the globe suffered, i.e., COVID-19. Studies showed that it was affecting humans by using ACE-2 receptors. Researchers proved that the ACE-2 receptor shows its expression in keratinocytes and sweat glands. Hence, it is clear that the skin is a potential target for the infection. Hence, we conducted this review to learn about different clinical aspects and presentations due to this infection. We conclude that all clinicians showed basic knowledge about its etiopathology, clinical features, and severity for treatment aspects.

Keywords: COVID-19, ACE-2 Receptor, Severity, Clinical Features & Basic Knowledge.

INTRODUCTION

As we know, not more recently COVID-19, has hit the world population over more than 142 million people & have taken 3 million lives across the globe.¹ Henceforth, the disease was declared a pandemic by World Health Organization on March 11, 2020.^{2,3} Furthermore, by approaching to MAY 9, 2021 death ratio & disease ratio have been increased upto 3 million & 157 million respectively.⁴ Additionally, alone India was contributing around 95% of the cases then 93% with Southeast Asia & rest 50% were from rest of nations which brought us

to a figure with 30% global death.⁵ Many researches by then including India had concluded that , the virus was using angiotensin cobnverting enzyme-2(ACE-2) receptor to invade human cells.⁶ It is also well known from previous studies that ACE-2 receptors are widely present in human cells. ⁴ A study conducted in 2021 concluded that , ACE-2 receptors showed their expression in keratinocyte & sweat glands. Thus, suggesting that skin is a potential target for infection by SAR-COV-2 virus.⁷

CUTANEOUS FINDINGS

As we know from primary data that ,the incidence of cutaneous manifestations in COVID-19 disease has been found to vary across different parts of the world which ranged from an early chinese study that reported around 0.2% incidence rate & Italian study which reported around 20.4% higher rate of patients.^{8,9} Thus, it is classified into various ways by various different authors.

CLASSIFICATION

A. Galván et al. (2019) proposed a classification system based on their examination of 375 patients within the Spanish population, as documented in their study. The researchers were able to classify five unique categories of lesions, which includes as follows:-

1. Maculopapular Exanthem (47%)
2. Urticarial Eruptions (19%)
3. Acral erythema with vesicles or pustules (19%)
4. Other vesicular eruptions (9%)
5. Livedo or necrosis (6%).

Thus authors had concluded from his study that, there was a diverse indications of skin involved surfaced at discrete phases of the ailment's & it was also associated with different durations, degrees & consequences.¹⁰

B. Case series of 15 patients, the cutaneous symptoms were classified according to their etiopathogenetic origins which includes:-

1. Cutaneous Vasculitides,
2. Papulosquamous
3. Pityriasis Rosea
4. Measles-Like
5. Papulovesicular

6. Urticarial
7. Cutaneous Adverse Drug Responses (CADR).¹¹

Thus , the prevalence of skin manifestations was as high as 20.45%,

C. Study that analyzed the data from 46 papers with a combined total of 998 patients from nine different countries. The symptoms that most closely resemble chilblains include were as follows:-

1. Vesicular Lesions (6.4%)
2. Maculopapular Lesions (22.7%)
3. Chilblain-Like Lesions (40.2%)
4. Urticaria (8.9%)
5. Livedoid/Necrotic Lesions (2.8%)
6. Other Non-Classified Skin Lesions (19.8%) Are The Next Most Often Reported Symptoms.

At least 85 people have reported experiencing pain or burning, while at least 256 have said they have experienced itching.¹²

D. Freeman et al conducted a study & described dermatologic findings in 171 COVID positive patients from 31 countries & found most common morphologies that were as follows:-

1. Morbilliform (22%)¹³
2. Pernio-Like (18%)¹³
3. Urticarial (16%)¹³
4. Macular Erythema (13%)¹³
5. Vesicular (11%)¹³
6. Papulosquamous (9.9%)¹³
7. Retiform Purpura (6.4%).¹³

E. Klejetman & his colleagues described & concluded from his study , 6 different dermatological patterns that can be seen that are as follows :-

1. Maculopapular/Morbilliform¹⁴
2. Urticarial, Vesicular¹⁴
3. Chilblain-Like, Petechiae¹⁴

4. Purpura¹⁴
5. Livedoid¹⁴

F. Wang and Worswick & his colleagues further subdivided the cutaneous manifestations into various types:-

1. Viral Exanthem¹⁵
2. Urticarial¹⁵
3. Vesicular¹⁵
4. Chilblains/Chilblains-Like¹⁵
5. Non-Chilblains Vasculopathy-Related¹⁵
6. Pityriasis Rosea-Like¹⁵
7. Erythema Multiforme-Like¹⁵
8. Kawasaki/Kawasaki-Like Disease & Others¹⁵

PREVALENCE

Cutaneous manifestation	Prevalence
Chilblain-like lesions	14.3-72%
Maculopapular rash	5-70%
Urticarial lesions	7-40%
Vesicular lesions	3.77-15%
Livedoid-like lesions	6%
Petechiae/Purpura	3%

TABLE 1 : PREVALENCE WITH VARIOUS SKIN DISEASE.⁴

LIST CLINICAL CUTANEOUS FEATURES

1. Maculopapular / Morbilliform eruptions/Exanthema

It is one of the most common type. Studies conclude that , its presence ranged feom 5 to 70 % in various studies. It can be due to viral infection or any drug reaction. It is most common in middle –aged or elderly patients but also been described & with evidence in young patients.⁴

2. Urticarial Eruption

According to various studies, its prevalence ranged from 7 to 40% . They were found most commonly in middeel –aged patients . However, in few of the cases, it can occur without



any systemic symptoms also. It mainly involves trunk, extremities & face along with this, generalized eruption was also seen.⁴

3. Vesicular Eruption

Studies revealed that, this type of feature is not very commonly seen. Its prevalence ranged from around 3.77 to 15%. They were mostly occurred in middle-aged individuals which are predominantly present on trunk & extremities. They can be diffuse, polymorphic or localized, monomorphic in nature. It can occur before, during & after development of systemic symptoms. Furthermore, average duration of lesion was between 8 to 10 days.⁴

4. Chilblain/Chilblain-like/Pernio-like lesions ('COVID toes')

Studies have reported that, this type normally range from 14.3% to 72%. Furthermore, it has been observed that, these lesions manifest as plaques with erythematous to violaceous coloration on the acral region, predominantly on the digits of the hands and feet. These lesions were accompanied by sensations of pain and pruritus. Infrequently, they were correlated with vesicles, bullae, and pustules. The aforementioned lesions were frequently observed in individuals belonging to the age groups of children, adolescents, and young adults. The onset of these lesions occurred subsequent to the manifestation of systemic symptoms, with an approximate latency period of 1-3 weeks. Nevertheless, such occurrences are infrequently documented prior to the manifestation of systemic indications. The duration of the lesions was observed to be approximately 1 to 2 weeks on average.^{15,16}

5. Petechiae/Purpura-like lesions

Cutaneous manifestations of COVID-19 infection, which have been less extensively documented, were found to have a prevalence of 3% in a cohort of 277 patients in a study conducted in France for this type of skin manifestation. The appearance of lesions was observed either in a widespread manner or on the limbs following the emergence of COVID-19 symptoms and was concurrent with a severe presentation of the illness. The proposed pathogenesis of the disease entails either a thrombotic vasculopathy characterized by negligible inflammation or the buildup of complement proteins (C5b-9 and C4d) in the cutaneous microvasculature, sometimes concomitant with SARS-CoV-2

spike glycoproteins.¹⁶ The histopathological analysis of the petechial lesion revealed the existence of parakeratosis, dyskeratotic cells, papillary dermal edema, superficial perivascular lymphocyte infiltrate, and significant red cell extravasation without thrombotic vasculopathy. The analysis of the purplish-red skin lesions using histopathological techniques revealed the existence of thrombogenic vasculopathy along with necrosis of the epidermal and adnexal structures, interstitial neutrophils, and leukocytoclasia in a particular case. Thrombosis was detected in deep dermal vessels in the remaining two instances, concomitant with the presence of C5b-9 deposition within the vessel walls.¹⁵ In the analysis of petechial and purpuric lesions, it is imperative to take into account a range of differential diagnoses, including scurvy, drug-induced petechiae and purpura, and immune thrombocytopenic purpura triggered by COVID-19.^{16,17,18}

6. Livedo-like lesions

The occurrence of these lesions is infrequent in the COVID-19 disease, as evidenced by a study of 375 confirmed cases that reported an incidence rate of 6%. The distribution of these entities was predominantly observed on the trunk, flexor surface of the forearms, dorsal hand, and dorsal foot. The appearance of the lesions was observed to be concurrent with the initiation of the symptoms and was found to be prevalent among individuals belonging to the elderly demographic. The aforementioned lesions were linked to a grave ailment that exhibits the greatest fatality rate among cutaneous afflictions, approximately 10%. Livedo-like lesions can be attributed to hypercoagulable states that result in the occurrence of disseminated intravascular coagulation, macrothromboses, and microthromboses.¹⁶

7. Retiform purpura lesions

According to various past studies, this lesion normally occur most commonly over extremities & sacral /buttock area & also associated with COVID-19 disease.^{19,20}

8. Erythema Multiforme-like lesions

The lesions mentioned above typically appear within a period of 14–21 days after the onset of systemic symptoms. The dimensions of the lesions exhibited a decrease, their

dispersion was confined, and their form deviated from the typical manifestation of erythema multiforme. Oral corticosteroids were administered as a therapeutic intervention by the medical team. The histopathological features that were observed encompassed epidermal spongiosis, dermal vasodilation in conjunction with neutrophilic infiltration, perivascular lymphocytic infiltration, and extravasation of red blood cells.¹⁵

9. Oral lesions

Here, study conducted by Iranmanesh concluded that it contains features like phthous stomatitis, herpetiform lesions, candidiasis, vasculitis, Kawasaki- like, erythema multiforme- like, mucositis, drug eruption, necrotizing periodontal disease, angina bullosa- like, angular cheilitis, atypical sweet syndrome, and Melkerson–Rosenthal syndrome.²¹

10. Nail lesions

Study conducted in 2020 concluded that ,in two weeks following the onset of symptoms, a red band with a distally convex, half-moon shape was observed encircling the distal margin of the lunula in all fingernails. This band persisted & increased in width after one month. The manifestation of COVID-19 known as the "red half-moon nail sign" is a newly identified phenomenon. The authors have put forth a hypothesis regarding a localized microvascular injury that occurs in the distal subungual arcade as a result of the inflammatory immune response and procoagulant state.²²

11. Hair abnormalities

12. Other lesions (Pityriasis rosea like lesion , conjunctivitis with eyelid dermatitis , periorbital dyschromia, diffuse melanoderma , erythema nodosum).

13. Findings in Children (Similar to Kawaski syndrome)

14. Colour of skin

The inadequacy of visual depictions portraying cutaneous manifestations of COVID-19 in individuals with darker skin is a noteworthy issue that necessitates attention. In light of the observed racial disparities in COVID-19 infections and associated fatalities, it is crucial to ensure that all manifestations of the disease incorporate a diverse representation of individuals from various racial and ethnic backgrounds. This methodology has the

potential to facilitate timely identification of potential indicators, which may subsequently result in enhanced health consequences.²³

Lester et al. conducted a study wherein they analyzed 130 clinical photographs of skin lesions associated with COVID-19. The findings of the study revealed that the majority of the images, specifically 92% (120 out of 130), portrayed skin types I–III. In contrast, only a small proportion of the images, specifically 6% (7 out of 130), exhibited patients with type IV skin. The inability to classify 3 out of 130 cases, constituting 2% of the sample, was attributed to the exclusive representation of acral skin in the images. Clinical images representing skin types V or VI, as per the Fitzpatrick scale, were not available.²⁴

Dalal et al. conducted a study in North India that revealed that 12.7% of the patients (n = 13) exhibited dermatological manifestations. Among the participants, a total of 3 individuals (2.9%) manifested a maculopapular rash, 2 (1.9%) displayed urticarial lesions, and 8 (7.8%) subjects reported pruritus, albeit without any observable cutaneous manifestations.²⁵

Das et al. conducted a study in which they observed a group of individuals who displayed erythematous-edematous chilblains. The onset of this condition was preceded by a sensation of burning and tingling.²⁶

Sukhavasi et al. conducted a study wherein they observed cutaneous manifestations in 4.51% of 1,065 South Indian patients who tested positive for COVID-19. The predominant symptoms reported by the subjects were pruritus and urticaria, which constituted a quarter of the cases. Subsequently, vesiculopapular rash, acral erythema, maculopapular rash, irritant contact dermatitis, aphthous ulcer, herpes zoster, purpura, and other symptoms were also reported.²⁷

According to a study carried out by Goyal et al., individuals of Indian descent with type IV Fitzpatrick skin type were found to exhibit three instances of maculopapular erythema, urticaria, and herpes zoster.²⁸

CONCLUSION

Several skin manifestations of COVID-19 have been reported; however, additional work is needed to acquire more information. The discovery of segregation on the skin should prompt a discussion between physicians and patients concerning segregation and appropriate testing. All healthcare providers should be aware of these increasingly common COVID-19 cutaneous manifestations since they may be associated with disease severity, prognosis, or infectiousness.

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