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Review

Dermatological Repercussions in the Storm of COVID-19

N. Sarat Anandh[1], Shivani Bhardwaj[2]*, Prachi Agrawal[2]

[1]P.G. Resident, [2]Assistant Professor

Department of Dermatology, Pacific Medical College and Hospital, Udaipur, Rajasthan, India

*Corresponding author Email: shivani00444@gmail.com

ABSTRACT

The current ongoing pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which was first isolated in Wuhan, China. The disease caused by this virus is called "corona virus disease-19" (COVID-19) which has spread far and wide since then. New research has shed light on the transmission, etiopathogenesis and symptomatology of this novel corona virus. Common symptoms include fever, cough, fatigue, dyspnoea and hypogeusia/hyposmia. Dermatological manifestations, a usual effect of viral infections, are being increasingly reported in patients with COVID-19 disease are seen preceding or concurrently with or after the systemic manifestations. Most commonly found skin manifestations are erythematous maculopapular eruptions, urticaria, livedo reticularis/racemosa-like pattern, purpuric "vasculitic" pattern, pseudo-chilblains, vesicular eruptions and alopecias. There have also been reports of cutaneous manifestations due to the use of personal protective equipments and increased hygiene measures such as contact dermatitis, erythemas, tinea infections, dry skin and exacerbation of pre-existing skin diseases. This review summarizes the display of COVID-19 and the consequence of its preventive measures on skin.

KEYWORDS: SARS-CoV-2, Gabrin sign, Cutaneous manifestations of COVID-19, Skin manifestation due to PPE and personal sanitising measures.

INTRODUCTION

SARS-CoV-2 also known as COVID-19 virus infection's first case was recorded in Wuhan, China, in the month of November 2019[1].Wuhan Municipal Health Commission, China, reported many cases of pneumonia in Wuhan, Hubei Province, in the month of December 2019[1].In the following months, COVID-19 having high rates of infectivity, low virulence and asymptomatic transmission has spread far and wide around the world[3]. In March 2020, the World Health Organisation announced COVID-19 as a pandemic[2].

Researches are being done to understand and classify the clinical features of SARS-CoV-2 infection. The most common symptoms are fever, anosmia, dysgeusia, cough, cold and breathlessness[4]. However, there have been many COVID-19 cases reporting with cutaneous manifestations ranging from pseudo chilblains, urticaria, maculopapular eruptions, vesicular eruptions, papulosquamous eruptions, purpura, and erythema[5,6].

The purpose of this article is to provide literature review of various cutaneous manifestations in COVID-19, post COVID-19 patients and because of undertaking the preventive measures to avoid transmission. This may also aid in identifying and diagnosingasymptomatic COVID-19 carriers which may aid in slowing down the spread of the virus.

Incidence and Prevalence

An initially regional epidemic has since rapidly spread to a global pandemic impacting at least 124 countries with significant morbidity and mortality and changing the lives of hundreds of millions of people globally. At the time of writing this article, COVID-19 has affected 178,837,204 people globally and still continues to infect many people daily. COVID-19 has a case fatality rate of ~2.16% globally. On 23rd June 2021 the total number of new cases globally was 296,106[7].

In India COVID-19 has affected 30,028,709 people, out of which 390,660 died due to severe illness caused by COVID-19[8]. Demographic determinants like increased population density, lack of access to basic amenities, migration, and elderly population, aggravated the COVID-19 infection in India[9]. The total number of new cases in India was 50,848 on 23rd June, 2021[8].

Vaccination has been found to be highly effective across all age group (more than 16 years) in preventing the transmission of COVID-19 infection and COVID-19 related hospitalisation, severe disease, and death. There is marked and sustained decline in COVID-19 cases after vaccination suggesting COVID-19 vaccine can aid in controlling the pandemic thus reducing the incidence of COVID-19[10].

Etiopathogenesis

COVID-19 pandemic is caused by novel coronavirus named SARS-CoV-2. Recent research from world health organisation suggest that the start of the outbreak resulted from a single point introduction by zoonotic transmission (bats or pangolins) or by introduction through a laboratory incident which was deemed unlikely[11].

The SARS-CoV-2 is transmitted via respiratory droplets, aerosols and faeces from person to person (95%) or through fomites to person (5%). After getting infected the person enters the asymptomatic phase.

Asymptomatic phase: After entering, the virus binds to host ACE-2 receptor and enters host cells through endocytosis or membrane fusion. Post membrane fusion, the virus enters the nasal epithelial cells in the upper respiratory tract then undergoes replication and formation of new viral components. The newly formed viral particles are transported to the cell membrane for exocytosis to the extracellular space by Golgi vesicles. The new viral particles are primed to occupy the adjacent cells as well as for providing fresh infective material for community transmission via respiratory droplets. The immune response is very limited during this phase. Even though the viral load is less the infected people are highly infectious. Even in the asymptomatic phase, the virus can be detected using nasal swab[12].

Symptomatic phase: Then the virus migrates from the nasal epithelium via the conducting airways and reaches the upper respiratory tract infecting the pulmonary alveolar epithelial cells; therefore the symptoms are presented in patients. The immune response is greater during this phase. Since the immune response is sufficient during this phase, most of the patients do not advance beyond this phase[12].

About 1/5th of the patients infected with COVID-19 have involvement of lower respiratory tract and progress to acute respiratory distress syndrome (ARDS). In this stage the pneumocytes release cytokines and inflammatory markers such as interleukins (e.g., IL-1, IL-6), tumour necrosis factor – α (TNF-α) and interferonλ (INF – λ). This leads to 'cytokine storm' which acts as a chemo attractant for Neutrophils, CD_4 helper T cells and CD_8 cytotoxic T cells. There is constant apoptosis due to viral replication and infection of adjacent cells leading to inflammation and diffuse alveolar damage. This eventually culminates into ARDS[12].

Moravvej *et al.* suggest that androgens may also play an important role in the severity of COVID-19 patients. It was noted that low total testosterone levels in patients with COVID-19 was associated with poor prognosis and severe illness in male patients while high levels were also associated with increased hospitalisation rates and need for supplemental oxygen. With this in mind, Moravvej *et al.* suggested that androgens have a dimorphic role in COVID-19 severity. Androgenetic alopecia (AGA) being a hyperandrogenic state can lead to increase in COVID-19 severity and hospitalisation rates[13]. This is known as "Gabrin sign". Dr. Frank Gabrin was the first American physician to die due to COVID-19. Dr. Gabrin suffered from androgenetic alopecia and long-term survivor of bilateral testicular cancer. Wambier *et al.* suggested the use of eponym "Gabrin sign" to visually identify patients who may be at higher risk for severe primary symptoms of COVID-19[14] while others have criticized the use of the eponym[15]. To confirm this hypothesis there is need for further studies in AGA patients with COVID-19.

COVID-19 AND SKIN DISEASES

In this review article, COVID-19-related maladies are being reviewed under the following categories:

1. Cutaneous manifestations of COVID-19

2. Cutaneous manifestations due to use of PPE and personal sanitising measures

1. Cutaneous Manifestations of COVID-19

Many skin manifestations were observed in COVID-19. The most commonly reported include acral lesions resembling pseudo-chilblains, erythematous maculopapular eruptions, vesicular eruptions, urticaria, livedo reticularis/racemose-like pattern, purpuric "vasculitic" pattern and other lesions including eruptive cherry angioma and herpes simplex-1 reactivation, erythema multiforme-like eruptions, telogen effluvium, flaring of pre-existing skin diseases and otherwise unspecified erythematous lesions. Most of these lesions may be due to a COVID-19 specific viral exanthem; however, some maybe due to the by-products of the thrombogenic and immune deregulatory effects of SARS-CoV-2[6].

Time of onset of cutaneous manifestations: The association

between COVID-19 symptoms and skin manifestations has been observed and studied. Sachdeva *et al.* reviewed 18 manuscripts and noted that in 12.5% of the patients, skin manifestations of COVID-19 were noted before the onset of primary symptom or COVID-19 diagnosis[3]. In another study 5.9% of cases showed manifestations before the primary symptoms, 56.8% cases show lesions along with the symptoms, while 37.3% showed manifestations after the primary symptoms[16] (Table 1). These manifestations may help in diagnosing COVID-19 and post COVID-19 skin diseases.

Locations of lesions: A study noted that the most common location of the skin manifestations was on the trunk (66.7%); however, 19.4% of patients had lesions over the extremities[1].

Healing time for skin manifestations of COVID-19: The skin manifestations of COVID-19 healed without any medical interventions. In all patients the lesions healed within 10 days[3].

Histological findings: Described in Table 3.

1.1. Erythematous maculopapular eruptions

Erythematous maculopapular eruptionsareone of the most

Table 1: Time of onset of various cutaneous manifestations[3,16]

Association between the skin manifestations and COVID-19	Manifestations
Before	Common: Acral lesions (pseudo-chilblains). Less Common: Erythematous maculopapular eruptions, urticaria and vascular lesions.
Concurrently with symptoms	Most Common: Erythematous maculopapular eruptions, urticaria and vascular lesions. Common: Acral lesions (pseudo-chilblains), vesicular lesions, non-specific erythematous lesions and cutaneous drug eruptions.
After	Most Common: Acral lesions (pseudo-chilblains), vesicular lesions, non-specific erythematous lesions and cutaneous drug eruptions. Common: Erythematous maculopapular eruptions, urticaria, vascular lesions.

Associations between skin manifestations and COVID-19 disease severity: There is little evidence to suggest that the appearance of skin lesions is related to disease severity[3,6,16] (Fig.1). In a study assessing 716 patients from 31 countries from the international registry, pernio-like lesions were seen in milder form of the disease whereas retiform purpura was noticed in critically ill patients[17].

Age and gender distribution of skin manifestations: Sachdeva et. al. noted that the mean patient age was 53.6 years, ranging from 15 days to 84 years of age. 38.9% of cases were males and 27.8% were females, and gender was not reported in the rest of the patients[3].

common cutaneous manifestations. These eruptions are most often seen in middle-aged patients and presented along with the other non-cutaneous symptoms, sometimes even before the diagnosis of COVID-19. Erythematous maculopapular eruptions are more commonly drug induced because of which it cannot be used as a COVID-19 diagnostic marker. These types of eruptions were seen in 21.3% patients in one study[6]. According to Casas *et. al.*, maculopapular eruptions presented in 47% of all cutaneous lesions[16] and in other study by Freeman et. al. these lesions were seen in 44% of the skin manifestations in COVID-19. This group of lesions is subdivided into macular erythema, morbilliform exanthems and papulosquamous lesions17 (Chart 1).

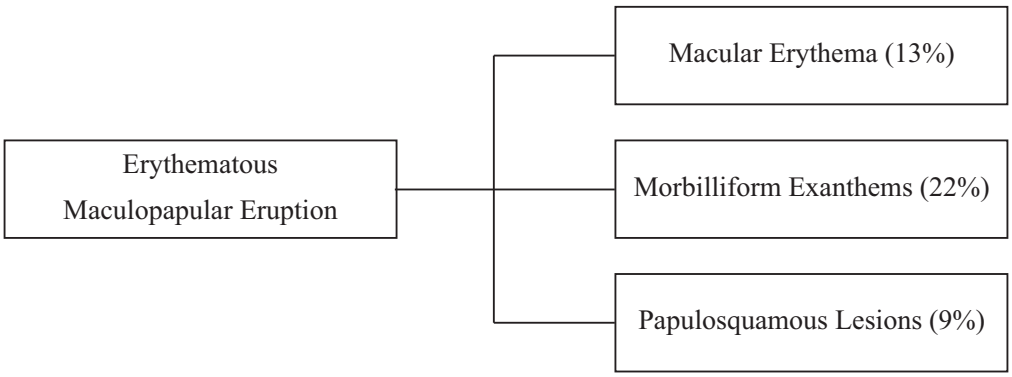

Chart 1: Classification of erythematous maculopapular eruption by Freeman *et al.*, in COVID-19.[17]

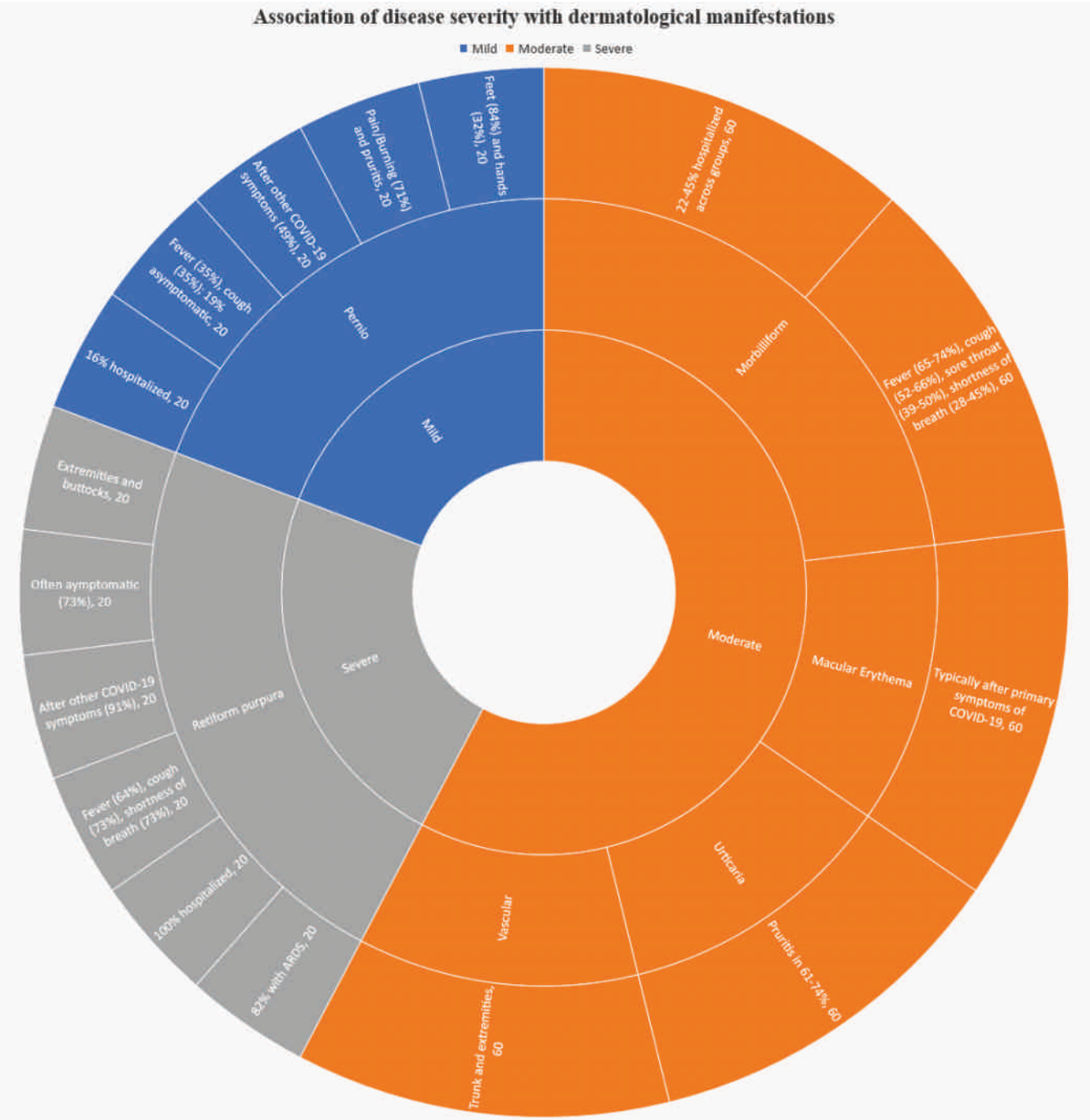

Figure 1: Association of disease severity with dermatological manifestations.[16]

1.2. Urticaria

Urticarial lesions were seen in 10.9% of the patients. Adults were most commonly affected (mean age, 38.3 years). Daneshgaran *et. al.* reported that these lesions appeared at the same time as of the non-cutaneous features. These lesions were thought to be drug induced due to which these lesions have very less significance as a COVID-19 diagnostic marker[6].

Algaadi, with a background of 'A systemic review in 2016' suggesting viral infections can trigger or cause urticaria, all the cases where possible drugs were suspected to cause urticaria were excluded and therefore presumed that all reported cases were triggered or caused by SARS-CoV-2. With this hypothesis, the review revealed that 55% of COVID-19 associated urticarial lesions were presented before or along with the classical symptoms of COVID-19[18,19] (Fig. 2). Furthermore, 10% of COVID-19 associated urticarial lesions presented prior to the classical symptoms. This was also seen in paediatric age group where the youngest was a 2-month-old girl baby who presented with only low-grade fever and urticarial lesions (nasopharyngeal swab test was positive). With these new findings, it is imperative for clinicians to consider diagnoses of COVID-19 in patients with asymptomatic urticaria with atypical COVID-19 presentation and early diagnosis in case of children with COVID-19 to curb the spread of SARS-CoV-2[19]. In one study, it was noted that angioedema may occur along with COVID-19 related urticaria[20]. However, to find the cause-effect relationship between angioedema and COVID-19 is difficult in case reports.

1.3. Livedo Reticularis/Racemosa-Like Pattern

Genovese *et al.* described livedo as a reticulate pattern of slow blood flow, with consequent denaturation of blood and bluish cutaneous discolouration[20,21](Fig.3). These lesions were classified into: (i) livedo reticularis and (ii) livedo racemosa[20] (Table 2).

The pathogenesis of livedo consisted of

i. Hyper congestion of the cutaneous venous vasculature due to restricted arterial inflow,

ii. Exaggerated venous dilation,

iii.Impaired venous outflow[21].

Shadi Khalil *et al.* reported that endothelitis was beginning to be a feature of COVID-19 and could have contributed to these lesions by producing vascular changes causing increased altered coagulation and vascular homeostasis. They also reported that COVID-19 associated coagulopathy was commonly seen in advanced and significant infection. It was hypothesized that health care workers may manifest cutaneous lesions more commonly than others due to difference in exposure, inoculation dose, or route of infection[21].

1.4. Purpuric "Vasculitic" Pattern

Table 2: Classification, clinical features, and pathophysiology as described by Giovanni *et al.*[20]

Livedo	
Livedo Reticularis	Clinical features: Develops as tight, symmetrical, lace like, dusky patches forming complete rings surrounding a pale centre. Pathophysiology: Cold induced cutaneous vasoconstriction or vascular flow disturbances.
Livedo Racemosa	Clinical features: Large, irregular, and asymmetrical rings than seen in livedo reticularis. Pathophysiology: Most commonly associated with focal impairment of blood flow.

The onset of purpuric lesions in COVID-19 is highly suggestive of poor prognosis. These lesions are associated with the highest mortality rate due to COVID-19 than any other cutaneous manifestations. Purpuric "vasculitic" patterns are most commonly seen in elderly patients and patients with severe COVID-19 infection[20,22] (Fig. 4). These patterns suggest that COVID-19 virus caused dysregulated host inflammatory responses that caused vasculitic changes by direct endothelial damage. These lesions are very rare, only representing a very few numbers of cases, according to a review article by Giovanni *et al.*[20].

Purpuric lesions may present as

i.Generalised

ii.Localised in the intertriginous regions

iii.Arranged in an acral distribution[20]

Vasculitic lesions in COVID-19 have the potential to change

Figure 2: Diffuse urticaria noted on lower extremities in a COVID-19 positive patient[18]

Figure 4: Papular-purpuric lesion present in COVID-19 positive patient on left thigh[22]

Figure 3: Livedo reticularis seen in 34-year-old female health care worker. After 2 days from the onset of lesion, she developed primary symptoms of COVID-19[21]

Figure 5: COVID toes[23]

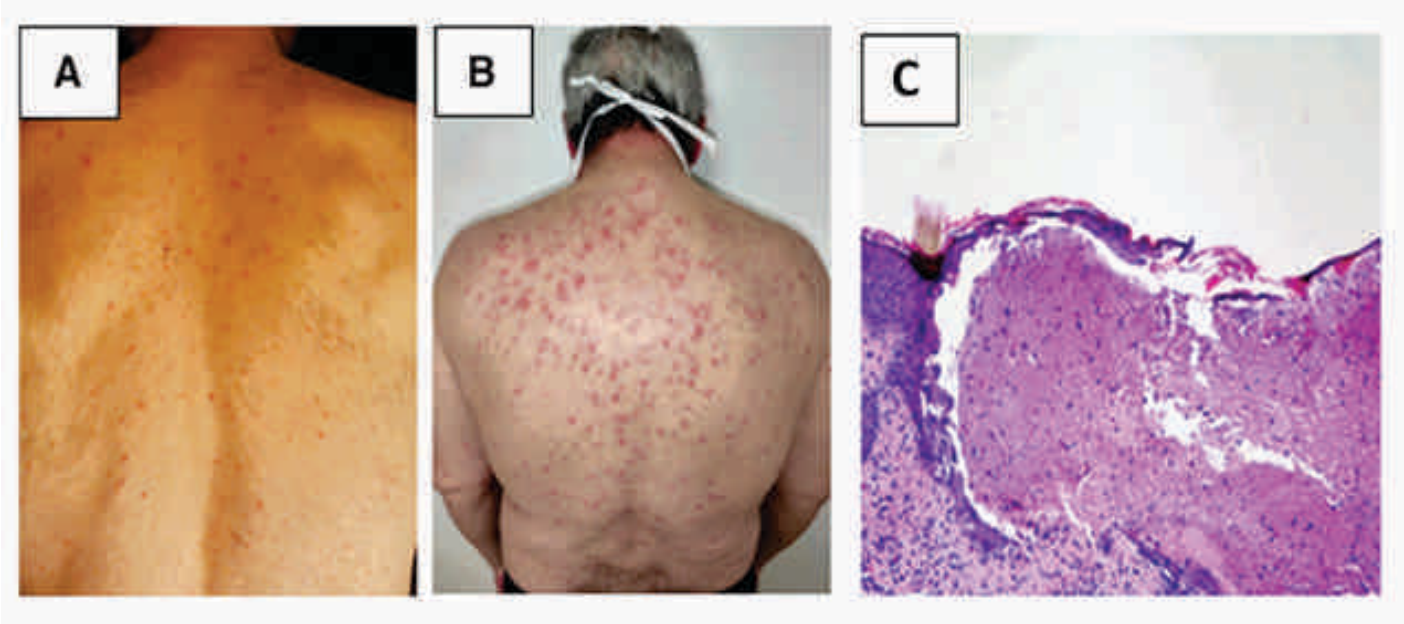

Figure 6: Vesicular lesions seen in COVID-19 pandemic. (A) Vesicular lesions, characterised by monomorphic on patient's back (B) Polymorphic vesicular lesions diffusely affecting patient's entire trunk (C) HPE showing intraepidermal vesicle containing scattered multinucleated and balloned keratinocytes, with mild acantholysis[25]

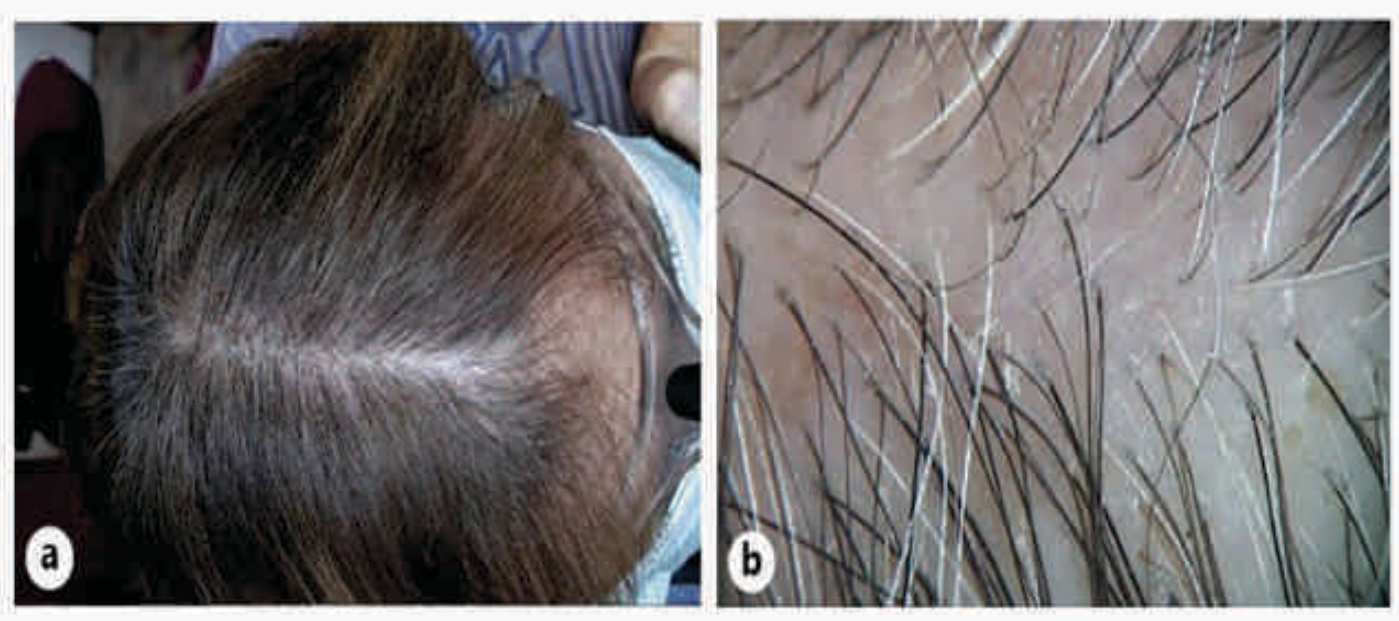

Figure 7: (a) Post COVID-19 telogen effluvium (b) Trichoscopic image showing several regrowing thin hairs and terminal hairs[32]

into haemorrhagic blisters. Extensive acute necrosis is seen in severe cases. These lesions may be associated with severe coagulopathies[20]. Dermoscopy of purpuric lesions showed multiple monomorphic papules with incomplete violaceous rim at the periphery. There is a central yellow globule in some papules while others had a central purpuric globule with an erythematous background[22]. Thus, these lesions can be used as a prognostic marker that can aid in appropriate management of the patient.

1.5. Pseudo-chilblains

Pseudo-chilblains, also known as COVID toes, acral lesions or pernio-like lesions is one of the most common type of skin lesion affecting young adult patients with a mild disease course, resolving disease or negative laboratory testing[6,23] (Fig. 5). This presents after the non-cutaneous COVID-19 symptoms. This could be due to rapid decrease in viral loads after initial symptoms. These cutaneous findings are more likely be due to COVID-19 and not due to primary pernio disease[6]. Galvan casas *et al.*, reported that the patients with acral lesions typically required fewer treatments than the other cutaneous manifestations such as livedo reticularis, erythematous maculopapular eruptions, urticaria and vesicular eruptions. The pseudo-chilblain pattern commonly appears late in the evolution of the COVID-19 disease (59% after other symptoms), while the others are seen along with the symptoms of COVID-19[16].

Pathogenesis of chilblain-like acral pattern can be due to:

i. Increased interferon release is induced by COVID-19 due to which cytokines are released causing higher inflammatory response

ii. Virus-induced endothelial damage

iii. Obliterative microangiopathy

iv. Coagulation abnormalities[20].

1.6. Vesicular eruptions

Vesicular eruptions are common dermatologic findings in COVID-19[6]. It is important to differentiate similar lesions from COVID-19 and other viral exanthems such as herpes virus or varicella zoster virus reactivation[24]. These eruptions were seen in 13% of the patients, most frequently seen in middle aged adults and it was presented after the onset of non-cutaneous symptoms. Vesicular lesions are more specific to viral exanthems, due to which it can be used as COVID-19 diagnostic tool[6].

The vesicular eruptions appeared in two patterns: the first is the diffuse pattern (75% of vesicular eruptions) with similarity to hand, foot and mouth disease, and the second is the localised pattern (25% of vesicular eruptions) resembling chickenpox but mostly with only trunk involvement[16,25] (Fig. 6). These lesions appeared most after 3 days of primary symptoms and spontaneously cleared after 8 days, without any scarring[20].

The histopathological examination of these lesions showed hyperkeratosis, epidermal atrophy, vacuolar degeneration, and dyskeratotic cells suggesting a viral etiology. The most distinctive features of vesicles include a "pomegranate-like" eosinophilic dyskeratosis, suprabasal non-ballooning acantholysis forming a unilocular vesicle, and absence of vasculitis. Real-time polymerase chain reaction (RT-PCR) assays for SARS-CoV-2 were negative for the contents of the vesicles[26].

1.7. Other COVID-19 and post COVID-19 dermatological manifestations

Erythema multiforme like Lesions: These are most commonly present in young patients and children[6] and patients admitted for the treatment of COVID-19[1]. In these patients, the mean time period between onset of primary symptoms and appearance of these lesions was 19.5 days. Typical target lesions are present in the back, face, and limbs, without affecting the palms and soles. Histopathological examination showed nonspecific findings. Most of these lesions are associated with oral findings such as palatal macules and

Table 3: Summary of histopathological examination of various cutaneous manifestation of COVID-19[20]

S.No.	Cutaneous Manifestations	Histopathological Findings
1.	Confluenterythematous/maculopapular/ morbilliform lesion	Superficial perivascular lymphocytic and/or neutrophilic infiltrate
2.	Urticaria	Vacuolar interface dermatitis associated with superficial perivascular lymphocytic infiltrate
3.	Livedo reticularis and Acral lesion (pseudo-chilblain)	Pauci-inflammatory micro thrombotic vasculopathy
4.	Purpuric "vasculitic" pattern	Leukocytoclastic vasculitis, severe perivascular neutrophilic and lymphocytic infiltrate, presence of fibrin and endothelial swelling
5.	Vesicular lesions	Prominent acantholysis and dyskeratosis associated with unilocular intraepidermal vesicles in a suprabasal location

petechiae[1].

Oral mucosa lesions: Painful ulcers and blisters (desquamating gingivitis) can be found in the oral cavity. Palatal macules and petechiae can also be seen in few cases[1,26].

Adverse cutaneous drug eruptions:

i. Hydroxychloroquine (HCQ): Hydroxychloroquine is an antimalarial drug which also has anti-inflammatory and immunomodulatory functions. Its use in short term treatment of COVID-19 is debatable. HCQ may cause adverse cutaneous drug eruptions. (ACDRs). The ACDRs can present as lichenoid, urticarial, exanthematous, generalized pustular figurate erythema, HCQ induced pruritis, acute generalised exanthematous pustulosis, mucocutaneous dyspigmentation, Stevens – Johnson – like eruptions and flaring of pre-existing psoriasis[1].

ii. Azithromycin: Azithromycin is used commonly all over the world and has adverse reactions such as fixed drug eruptions, Stevens – Johnson syndrome, drug reactions with eosinophilia and systemic symptoms (DRESS), hypersensitivity syndromes, etc[1,27].

iii. Remdesivir: It is a monophosphoramidate prodrug of adenosine analog. ACDRs can present as itching and swelling of the face, tongue, and throat. Gül analysed two studies in which skin lesions were found in 7% COVID patients being treated with Remdesivir and the same was discontinued in 2 cases out of 200 cases due to cutaneous adverse effects in one study and while skin lesions were seen in 9% of the cases treated with invasive ventilation and 5% of cases with non-invasive oxygen support in another study[1].

The crucial part in the management in these conditions is discontinuation of the offending drug and providing the appropriate treatment according to patient's condition with supportive care[1].

Pityriasis rosea: These lesions were rarely observed. It was noted that the number of cases of pityriasis rosea might be under-reported since many of these lesions could have been reported in other categories[6]. Further studies are required to assess whether these lesions are due to SARS-CoV-2 or are drug induced.

Alopecia: Hair loss is thought to be one of the most common effects of any febrile states, stress, drugs, hormones, organ dysfunction and nutritional deficiency[28]. In COVID-19 pandemic, there is increased incidence of alopecia in post-COVID-19 patients manifesting as androgenetic alopecia, anagen effluvium and telogen effluvium. Telogen effluvium is the most common post-COVID-19 manifestation in alopecias[29]. (Table 4).

Telogen effluvium (TE) is characterized by diffuse hair shedding few months after a stressor, and COVID-19 infection is possibly one such stressor, not only causing severe physical and physiologic but psychological and social stress[30]. In a study, the patients presented with increased hair loss following SARS-CoV-2 infection. All the patients were female, with no previous history of hair loss. Some patients from the study had milder disease while some had severe disease requiring hospitalisation. The duration of onset varies from weeks to months after the infection. With absence of any signs and symptoms of other causes and along with the recent history of COVID-19 recovery, the patients can be diagnosed with COVID-19 associated telogen effluvium[31]. In another study, the trichogram showed different telogen/anagen ratio depending on the time of onset and visit to the dermatologist. On observing the patients who presented to the dermatologist 3 months after COVID-19 cure had telogen rate of < 20%and regrowing hair which suggested TE in regression[32] (Fig. 7). In light of these new findings, SARS-CoV-2 infection should be suspected in patients presenting with acute TE.

According to a case report, a patient was hospitalised for the primary symptoms due to COVID-19, later developed urticarial and erythematous maculopapular eruption on the extremities along with moderate hair loss 10 days after admission. With no known allergy to any of the prescribed medications, the eruption was diagnosed as COVID-19 associated cutaneous manifestation and the sudden hair loss as COVID-19 related anagen effluvium. The cause of hair loss was hypothesised as immune dysregulation due to COVID-19[33].

2. CUTANEOUS MANIFESTATIONS DUE TO USE OF PPE AND PERSONAL SANITISING MEASURES

Due to heightened use of personal protective equipment (PPE) (such as masks, gloves, face shields and gowns) and increased sanitisation measures such as washing (face and hands) and use of disinfectants during the pandemic to avoid contracting the virus caused hyperhydration (by PPE), increased friction, epidermal barrier breakdown and contact reactions. This further led to aggravation of existing skin lesions and new cutaneous manifestation in the form of contact and pressure urticaria, contact dermatitis, pigmentation of the nasal bridge, dryness of the skin, erythemas and papular eruptions (Table 5)[1,35,36].

2.1. Skin manifestations due to personal protective equipments

It is majorly caused due to extended usage of PPE (such as goggles and face masks). The clinical manifestations are burning, itching, stinging, contact dermatitis, urticarial lesions, and aggravation of the pre-existing diseases. This study pointed out that more than 30% of the health care workers had complaints of acne, facial itching, and other eruptions due to prolonged wearing of masks[36].

In another review, the authors found prolonged wearing of masks and goggles were associated with aggravation of pre-existing acne vulgaris. They hypothesised that rupture of comedones due to pressure and friction, occlusion of the pilosebaceous duct and microcirculation dysfunction due to long-term pressure and humid environment (which can be a

Table 4: Demographic and clinical details of alopecia observed in post-COVID-19 patients

Article and Year	Number of patients, age, Gender	Suspected or Confirmed COVID-19	Severity of COVID-19	COVID-19 Manifestations	Bedside test	Diagnosis
Hailey Olds, *et. al.* (2021)[30]	Total Population:10 patients Age, median (range): 48.5 (28-62) 1 Male (10%), 9 female (90%)	Confirmed = 10/10 (100%)	Mild to Moderate: 3 patients Severe: 7 patients (requiring hospitalisation)	Diffuse hair loss and thinning	Hair pull test – Positive in 4/10 patients Negative in 2/10 patients Could not be in 4/10 patients performed due to limitations.	Telogen effluvium
Karolina Mieczkowska, *et. al.* (2020)[31]	Total Population:10 patients Age, median (range): 55 (38-68) 0 Male (0%), 10 female (100%)	Total Confirmed =10/10 (100%)	Mild: 6 patients Moderate: 0 patients Severe: 4 patients (requiring hospitalisation)	Noncicatricial hair loss, pronounced thinning along the frontal hairline. One patient had global loss of hair volume	Hair pull test – Positive in 3/10 patients (30%) Could not be performed in 7/10 patients due to limitations.	Telogen effluvium
Alfredo Rossi, *et. al.* (2021)[32]	Total Population:14 patients Age, median (range): 49 (23-64) 3 Male (25%), 12 female (75%)	Confirmed = 14/14 (100%)	Mild: 10 patients Moderate: 4 patients (requiring ordinary hospitalisation) Severe: 0 patients	Acute hair loss	Hair pull test – Positive in 7/14 patients Negative in 7/14 patients	Telogen effluvium
Michela Starace, *et. al.* (2021)[34]	Total Population:67 patients Age, median (range): 46.5 (28-61) 7 Male (10.4%), 60 female (89.6%)	Confirmed = 67/67 (100%)	Mild: 33 patients Moderate: 28 patients Severe: 6 patients (requiring hospitalisation)	Acute hair loss (62.7%), Itching, burning sensation, pain or paraesthesia of scalp along with acute hair loss (37.3%)	Data not available	Telogen effluvium (42 patients) Telogen effluvium and trichodynia (25 patients)
Mohammed Shanshal (2020)[33]	Total population: 1 Age: 35	Confirmed	Severe (requiring hospitalisation)	Urticarial lesions, erythematous	Hair pull test – Positive	Anagen effluvium

Table 5: Cutaneous manifestation of PPE and personal hygiene measures[1]

Protection Type	Personal protective equipment		Personal hygiene measures
Protection agents	Masks, goggles and face shields	Masks, goggles, gowns, gloves	Disinfectants, soaps, frequent washing
Diseases	○ Pressure injury ○ Pressure urticaria	○ Contact dermatitis ○ Itching ○ Exacerbation of pre-existing skin diseases ○ New skin disease	○ Contact dermatitis ○ Itching ○ Exacerbation of pre-existing skin diseases ○ New skin disease

good environment for bacterial proliferation) could have been the trigger for aggravating acne vulgaris. It was also noted that exacerbations were also reported for seborrheic dermatitis[1].

The use of protective hats could induce pruritus and folliculitis or exacerbate seborrheic dermatitis. Macerations and erosions could have been the cause for contact dermatitis, in case of gloves[36].

Prolonged use of protective equipment will produce sweaty, humid and warm environment in the skin folds. This could lead to secondary superficial fungal infections such as tinea corporis, tinea cruris and tinea manuum/tinea pedis[37].

Pompholyx or vesicular eczema may be caused due to prolonged occlusion of gloves and rubber boots. These lesions present as small vesicles on both hands and/or feet. These manifestations may be associated with itching, tingling, or burning sensation[37].

2.2. Skin manifestations due to increased personal hygiene measures.

Excessive washing or disinfectant use in patients and as well as in health care workers is the major cause for impaired epidermal barrier breakdown, irritation being the root cause for the development of contact dermatitis. Allergy, low humidity, frequency of hand washing or sanitizer use, wet work, glove use and duration of PPE use were important risk factors in the manifestation of contact dermatitis[36].

In case of face, frequent face washing, or cleansers use may cause contact dermatitis[36]. Since hand hygiene is extremely important in COVID-19 pandemic, the frequent use of disinfectants such as (60%-80% alcohol, chlorine-based disinfectants, peroxyacetic acid and chloroform) may cause irritant contact dermatitis[1,36].(Fig. 8). The cutaneous manifestations of irritant contact dermatitis can present as erythema, papules, vesicles, and dry skin which are mostly associated with itching[37].

Allergic contact dermatitis commonly occurs due to the atopic diathesis. The development of contact allergy to an allergen requires sensitisation on first contact and is followed by elicitation of the inflammatory response after the secondary exposure to the allergen[38]. The lesions may present as eczematous erythema and is seen only at the area of contact which can be well defined and associated with swelling, pruritis and stabbing pain. The most common hygiene ingredients in atopic diathesis are preservatives, surfactants, and antimicrobial ingredients. The usage of latex gloves, nitrile gloves can also lead to ACD due to latex and rubber sensitisation. In sub acute and chronic stages, the lesions may manifest with scaling, crusting and lichenification. In severe cases, it can present as papules, vesicles or even erosions. These lesions can become secondarily infected in some cases[37].

Long *et al.* noted that the usage of alcohol-based hand sanitizers with moisturizers has the least sensitizing and irritant prospects[37]. For the prevention of hand dermatitis, usage of products which lack common allergens, (Table 6) usage products with added moisturizers and application of moisturizers (one fingertip unit per hand) immediately after washing hands or before wearing gloves should be advised to the patients at risk of developing contact dermatitis[38].

CONCLUSION

COVID-19 being a multispecialty concerning disease, the collective knowledge and effort of the entire medical fraternity is required to treat and cure this malady. COVID-19 and its relationship with dermatology can aid doctors in early diagnosis of SARS-CoV-2 in case of asymptomatic patients, especially in India, being the 2nd most populated country in the world. Furthermore, understanding the post-COVID-19 effects and the consequences of prolonged personal protective equipment use and increased personal hygiene measures could help physicians in counselling and reassurance, thereby reducing the psychological distress to the patients. The purpose of this article is to provide awareness by literature review as COVID-19 cases increase day by day, the risk of developing these manifestations will likely continue in the near future.

Table 6: Allergens commonly encountered with regular hand hygiene[38]

Gloves	Soaps, synthetic detergents, and antiseptics		Hand sanitizers
I. Latex II. Rubber accelerators • Thiurams • Carbamates • Diphenylguanidine • Mixed dialkyl thioureas • Benzothiazoles	III. Fragrance IV. Surfactants • Cocamidopropyl betaine • Cocamide diethanolamine • Decyl glucoside • Dimethylaminopropylamine • Oleamidopropyl dimethylamine	V. Preservatives • Dimethyloldimethyl hydantoin • Diazolidinyl • Formaldehyde • Iodopropynyl butylcarbamate • Imidazolidinyl urea • Isothiazolinones • Quaternium-15	• Fragrance • Benzoates • Cetylstearyl alcohol • Tocopherol

Figure 8: (a) Facial erythema and papules in a patient who disinfected her face with 60% ethanol and used protective facial mask for 6 hours a day. (b) Hand dermatitis due to excessive hand washing as a preventive measure during COVID-19 pandemic to avoid transmission[36]

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