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Unveiling the Dermatological Manifestations of COVID-19 Infections

Sankalp Khanke [a≡], Sanket Bakshi [a≡] and Sandip Mohale [b*#]

[a] Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Wardha–442001, India.
[b] Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Wardha–442001, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: There have been over 86 million global confirmed cases to date, and the disease is known to have a 2.2% case fatality rate, having claimed over 1.87 million lives. They were initially regarded as a purely respiratory disease with symptoms of viral pneumonia such as fever, fatigue, dry cough, and lymphopenia. The widespread coronavirus disease is aimed at the Arial route of the tramsmission. Furthermore, the constant mutations in the virulence factors of the virus lead to the effectiveness of the treatment regimens. Covid-19 disease is mainly known to be a pulmonary infection, giving rise to pulmonary fibrosis, focuses and leads to severe pneumonia and ulyimately gives a fatal result iof not treated promptly. The pulmonary but extrapulmonary manifestations of this disease are also seen—cardiovascular, renal, nervous and dermatological, and immune system. The exact pathogensis and the etiology of the extra pulmonary manifestation of covid to the cutaneous prognosis are not yet well known. The virulence factors, the antigens of the virus that exacerbate the dermatological symptoms. The virus causes dermatological symptoms in urticarial rashes, eczematous infections, and mucocutaneous depositions. The exact mechanisms of the disease's progress to the dermatological variant are not known; however, this review will concentrate on the cutaneous manifestations of Covid-19 disease and the variant nature of the

[≡]MBBS Student;
[#]Associate Professor;
**Corresponding author: E-mail: sandipmohale@yahoo.com;*

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Keywords: COVID-19; coronavirus– COVID-19; skin manifestations; skin – pathology; systematic literature search; disease severity; mortality; prognosis.

1. INTRODUCTION

The virus utilised the angiotensin converting enzyme-two ACE-2 receptor to infect human cells, which is demonstrated differently in different human organs. ACE-2 receptors are abundantly expressed in keratinocytes and then in sweat glands,, according to "Xue et al.," suggesting that the skin is the vulnerable site for infection by the coronavirus. The numerous cutaneous presentations of corona disease, their clinical importance, and the therapy plan for these manifestations are described in this study. The gripping infection Covid-19, known initially as 2019-nCov, has been dubbed by the International Committee on Virus Taxonomy (ICTV) as a rapidly spreading pandemic. It is an upcoming acute respiratory illness, and it mainly transmits by the respiratory tract, through droplets, resp. secretions, and direct contact [1]. The virus has been demonstrated to transmit by resp. Droplet Droplets membranes exposure by gomites & by aerosols and is classified in the subgroup beta COVID as a membethe r of the Coronaviridae family. The RNA of SARS-CoV2 was also seen in the stools of Covid-19 infected sufferers . The outcome of this research established the hypothesis that *SOD3*/*ATF4*-associated antioxidants that is particularly in the pulmonary will function in synergy [2]. This type of coronavirus has a polymorphic nature. This virus is enveloped with +ve sense ssRNA & is a member of the coronavirus family.Cells are infected by the virus binding to the angiotensin converting enzyme 2 ACE2 receptor present on the cell's surface. COVID-19 is mostly transmitted through the lungs, with manifestation varying from flu-like features which are mild to features like hazardous pneumonia and fatal respiratory distress. 9 This disease is mostly seen as producing fever & respiratory problems, but it is also seen linked to a variety of extrapulmonary symptoms, including dermatological indications [3]. There have been over 86 million global confirmed cases till date, and the disease is known to have a 2.2% case fatality rate, having claimed over 1.87 million lives. Initially,y having was regarded as a purely respiratory disease with symptoms of viral pneumonia such as fever, fatigue, dry cough, and lymphopenia. The widespread coronavirus disease is aimed at the Arial route of the tramsmission. Furthermore, the constant mutations in the virulence factors of the virus lead to the ineffectiveness in the treatment regimens. Covid-19 disease is mainly known to be a pulmonary infection, giving rise to pulmonary fibrosis, focuses and leads to severe pneumonia and ulyimately gives a fatal result if not treated promptly. Not only pulmonary but extrapulmonary manifestations of this disease are also seen. Cardiovascular, renal, nervous dermatological, and immune systems. The exact pathogensis and the etiology of the extra pulmonary manifestation of covid to the cutaneous prognosis are not yet well known. The virulence factors, the antigens of the virus that exacerbate the dermatological symptoms. The virus causes dermatological symptoms in urticarial rashes, eczematous infections and mucocutanous depositions. The exact mechanisms of actions of the disease progress to the dermatological variant are not known. However, this review will concentrate on the cutaneous manifestations of Covid-19 disease and the variant nature of the infection. The widespread coronavirus disease is aimed at the Arial route of transmission. Furthermore, the constant mutations in the virulence factors of the virus lead to ineffectiveness in the treatment regimens. Covid-19 disease is mainly known to be a pulmonary infection, giving rise to pulmonary fibrosis, focuses and leads to severe pneumonia and ultimately gives a fatal result iof

not treated promptly. Not only pulmonary but extrapulmonary manifestations of this disease are also seen. Cardiovascular, renal, nervous dermatological, and immune systems. The exact pathogensis and the etiology of the extra pulmonary manifestation of covid to the cutanenous prognosis are not yet well known. The virulence factors, the antigens of the virus that exacerbate the dermatological symptoms. The virus causes dermatological symptoms in urticarial rashes, eczematous infections, and mucocutanous depositions. Furthermore, evidence is mounting that COVID-19-related skin symptoms are exceedingly polymorphic. Keratinocytes have much greater levels of ACE2 expression compared to other cellular parts in the dermis, for instance, fibroblasts and melanocytes. It is confirmed by individualistic ss (RNA) sequencing information that revealed that keratinocytes account for 97.37 percent of the total “ACE 2” +ve dungeon in dermis, after the sweating gland dungeon, which is of total 2.63%. The significant extensive appearance of “ACE two” [4] appears as microorganisms that can contaminate other man cells along with pleura , potentially leading to new clinical symptoms.

2. METHODOLOGY

Composition exploration was run using OVID, PubMed, and Google search engines for indigenous and review articles issued at the beginning of the ongoing COVID-19 epidemic afterward to April 20, 2020. Forage words such as (COVID-19), (2019-nCoV), (SARS-CoV-2) & (coronavirus) are utilized in union with (skin), (dermatology), (cutaneous), (urticaria) and (rash).

3. RESULTS

The most general dermatological appearance in “COVID-19” seems to be a widespread macular or maculopapular exanthem, with 36.1 percent (26/72) of individuals having such lesions on their skin. 34.7 percent (25/72) [5] of individuals had a papulovesicular rash (blisters). Urticaria was seen , with nine point seven percent “seven out of seventy two” diseased who were reported, and a tender purple-red pastule that may or may not contain vesicles was noticed in fifteen point three percent diseased “eleven out of seventy-two.” Finally, two-point eight percent (2/72) of the patients had life do reticulates wound, while one diseased (one point four percent) had petechiae. In (67/72)cases, the lesion site was described; most were located at hands, feet & trunks. Lesions on the trunk were found in 69.4 percent (50/72) of patients [6]. In addition, 19.4 % of diseased (14/72) had skin symptoms at their feet & hand. The patient's onset of cutaneous lesions ranged from 3 days before “Covid-19 ” identification to thirteen days following the confirmation. Within case’s studied, 12.5 percent (9 / 72) of diseased had skin lesions by the time of confirmation of the beginnings of “covid - 19” features, 69 . 4 %(50/72) had cutaneous manifestations following the start of pulmonary features or the confirmation of covid - 19. In 18.1 percent (13/72) of patients, the onset of a cutaneous lesion was not reported. 74.0 percent (37/50) of the 49 patients who had lesions within seven days of the beginning of pulmonary features or “COVID - 19” confirmation developed skin manifestation in seven days, while six percent reported manifestation following seven days. Out of the total cases, 50 reported healing times, 100% Healing of cutaneous lesions was recorded by patients, with healing durations ranging from a few days to a few weeks. (25/50). (2.0 percent) [7].

4. DISCUSSION

The vigorous spread of the Covid-19 pandemic has affected almost every sector in the community and the medical fraternity. While many countries have been facing the consequences of this insisted state of lockdown and medical burdens due to the pandemic, India is suffering under the wrath of the widespread of this Covid-19 virus. The said pandemic has recently taken a general aggressive course, resulting in an increased number of cases succumbing to the pathogenesis of this disease. The rapidly elevating graph of the fatalities is observed due to the extra-pulmonary advancing ability of the coronavirus infection. In the cases presenting with severe Covid-19 infection, almost 5% of patients are seen progressing to the pathology known as multi-organ dysfunction syndrome [MODS]. The COVID19 infection has been recorded to exhibit a broad range of manifestations from asymptomatic to severe [5]. In general, a high rate of patients are asymptomatic, and the ones with mild infection exhibit the common cold manifestations, fever, dry cough, and myalgia [5] and show a favorable prognosis. Healthcare professionals are working tirelessly and honoring their services towards the general population, despite the threat of getting infected. Worse outcomes have been observed in middle-aged and elderly patients with primary chronic diseases. Especially, CVDs, diabetes,

obesity, thyroid abnormalities, renal diseases, and chronic respiratory diseases, among others, who, therefore, had poorer prognoses and comparatively little chances to recover successfully. COVID-19, mainly in severe cases, can progress as a severe condition with hypoxemia and dyspnea and could develop as ARDS, one week after the onset of the illness. In addition to the lungs, the virus has been known to cause detriment to other organs such as the kidneys, liver, heart, and body systems such as nervous and hematological, and induce multiorgan failure [8].

The blood biochemistry indices give an idea about the disease severity in COVID-19 infection. When compared to healthy individuals, patients infected with SARS-CoV-2 showed a marked increase in the serum concentrations of interferons (IFN), tumor necrosis factor-α (TNF-α), interleukins like IL-1β, IL-2, IL-6, IL-7, IL-8, platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF) among others pro-inflammatory mediators [9]. Patients have also been known to present with hypoalbuminemia, lymphopenia, leukopenia with leukocytosis, and an increase in LDH, AST, ALT, bilirubin, and especially D-dimer. Another high mortality risk factor in COVID infected patients was a high neutrophil-to-lymphocyte ratio (NLR) [10]. In addition to this, activation of the complement system leading to cytokine storm that results in inflammatory cells infiltration, amplified and poorly regulated immune responses, and impaired coagulation in SARS-CoV2 infection has been known to induce multi-organ failure in the patients. Counteracting effects such as these hinder the complete obliteration of the virus and pave the way for opportunistic pathogens to cause secondary infections, thus resulting in a sepsis-like state, which was recorded in 17% of patients, 65% of whom have worsened and succumbed to the illness. More significant increases in serum concentration of several pro-inflammatory mediators brought on by the cytokine storm have been recorded in the patients admitted to the ICU, which directly correlates with the severity of the disease [11]. Therefore, there is a dire need for evaluation of viral sepsis and multiple organ failure scores in COVID-19 patients, and further information about the precise mechanisms of pathogenesis of sepsis caused by the novel coronavirus needs to be computed to increase the clinician's knowledge facilitating their determination of the clinical characteristics of viral sepsis and the identification of the risk factors more accurately so that the mortality and morbidity rate decreases and the outcomes become more favorable.

According to the survey conducted by Mehta and McAuley in March 2020, the majority of the cases admitted to ICU showed a dysregulated host response, wherein characteristic features such as hyper inflammation along with the alterations in the coagulation cascade and dysregulation in the immune response were noted, [12] that further contributed to multi-organ dysfunction syndrome (MODS), like occurs in the presentation of sepsis [13]. The cases are landing into septic shocks associated with the multi-systemic pathologies. The prognosis of such cases is substandard, considering the mysterious virulent characteristics of the recently discovered mutant strains of Sars-coV-2. Recently, Collange and Jacquard conducted a research study in France [14] in which they reported the cases showing extra-pulmonary pathologies associated with Covid-19 infection. These patients' examination, revealed multi systemic findings such as Mesenteric vascular ischemia resulting in bowel resection, thrombotic microangiopathy, and Anti-phospholipid syndrome. From the study done by the researchers of China and Iran, it was concluded that, Covid-19 virus, mainly in severe cases, in addition to respiratory impact, also involves different organs such as the heart, liver, and kidney, and it also affects hematological parameters and nervous system and induces multi-organ failure. An eminent arthor [15] reported that patients with COVID-19 disease present with some neurologic manifestations. The patients in his study did develop severe consciousness disorders. When investigated, MRI images suggested occurrence of the pathological entity called as necrotizing-hemorrhagic encephalitis. As long as its inception in dec. 2019 Wuhan, China, the world has been witness to the horrors of a new viral sickness produced by the novel severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). The WHO On [16] 11th march 2020, announced the illness 2019 coronavirus (COVID-19) & called it a pandemic.¨ As of May 9, 2021, the global burden of the disease has increased to greater than 1570 lakh cases and greater than 30 lakh mortality There have been over 86 million global confirmed cases till date, and the disease is known to have a 2.2% case fatality rate, having claimed over 1.87 million lives. Initially having being regarded as a purely respiratory disease with symptoms of viral pneumonia such

as fever, fatigue, dry cough, and lymphopenia. The widespread of this coronavirus disease is aimed at the arial route of the tramsmission. Furthermore, the constant mutations in the virulence factors of the virus leads to the in effectivnerss in the treatment regimens. Covid-19 disease is mainly known to be a pulmonary infection, giving rise to the pulmionary fibrosis, focuses and leads to severe pneumonia and ulyimately gives a fatal result iof not treated promptly. Not only pulmonary but extrapulmonary manifestations of this disease are also seen. Cardiovascular, renal, nervous and dermatological and immune system. The exact pathogensis and the etiology of the extra pulmonary manifestation of covid to the cutanenous prognosis, is not yet well known. The virulence factors, the antigens of the virus that exacerbate the dermatological symptoms. The virus causes the dematological symptoms in the form of urticarial rashes, eczematous infections and mucocutanous depositions. The exact mecahnisms of actions of the disease progresses to the dermatological variant is not known, however this review will concentrate on the cutaneous manifestations of Covid-19 disease and the variant nature of the infection. The widespread of this coronavirus disease is aimed at the arial route of the tramsmission. Furthermore, the constant mutations in the virulence factors of the virus leads to the in effectivnerss in the treatment regimens. Covid-19 disease is mainly known to be a pulmonary infection, giving rise to the pulmionary fibrosis, focuses and leads to severe pneumonia and ulyimately gives a fatal result iof not treated promptly. Not only pulmonary but extrapulmonary manifestations of this disease are also seen. Cardiovascular, renal, nervous and dermatological and immune system. The exact pathogensis and the etiology of the extra pulmonary manifestation of covid to the cutanenous prognosis, is not yet well known. The virulence factors, the antigens of the virus that exacerbate the dermatological symptoms. The virus causes the dematological symptoms in the form of urticarial rashes, eczematous infections and mucocutanous depositions.

In the Southeast Asia region, India accounts for 95% of cases and 93 percent of deaths, as well as 50% of global cases and 30% of global deaths. To infect human cells, the virus utilised the angiotensin converting enzyme-two ACE-2 receptor, that is demonstrated differently in different human organs. ACE-2 receptors are abundantly expressed in keratinocytes and then in sweat glands,, according to "Xue et al" suggesting that the skin is the vulnerable site for infection by the coronavirus. The numerous cutaneous presentations of corona disease, their clinical importance, and the therapy plan for these manifestations are described in this study. The gripping infection Covid19, originally known as 2019-nCov, has been dubbed by the International Committee on Virus Taxonomy (ICTV) as a rapidly spreading pandemic. It is an upcoming acute respiratory illness, and it mainly transmits by the respiratory tract, through droplets, resp. secretions, and also by direct contact The virus has been demonstrated to transmit by resp. droplets,mucous membranes exposure by gomites & by aerosols and is classified in the subgroup beta COVID as a member of Coronaviridae family .The RNA of SARS-CoV2 was also seen in the stools of Covid-19 infected sufferers . The outcome of this research established the hypothesis that *SOD3*/*ATF4*-associated antioxidants, that is particularly in the pulmonary,will function in synergy . This type of coronavirus has a polymorphic nature. This virus is an enveloped virus with +ve sense ssRNA & is a member of coronavirus family.Cells are infected by the virus binding to the angiotensin converting enzyme 2 ACE2 receptor present on the surface of the cell. COVID-19 is mostly transmitted through the lungs, with manifestation varying from flu-like features which are mild to features like hazardous pneumonia and/or fatal respiratory distress. This disease is mostly seen as producing fever & respiratory problems, but it is also seen linked to a variety of extrapulmonary symptoms, including dermatological indications [17-21].

5. CONCLUSION

The presentation of skin manifestations varies greatly, yet this systematic study aids in the classification of these diverse patterns . Clinicians are the first to observe the manifestation in “COVID - 19” cases and must be ready to spot a COVID-19-related dermatologic presentation. The predictive value of each dermatologic symptom should be investigated further. COVID-19-related cutaneous symptoms have become more widespread in recent months, drawing international scientific attention as well as media attention. Right after the outbreak broke out ,in few months numerous reports and structured evaluations about the cutaneous aspects of “COVID - 19” were issued.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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