MUCOCUTANEOUS MANIFESTATIONS OF COVID-19 IN AN ISOLATION UNIT OF PESHAWAR, KHYBER PAKHTUNKHWAI

Abdur Rahim Khan1, Farah Gul2, Durdana Jalal3, Iqbal Haider4, Hamza Ali Khan5

ABSTRACT
OBJECTIVES
This study aimed to determine the frequency of mucocutaneous manifestations in patients with COVID-19.

METHODOLOGY
This prospective cross-sectional study was conducted in the isolation ward of Hayatabad Medical Complex, Peshawar, for COVID-19-positive patients from 20th June to 30th July 2020. One hundred and twenty COVID-19-positive patients were included in our study. Patients fulfilling the inclusion criteria were subjected to a detailed clinical history and mucocutaneous and systemic examination. Relevant investigations were done. Data was recorded in predesigned proforma and analyzed for various statistical variables.

RESULTS
Among 120 patients included in our study, 87 were male and 33 female. Most patients belonged to the age group 21-40 years. A total of 17 patients showed mucocutaneous manifestations. Generalized pruritus and petechial rash were the most common, and the maculopapular rash were the least common. Mucosal involvement was seen in 2 patients.

CONCLUSION
Mucocutaneous manifestations are essential clues in the diagnosis of COVID-19. Early recognition may help in the effective management of patients.

KEYWORDS: COVID-19, Mucocutaneous Manifestations

INTRODUCTION
Coronavirus disease 2019 (COVID-19) first appeared in December 2019 in Wuhan, China, and since then has spread quickly throughout the world. According to WHO, confirmed cases of COVID-19 were 26823011 by 7th September 2020.1 It has been declared a pandemic since March 2020. SARS-COV-2 causes COVID-19, an enveloped RNA virus that invades the cell through angiotensin-converting enzyme (ACE-2) receptors.2 Pulmonary system is mainly affected, and symptoms range from fever, dry cough and dyspnea to pneumonia and respiratory distress.3 Different organ systems including skin are affected by COVID-19. Skin lesions are primarily observed in the active phase of infection, although skin rash can appear in the prodromal phase.4 According to their pathomechanisms, mucocutaneous manifestations of COVID-19 are divided into two groups. First, cutaneous features similar to viral exanthems; which are an immune response to nucleotides of virus.5 Second, mucocutaneous eruptions secondary to systemic consequences of vasculitis and thrombotic vasculopathy.6 Histopathological characteristics of respiratory dysfunction are fatal microvascular injury syndrome, mediated by activation of complement pathways and an associated procoagulant state. A complement-mediated micro thrombotic disease characterized by pauci-infiltrate is seen in the skin.7 It is of great importance to all clinicians to keep cutaneous lesions in mind as these may be acute symptoms of COVID-19. Cutaneous lesions may warn about the asymptomatic carriers as well.8 The types of skin lesions in COVID-19 are not well recognized &understood. Hence dermatologists and general practitioners require a clear understanding of skin lesions of COVID-19 in order to diagnose this disease promptly. This study aimed to determine the frequency of mucocutaneous manifestations in patients with COVID-19.

METHODOLOGY
It was a descriptive cross-sectional study, and a non-probability consecutive sampling technique was used for data collection. Ethical approval for the study was taken from the hospital’s ethical committee. The study was conducted in the isolation ward of Hayatabad Medical Complex (HMC), Peshawar, for COVID-19 positive patients from 20th June to 20th July 2020. A total of 120 COVID-19 positive patients were included in our study. They were the patients who were admitted to the isolation ward during our duty hours. Patients of all ages and both genders presenting with positive reverse transcriptase PCR assay in the inpatient department were included in our study.
Patients with chronic concurrent skin ailments and those taking drugs for other conditions were excluded. Informed consent was taken. A detailed history and mucocutaneous examination were carried out. Relevant investigations like complete blood count, coagulation profile, liver function tests, renal function tests and PCR were done. Data was entered in predesigned proforma and later analyzed. The frequency and pattern of various mucosal and cutaneous findings were noted. Data were analyzed using SPSS version 22. Frequency and percentages were calculated for all categorical variables like gender, age range, and skin and mucosal manifestations. Mean ± standard deviation was calculated for a continuous variable like age.

**RESULT**

A total of 120 patients, including 87 males and 33 females, participated. The majority of the patients were in the age range of 41 to 60 years. A total of 17 patients showed mucocutaneous manifestations; out of these, seven patients had two or more mucocutaneous manifestations. Generalized pruritus and petechiae were the most common cutaneous manifestations seen in 29.4% of patients each, while maculopapular rash was the least common, present in only 5.8% of patients. Mucosal involvement was seen in 2 patients. One patient had only oral mucosal involvement, while the second had oral and conjunctival involvement and a maculopapular rash on the body. In most patients, the mucocutaneous lesions appeared after covid-19 symptoms. In most patients, cutaneous lesions were present on the trunk.

**DISCUSSION**

Covid-19 is a rapidly growing public health problem and a WHO-declared pandemic. A variety of mucocutaneous manifestations have been observed in patients presenting with covid-19. In our study, male patients outnumbered females by 2.6:1. This observation was consistent with the findings of Keyung Tang and his colleagues. They also reported male predominance. Its reason may be that males of reported age are mostly responsible for earning livelihood for their families in our part of the country. So they have to go outside due to their job nature and hence also more exposed to infection. Furthermore, it has been reported in the literature that males have a higher expression of Angiotensin Converting Enzyme 2 (ACE 2) encoded by the ACE 2 gene than females. This gene has been proven to be the receptor for SARS coronavirus (SARS-CoV) and human respiratory coronavirus NL63. ACE 2 receptors responsible for SARS-CoV-2. Since males have a higher expression of ACE 2 than females, the chances of COVID are higher in males than females. Most of our enrolled patients with COVID-19 were above 20 years of age (Table 1). The literature review also shows that most patients suffering from COVID-19 are more than 20 years old. The plausible reason for this could be that patients below 20 develop more respiratory viral infections than those above 20, which can provide nonspecific protection against coronavirus infection due to immune cross-reaction. In our study, 17 patients developed cutaneous manifestations, of which pruritus and petechiae were most common; present in 6 patients each (29.4%), and the maculopapular rash was least common and present in only one patient (5.8%) (Table 2). Similar findings were observed by Angelo Valerio where pruritus was the most typical observed manifestation, present in 40.9% of COVID -19 positive patients. The predominant finding of these two manifestations could be that these two findings are present in many other viral infections as well. Since COVID-19 is a viral infection, these two findings are seen in most cases. It has also been observed that frequent hand washing using alcohol and other chemical preparations has been recommended.

**Table 1: Age of Patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>f</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20</td>
<td>10</td>
<td>8.3</td>
</tr>
<tr>
<td>21-40</td>
<td>50</td>
<td>41.6</td>
</tr>
<tr>
<td>41-60</td>
<td>40</td>
<td>33.3</td>
</tr>
<tr>
<td>More than 60</td>
<td>20</td>
<td>16.6</td>
</tr>
</tbody>
</table>

**Table 2: Covid-19 Positive Patients Having Mucocutaneous Manifestations (n= 17)**

<table>
<thead>
<tr>
<th>Cutaneous Lesions</th>
<th>Number of Patients</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>02</td>
<td>11.7</td>
</tr>
<tr>
<td>Petechiae</td>
<td>05</td>
<td>29.4</td>
</tr>
<tr>
<td>Maculopapular Rash</td>
<td>01</td>
<td>05.8</td>
</tr>
<tr>
<td>Bullae</td>
<td>02</td>
<td>11.7</td>
</tr>
<tr>
<td>Urticarial</td>
<td>02</td>
<td>11.7</td>
</tr>
<tr>
<td>Pruritus</td>
<td>05</td>
<td>29.4</td>
</tr>
</tbody>
</table>

**Table 3: Characteristics of Mucocutaneous Lesions**

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Number of Patients</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Ulcers</td>
<td>01</td>
<td>50</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>01</td>
<td>50</td>
</tr>
<tr>
<td>Symptoms before COVID-19</td>
<td>02</td>
<td>11.76</td>
</tr>
<tr>
<td>Symptoms simultaneous with COVID-19</td>
<td>05</td>
<td>29.41</td>
</tr>
<tr>
<td>Symptoms After COVID-19</td>
<td>05</td>
<td>17.64</td>
</tr>
<tr>
<td>Face &amp; limbs</td>
<td>03</td>
<td>17.64</td>
</tr>
<tr>
<td>Trunk</td>
<td>14</td>
<td>82.35</td>
</tr>
</tbody>
</table>
These chemicals might lead to pruritus on hands and other body parts, as Stefaniak and his colleagues discussed. Petechiae have been reported to be one of the most typical cutaneous manifestations by Recalcati S as well. According to him, COVID-19 is associated with thrombocytopenia, just like dengue fever. Hence patients suffering from COVID-19 may present with purpura as one of the cutaneous manifestations. Keyung Tang mentioned that mainly skin lesions were erythematous patches, urticaria, vesicles and petechiae. Another study conducted by Muskan Sachdeva et al.; showed results from 18 articles, according to which mucolopapular rash was most common (36.1%), followed by vesicles(34.1%) and urticaria(9.7%). The cutaneous findings are varied in different studies. It may be because COVID-19 is a new disease, and more studies and findings are needed for consensus. In our study, two patients had mucosal involvement, one having oral ulcers with overlying candida and the other with conjunctivitis only (Table 3). A variety of oral manifestations are observed in COVID-19. Juliana and Eliete described a man who tested positive for coronavirus and presented with oral manifestations like herpes simplex, candidiasis and geographical tongue. Filizand Huliya reported a confirmed case of COVID-19 positive patient who had characteristic exanthema of the disease and erythema of the oropharynx and hard palate and some petechiae and purpurant exanthem near the soft palate. There is still a question whether these are due to coronavirus infection primarily or secondary manifestation from patient’s systemic condition. Erbas and his colleagues, in their systemic review, have reported a wide range of mucosal features ranging from oral erosions to ulcers, aphthae, and mucolopapular exanthema erythema multiforme-like lesions. In our study, most patients developed mucocutaneous manifestations after diagnosis of covid-19 (Table 3). Our findings were consistent with the study by Recalcati S, who in March 2020 collected data from 88 patients, 18 (20.4%) who developed cutaneous manifestations. Eight patients developed cutaneous manifestations at the onset, and ten patients after hospitalization. Such appearance of mucocutaneous lesions in COVID-19 is vital because if appearing early, these may be the first sign of infection, and these mucocutaneous findings may be the only sign in asymptomatic COVID-19-positive patients. In our study, in most patients, the cutaneous presentation was limited to the trunk (Table 3). This finding is consistent with the study by Recalcati S in which the trunk was the central active region. The study by Muskaan Sachdeva also showed that most lesions were found on the trunk. It may be because, like other viral exanthems, most lesions are present on the trunk as compared to extremities, same is the case with COVID-19 exanthem being viral.

LIMITATIONS

Our study shows the frequency of mucocutaneous manifestations from a single centre. Similar studies must be done at multiple centres to identify the frequency of mucocutaneous manifestations of COVID-19 in a larger sample size.

CONCLUSION

A variety of mucocutaneous manifestations have been observed in patients presenting with COVID-19. Pruritis and the petechial rash was the most common cutaneous manifestation, followed by erythema and urticaria. Like other viral diseases, mucosal involvement should be considered a potential symptom of COVID-19 infection. Awareness regarding mucocutaneous features of COVID-19 can help in early diagnosis and timely treatment of patients.

CONFLICT OF INTEREST: None

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REFERENCES


CONTRIBUTORS

1. Abdur Rahim Khan – Concept & Design; Critical Revision; Supervision

2. Farah Gul – Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Final Approval

3. Durdana Jalal – Data Acquisition; Data Analysis/Interpretation; Analysis/Interpretation Drafting Manuscript

4. Iqbal Haider – Drafting Manuscript; Critical Revision; Supervision; Final Approval

5. Hamza Ali Khan – Drafting Manuscript; Critical Revision; Final Approval