Eastern-European Journal of Medical Humanities and Bioethics

ISSN: 2559-7604 Covered in: CrossRef; RePEc; CEEOL; KVK; WorldCat; Google Scholar 2021, Volume 5, Issue 1, pages: 13-23 | https://doi.org/10.18662/eeimhb/5.1/29

Skin Manifestations of COVID-19

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Abstract: Coronavirus-19 (COVID-19) is an ongoing global pandemic, which was isolated for the first time in Wuhan (China), in December 2019. Although this virus is most well known for causing respiratory pathologies, in medical practice, there are being reported more cases with heterogenous cutaneous presentations. These lesions manifest at various times in relation to COVID-19 symptoms, which may indicate whether the lesions are virus-induced or are delayed immunological responses to the infection. The main purpose of this study is to evaluate the distribution, types, and highest skin manifestations of Covid-19. Finding the potential link between Covid-19 and cutaneous manifestations may help to understand the pathogenesis and best policies in disease control. The pathophysiology of these lesions remains under study and still unclear. To achieve this goal, a transversal study was conducted on the population, the period March 1, 2021, to July 16, 2021. Out of 205 suspected / laboratory-confirmed people, there were 13 people with cutaneous signs, of which 13 were female and 9 were male. The most common morphological form was morbilliform rash, chicken-pox-like vesicles, and urticarial rash.

Keywords: COVID-19, cutaneous manifestations, morbilliform rash, chicken-pox like vesicles, urticarial rash.

How to cite: Caushaj, S. (2022). Skin Manifestations of COVID-19. *Eastern-European Journal of Medical Humanities and Bioethics*, *5*(1), 13-23. https://doi.org/10.18662/eejmhb/5.1/29

Introduction

The pandemic spread rapidly throughout the world. The symptoms of the disease vary from person to person and involve a wide range of clinical manifestations. According to studies, the most common symptoms are fever, fatigue and dry cough. Also, some patients may experience muscle aches, congested nose, sore throat, gastrointestinal symptoms and loss of olfactory and taste (Lei et al., 2020; Lechien et al., 2020; Rodriguez-Morales et al., 2020). During the pandemic, it became clear that the SARS-CoV-2 virus, while mainly targeting the lungs, also affected other organs (Phelan et al., 2020). Cutaneous manifestations were slower to report, probably because the need to document cutaneous changes in patients in critical conditions was less pressing.

Literature review

The very first description of the skin involving COVID-19 came out of "The New England journal of Medicine" article that describes over 1000 patients from 552 hospitals in China and the majority of those patients had fever and cough and 2 (0.2%) patients were described as having a rash. They both were described as having severe disease, but we have no idea what that rash was (NEJM, 2002).

The first article that actually looked at the skin came out of Italy in May 2020 and it was about 148 patients with confirmed COVID-19. They had excluded 60 of the patients with new medications in previous 15 days, in case the medication was the cause of the rash. 18 out of 88 patients had a new unknown rash (8 patients had a rash on onset of COVID-19 and 10 patients developed rash after hospitalization), 14 patients had erythematous rash, 3 patients had urticaria and 1 patient had chicken-pox like vesicles. There are no pictures and no other information about these cases (Recalcati, 2020).

Then the American Academy of Dermatology along with Harward University and an international dermatolody european association created an international registry of COVID-19 cutaneous manifestations that is open to medical professionals from any specialty [7]. They collected the data from April to May and there were submitted 716 cases from a variety of countries. Only 171 of those cases were confirmed with COVID-19 and of those, the average age was 44 and there were more women than men declared. 22% of those patients had a morbiliform rash, 18% had a pernio like rash, 16% had urticaria and then there was a variety of other rashes: macular erythema,

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vesicular, papulosquamous, retiform purpura. It was unable to determine the duration of rashes because 72% of the patients had ongoing rash at the end of the study and the majority (56%) had received treatment prior to onset of rash. Most of the professionals did not submit pictures (AAD, 2021).

There is another prospective study out of China and Italy presenting 678 patients with PCR confirmed COVID-19. 7.8% (n=53) of those patients showed with new skin eruptions, 70% (n=37) had a "morbiliform" eruption, 26% (n=14) were presented with urticaria and 4% (n=2) had chicken-pox like rash. 44% of rashes were presented at time of COVID-19 diagnosis while 56% developed a rash during theier hospitalization. Most of these rashes did tend to be very mild and self-limiting, lasting 3-5 days. However patients with patachiae, purpura and acroischemia tended to be sick, admitted at ICU, with elevated PT, fibrinogen and D-dimer (De Giorgi et al., 2020).

Another interesting study out of Spain asked all the Spanish dermatologists over a two week period during April 2020. They had to enroll all the patients with a new unexplained skin eruption with suspected or confirmed COVID-19. They had 375 patients and 19% of those had pernio like lesions which tended to be on the feet more than the hands, 9% had vesicular lesions, 19% had urticarial rash, 47 % had maculopapular rash and the other patients had livedo reticularis rash. The most important thing about this study was that the patients who had pernio like lesions were younger and their rash lasted longer. On the other hand, the patients who had livedo/necrosis were older and much sicker (the most admitted in the ICU) (Docampo-Simón et al., 2020).

Methodology

The methodology is the whole framework or model of the research which includes the choice of methods, tools and techniques to be applied in the study. It is important to ensure that the study can be carried out and function as planned.

The research was developed in several phases:

1) There was conducted and defined the purpose and objectives of this study and there was done a literature review on our subject.

2) In the second phase, a questionnaire was designed with simple and easily understandable questions.

3) In this phase, it was done the extraction, processing of data and compilation of the results. In the end, conclusions on the study were conducted.

Questionnaire in Google Form

A short questionnaire was organized, via Google Form, and launched for the first time in 1st of March 2021. The study population included anyone capable of using this software, over 18 years old. For the elderly that were unable to use this software, this questionnaire was printed and distributed manually. During this time there was collected information about the type of diagnosis (suspected or laboratory confirmed), patient demographics, concomitant diseases, details about the new dermatological condition of patients, time of onset of marks on the skin and the patients' reaction to them.

Population study

This study included people aged 18 to 87 who suspected they had passed or were laboratory confirmed positive for Covid-19. We excluded 1 to 17 and over 87 year old individuals, pregnant women and people who were not infected with Covid-19. We removed from the study those who reported they had no marks on the skin, but in the meantime completed other questions about the new dermatological condition.

In total, the number of people who participated in the study was 205. Only 22 of them had marks on their skin. This group, was defined as the target group where our study was focused. Data processing and analysis was done through Microsoft Excel software.

Cutaneous manifestations in patients with COVID-19

Skin manifestations of COVID-19 are separated in two main categories: inflammatory/exanthematous and vasculopathic rashes.

The first are non-specific rashes that are related to it being a viral process. These are rashes that present with classic viral exanthems, classic maculopapular eruptions, urticarial lesions and vesicular rash.

Morbiliform/maculopapular rash

Morbiliform essentially means it looks like measles rash which gives rise to the flat patches and raised bumps on the body. In our transversal study, there were self-declered 6 people with morbiliform rash. The predominant age groups were 70-87 years old (n=2) and 51-68 years old (n=2). Except skin manifestations they reported other symptoms like: itching, burning. There were predominantly males who declared skin findings (n=4). This rash was tipically presented on the convalescente phase, but there was a person (n=1) who had had this skin rash at the beginning of

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the disease. Another person declared that he found this rash during the active phase of the disease. All these 6 patients had concomitant diseases and 2 of those used to smoke, too. This type of exanthematous rash loves the trunk, but it also spreads on the legs and arms. So this rash is mostly associated with a mild/severe COVID infection.

There is a challenge in diagnosing these patients with maculopapular rashes, because an exanthematous drug reaction is a very similar presentation and the main differential diagnosis that we have to consider. Patients with a drug reaction present with the same skin findings of that widespread maculopapular rash, but tipically this is going to occur 1 to 2 weeks after the introduction of the medication. But this rash tends to be self-resolving and not severe.

Urticarial rash

Urticarial rash tipically looks like hives, a variety of shapes. It appears as raised, itchy bumps that come and go within the day. These lesions do not stay in the same area for more than 24 hours. In our study, there were self declared 3 people with urticarial rash. They appeared mostly in the face, neck, and back. One person (n=1) reported that urticaria was the first presentation of the disease. At this people, the severity of the disease was mild.

Vesicular lesions

Vesicular lesions look the same as chicken pox or varicella rash. In China this was the first skin manifestation of COVID-19 found (Eastin, & Eastin, 2020). In our study there were found 9 people with these lesions. This was the most encountered skin rash. Vesicular lesions predominated in age group 70-87 years old (n=5), followed by age group 51-69 years old (n=3) and 35-50 years old (n=1). The predominated gender was female. They complained of other symptoms like: itching and burning. These lesions appeared on arms, legs and the trunk. Most of these self-declared people had concomitant diseases and also used to smoke and drink alcohol. The severity of the disease was mild to moderate.

The second type of rash are those related to vascular insufficiency. This means that here is not enough skin perfusion because of micro or macro thrombosis. Clinically this patients present with livedo reticularis or skin necrosis or pernio.

Livedo reticularis

Livedo reticularis presents like network of dusky purplish blotches on the skin. This suggests that there is some occlusion in the blood vessels supplying the skin. In our study there were only two people with livedo reticularis. They had been hospitalized and severity of their disease was moderate. These lesions had appeared during the active phase of the disease, after some days of the hospital admittion.

Chilblain/ pernio lesions

Chilblain/ pernio lesions are small erythematous lesions seen distally usually on leg digits. In our study there were 2 people of age group 18-34 years old. They reported some other symptoms like: pain, burning and itching. These skin findings had appeared during the active phase of the disease and had lasted for a long time. Severity of the disease was light to mild.

These lesions can be seen during the prodormal, active or convalescente phase of the disease. Patients tend to be younger and have a milder form of COVID-19 infection. We have to be interested of the wide range of differential diagnosis. We all know that if we see persistence of these pernio lesions beyond cold seasons, then they have a higher chance of an underlying systemic disease.

Results and discussions

Description of people who participated in the study

Cutaneous manifestations are seen in different age groups. In our 5 month study, took part 205 people. 53.2% of these individuals (n = 109) declared themselves to have been laboratory confirmed COVID-19 positive, the rest suspected of being infected, based on the symptoms they had had. Cutaneous manifestations were observed in laboratory confirmed individuals. 22 out of 109 people (20.1%) had marks on the skin. 59.1% of those (in 13) were female, with a ratio female: males almost 2: 1. The predominant age group was 70-87 years old.

In the age-gender relationship these were the observations:

Age group	Females	Males
18-34	3	1
35-50	2	0
51-69	2	3
70-87	6	5

Table.1 | Age-gender relationship

Source: Authors' own conception



Figure.1 | Age-gender relationship Source: Authors' own conception

The concomitant diseases that these people may have according to age groups were also studied:

Concomitant diseases					
Age group	Cardiovascular diseases	Renal Diseases	Mellitus diabetes	Bronchial Asthma	None
18-34	0	2	0	1	1
35-50	1	1	0	0	0
51-69	3	0	0	0	2
70-87	7	0	3	0	1

 Table. 2 | Concomitant disease-age group relationship

Source: Authors' own conception

Out of 6 types of diseases included in the study, cardiovascular disease, renal disease, asthma and diabetes mellitus were the most commonly reported in individuals with cutaneous manifestations.

In an attempt to obtain as much information as possible about these people, the following data were obtained:

Table.3 | Age group relationship - alcohol, smoking and other drugs

	User of:			
Age group	Smoking	Alcohol	Other	None
18-34	0	1	0	3
35-50	0	0	0	2
51-69	0	2	0	3
70-87	5	1	0	5

Source: Authors' own conception

Clinical symptoms in persons with COVID-19 with cutaneous manifestations were also monitored. According to results of the studies, there were reported 9 types of clinical symptoms. Of these, headache and muscle (63.6% each), fever (54.5%), dyspnea and breathing problems (50% each), loss of taste (36.4%) and diarrhea (27.3%) were the most common clinics in people with cutaneous manifestations



Frequency

Figure 2 | Other clinical symptoms of COVID-19 Source: Authors' own conception

Patients with cutaneous manifestations

22 was the number of people who appeared with cutaneous manifestations. 40.9% (n = 9) of these people received care and treatment in the hospital, the others chose to stay at home under the care of a family doctor.

The majority, 72.7% (n = 16), reported that the marks on the skin had appeared after the other difficulties of COVID-19 had gone away. 22.7% (n = 5) indicated that the marks had appeared during the period they were suffering from the symptoms of other COVID-19 disease and a very small proportion, around 4.5% (n = 1) had cutaneous manifestations as the initial presentation.

Signs on the skin may also appear as a result of drug reaction during the treatment of COVID-19 disease. In our study, this was observed in 22.7% (n = 5) of patients with cutaneous manifestations.

The numbers and types of cutaneous manifestations in patients with COVID-19 were as follows: urticarial rash (3/22), petechial rash (1/22), pseudo-chilblain (2/22), blister-like vesicles (9/22), livedo reticularis (2/22) and morbiliform rash (6/22).

Conclusions

Between 22 self-assessed people with cutaneous manifestations, the majority were female and the female: male ratio was almost 2: 1. The most affected age group was over 50 years old. The number could have been even higher as people may have neglected the marks on the skin, due to the other more severe symptoms of COVID-19 disease. Another expected reason might have been because the older age group may not have paid attention to the signs. because they may have thought of them as part of old age.

This study highlights the wide variety of cutaneous manifestations of COVID-19 simultaneously with or after the diagnosis of COVID-19. Based on the results of the study, the most common morphologies, in laboratory-confirmed cases, include urticarial, morbiliform, vesicular rash, and chilblain/ pernio lesions. Many of these morphologies occur with various viral infections and, thus, may not provide specific explanation into the pathophysiology or treatment. Cutaneous manifestations of COVID-19 generally occurred concurrently with or after other COVID-19 difficulties. However, 4.5% occurred before other symptoms of COVID-19, thus those emphasize their importance in early diagnosis.

Many of the people with cutaneous manifestations had concomitant diseases and used tobacco or alcohol. These could be favorable factors in the appearance of skin rashes. It was noticed that there were people who reported cutaneous manifestations DURING treatment of the disease.

As a result, the importance of this study is to help to stop the spread of COVID-19 and to protect other people. Drug interactions during therapy should be the focus; cutaneous manifestations may be due to drug reactions and not COVID-19 itself. These patients present with the same skin findings of that widespread maculopapular rash, but tipically this occurs one to two weeks after the introduction of the medication (those patients had never previously been exposed to that therapy). So if it is a really short time between medication initiation and the development of the rash, it is likely related to the underlying COVID-19.

Key points to remember:

• COVID-19 can cause a variety of rashes

• Skin findings can precede COVID-19 diagnosis, arise during illness or follow illness.

• Most rashes and symptoms will resolve on their own within days or 1-2 months. They respond well to simple treatments like topycal creams or antihistamins.

In conclusion, physicians should consider cutaneous manifestations as clinically important features. Further studies and investigations are needed to confirm and explain an understanding of the cutaneous manifestations associated with COVID-19.

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