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CUTANEOUS MANIFESTATIONS RELATED TO COVID-19 IN SOUTH ASIAN YOUNG ADULTS

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COVID-19 – თან დაკავშირებული კანის გამოვლინებები სამხრეთ აზიის ახალგაზრდებში

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რეზიუმე

ცოტა ხნის წინ გაირკვა, რომ COVID-19, დაავადება, რომელიც გამოწვეულია SARS-CoV-2-ით და იწვევს რესპირატორული ტრაქტის დაზიანებას, ასევე იწვევს კანის გამოვლინებებს პაციენტთა უმეტესობაში. კვლევის მიზანი იყო სამხრეთ აზიის ახალგაზრდებში კოვიდ 19 - ის დერმატოლოგიური გამოვლინების მახასიათებლების შესწავლა. 53 მონაწილის გამოკითხვა ჩატარდა სპეციალურად შემუშავებული კითხვარის გამოყენებით, რომელიც შეიცავს კითხვებს სქესის, ასაკის, SARS-CoV-2 დაავადების ისტორიის და მიმდინარეობის შესახებ, შემდგომი დაკვირვებისას, მედიკამენტების გამოყენების და კანის გამოვლინების არსებობის შესახებ. მიღებული მონაცემების ანალიზი განხორციელდა ამ ფაქტორების კორელაციის დასადგენად და კანის სხვადასხვა გამოვლინების სიხშირეს შორის.

შედეგებმა აჩვენა, რომ ჩვენს 53 მონაწილეს შორის ყველაზე გავრცელებული კანის გამოვლინება იყო მაკულოპაპულური გამონაყარი 27% (n = 14), ასევე გენერალიზებული ქავილი, პეტექია ქვედა კიდურებზე და ვეზიკულოპაპულური გამონაყარი. ამ გამონაყარის უმეტესობას გავრცელებული ხასიათი ჰქონდა. საინტერესოა, რომ ახალგაზრდა მონაწილეს, რომელმაც 2020 წლის აგვისტოში გადაიტანა COVID-19, 2021 წლის თებერვლიდან აწუხებდა მომატებული დერმატოგრაფიზმი.

ჩვენი კვლევის მონაცემები აჩვენებს, რომ COVID-19- ის კანის გამოვლინებები იშვიათად გვხვდება ფერადკანიან პაციენტებში, შესაძლოა კანში მელანოციტების შემცველობისა და ACE რეცეპტორებთან ასოცირების გამო, კანის სხვადასხვა გამოვლინება შეიძლება აღმოჩნდეს გარკვეულ ასაკობრივ ჯგუფში, რესპირატორულ პრობლემებთან ერთად, რაც უნდა ჩაითვალოს სპეციფიკურ სიმპტომატიკად.

INTRODUCTION

“Severe Acute Respiratory Coronavirus 2” (SARS-COV-2), is the causative agent of the COVID-19 pandemic which started in December 2019. It was recognized as a pandemic, by WHO in March 2020, triggering a global outcry and public health emergency [1]. Coronaviruses are enveloped RNA viruses that are distributed broadly among humans, other mammals, and birds, and can cause respiratory, enteric, hepatic, and neurologic diseases.

Since the first reported case of COVID-19, the number of cases and mortality has been increasing exponentially. The estimated death toll so far is a whopping 4.16 million and still counting, and the total cases so far is an estimated 194 million. This is a massive burden on the economy, causing an increase in health care expenditure.

Since then, there have been several developments related to COVID-19. Many scientists and first-line health workers have been on a continuous lookout for these developments. Many research papers on various topics concerning the COVID-19 pandemic ranging from symptoms, pathogenesis to vaccine efficacy on new strains have been published.

The classical symptoms of COVID-19 are respiratory tract disorders such as sore throat, dry cough, dyspnoea, damage to the lung parenchyma, and in extreme cases pneumonia and pulmonary embolisms [2]. Non-respiratory symptoms include fever, headache, body pains, fatigue, loss of taste and smell, diarrhoea, etc. However, recent studies have shown that there have been cutaneous manifestations, too.

Concerns about the development of cutaneous manifestations such as maculopapular rash, vesicular lesions, urticaria-like lesions, and chilblain-like lesions are reported [2]. The first article to be cited throwing light on cutaneous manifestations is Cutaneous Manifestations in COVID-19: a first perspective [3].

Although this virus primarily attacks the respiratory tract, the role of ACE2 gene has been discovered in the pathogenesis of the COVID-19 infection, and it is seen in several human tissues, including gastrointestinal and skin tissue [4]. In a recent analysis of 31 Genotype-Tissue Expression human tissue, Li et al have found that among human organs, small intestine, testis, kidneys, heart, thyroid, and adipose tissue have the highest ACE2 expression levels, while blood, spleen, bone marrow, brain, blood vessels, and muscles have the lowest ACE2 expression levels. To explore whether the skin was a probable target for SARS-CoV-2 infection, the public domains (GEPIA2 and ARCHS4) are available to study ACE2 mRNA expression and ACE2- positive cell composition in skin tissues. ACE2 expression was considerably elevated in keratinocytes compared to fibroblasts and melanocytes found in skin tissue [3, 5]. This could be the possible explanation as to why coloured skin or Asian populations have not reported cutaneous manifestations post - COVID-19 as much as Caucasians.

Our main goal is to study the cutaneous manifestations related to COVID-19 in South Asians between the ages of 20-29, and to compare our findings with published data to understand the development/pathogenesis of cutaneous manifestations and their variation in the above-mentioned population. This will enable us to improve the diagnosis and initial treatment of COVID-19 infection in patients who may present with cutaneous manifestations and may go undetected and create awareness of possible COVID-19 vaccine-induced cutaneous manifestations.

MATERIALS AND METHODS

A combination of both theoretical and practical approaches was used in the making of this research such as reviewing various articles from multiple resources, comparing the articles with the data obtained from conducting a survey and analysing it. The literature used was from database sources such as: Wiley Online Library, National Centre for Biotechnology Information (NCBI), PubMed and from articles published in dermatology digests and journals such as Journal of the European Academy of Dermatology and Venereology: JEADV. An online survey was conducted via Google forms and students were asked to fill the personal details and contact for further questioning. This survey was used to collect the contact information of potential participants. Then, participants were called, and once verbal consent was obtained, they were interviewed personally where information on their COVID-19 infection was collected.

Pictures of the cutaneous manifestations of COVID-19 were also shown to participants to help them identify if they have experienced any. We see that the majority were medical students from Tbilisi State Medical University because of the age group required for our criteria, and most were Indians since we focused our study on South Asians. This gives us a total of 53 participants from TSMU, belonging to the age group 20-29, out of which 51 had tested positive for COVID-19 recent to this study.

RESULTS

From a total of 51 participants who had tested positive for COVID-19, 25 (49%) had cutaneous manifestations of COVID-19. 14 of these 25 participants were male, and 11 were female. The most common cutaneous manifestation, experienced by 13 participants, is maculopapular rash. 2 participants experienced chilblain-like lesions on the toes, 1 had generalized pruritus, 1 had petechiae on the feet, 1 had urticaria on the arms, 1 had purpura on the arms, 1 had pityriasis alba, 1 had generalized vesiculopapular rash, and 1 had xerosis on the hands. These manifestations were observed during the COVID-19 infection (**Table 1**).

Additionally, one female participant had tested positive for COVID-19 in August 2020, and since February 2021, she has been experiencing dermatographism. One female participant had pre-existing tinea

versicolor on her trunk and shoulders, and this worsened after her COVID-19 infection. Finally, another female participant reported hyperpigmentation on her hands (**Table 2**).

3 participants, 2 females and 1 male have reported cutaneous reactions after receiving the COVID-19 vaccine. One female participant reported maculopapular rash at the injection site after receiving the first dose of the Sinopharm vaccine (BBIBP-CorV vaccine), and the second had a delayed hypersensitivity reaction on the injected arm after the first dose of the Pfizer vaccine (BNT162b2) (Figure 1). The male participant had noted urticaria on his arm after receiving the first dose of AstraZeneca.

Delayed hypersensitivity reactions (Fig. 1&2)

Fig. 1.



Fig. 2



Vaccine Reactions

Table 1
Reactions caused due to vaccine

s.no	Name of the vaccine	Side effects
1	Sinopharm	Maculopapular rash
2	Pfizer	Delayed hypersensitivity reaction
3	AstraZeneca	Erythematous papule

Table 2. Manifestations during COVID-19

s.no	Age	Gender	Manifestations	Site
1	22	Male	Maculopapular rash	Forehead
2	21	Female	Maculopapular rash	Arms
3	21	Male	Maculopapular rash	Generalized
4	23	Male	Maculopapular rash	Generalized
5	22	Female	Maculopapular rash	Generalized
6	28	Male	Maculopapular rash	Generalized
7	20	Female	Maculopapular rash	Arms
8	20	Male	Maculopapular rash	Chest
9	20	Female	Maculopapular rash	Legs
10	24	Male	Maculopapular rash	Generalized
11	21	Female	Maculopapular rash	Hands
12	21	Male	Maculopapular rash	Trunk
13	23	Female	Maculopapular rash	generalized
14	20	Male	Chilblain like lesions	Toes
15	22	Female	Pruritis	Generalized
16	22	Female	petechiae	Feet
17	23	Male	Urticaria	Arms
18	20	Male	purpura	Arms
19	20	Male	Pityriasis alba	Face
20	24	Male	Vesiculopapular rash	Generalized
21	20	Male	Chilblain like lesions	Toes
22	21	Male	Xerosis	Hands

Table 3
Manifestations after COVID-19

s.no	Age	Gender	Manifestations	Site
1	23	Female	Dermographism	Generalized
2	22	Female	Tinea versicolor (pre-existing before COVID-19 that got worse after COVID-19)	Trunk and shoulders

DISCUSSION

The objective of this paper is to analyse the cutaneous manifestations of COVID-19 in South Asians aged 20-29. According to the results, after detailed interviewing, most of the participants had mild to moderate symptoms and all of them took erythromycin/azithromycin, Dolo 500, Ivermectin, and multivitamins. Only after individually assessing their symptoms, the participants could give us a positive response to have seen/experienced cutaneous manifestations.

In current available studies, COVID-19 has been associated with multiple cutaneous manifestations [6]. Six main clinical patterns are reported: (i) urticarial rash, (ii) confluent erythematous/maculopapular/morbilliform rash, (iii) papulovesicular exanthem, (iv) chilblain-like acral pattern, (v) livedo reticularis/racemosa-like pattern, (vi) purpuric "vasculitic" pattern [7].

The most common cutaneous manifestation among our 51 participants is maculopapular rash 27% (n=14). The majority of these rashes were generalized. In a study conducted in a COVID hospital in Guntur, Andhra Pradesh, India, urticaria, and pruritus were reported as the most prominent cutaneous manifestation [8]. Moreover, in this study, the abdomen was the most common site of the rash. These differences may be attributed to the fact that the study was conducted in hospitalized patients, whereas our study involved participants in the outpatient setting, and also due to the possibility that the strain in both these countries at the time of research was different.

Studies from one case series suggest that maculopapular rashes are associated with greater severity of COVID-19 infections that show higher viral exanthem.

No participants in this study had any pre-existing dermatological conditions except one female participant who reported tinea versicolor with distribution over the trunk and shoulders. She reported aggravation of the tinea versicolor after her COVID-19 infection.

A participant who tested positive for COVID-19 in August 2020 had reported the onset of urticarial dermatographism in February 2021. Dermatographism can be described as a wheal and flare reaction noted after pressure is applied to the skin by stroking or scratching, and usually arises within minutes, lasting up to an hour, in her case a more chronic urticarial form [9]. During her COVID-19 infection, she had experienced fever, body ache, loss of smell, and a generalized maculopapular rash. Her urticarial dermatographism is ongoing.

One case of hyperpigmentation was reported by a female participant. Her COVID-19 infection was symptomatic with a cough and high fever. Hyperpigmentation was noted on her hands and resolved after one month.

The possible reason behind our above findings' similarity to the European data could be the similarity in COVID-19 strain found here at the time of this study and geography.

As populations worldwide are being vaccinated against COVID-19, it is vital to identify and report any side effects. Through our research, we have identified 3 participants who have experienced cutaneous reactions upon vaccination. 72 hours after receiving the first dose of the Sinopharm vaccine (BBIBP-CorV), a female participant developed a maculopapular rash at the injection site. Local injection site reactions are reportedly higher in the younger population compared to participants aged 60 years and older [10].

The second female participant had a delayed hypersensitivity reaction at the injection site on her left arm, after receiving the first dose of Pfizer (Figure 1). These delayed large local reactions have been reported in patients vaccinated with the mRNA vaccines Pfizer and Moderna, with a median onset of 8 days after the first dose and have been termed in mass media as "COVID arm" or "red arms" [10,11,12,14]. It is a swollen, indurated, erythematous, itchy, or painful rash that may mimic, and may be incorrectly diagnosed as cellulitis [13]. They can be managed with antihistamines if itchy, analgesics, topical steroids, and cold compresses [12]. However, most are mild and self-limited, resolving spontaneously, and should not deter vaccination [10,14].

The third participant was a male who experienced an urticarial eruption on his arm 9 hours after receiving the first dose of AstraZeneca. He also reported fever and body pain lasting 3 days.

LIMITATIONS

The pitfalls of the study included the sample size, which consisted of a relatively small group of 51 individuals.

Since the study was conducted as a retrospective study, the data obtained was based on previously recorded information, thus susceptible to memory or registry bias when retrieving data.

CONCLUSION

At the end of this research, after extensive reviewing, we saw that the number of COVID-19 patients who developed cutaneous manifestations was considerably small but significant enough to add cutaneous manifestation as a symptom seen in South Asians battling COVID-19. We learned that coloured populations are less likely to present with cutaneous manifestations possibly because of the melanocyte content in the skin, and its relation to ACE receptors. The most common cutaneous manifestation observed is maculopapular rash, which could be due to high viral exanthem, or any drug-related interaction seen during treatment. In addition, there were three cases of vaccine-induced cutaneous manifestations in our study, which threw light on possible but rare side effects of the COVID vaccines. Identifying these skin manifestations can be a quick way to diagnose some COVID-19 patients. As a result, the importance of this issue is to help stop the spread of COVID-19 and protect other people as well as prospects where research could be conducted in regard to the causes of the cutaneous manifestations, which would help in improving the treatment and hence the outcomes.

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КОЖНЫЕ ПРОЯВЛЕНИЯ, СВЯЗАННЫЕ С COVID-19, У МОЛОДЫХ ЛЮДЕЙ ИЗ ЮЖНОЙ АЗИИ

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РЕЗЮМЕ

Не так давно было обнаружено, что COVID-19, заболевание, вызываемое SARS-CoV-2, которое, как известно, вызывает симптомы со стороны верхних дыхательных путей, вызывает также кожные проявления у значительного количества пациентов. Целью исследования было изучение особенностей дерматологических проявлений COVID-19 у молодых людей из Южной Азии. Проведен опрос 53 участников по специально разработанной анкете, содержащей вопросы о поле, возрасте, наличии заболевания по SARS-CoV-2 в анамнезе и характере течения, применении медикаментов во время наблюдения и наличии кожных проявлений у данной категории больных. Анализ полученных данных был проведен для выявления корреляции между этими факторами и заболеваемостью SARS-CoV-2 и различными кожными проявлениями.

Результаты показали, что наиболее частым кожным проявлением среди наших 53 участников является макулопапулезная сыпь 27% (n = 14), а также генерализованный зуд, петехии на стопах и везикулопапулезная сыпь. Большинство этих высыпаний были генерализованными. Интересно, что молодая участница, у которой в августе 2020 года был положительный результат теста на COVID-19, с февраля 2021 года страдает усиленным дермографизмом.

Данные наших исследований свидетельствуют, что у пациентов с цветной кожей кожные проявления COVID-19 встречаются реже, возможно, из-за содержания меланоцитов в коже и его связи с рецептором АПФ, различные кожные проявления могут быть обнаружены в определенной возрастной группе наряду с респираторными проблемами, и должны рассматриваться как специфическая симптоматика.

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CUTANEOUS MANIFESTATIONS RELATED TO COVID-19 IN SOUTH ASIAN YOUNG ADULTS

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SUMMARY

COVID-19, a disease caused by SARS-CoV-2, which is mostly known to cause upper respiratory tract symptoms is recently found to cause cutaneous manifestations in a considerable number of patients.

The purpose of the study was to study the features of dermatological manifestations of COVID-19 in young South Asian adults.

After the initial survey obtaining the contact details, personal interviews of 53 participants were conducted personally asking them questions about gender, age, the presence of the disease on SARS-CoV-2 in the anamnesis and nature of the course, the presence of nosocomial infection, the use of medications during supervision and the presence of dermatological lesions. Analysis of obtained data was performed to identify the correlation between these factors/incidences of SARS-CoV-2 and different skin manifestation.

The results displayed that the most frequent cutaneous manifestation among our 53 participants is maculopapular rash 27% (n=14). This is thought to develop because of high viral exanthem or due to possible drug related interactions through treatment. Others had skin manifestation such as generalized pruritus, petechiae on the feet and vesiculopapular rash. Majority of these rashes were generalized. Interestingly, a young female participant who had tested positive for COVID-19 in August 2020 has been experiencing dermographism since February 2021.

Our research data show that coloured populations are less likely to present with cutaneous manifestations possibly because of the melanocyte content in the skin, and its relation to ACE receptor and that cutaneous manifestations can be detected in a specific age group, along with the respiratory problems that arise from infection with this strain and should be considered as a symptom.

Keywords: COVID-19, cutaneous, vaccine, South Asian, SARS-CoV-2

