Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19: Important Updates and Developments
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Immunosuppressive and immunomodulatory therapies in dermatology and coronavirus disease 2019 (COVID-19)

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Abstract COVID-19 infection may affect the individuals with many underlying conditions including skin diseases. This cross-sectional study was conducted to provide an overview regarding the prevalence of COVID-19 disease in the patients with several skin diseases. Overall, 703 patients with several skin diseases participated in the study and completed our online-designed questionnaire. Among the total participants, only 32(4.6%) subjects reported the COVID-19 infection. The prevalence rate was equal to 0.04%. In the patients with psoriasis, 14 out of 322 people (4.3%) developed the COVID-19. Three out of 159 patients (1.9%) with alopecia areata had been affected with the COVID-19 and 4 (5.2%) patients with vitiligo had caught the disease. Only one subject (2%) with the lichen planus, and 6 (6.8%) patients with other skin diseases had developed the COVID-19 but in the patients with GVHD (Graft Versus Host Disease), 4 (80%) out of 5 patients had caught the COVID-19 disease. The frequency of COVID-19 infection was low in the studied population however; more studies with larger sample size are needed to determine the exact prevalence of the infection in the patients with skin diseases undergoing the treatment with several systemic medications.

In some patients with coronavirus disease 2019 (COVID-19), preexisting skin diseases, such as atopic dermatitis, psoriasis, and rosacea, have been exacerbated.[1] It is not known whether the patients receiving immunotherapy for skin diseases are more susceptible to severe acute respiratory syndrome coronavirus 2.[2,3]

Cross-sectional study

This cross-sectional study was performed on the participants who completed our questionnaire and had dermatologic diseases. Some patients were under treatment with various immunosuppressive and immunomodulatory and biologic agents. The data were collected by a web-based designed questionnaire. Statistical analyses were performed using SPSS software version 24 (IBM Statistics, Chicago, Illinois), and R statistics (R Core Team, 2019). A P value of $\leq .05$ was considered statistically significant. Descriptive

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Table 1 Distribution of the disease types in the population in our study

Disease	n	%
Psoriasis	322	45.8
Lichen planus	50	7.1
Vitiligo	77	11
Alopecia areata	159	22.6
Hidradenitis suppurativa	3	0.4
Pemphigus	2	0.3
GVHD	5	0.7
Other diseases	85	12.1
Total	703	100
COVID-19		
Positive	32	4.6
Negative	671	95.4
Total	703	100
Underlying diseases		
Hypertension	61	8.7
Cardiovascular disease	34	4.8
Diabetes	29	4.1
Obesity	126	17.9
Fatty liver	124	17.6
Hypothyroidism	92	13.1
Hyperthyroidism	5	0.7
Hyperlipidemia	84	11.9
Psychosocial disease	51	7.3
No underlying disease	370	52.6

COVID-19, coronavirus disease 2019; GVHD, graft versus host disease.

statistics were reported using the frequencies and percentages. The quantitative data were summarized as mean ± standard deviation.

Pearson χ^2 test was used to evaluate the association between two categoric responses as well as Spearman rank-order correlation to measure and test the association between two continuous or ordered categorical responses if the data met the assumptions for using the χ^2 test. Fisher exact test was used to determine the associations between two categorical variables.

A total of 703 patients participated in this study and completed our questionnaire. The majority of the participants (322 individuals) had psoriasis. Table 1 shows the frequency of other dermatologic diseases. Seven patients had psoriasis and lichen planus, seven patients had psoriasis and alopecia areata, three patients had lichen planus and alopecia areata, and seven patients had psoriasis and vitiligo.

Among the participants, only 32 (4.6%) patients reported COVID-19. This included those who did not have signs and clinical manifestations of COVID-19. Only two (6.3%) patients became positive for COVID-19, but 30 (93.8%) of those with signs and clinical manifestations of COVID-19 also became positive. All COVID-19–positive patients reported in this study were based on a positive result from a polymerase chain reaction test. A statistically significant difference was detected between these groups (Fisher exact test, $P = .0001$).

In the patients with psoriasis, 14 of 322 patients (4.3%) developed COVID-19. Three of 159 patients (1.9%) with alopecia areata had contracted COVID-19. In the patients with vitiligo, four (5.2%) patients had developed the disease. Only one patient (2%) with lichen planus and six (6.8%) patients with other skin diseases had developed COVID-19, but in the patients with graft versus host disease, four (80%) of five patients had contracted COVID-19. There were no positive cases of COVID-19 among the patients with pemphigus and hidradenitis suppurativa. There were also no reports about positive cases of COVID-19 in patients with concomitant conditions, such as psoriasis and alopecia areata or psoriasis and vitiligo, etc.

The mean age of the patients was 35.45 ± 12.67 years. The highest number and percentage belonged to the age group between 30 and 40 years, which was equivalent to 277 (39.4%) participants. Among the patients, 497 (70.7%) individuals were overweight, 137 (19.5%) of them were obese, and 48 (6.8%) of them had normal body mass index. Twenty-one (3%) were underweight. No positive significant correlation was found between high body mass index and COVID-19 development (χ^2, $P = .9$).

Table 2 shows the frequency of COVID-19 according to the skin diseases and the type of received medications.

Among the patients, 152 (21.6%) had discontinued their medications after the onset of the COVID-19 pandemic, and only 21 (30.2%) patients had continued their treatment regularly, whereas 102 (14.5%) had continued their treatments irregularly and 237 (33.7%) did not answer this question. Based on the data, the patients were divided into two groups, one group undergoing biologic treatment and the other on nonbiologic therapy. Adalimumab, etanercept, infliximab, and tofacitinib as the small molecule Janus kinase inhibitor were classified as the biologic drugs, and other drugs were classified as the nonbiologic. Only four (12.5%) patients treated with biologic drugs had developed COVID-19. No significant statistical correlation was detected between receiving the biologic and nonbiologic therapies and the development of COVID-19 (Fisher exact test, $P = .7$).

None of the patients taking hydroxychloroquine had uncontracted COVID-19, but no statistically significant difference was found between the use of this drug and other ones and COVID-19 development (Fisher exact test, $P = .6$). No findings have been reported on the prevalence of COVID-19 in the patients with various skin diseases as well as the correlation of the disease with the drugs used.

Additional observations

In this cross-sectional study, the frequency of COVID-19–positive cases in various dermatologic diseases was reported. The overall prevalence of COVID-19 in the studied population was low, about 0.04%; however, applying the poly-

Table 2 Frequency of COVID-19–positive cases based on the type of disease and received medications

Drugs	Psoriasis	Lichen Planus	Vitiligo	Alopecia areata	Hidradenitis suppurativa	Pemphigus	GVHD	Other diseases	Total
Methotrexate	33 (0)	1 (0)	0 (0)	11 (0)	0 (0)	0 (0)	1 (1)	10 (1)	56 (2)
Adalimumab	45 (3)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	46 (3)
Azathioprine	1 (0)	0 (0)	1 (0)	8 (1)	0 (0)	1 (0)	0 (0)	1 (0)	12 (1)
Prednisolone	15 (1)	14 (0)	2 (0)	15 (0)	0 (0)	1 (0)	1 (1)	3 (1)	51 (3)
Tofacitinib	1 (0)	0 (0)	1 (0)	18 (1)	0 (0)	0 (0)	0 (0)	0 (0)	20 (1)
Etanercept	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0)
Cyclosporine	10 (0)	0 (0)	0 (0)	5 (0)	0 (0)	0 (0)	0 (0)	3 (0)	18 (0)
Isotretinoin	1 (0)	14 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)	17 (1)
Hydroxychloroquine	0 (0)	10 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	2 (0)	13 (0)
Acitretin	9 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)	11 (1)
Mycophenolate mofetil	0 (0)	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0)
Infliximab	2 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)
Sulfasalazine	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Other medications	168 (7)	6 (1)	72 (4)	89 (0)	3 (0)	0 (0)	2 (1)	60 (2)	400 (15)
Combination therapy	33 (3)	2 (0)	0 (0)	12 (1)	0 (0)	0 (0)	1 (1)	2 (0)	50 (5)
Total	322 (14)	50 (1)	77 (4)	159 (3)	3 (0)	2 (0)	5 (4)	85 (6)	703 (32)

Values represent the number of patients who received the medication and (n) represent the number of COVID-19 positive cases.

merase chain reaction test during the course of the study was limited to very few cases, and it is assumed that the actual prevalence was higher than the reported one.

Many patients with several skin conditions are being treated with various immunosuppressive drugs, so it is important to investigate the correlation between taking these drugs and development of COVID-19. Currently, there are no data available to describe the benefits or risks of stopping immunomodulators and immunosuppressants during the COVID-19 outbreak.[4]

There are numerous opinions on the use of biologic drugs for treatment of psoriasis during the COVID-19 outbreak.[3]

In the current studies, patients on systemic immunomodulatory therapy had similar infection rates compared with the general population.[5-8] The mortality rate adjusted by age and sex did not increase in the patients who had received immunosuppressive therapies.[9]

In a recent study, an evidence-based approach to the risk of infection along with receiving dermatologic therapeutics was evaluated. Most biologics and conventional immunotherapies, such as methotrexate, cyclosporine, and azathioprine when based on the doses and indications in dermatology, did not appear to increase the risk of viral vulnerability. They are most likely safe to be used during the COVID-19 pandemic.[10]

In our studied population, only two of 56 patients treated with methotrexate, as well as one in 12 patients treated with the azathioprine and three of 51 patients treated with the prednisolone had developed COVID-19. There were no reports of COVID-19 in the patients treated with cyclosporine and mycophenolate mofetil.

Although 703 patients completed our questionnaire, the sample size in the subgroup of diseases was small, which was among one of the limitations of this study. The small sample size in the subgroups and those who had received the biologics may have prevented us from finding a statistically significant correlation between the use of biologics and development of COVID-19.

Unknown number of possible asymptomatic infections and the lack of available confirmatory COVID-19 tests were also limitations of this study.

Conclusions

We have presented an overview of the prevalence of COVID-19 in 703 patients with skin diseases undergoing treatment with a wide range of medications. Despite the addressed limitations, no positive correlation was observed between the development of COVID-19 infection and the use of immunosuppressive and immunomodulatory therapies. Other prospective studies with larger sample sizes are needed to prove the benefits and risks of using these agents during the ongoing COVID-19 pandemic.

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