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Report

The effect of COVID-19 on development of hair and nail disorders: a Turkish multicenter, controlled study

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Abstract

Background A broad spectrum of skin diseases, including hair and nails, can be directly or indirectly triggered by COVID-19. It is aimed to examine the type and frequency of hair and nail disorders after COVID-19 infection.

Methods This is a multicenter study conducted on consecutive 2171 post-COVID-19 patients. Patients who developed hair and nail disorders and did not develop hair and nail disorders were recruited as subject and control groups. The type and frequency of hair and nail disorders were examined.

Results The rate of the previous admission in hospital due to COVID-19 was statistically significantly more common in patients who developed hair loss after getting infected with COVID-19 ($P < 0.001$). Telogen effluvium (85%) was the most common hair loss type followed by worsening of androgenetic alopecia (7%) after COVID-19 infection. The mean stress scores during and after getting infected with COVID-19 were 6.88 ± 2.77 and 3.64 ± 3.04, respectively, in the hair loss group and were 5.77 ± 3.18 and 2.81 ± 2.84, respectively, in the control group ($P < 0.001$, $P < 0.001$). The frequency of recurrent COVID-19 was statistically significantly higher in men with severe androgenetic alopecia (Grades 4–7 HNS) ($P = 0.012$; Odds ratio: 2.931 [1.222–7.027]).The most common nail disorders were leukonychia, onycholysis, Beau's lines, onychomadesis, and onychoschisis, respectively. The symptoms of COVID-19 were statistically significantly more common in patients having nail disorders after getting infected with COVID-19 when compared to the control group ($P < 0.05$).

Conclusion The development of both nail and hair disorders after COVID-19 seems to be related to a history of severe COVID-19.

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Introduction

Coronavirus disease 2019 (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can progress with numerous symptoms such as weakness, fever, cough, loss of taste and smell and affects numerous organs including the skin.[1]

As the COVID-19 pandemic approaches its third year, it has been revealed that a wide spectrum of skin disorders, including hair and nails, can be directly or indirectly triggered by COVID-19.[2–5] Cytokine dysregulation and activation of inflammatory pathways due to the increase in numerous cytokine secretions such as interferon γ, tumor necrosis factor (TNF), interleukin (IL) 6, IL-1 β, IL-2, and IL-17A during COVID-19, may cause certain skin, hair, and nail diseases.[6] In the context of studies that revealed cytokines such as IL-17 causing psychiatric comorbidities including stress, a correlation has been established between the presence of stress due to COVID-19 and hair loss.[7,8] In addition, it has been suggested that stress is associated with a decrease in the number of melanocyte stem cells in the hair and gray hair.[9,10] Currently, there are a number of reports that proposed an increased rate of hair diseases such as telogen effluvium (TE), androgenetic alopecia (AGA), alopecia areata (AA) after COVID-19; however, reports with respect to graying/whitening of hair (GWH) are quite limited. Meanwhile, to the best of our knowledge, no studies have been conducted on the relationship between the presence of recurrent COVID-19 and hair/nail disorders.

There are certain case reports that assert nail findings such as Beau's lines, red half-moon appearance, and onychomadesis may occur after COVID-19.[2] However, there are no studies regarding the most common nail disorders developed after COVID-19 and the association between nail disorders and the severity of COVID-19.

In this study, the type and frequency of hair and nail disorders that occur after COVID-19 in patients presented to the dermatology outpatient clinics were examined. In addition, the association between hair/nail disorders and emotional stress, recurrent and severe COVID-19 status was investigated.

Material and methods

In seven different regions of Turkey, 1102 patients who consecutively presented to the dermatology outpatient clinics at secondary and tertiary care hospitals due to the development of hair and nail disorders after being infected with COVID-19 and 1069 patients who consecutively presented due to dermatologic conditions other than hair and nail disorders after being infected with COVID-19 were included in this study. SARS-CoV-2 infection was confirmed by detection of viral RNA using real-time reverse transcription polymerase chain reaction (RT-PCR). Patients who were under 18 years of age, who had hair/nail disorders before COVID-19, those with intellectual disability, and those with suspicion of COVID-19 but not confirmed by RT-PCR, and infected with COVID-19 within 2 months were excluded from the study.

The collected data from patients consisted of age, gender, and clinical presentations. A complete history was taken from every patient regarding comorbidities, the onset and duration of COVID-19 infection, history of COVID-19 related hospitalization and/or intensive care unit admission, history of systemic symptoms of COVID-19, stress levels during and after being infected with COVID-19, and the onset of hair and nail disorders.

The presence of nail disorders and AA, AGA, TE, and GWH status of the patients after being infected with COVID-19 were examined. The diagnosis of nail disorders, TE, AGA, and AA was made by specialist dermatologists. The diagnosis of TE depended on a history of shedding following COVID-19, physical examination, and confirmed by a hair pull test. Hamilton-Norwood classification system for males and Ludwig system for females were used for classification of AGA. The worsening of AGA was described by statements of the patients. The stress status of patients during and after COVID-19 was evaluated using a visual analog scale (from 1 to 10). Hospital and intensive care hospitalization criteria for COVID-19 were according to the "Ministry of Health Scientific Advisory Board Study" criteria across the country and evaluated as severe COVID-19.

The study protocol was approved by the Review Boards at all the participating institutions. The ethical approval was obtained from the Ministry of Health Scientific Research Study Applications (2021–03-2ITI3-24-13) and Van Yüzüncü Yıl University Ethic committee (2021/05–25). Written informed consent was obtained from the patients to publish the case details.

All statistical analyses were performed using IBM SPSS 26.0 Statistics (SPSS Inc., Chicago, IL, USA). Frequencies were used to summarize qualitative data. Kolmogorov–Smirnov and Shapiro–Wilk tests were used to find normality. The student *t*-test or Mann–Whitney test was used to compare scale variables according to a parametric or nonparametric distribution. The Kruskal-Wallis H test was used to search for any significant differences between two or more groups of an independent variable on a continuous or ordinal dependent variable. The association between categorical variables was tested using the chi-square test. $P < 0.05$ was considered statistically significant.

Results

Demographic characteristics

A total of 2171 patients including 1102 cases and 1069 controls were recruited in this study. Of the patients participating in the study, 1454 were females and 717 were males. In the case group, the mean age was 37.75 ± 13.32 years and mean body mass index (BMI) was 26.17 ± 5.15 kg/m^2, while in the control group the mean age was 38.44 ± 13.11 years and the mean BMI was 26.13 ± 4.87 kg/m^2. There was no statistically significant difference in mean age and BMI between the case and control group ($P = 0.117$, $P = 0.421$).

Hair disorders and COVID-19

Types of hair loss

Telogen effluvium (85%) was the most common hair loss type after getting infected with COVID-19. The frequency hair loss type is shown in Figure 1. The mean onset of hair loss was 5.43 ± 4.10 weeks regardless of types of hair loss while it was 5.30 ± 4.7 weeks in TE, 5.00 ± 3.87 weeks in worsening of AGA, and 9.44 ± 6.49 in AA.

Hair loss and systemic comorbidities

Thyroid diseases (hypo- and hyperthyroidism) and iron deficiency were significantly higher in patients who developed hair loss after getting infected with COVID-19 ($P = 0.009$, $P < 0.001$, respectively). The statistical differences between the rate of comorbid systemic diseases in patients with hair loss and the control group are given in Table 1.

Hair loss and COVID-19 symptoms

The main symptoms of COVID-19 including fever, fatigue, loss of taste and smell, cough, nausea, and vomiting were statistically more frequent in the hair loss group when compared with the control group ($P < 0.05$) (Table 2).

Hair loss and stress during and after COVID-19

The mean stress scores during and after getting infected with COVID-19 were 6.88 ± 2.77 and 3.64 ± 3.04, respectively, in the hair loss group while they were 5.77 ± 3.18 and 2.81 ± 2.84, respectively, in the control group ($P < 0.001$, $P < 0.001$). In addition, the mean stress levels during and after getting infected with COVID-19 were 7.77 ± 2.6 and 4.65 ± 3.07, respectively, in patients who were previously hospitalized due to COVID-19, while the levels were 6.13 ± 3.03 and 3.05 ± 3.07 in patients without hospitalization due to COVID-19 ($P < 0.001$, $P < 0.001$).

The types of hair loss were examined with each other in terms of mean stress score during and after COVID-19. There was no statistically significant difference between types of hair loss and mean stress scores during COVID-19 ($P = 0.596$), while there was a statistically significant difference between hair loss types and mean stress scores after COVID-19 ($P < 0.001$) (Table 3).

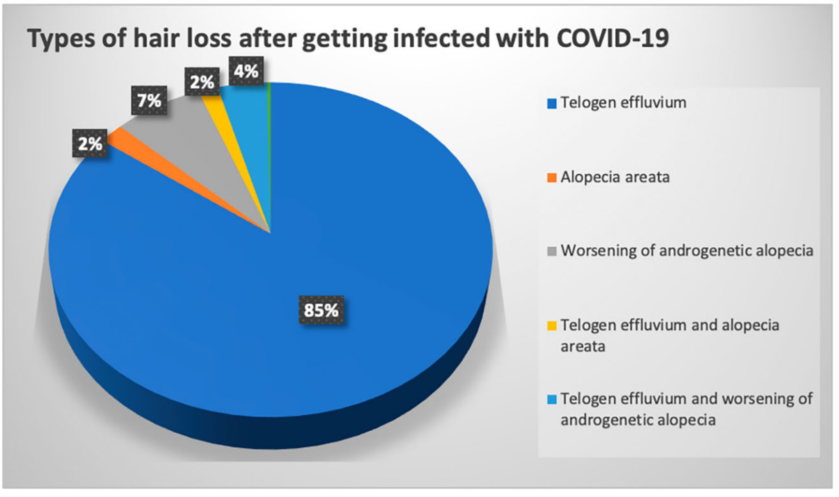

Figure 1 Types of hair loss after getting infected with COVID-19

Table 1 The differences between comorbid systemic diseases in hair loss and control group

Comorbid systemic diseases	Hair loss group [%]	Control group [%]	P value	Odds ratio	Odds ratio (lower-upper)
Thyroid diseases	8.5	5.6	0.009	1.588	1.119–2.254
Hypertension/CVD	12.3	13.6	0.399	0.892	0.684–1.163
Cerebrovascular disease	0.6	0.8	0.513	0.695	0.232–2.080
Diabetes mellitus	6.9	7	0.946	0.988	0.697–1.400
Asthma	5.9	4.3	0.097	1.407	0.938–2.109
Chronic renal failure	0.3	0.7	0.364	0.468	0.124–1.770
Benign prostate hyperplasia	3.2	2.4	0.966	1.031	0.256–4.160
Malig	1.3	0.5	0.075	2.751	0.952–7.947
Psychiatry	3.5	2.5	0.169	1.442	0.854–2.435
Iron deficiency	22.7	15.4	<0.001	1.615	1.286–2.028

CVD, cardiovascular disease.

Table 2 The frequency of COVID-19 symptoms in patients with hair loss and control group

Symptoms	Hair loss group [%]	Control group [%]	P value	Odds ratio
Fever	50.7%	40.6%	<0.001	1.501 (1.254–1.797)
Fatigue	90.1%	83.9%	<0.001	1.744 (1.324–2.297)
Loss of taste and smell	59.9%	52.7%	0.002	1.336 (1.1062–1.305)
Cough	64.5%	51.1%	<0.001	1.740 (1.447–2.092)
Nausea and vomiting	25.8%	21.9%	<0.001	1.563 (1.270–1.922)

Table 3 Types of hair loss and mean stress scores during and after COVID-19

Types of hair loss	Mean stress scores	
	During COVID-19	After COVID-19
Telogen effluvium	6.90 ± 2.76	3.60 ± 3.06
Alopecia areata	6.29 ± 2.37	3.41 ± 2.21
Worsening of androgenetic alopecia	6.69 ± 2.77	3.00 ± 2.74
Telogen effluvium & alopecia areata	8.38 ± 1.06	6.12 ± 3.52
Telogen effluvium & androgenetic alopecia	6.81 ± 3.37	5.28 ± 2.71
Telogen effluvium & androgenetic alopecia & alopecia areata	7.67 ± 4.04	8.33 ± 2.89
Total	6.88 ± 2.77	3.65 ± 3.05

Hair loss and hospitalizations due to COVID-19

There was a 16% history of hospitalization due to COVID-19 in the hair loss group while 10.3% in the control group. The rate of previous admission to the hospital due to COVID-19 was statistically significantly more common in patients who developed hair loss after getting infected with COVID-19 ($P < 0.001$). The odds ratio for hair loss after hospitalization due to COVID-19 was 1.655 (1.266–2.163).

The intensive care admission was 2.2% in the hair loss group while 1.3% in the control group. There was no statistical difference between the two groups in terms of previous intensive care admission ($P = 0.122$).

Androgenetic alopecia and hospitalization due to COVID-19

Women with and without AGA were examined in terms of hospitalization due to COVID-19. A total of 22.3% of women with AGA had admission to the hospital previously due to COVID-19, while 11.1% of women without AGA had admission to the hospital ($P < 0.001$). The odds ratio for admission to the hospital due to COVID-19 in women with AGA was 2.30 (1.47–3.60). There was no significant correlation between Ludwig severity and the number of days in hospital ($P = 0.129$). No statistically significant difference was found between having recurrent COVID-19 and the presence of AGA in women ($P = 0.484$).

A total of 2.3% of the women with AGA and 1.7% of the women without AGA had recurrent COVID-19. While recurrent COVID-19 was 6.5% in women with Ludwig 2 and 3 stage AGA, it was in 1.6% in women with Ludwig 1 stage and absence of AGA ($P = 0.097$). The odds ratio for women with Ludwig 2 and 3 stage AGA was 4.198 (0.945–18.644) in terms of recurrent COVID-19.

Men with AGA were compared to men without AGA in terms of admission to the hospital due to COVID-19, and no statistical difference was found between the two groups ($P = 0.196$). Men with AGA had 17.3% admission to the hospital due to COVID-19 previously, while men without AGA had 13.8% admission to the hospital.

A significant correlation was found between Hamilton grades and the number of days in hospital/number of days with COVID-19 symptoms ($P < 0.001$, Rho = 0.245; $P = 0.035$ Rho: 0.120, respectively).

There was no statistically significant difference between having recurrent COVID-19 and the presence of AGA in men ($P = 0.549$).

The frequency of recurrent COVID-19 was statistically significantly higher in men with over grades 3 AGA. The frequency of recurrent COVID-19 was 7.3% in men with over grades 3 AGA according to Hamilton classification while it was 2.6% in men with absence of AGA and presence of AGA grades 1–3 ($P = 0.012$; Odds ratio: 2.931 [1.222–7.027]).

Hair loss and trichodynia/itching

A total of 16.24% of patients with hair loss had concomitant trichodynia while 23.78% had itching. In addition to hair loss, trichodynia appeared at an average of 5.19 ± 5.32 weeks, while itching appeared at 4.71 ± 4.57 weeks.

Graying/whitening hair and COVID-19

A total of 321 (29.13%) patients developed GWH after getting infected with COVID-19. Among them, 20 had full (6.23%) and 301 (22.89%) had partial GWH. The graying/whitening hair occurred at an average of 6.71 ± 5.51 weeks. There were statistically significant differences between the presence of GWH before getting infected with COVID-19 and admission to the hospital/intensive care unit due to COVID-19. Similarly, there were statistically significant differences between the occurrence of GWH after getting infected with COVID-19 and admission to the hospital/intensive care unit due to COVID-19 (Table 4).

The mean age of patients who developed GWH after COVID-19 was 40.14 years while the mean age of patients who did not develop GWH after COVID-19 was 37.69 years ($P < 0.001$).

The mean stress scores during and after getting infected with COVID-19 were 7.33 ± 2.59 and 4.18 ± 2.94, respectively, in patients who developed GWH after COVID-19 and were 6.16 ± 3.08 and 3.09 ± 2.95 in patients who did not develop GWH ($P < 0.001$, $P < 0.001$).

The mean stress levels during and after getting infected with COVID-19 were 7.30 ± 2.60 and 4.14 ± 2.94, respectively, in patients who developed partial GWH after COVID-19 and were 7.95 ± 2.40 and 5.1 ± 2.92 in patients who developed full GWH ($P = 2.60$, $P = 0.156$).

Nail disorders and COVID-19

There were 165 patients who developed nail disorders after getting infected with COVID-19 in the study group. The most common nail disorders were leukonychia, onycholysis, Beau's lines, onychomadesis, onychoschisis, bruising on fingers and nails, and onychorrhexis (longitudinal ridging), respectively (Fig. 2). Increased fragility, orange color appearance, red half-moon, yellow discoloration of the nail, thickening, melanonychia, trachyonychia, pitting, slowing of elongation, and cuticle dystrophy were other rare nail disorders that occurred after getting infected with COVID-19. The time of the nail disorders onset is shown in Table 5.

The most common diseases accompanying nail disorder were iron deficiency (26.8%), thyroid disease (11.1%), hypertension and cardiovascular diseases (22.2%), asthma (9.6%), and diabetes mellitus (6.3%).

The symptoms of COVID-19 were statistically significantly more common in patients having nail disorders after getting infected with COVID-19 when compared to the control group ($P < 0.05$) (Table 6). No difference was found between the frequency of recurrent COVID-19 in patients who developed and did not develop nail disorders ($P = 0.124$).

The patients who developed nail disorders after getting infected with COVID-19 had a statistically significantly more common history of admission to the hospital and intensive care unit due to COVID-19 than patients who did not develop nail disorders ($P < 0.001$, $P = 0.002$). The odds ratios were 2.85 (1.920–4.230) and 4.034 (1.809–8.990), respectively.

Concomitant hair loss was present in 63% of individuals with nail disorders. There was a significant difference between the

Table 4 The presence of graying/whitening of hair before and after COVID-19 and admission to the hospital/intensive care unit due to COVID-19

	Admission to the hospital			Admission to the intensive care unit		
	%	**P value**	**Odds ratio**	**%**	***P* value**	**Odds ratio**
Graying/whitening of hair before COVID-19						
Yes	18.8	<0.001	2.379 (1.836–3.084)	3.2	<0.001	3.530 (1.707–7.314)
No	8.8			0.9		
Graying/whitening of hair after COVID-19						
Yes	20.4	<0.001	1.918 (1.424–2.584)	5.1%	<0.001	3.904 (2.026–7.521)
No	11.8			1.4%		

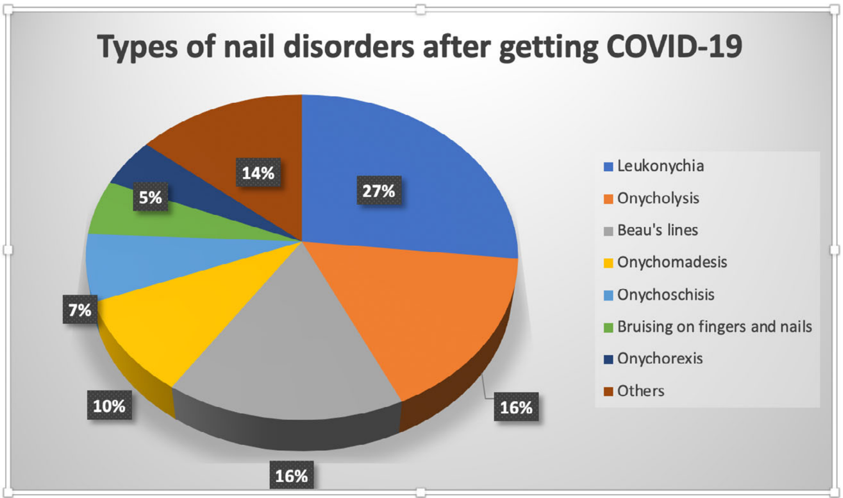

Figure 2 Types of nail disorders after getting infected with COVID-19

Table 5 The time of the nail disorders onset after getting infected with COVID-19

Nail disorders	The onset time (week)
Leukonychia	7.41 ± 5.77
Onycholysis	6.14 ± 4.77
Beau's lines	7.89 ± 5.18
Onychomadesis	9.46 ± 8.65
Onychoschisis	7.33 ± 2.73
Bruising on fingers and nails	4.86 ± 3.58

Table 6 The frequency of COVID-19 symptoms in patients with and without nail disorders

Symptoms	Case %	Control%	*P* values	Odds ratio
Fever	58.4	44.3	0.001	1.763 (1.241–2.505)
Fatigue	92	86.6	0.065	1.794 (0.956–3.368)
Loss of taste and smell	63.7	56	0.080	1.380 (0.961–1.982)
Cough	68.4	56.5	0.007	1.663 (1.146–2.414)
Nausea and vomiting	39.8	25.9	0.001	1.891(1.317–2.715)

presence of onycholyses ($P = 0.007$, OR = 3.249), Beau's lines ($P < 0.001$, OR = 4.69), and onychomadesis ($P = 0.002$, OR: 5.32) and history of admission to the hospital due to COVID-19, while there was no statistically significant difference between the presence of leukonychia and history of admission to the hospital ($P = 0.054$).

Discussion

There are important reports that highlighted the increased rate of any types of hair loss during the current pandemic.[4,11,12] Some of these studies proposed that an increased rate of hair loss may be due to the effect of pandemic-related emotional stress or COVID-19-related proinflammatory cytokines.[13] In the meantime, hair loss after severe/long-term febrile diseases has already been described. Therefore, it can be speculated that the worldwide effect of the current febrile and stress-based COVID-19 may trigger and increase the number of hair and nail diseases such as any infectious diseases.

In our study, the mean stress scores were 7.77 and 4.65 during and after hospitalization due to COVID-19. However, the mean stress scores were 6.88 and 3.65 in those with hair loss while they were 5.77 and 2.81 in those without hair loss regardless of hospitalization status. This condition may lead to the perspective that the severity of stress during the COVID-19 infection influences hair loss. On the other hand, the fact that the level of stress in patients with hair loss is relatively lower than in hospitalized patients may indicate that stress is a priority for individual psychological susceptibility rather than COVID-19-related cytokine storm in hair loss. We also found that the stress level after COVID-19 was most commonly associated with an increase in TE followed by AA and a worsening of AGA, respectively. Moreover, different types of hair loss together have been increased significantly in cases where the stress level was severe. This may shed light on new studies on the role of stress levels on the etiopathogenesis of different types of hair loss.[14]

A correlation between the duration of certain types of hair loss and the severity of COVID-19 has been postulated previously.[6,15,16] In our previous reports, we found an increased percentage of patients with TE from 0.4% to 2.17 and AA from 0.97% to 1.48% after 2 months since the pandemic's onset. Basically, these results did not include patients who got infected with COVID-19 because the pandemic has just begun. Subsequently, certain reports have been published to pay attention to the types of hair diseases and average time onset of hair diseases such as TE and AA in patients infected with COVID-19. In the multicenter study, Moreno-Arrones et al. reported the average time onset of 214 TE was about 8 weeks in the post-

COVID-19 term.[13] Similarly, Tatiana F. Abrantes et al. reported the median onset time of acute TE was 45 (about 6 weeks) days after PCR positivity.[16] Italian survey reported that 42.5% of patients with AA had recurrence after COVID-19, and the median duration of time for recurrence was 2.14 months.[7] In this study, we found that TE (85%) was the most common type of hair loss followed by worsening of AGA (7%). The onset of the hair loss after COVID-19 was about 5 weeks in both types of hair loss. On the other hand, the average onset time of AA was 9.44 weeks after getting infected with COVID-19. Although TE typically occurs 3–4 months after triggering events including stress, drugs, or postpartum, it can be suggested that TE which occurs after COVID-19 may have a short time to onset.[17] Moreover, our results show that a history of emotional stress may extend to 3 months for AA.

We found that the most common comorbidities for hair loss after COVID-19 infection were thyroid diseases along with iron deficiency. This condition is also anticipated in the common etiology of hair losses regardless of getting infected with COVID-19.[17,18] We did not find common comorbidities such as hypertension, diabetes mellitus, asthma, and malignancy as risk factors for post-COVID-19 hair losses. On the other hand, the main symptoms of COVID-19 such as fever, fatigue, loss of taste and smell, cough, nausea, and vomiting were higher in the hair loss group. The relative risk for hair loss was highest in patients who have fatigue and cough symptoms during COVID-19.

The hypothetical effect of AGA on COVID-19 was first identified by Goren et al. during the pandemic. The authors revealed that men with AGA had a higher incidence of hospital admission due to COVID-19.[3] Similarly, Wambier et al. examined 175 patients with SARS-CoV-2 infection and reported that patients with COVID-19 have a remarkable proportion of AGA.[19] Another study consisted of 1941 symptomatic males that tested for COVID-19 (336 PCR-positive, 1605 PCR-negative) found that severe AGA (HNS 4–7) was significant with a higher rate of COVID-19 positivity.[20] In concordance with the literature, we found a higher incidence of patients with AGA in hospital admission due to COVID-19 when compared to patients who did not have AGA in both genders.[3,19,20] In addition, in spite of low Rho factors, a significant correlation was firstly found between HNS score and the number of days in hospital/the number of days with COVID-19 symptoms due to COVID-19.

To the best of our knowledge, this is the first study to determine the effect of severity of AGA on recurrent COVID-19. We found a statistically significant increased proportion of recurrent COVID-19 in males with severe AGA (Grades 4–7 HNS). The relative risk of recurrent COVID-19 in males with severe AGA was approximately 3 times. In addition, although it is not significant, females with severe AGA (Ludwig 2–3) had approximately 4 times more frequent recurrent COVID-19 when compared with other females. The current studies revealed that the main pathogenesis of COVID-19 is associated with the angiotensin converting enzyme-2 (ACE-2) receptor localized in alveolar epithelial cells.[21] Subsequent studies reported that the entrance of the virus to the cells via ACE-2 receptor depends on androgen-related transmembrane protease, TMPRSS2.[22] TMPRSS2 cleaves ACE-2 receptors and leads to binding spike protein to the receptor more easily which resulted in the viral spread.[23–25] To date, no promoters were determined beyond androgens for TMPRSS2.[26] It can be speculated that the high androgen activity-related-TMPRSS2 leads to the entrance of the virus more easily and causes recurrent COVID-19 in patients with AGA. The result of our study may raise the question of whether individuals with severe AGA need extra precautions such as the number/time duration of booster shots of vaccines in order to protect themselves from recurrent infections.

It has been previously reported that trichodynia is associated with TE and AGA while the severity of trichodynia is not correlated with the hair loss activation. In previous reports, Williman and Trüeb reported that trichodynia was positive in 29% of patients with hair loss including TE and AGA.[27,28] To date, there is only one report regarding trichodynia and TE in patients with COVID-19 that reported trichodynia was present in 42.4% of patients with post-COVID-19. In our study, we found the proportion of trichodynia in hair loss was approximately similar to studies conducted in the pre-pandemic period. The onset of trichodynia was at the same time as the onset of hair loss (about 5 weeks after COVID-19).

Ramos et al. performed the online questionnaire-based cross-sectional study and found that severe COVID-19 was considerably associated with extensive gray hair. The study also confirmed previous studies which found gray hair and AGA was correlated with cardiovascular diseases, which is one of the critical factors for COVID-19 severity.[10,29] In our study, approximately one-third of patients developed GWH after getting infected with COVID-19. The average age of patients who developed GWH after COVID-19 was higher when compared with patients who did not develop GWH after COVID-19. In concordance with previous studies, we found patients who had GWH previously have 2.4 and 3.5 times higher admission to the hospital and intensive care units due to COVID-19, respectively. In addition, we found patients who developed GWH after COVID-19 have also considerable more admission to hospital and intensive care units previously due to COVID-19. This may be related to the significant increase in stress levels both during and after COVID-19. It is well known that restraint stress along with chronic unpredictable stress can result in increased numbers of white hairs over time.[30,31] Furthermore, it has recently been found that acute stress leads to hair graying via rapid depletion of melanocyte stem cells.[32] Further studies are required in order to know whether acute or chronic stress has more effect on GWH after getting infected with COVID-19.

In addition to hair involvement, nail involvement has also been reported after COVID-19 infection. The exacerbation of certain cytokines including IFN-α and microthrombosis resulting from microvascular inflammation microthrombosis may lead to certain nail changes in patients with COVID-19.[33,34] To date, most of the reports related to nail findings and COVID-19 are in the setting of case reports or letters to the editor.[2] To the best of our knowledge, there are currently no studies on the frequency of nail findings in patients who recovered from COVID-19. According to our study, the most common nail disorders after COVID-19 were leukonychia (punctate, striate, diffuse, striate longitudinal or transverse) (27%) followed by onycholysis (16%), Beau's lines (16%), onychomadesis (14%), onychoschisis (7%), bruising on fingers and nails (5%), and onychorrhexis (longitudinal ridging) (5%), respectively. In previous case reports, the time onset of leukonychia after COVID-19 was from 5 days to 1.5 months; on the other hand, the time onset of Beau's lines after COVID-19 was 1.5–3.5 months, and onychomadesis was about 3 months.[35–38] In our study, we found the average time onsets of leukonychia, Beau's lines, and onychomadesis were 7.41, 7.89, and 9.46 weeks, respectively. It is well-known that the nail growth rate is about 3.47 mm/month for fingernails, which are the most common site for occurrence of Beau's lines; therefore, the distance between the Beau lines and nail matrix may give the history of presence and time onset of COVID-19.[39] Among the nail findings, onychomadesis appeared for the longest time. This timeline may also give some clues whether patients—although they do not know—were experiencing asymptomatic COVID-19 previously. The development of trachyonychia, pitting, slowing of elongation, and cuticle dystrophy has not been reported yet after being infected with COVID-19. However, rare presentation of these findings makes strength to make them associated with COVID-19. The orange color appearance, red half-moon that are the new findings related to COVID-19 have also been observed in our study, though they were observed rarely. Interestingly, these findings have also been observed in patients with Kawasaki syndrome that is characterized by vascular inflammation.[40] Therefore, it can be speculated that these nail findings may be associated with vascular microinflammation.

We found that the most common systemic diseases accompanying nail disorder were iron deficiency which may explain the reason for nail fragility after COVID-19 followed by hypertension and cardiovascular diseases.[41] In addition, the history of severe COVID-19 was associated with development of nail disorder. According to our study, as the severity of COVID-19 was increased, the risk of development of nail disorders increased. The relative risk of nail disorder was highest in patients with a history of gastrointestinal symptoms such as nausea and vomiting due to COVID-19.

In previous reports, it has been proposed that severe cases of COVID-19 may be associated with nail disorders including onychomadesis and half and half nail.[2,38] To our knowledge, our study is the first study in the literature that reported a significant relationship between certain nail disorders and the severity of COVID-19. Among the frequent nail disorders, we found that onycholysis, Beau's lines, and onychomadesis developed significantly in patients who were previously admitted to the hospital due to COVID-19. The relative risk of onychomadesis was highest with about five times as much as the control group. On the other hand, there was no statistical difference between the occurrence of leukonychia and history of admission to the hospital due to COVID-19.

Although the current study includes a wide aspect of hair and nail disorders, there are some limitations. The fact that lack of follow-up after COVID-19 and the onset of diseases is based on declaration leads to increases in the possibility of recall bias. In addition, the whole course of hair and nail disorders has not been evaluated. Additional clinical investigation such as long-term follow-up are currently underway in order to observe the progress of diseases.

In conclusion, as we are about to leave behind the second year of COVID-19, there are still multiple gaps regarding the post-COVID-19 manifestations of hair and nail disorders. There are numerous types of hair and nail disorders that appeared after COVID-19. It seems that the development of both nail and hair disorders after COVID-19 may be related to a history of severe COVID-19. The current study encourages further researches in order to achieve a precise relationship between COVID-19 and hair/nail disorders.

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