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COVID-19 induced telogen effluvium

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Abstract

COVID-19 is a febrile, infectious illness that has previously been associated with telogen effluvium (TE). However, to date, no study has been conducted to determine the incidence of TE in those who have had COVID-19. To assess the frequency of TE in post-COVID-19 patients and the correlation between the development of TE and the severity of COVID-19, to understand whether emotional stress or medications are responsible for the development of TE. Totally 204 patients with a history of SARS-CoV-2 infection in the last 3 months were included in the study. The diagnosis of TE was made by history of excessive hair shedding, hair pull test, diffuse or bitemporal thinning, and absence of anisotrichosis in trichoscopy. Patients who did not have any TE cause other than COVID-19 and whose hair loss started after COVID-19 were considered as “COVID-19 associated TE (CATE).” We found TE in 75 (36.7%) cases and androgenetic alopecia (AGA) in 85 (41.7%) cases. CATE was present in 27.9% of cases and developed on average 53.76 ($\pm$ 23.772) days after COVID-19 real-time reverse transcription polymerase chain reaction (RT-PCR) positivity. The proportion of patients with CATE was numerically higher in hospitalized patients compared to outpatients (31.7% vs. 24.3%; $p = 0.238$); and significantly higher in women compared to men (42.3% vs. 6.2%; $p < 0.001$), in patients with hypertension compared to those without hypertension (40.4% vs. 23.1%; $p = 0.014$), and in patients who had respiratory symptoms compared to those who had not (31.7% vs. 14.0%; $p = 0.021$). The patients with and without CATE were similar in terms of stress level and usage of COVID-19 medications. Patients with AGA had a higher rate of hospitalization (69.4% vs. 35.3%; $p < 0.001$) and a higher incidence of fever (69.4% vs. 54.6%; $p = 0.033$) during COVID-19, compared to those without. TE developed in approximately one-quarter of people who have had COVID-19, and our study is the first to detect it. The time to onset of CATE, which was 7–8 weeks after the SARS-CoV-2 RT-PCR positivity, was not much different from post-infectious TE. Patients with severe COVID-19 seem to be more prone to develop TE. The presence of AGA is associated with a more severe COVID-19. During the pandemic, clinicians should consider a previous SARS-CoV-2 infection in patients presenting with hair loss.

KEYWORDS

androgenetic alopecia, COVID-19, SARS-CoV-2, telogen effluvium

1 | INTRODUCTION

Telogen effluvium (TE) is the most common cause of nonscarring alopecia. It is characterized by a diffuse hair shedding, which manifests 2–3 months after a triggering event. Several triggering factors such as febrile diseases, physiological or emotional stress, medications, endocrine abnormalities, organ failure, or nutritional deficiencies may result in TE. Immediate anagen release, abrupt termination of the anagen phase and premature entry into the telogen phase, is the pathomechanism of TE caused by febrile states, infectious diseases, or drugs.¹

The novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has previously been linked to TE. In several reports, TE has developed 2–12 weeks after the SARS-CoV-2 infection.^{2,3} The incidence of TE in New York City has been shown to increase by more than 400%, approximately 3–4 months after the COVID-19 was declared a pandemic.⁴ However, to date, no studies have been conducted on the incidence of TE in the patients who have recovered from the COVID-19. Besides, the relationship between the severity of COVID-19 and the development of TE is unknown.

In the present study, we aimed to assess the incidence of TE developed following COVID-19 and the correlation between the development of TE and the severity of infection. Our secondary objectives were to determine whether psychological stress during infection or COVID-19 treatments caused TE.

2 | METHODS

We designed a prospective study in Istanbul Medeniyet University Prof. Dr. Suleyman Yalcin City Hospital between February 2021 and April 2021. Ethics approval was obtained from local ethics committee (2021/0123, clinicaltrials.gov NCT04834102). Patients who admitted to dermatology or infectious diseases outpatient clinics with any complaints and had a history of SARS-CoV-2 infection confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) in the last 3 months were enrolled in the study. Informed consent was obtained from all subjects.

The diagnosis of TE was made by typical history of excessive hair shedding (e.g., reduction of the ponytail in diameter, clogging of the shower drain by hairs) and following physical findings: positive pull test, diffuse or bitemporal thinning, and absence of anisotrichosis in trichoscopy. Hair pull test was done by grasping about 40–60 hairs between the thumb and index finger and pulling gently-firmly from the scalp. Pulling out of more than 10% of hair (≥ 4 –6 hairs) was considered positive. Anisotrichosis in trichoscopy ($>10\%$ miniaturized hair) was deemed compatible with androgenetic alopecia (AGA).

Demographics, comorbidities, therapeutic agents used for COVID-19, and any history of alopecia or iron deficiency prior to COVID-19 were noted; and as an indicator for the severity of COVID-19; hospitalization status and -if hospitalized- length of hospital stay, peak body temperature, peak level of C-reactive protein (CRP),

COVID-19 symptoms and their duration were recorded for all participants. Patients' stress levels during infection were assessed using a scale of 1–10; where 1 refers to “low or no stress” and 10 indicates “very high stress.”

If the diagnosis of TE was made, subjects were investigated to exclude other common causes of TE such as anemia, iron deficiency, or thyroid dysfunction. Patients who had no other potential cause for TE except COVID-19 or who had anemia but had a history of hair loss started subsequent to COVID-19 were considered “COVID-19 associated TE (CATE).”

Statistical Package for Social Sciences (SPSS) v17.0 was used to analyze data. χ^2 test was used for categorical variables, Mann-Whitney or independent samples t tests were used for quantitative variables. *p* value of <0.05 was considered significant.

3 | RESULTS

A total of 204 subjects, 103 of whom had been treated at home and 101 had been hospitalized during COVID-19 infection, were recruited to the study. One hundred twenty-three of the cases were female and 81 were male. The mean age was 47.23 (± 16.471). COVID-19 symptoms were constitutional (87.3%), respiratory (78.9%), fever (60.8%, mean: 38.04 [± 1.054]°C), anosmia (54.9%), and gastrointestinal (33.8%), respectively. Fifty-seven of patients had hypertension (27.9%), 36 (17.6%) had diabetes, and 29 (14.2%) had anemia. Hypertension and diabetes were more common in hospitalized patients than in outpatients (37.6% and 27.7%; respectively). Favipiravir was the most commonly used medication.

Scalp examination revealed TE in 75 (36.8%) cases, AGA in 85 (41.7%) cases, and alopecia areata in three (1.5%) cases. Of the 75 patients with TE, 57 (27.9%) were considered COVID-19 associated TE (Table 1). The development of CATE was an average of 53.76 (± 23.772) days after COVID-19 RT-PCR positivity. COVID-19 associated TE was more frequent but not statistically significant in hospitalized patients compared to outpatients (31.7% vs. 24.3%; *p* = 0.238).

TABLE 1 Distribution of patients with hair loss by diagnoses and possible causes

Diagnosis	N (%)	
Telogen effluvium (TE)	Total	75 (36.8%)
	1. COVID-19 associated TE	57 (27.9%)
	-No other cause except COVID-19	42 (20.6%)
	-Anemia is present but hair loss started after COVID-19	15 (7.4%)
	2. TE probably due to anemia	7 (3.4%)
	3. No other identifiable cause for TE but no time link to COVID-19	7 (3.4%)
	4. TE due to other causes	4 (2.0%)
Androgenetic alopecia (AGA)		85 (41.7%)
Alopecia areata		3 (1.5%)

The proportion of patients with CATE was significantly higher in women compared to men (42.3% vs. 6.2%; $p < 0.001$), in patients with hypertension compared to those without hypertension (40.4% vs. 23.1%; $p = 0.014$), and in patients who had had respiratory symptoms compared to those who had not (31.7% vs. 14.0%; $p = 0.021$) (Table 2). There was no significant difference between patients with and without CATE in terms of age, body mass index, length of hospital stay, duration of COVID-19 symptoms, usage of several therapeutic agents for COVID-19, stress level, peak body temperature, and peak level of CRP (Table 3).

Of the 85 patients with AGA, 30 (35.3%) were female and 55 (64.7%) were male. Patients who had AGA had a significantly higher rate of hospitalization (69.4% vs. 35.3%) and higher incidence of fever during COVID-19 (69.4% vs. 54.6%) compared to those who did not ($p < 0.001$ and $p = 0.033$; respectively).

4 | DISCUSSION

COVID-19 is a febrile, infectious disease, a cause of emotional stress, and a reason to use several medications; all of which make it a potential cause of TE. There have been a few studies investigating the development of TE as a consequence of COVID-19. Kutlu and Metin have found that the incidence of TE was 5.51 times higher during the COVID-19 pandemic period compared to the corresponding month of the previous year, which increased from 0.40% to 2.17%.⁵ Likewise, Cline et al. showed an increase in the incidence of TE from 0.5% to 2.3%, nearly 3–4 months after COVID-19 became a pandemic.⁴ These

two studies determined the incidence of TE in all hospital admissions but not in patients with a history of COVID-19. In a recent study of 128 post COVID-19 patients who presented to hair clinics with hair loss and/or scalp complaints, TE was observed in 66.3%.⁶ However, this study was conducted only in those with hair loss and/or scalp complaints and does not provide data on the frequency of COVID-19 associated TE in all post COVID-19 patients. To our knowledge, this is the first study to determine the incidence of TE in patients who have recovered from COVID-19.

We found TE in 36.7% of the patients. After excluding cases with other potential causes of TE (e.g., anemia) or who have already been having hair loss prior to COVID-19; we determined CATE in 27.9% of the patients. Compared to the incidence of TE which has been found to be 2.17% and 2.3% during the pandemic period, the TE frequency of 27.9% in post-COVID-19 cases in our study suggests that COVID-19 is an important trigger for the development of TE.^{4,5}

COVID-19 associated TE was more common in women than men. Some authors attribute the higher incidence of TE in women to the fact that women take hair loss more seriously than men and that they are more prone to consult a physician with this complaint.¹ However, this explanation cannot be valid for our study in which all post-COVID-19 patients were examined, regardless of whether they had symptoms or not. In our opinion, the fact that men keep their hair shorter and many have male pattern baldness makes it difficult to diagnose TE.

COVID-19 associated TE developed 53.8 days after COVID-19 RT-PCR positivity, which was consistent with literature data. In a prospective study of 191 acute TE cases with prior SARS-CoV-2 infection, hair shedding occurred 57.1 days after the infection was detected.⁷ In a survey performed by hair experts, the time until TE develops after COVID-19 was determined as 3 weeks for 25 cases with trichodynia and 13 weeks for 42 cases without it.⁶ Although the authors of this study defined this situation as “early onset TE” and “late onset TE”; the time to CATE after RT-PCR positivity in our study was unimodal and not much different from usual post-infectious TE.⁸

Mean ages, body mass index, the highest body temperature values, and CRP levels during COVID-19, recovery times from infection, and length of hospital stay of those who have CATE; were not different from those who have not. Although statistically not significant, the frequency of CATE was slightly higher in hospitalized patients than in outpatients (31.7% vs. 24.3%). Consistent with the well-known relationship between hypertension and the severity of SARS-CoV-2 infection, the hospitalization rate in patients with hypertension was significantly higher than in patients without hypertension, in our study.⁹ Moreover, CATE was more common in those with hypertension than in those without. Lastly, we found the incidence of CATE to be higher in patients with respiratory symptoms compared to those without. Considering that hospitalization status, the presence of hypertension, and the presence of respiratory symptoms are important indicators of COVID-19 severity, the abovementioned findings in our study can be interpreted as that CATE is more common in those with severe COVID-19.

TABLE 2 Comparison of the frequencies of COVID-19 associated telogen effluvium in various groups

Comparison of the frequencies of COVID-19 associated telogen effluvium in various groups	Frequency of CATE (%)	<i>p</i>
In hospitalized patients	31.7	0.238
In outpatients	24.3	
In women	42.3	<0.001*
In men	6.2	
In patients with hypertension	40.4	0.014*
In patients without hypertension	23.1	
In patients with diabetes mellitus	36.1	0.229
In patients without diabetes mellitus	26.2	
In patients who have had respiratory symptoms during COVID-19	31.7	0.021*
In patients who have not had respiratory symptoms during COVID-19	14.0	
In patients who have had fever during COVID-19	29.0	0.665
In patients who have not had fever during COVID-19	26.3	

Abbreviation: CATE, COVID-19 associated telogen effluvium.

* $p < 0.05$.

TABLE 3 Comparison of patients with and without CATE

	In patients with CATE	In patients without CATE	<i>p</i>
Age	48.8	46.6	0.481
Mean BMI	28.4	27.9	0.549
Comorbidities			
Hypertension	40.4%	23.1%	0.014*
Diabetes mellitus	22.8%	15.6%	0.229
Indicators of COVID-19 severity			
Rate of hospitalization	56.1%	46.9%	0.238
Presence of fever	63.2%	59.9%	0.665
Peak body temperature (°C)	38.0	38.0	0.666
Peak level of CRP	6.8	10.8	0.265
Length of hospital stay (days)	7.0	8.6	0.083
Duration of COVID-19 symptoms (days)	13.8	14.2	0.924
Mean stress scores (1–10) during infection	7.7	7.1	0.171
Usage of drugs during infection			
Favipiravir	59.6%	70.1%	0.155
Antibiotics	57.9%	47.6%	0.188
Enoxaparin	52.6%	46.3%	0.414
Corticosteroids	40.4%	35.4%	0.508
Parasetamol	33.3%	35.4%	0.784
Lopinavir/Ritonavir	26.3%	15.0%	0.059
Acetylsalicylic acid	12.3%	23.1%	0.075
NSAID	8.8%	8.8%	0.987
Hydroxychloroquine	3.5%	2.7%	0.765

Abbreviations: BMI, body mass index; CATE, COVID-19 associated telogen effluvium; CRP, C-reactive protein; NSAID, non-steroidal anti-inflammatory drugs.
**p* < 0.05.

The medications used for COVID-19 may also play a role in the development of TE. In particular, the use of anticoagulants has been linked to the occurrence of TE previously.¹⁰ However, in the present study, TE was not found more frequently in patients who have used any drug than in those who have not used it. It is known that emotional stress is another potential cause of TE.^{1,11} In previous publications on the relationship between the COVID-19 pandemic and TE, it has been speculated that the psychosocial stress resulting from the pandemic itself and/or “stay at home” orders may be responsible for the increased incidence of TE.^{4,12} However, we found the mean stress scores of patients with CATE during infection to be similar to those without CATE. These findings suggest that CATE is caused by the infection itself, not the drugs or emotional stress.

The higher incidence of fever and hospitalization rates in those with AGA in our study is consistent with literature data suggesting that AGA is associated with a more severe course of COVID-19. The relationship between AGA and severe COVID-19 may be due to androgen receptor hyperactivation, since androgen receptors involved in the pathogenesis of AGA regulate the transmembrane protease serine-2, which plays a role in the entry of SARS-CoV-2 into the cell.¹³

Several pathogenetic mechanisms have been suggested previously to explain COVID-19 associated TE. Pro-inflammatory cytokines

such as IL-6, TNF α , IL-1 β , and IFN γ , which are released during systemic hyperinflammation of the COVID-19 may be responsible for the inhibition of hair shaft elongation, damage to matrix cells, and catagen development.^{14–16} Microthrombotic reaction due to decreased concentration of anticoagulant proteins, occlusion of the hair follicle vasculature, and the resulting cell death is another hypothesis.^{6,17} Lastly, direct infection of the hair follicle by SARS-CoV-2 has also been implicated in the development of CATE.⁶

Our study has several limitations. First, we did not utilize relatively objective methods such as trichogram or modified wash test to diagnose TE. Second, we did not record whether trichodynia, a scalp complaint sometimes accompanies hair loss, was present in our cases. Finally, since we did not maintain a long-term follow up, we do not know how long the hair loss lasted in the patients.

To conclude, hair loss develops in about a quarter of people who have had COVID-19, and the present study is the first to provide data on this issue. The time to onset of COVID-19 associated TE is not much different from post-infectious TE, which occurs approximately 2 months after the triggering factor. Those who have had more severe COVID-19 appear to be more likely to develop TE. In line with the previous reports, the presence of AGA seems to be associated with a more severe SARS-CoV-2 infection. These data again prove that just

as COVID-19 can affect hair health, existing hair disease can also be an indicator for the course of COVID-19. During the pandemic period, clinicians should consider a previous COVID-19 infection in patients presenting with hair loss.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Hasan Aksoy, Umut Mert Yıldırım, Pınar Ergen, and Mehmet Salih Gürel performed the research. Hasan Aksoy and Mehmet Salih Gürel designed the research study. Hasan Aksoy, Umut Mert Yıldırım, and Pınar Ergen collected and processed the data. Hasan Aksoy and Mehmet Salih Gürel analyzed and interpreted the data. Hasan Aksoy wrote the paper. Mehmet Salih Gürel performed the critical review. All authors have read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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