COVID-19-associated Telogen Effluvium After Hospital Discharge: A Prospective Cohort Study

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ABSTRACT

Introduction Telogen effluvium (TE) is a common sequela of SARS-CoV-2 infection. Existing studies are highly heterogeneous. We aimed to assess the prevalence of TE in a cohort of patients with severe disease hospitalized for acute COVID-19.

Methods This prospective cohort study was conducted at the University Clinic of Dermatology, part of the COVID-19 University Hospital Network throughout the pandemic. The acute phase data were extracted from electronic hospital records. Details about hair loss were obtained at two follow-up points, 3 and 6 months after hospital discharge, using telephone interviews.

Results A total of 77 patients were successfully followed up, and 40 (48.8%) were male. The mean age was 55.91, SD=10,588. Overall, 68.8% of patients reported TE. Among these, 52.8% reported early onset, and 50.9% reported moderate hair loss. 11 (20.7%) reported complete hair regrowth within three months, and an additional 32 (60.3%) reported complete regrowth within six months. 4 (7.5%) patients have chronic TE. Female sex ($p<0.0001$), anemia ($p=0.019$), hypoproteinemia ($p=0.037$), and severe pneumonia ($p=0.004$) were associated with TE. Age, fever, SpO2, CRP levels, in-hospital complications, and raised D-dimers were not associated with TE.

Discussion Our study confirmed a high prevalence of COVID-19-associated TE in hospitalized patients. Anemia and hypoalbuminemia were associated with TE, shedding new light on the possible pathogenesis. COVID-19-associated TE occurs earlier than classic TE and has a good prognosis in most patients. However, chronic TE was reported by 7.5%. Even a small incidence of long-term sequelae during a pandemic could have substantial health consequences.

KEYWORDS: anemia, hypoalbuminemia, COVID-19, SARS-CoV-2, telogen effluvium

INTRODUCTION

The spectrum of hair loss in coronavirus disease 2019 (COVID-19) includes acute and chronic telogen effluvium (TE), worsening of androgenic alopecia, alopecia areata, including alopecia universalis, and rarely anagen effluvium (1-4). COVID-induced TE likely results from immediate anagen release due to acute-phase infection (5). The proposed mechanisms based on current knowledge are direct viral damage of hair

Table 1. Clinical characteristics and laboratory findings of interest in enrolled patients hospitalized for COVID-19 (N=77)

Variable	Participants (N=77)
Age, mean (range), SD, years	55,91 (29-84), 10.588
Male, n (%)	40 (48.8)
TE, n (%)	53 (68.8)
Effluvium before COVID-19, n (%)	30 (38.9)
Admission SpO2, mean (range), SD	89.92 (60-99) 7.576
Fever on admission, n (%)	62 (75.6)
Severe pneumonia, n (%) No Yes	 10 (12.9) 67 (87.1)
CCI, n (%) No comorbidities Mild (CCI scores of 1-2) Moderate (CCI scores of 3-4) Severe (CCI scores ≥5)	 34 (41.5) 33 (40.3) 7 (8.5) 3 (3.6)
Mean CCI, (SD)	1.06 (1.389)
In-hospital medical complications, n (%) DM GI Neurological Psychiatric	 10 (12.2) 5 (6.1) 1 (1.2) 1 (1.2)
Anemia, n (%)	27 (32.9)
CRP, mean, range, SD, mg/L	90.65 (0-368) 70.761
Hypoalbuminemia, n (%)	36 (43.9)
Elevated D-dimer, n (%)	66 (80.4)

TE: telogen effluvium; SD: standard deviation; DM: diabetes mellitus; CCI: Charlson Comorbidity Index; CRP: C-reactive protein; SpO2: peripheral oxygen saturation; GI: gastrointestinal

follicles (6) and the immune-mediated phenomenon triggered by the virus (7). Hypoxia, feverish condition, emotional stress, metabolic stress, iron deficiency, thyroid dysfunction, and the medications used in the management of COVID-19, particularly anticoagulants, can also be a contributing factor (8-11). Notably, some or all of these may coexist in a given patient (7).

COVID-induced TE is a common post-acute sequela of SARS-CoV-2 infection; existing studies are highly heterogeneous, as they include patients with various COVID-19 severity levels and different time frame analyses (3,4,6,7,12). Our aim was to assess the prevalence of TE in a cohort of patients with severe disease hospitalized for acute COVID-19 during the predominance of the Alpha variant of the disease.

PATIENTS AND METHODS

Study design and participants

This prospective cohort study was conducted at the University Clinic of Dermatology in Skopje, which was part of the COVID-19 University Hospital Network throughout the pandemic. The study population included all patients aged 18 years or older who had survived until discharge after hospitalization with COVID-19 from January 1, 2021 to March 31, 2021, a period in which the Alpha variant was the predominant SARS-CoV-2 variant circulating in Macedonia. This study adheres to the STROBE statement (Supplementary material S1) (13). The study protocol was approved by the Ethics Review Committee (03-50881/13).

Data collection and follow-up

The acute phase data of the patients were extracted from electronic hospital records that included demographics, date of first symptoms appearance, vital signs, and laboratory results of interest. For patients with repeated measurements, the highest/peak measurements were extracted. Charlson index (14) was employed to summarize pre-existing comorbidities. We used the National E-health system ("Moj Termin") to confirm COVID-19-related deaths after discharge.

Details about hair loss were obtained at two follow-up points, 3 and 6 months after hospital discharge. The interviewers were dermatologists and dermatology residents, all involved in the treatment of the patients during hospitalization. The interviews were conducted in Macedonian or Albanian based on patients' language fluency. The research objectives were explained to the patients, and verbal consent

Table 2. Severity, timing, and outcomes of COVID-19-associated telogen effluvium (N=53)

Time to onset of TE, n (%) <1 month 1-2 months >3 months Uncertain	 28 (52.8) 18 (33.9) 6 (11.3) 1 (1.8)
Intensity of TE, n (%) Mild Moderate Severe Uncertain	 19 (38.8) 27 (50.9) 5 (9.4) 2 (3.7)
Outcome, n (%) Complete regrowth within 3 months Complete regrowth within 6 months Partial regrowth within 6 months Persistent or intermittent hair loss after 6 months of follow-up	 11 (20.7) 32 (60.3) 6 (11.3) 4 (7.5)
Trichodynia, n (%)	7 (13.3)
Treatment, n (%) No Oral supplements prescribed for hair loss Topical minoxidil Other	 41 (77.3) 7 (13.3) 3 (5.6) 2 (3.7)

TE: telogen effluvium

Table 3. Comparison between patients with and without COVID-19-associated telogen effluvium

Characteristic	Total (n=77)	With TE (n=53)	Without TE (24)	*P*-value
Sex, n (%) Female Male	 37 (48.1) 40 (51.9)	 34 (91.9) 19 (47.5)	 3 (8.1) 21 (52.5)	**0.000**
Age, Mean ± SD, years	55.91 (10.588)	56.60 (9.761)	54.38 (12.307)	0.396
Fever >39 Yes No	 62 (81.6) 14 (18.4)	 44 (71) 8 (57.1)	 18 (29) 6 (42.9)	0.350
SpO2 on admission, mean (SD)	89.92 (7.576)	89.23 (6.821)	91.46 (8.993)	0.234
CRP, mg/L, mean, ± SD	90.65 (70.761)	82.30 (50.147)	109.08 (101.709)	0.231
Hypoalbuminemia, n (%) Yes No	 36 (46.8) 41 (53.2)	 29 (80.6%) 24 (58.5%)	 7 (19.4) 17 (41.5)	**0.037**
Anemia, n (%) Yes No	 27 (35.1) 50 (64.9)	 23 (85.2%) 30 (60%)	 4 (14.8) 20 (40)	**0.019**
Severe pneumonia, n (%) Yes No	 67 (87) 10 (13)	 50 (74.6) 3 (30)	 17 (25.4) 7 (70)	**0.004**
CCI, mean (SD)	1.06 (1.389)	1.46 (1.414)	0.89 (1.354)	0.095
Effluvium before COVID-19 Yes No	 47 (61) 30 (39)	 17 (63.8) 7 (23.3)	 30 (36.3) 23 (76.7)	0.236
In-hospital complications, n (%) Yes No	 58 (75.3) 19 (24.7)	 16 (27.6) 8 (42.1)	 42 (72.4) 11 (57.9)	0.236
Elevated D-dimers, n (%) Yes No	 11 (14.3) 66 (85.7)	 2 (18.2) 22 (33.3)	 9 (81.8) 44 (66.7)	0.315

TE: telogen effluvium; CCI: Charlson Comorbidity Index; SD: standard deviation; SpO2: peripheral oxygen saturation; CRP: C-reactive protein;

was obtained. Patients were asked to report whether they observed new onset hair loss or trichodynia following the acute COVID-19. Data collected included time of onset, duration, and treatment regimens. Patients were also asked to grade their hair loss as mild (<30%), i.e., some skin visible; moderate (30-50%), i.e., more skin visible than hair; and severe loss (>50%), i.e., much more skin visible than hair.

Post-COVID-19 TE was defined as diffuse hair loss, which started no later than three months after the initial symptoms of COVID-19. The course of TE was defined as acute or chronic when its duration exceeded six months (8).

Statistical analysis

We conducted our analysis by comparing patients with COVID-associated TE and patients without COVID-associated TE. Differences between the groups (according to TE) were tested using the Mann-Whitney test for numerical variables or the Fisher exact test for categorical variables. The level of significance was set as a two-tailed $P<0.05$.

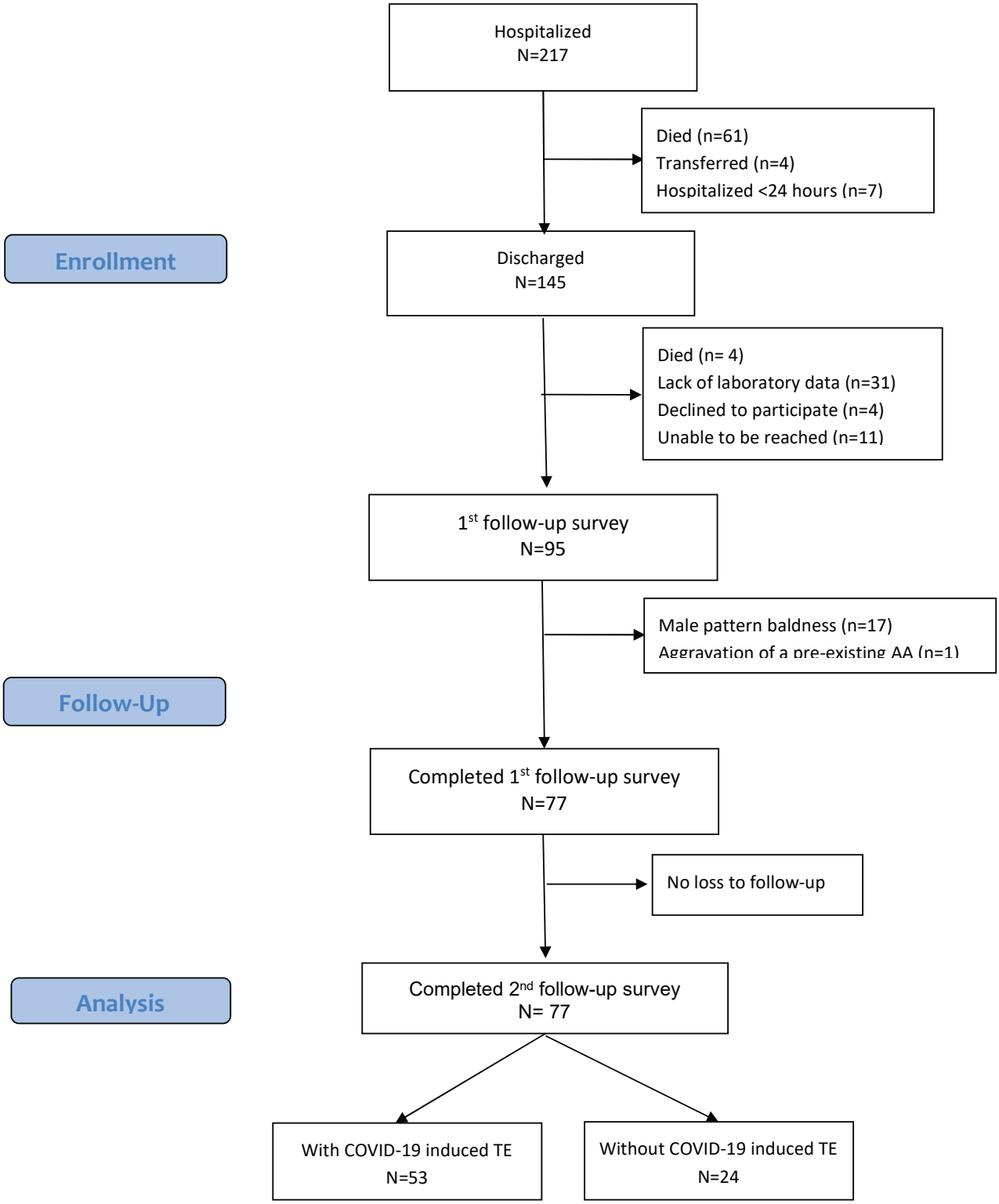
RESULTS

Among the 217 patients hospitalized with PCR-confirmed SARS-CoV-2 infection between January 1 and March 31, 2021, and assessed for enrollment, 140 (64.5%) were excluded. Figure S2 (Supplementary Material) illustrates the patient selection process.

A total of 77 patients were successfully followed-up, and 40 (48.8%) were male. The mean age was 55.91 (29-84), SD=10.588. Table 1 details clinical characteristics and laboratory findings of interest. The majority of patients in this study (53/77, 55%) had at least one comorbidity. Overall, 53 (68.8%) individuals in our sample reported COVID-19-associated TE, and among these, 28 (52.8%) reported early onset and 27 (50.9%) reported moderate hair loss. 11 (20.7%) reported complete hair regrowth within three months, and an additional 32 (60.3%) reported complete regrowth within six months. 4 (7.5%) patients still reported TE after 6 months and were defined as chronic TE; 12 (22.6%) were prescribed medication related to hair loss (Table 2). Two of 7 patients who self-reported trichodynia at the first follow-up still had scalp sensitivity at the second follow-up interview.

Supplementary Material

Fig.S1. Flow Diagram of patient selection



Female sex ($P<0.0001$), anemia ($P=0.019$), hypoproteinemia ($P=0.037$), and severe pneumonia ($P=0.004$) were significantly associated with TE (Table 3).

The mean CCI was higher in patients with TE than in those without TE (1.414 vs. 0.890); however, the difference was not statistically significant ($P=0.095$).

There was no statistically significant difference between the two groups regarding age, high fever, SpO2, CRP levels, history of effluvium before COVID-19, in-hospital complications, and elevated D-dimers.

DISCUSSION

In this cohort of hospitalized patients with confirmed COVID-19 who were followed up for 6 months after illness, 64.6% reported TE. A unique aspect of our cohort was the high proportion of patients with severe disease and high CCI.

Our study results were in line with reports suggesting that the prevalence of COVID-19-associated TE is higher in hospitalized patients, reflecting the effects of the severity of the disease (15,17).

The female sex has already been described as a risk factor for TE in ambulance (16) and hospitalized patients (15,16), which was also confirmed in this prospective cohort.

Notably, the severity of acute COVID-19 infection, evaluated by oxygen requirements and fever, was not associated with TE.

Half of the patients in our study reported early onset of TE, consistent with previous studies (16-18), confirming that COVID-19-associated TE occurs earlier than classic acute TE, which occurs approximately 3-4 months after a triggering event (8).

Consistent with the existing literature, the majority of patients in the present study reported a complete regrowth within 6 months of illness (6,7,17). Persistent active TE occurred in 7.5% of patients in this study, lower than the 10% reported in the survey by Starce *et al.* (6), likely reflecting the longer follow-up in our cohort. During a pandemic, with millions of cases worldwide, even a low incidence of long-term sequelae could have substantial health consequences.

Systemic inflammation is considered a triggering factor of TE in a subset of patients (12). In COVID-19, D-dimer levels are elevated and they correlate with the levels of other inflammatory markers such us ferritin, fibrinogen, and CRP (19). However, no association was found between TE and CRP and D-dimers, consistent with the study by Monary *et al.* (18), in which serum ferritin was not associated with TE.

Anemia and hypoalbuminemia, indicators of both poor nutrition and poor health, were associated with TE, shedding new light on the possible pathogenesis of COVID-associated TE.

Postinfectious hair loss has traditionally been linked with fever, with a cut-off for fever >39.2, as originally described during the influenza pandemic in 1918 (20). However, we did not find a statistically significant association between high fever and TE.

A major strength of this study was the long follow-up. To our knowledge, this study represents the longest follow-up assessment of TE after COVID-19 hospitalization.

Study limitations include a small sample size and potential bias from self-reporting of symptoms.

Firstly, we used self-reported hair loss, which is likely to be subject to reporting bias. Secondly, we performed the study in a single university center, and thus the results might not reflect all hospitalized patients. The majority of our cohort comprised relatively old women with severe COVID-19; this may limit the generalizability of our findings to more diverse populations.

CONCLUSION

High prevalence of TE was observed in this cohort of patients hospitalized for COVID-19. Female sex, anemia, hypoproteinemia, and severity of pneumonia were associated with TE.

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