

Post-SARS-CoV-2 Acute Telogen Effluvium

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Telogen effluvium (TE) is a scalp disorder characterized by diffuse, non-scarring hair shedding. The term “telogen effluvium” was proposed to differentiate the disorder from the excessive shedding of normal club hair. It affects both males and females, with a higher incidence rate in females. Various hypotheses have been proposed for the pathophysiology of TE, based on abnormalities in the normal hair cycle, triggered by different factors.

SARS-CoV-2

COVID-19

telogen effluvium

alopecia

1. Introduction

In December 2019, an outbreak of coronavirus disease (COVID-19)—caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-sense single-stranded RNA virus—was reported as a public health emergency of international concern ^[1]. COVID-19 rapidly spread from China to the entire world, affecting from January to June 2020, over 22 million people across 215 countries ^[2]. No specific treatment is yet available for COVID-19, and patient management relies on supportive care ^[3].

2. Detailed Analysis

2.1. Characteristics of Participants

Ninety-six patients were consecutively enrolled in the study (**Table 1**). The mean age of the patients was 59.0 years (54.5–65.0) and the majority were males ($n = 62$, 64.6%; females $n = 34$, 35.4%), with no significant difference in mean age. Patients were hospitalized for an average of 13 days (9.0–16.5). The mean duration of COV-2 positivity was 31.0 days [26.0–37.0], while the mean duration of fever was 11.0 days (9.0–13.0). As for treatment, 83 (86.5%) patients received hydroxychloroquine, 24 (25%) steroids, 59 (61.5%) azithromycin, 31 (32.3%) anticoagulants or antiplatelet agents for pulmonary embolism prophylaxis, and 73 (76%) needed oxygen therapy. Ritonavir was the most used antiviral drug (94 patients, 97.9%), followed by darunavir, administered to 84 patients (87.5%), while lopinavir was given to 24 patients (25%).

Table 1. General characteristics of patients involved in the study.

Variable	OVERALLN = 96	No-Alopecia n = 66	Alopecia n = 30	p-Value
Gender:				<0.001

Variable	OVERALL <i>N</i> = 96 No-Alopecia <i>n</i> = 66 Alopecia <i>n</i> = 30			<i>p</i> -Value
F	34 (35.4%)	12 (18.2%)	22 (73.3%)	
M	62 (64.6%)	54 (81.8%)	8 (26.7%)	
Age (years)	59.0 (54.5-65.0)	59.0 (55.2;64.8)	59.0 (53.2;66.5)	0.880
Swab positivity(days)	31.0 (26.0-37.0)	31.0 (26.0;37.0)	29.5 (25.2;34.5)	0.274
Hospitalization (days)	13.0 (9.0-16.5)	14.0 (8.25;17.0)	11.5 (10.0;15.0)	0.444
Fever (days)	11.0 (9.0-13.0)	10.5 (8.25;13.0)	11.0 (9.25;14.8)	0.225
DRUG				
Lopinavir:				0.611
No	72 (75.0%)	48 (72.7%)	24 (80.0%)	
Yes	24 (25.0%)	18 (27.3%)	6 (20.0%)	
Darunavir:				0.330
No	12 (12.5%)	10 (15.2%)	2 (6.67%)	
Yes	84 (87.5%)	56 (84.8%)	28 (93.3%)	
Ritonavir:				0.847
No	2 (2.1%)	2 (3.03%)	0 (0.00%)	
Yes	94 (97.9%)	64 (97.0%)	30 (100%)	
Chloroquine:				0.778
No	13 (13.5%)	9 (13.6%)	4 (13.3%)	
Yes	83 (86.5%)	57 (86.4%)	26 (86.7%)	
Azithromycine:				0.977
No	37 (38.5%)	25 (37.9)	12 (40.0%)	
Yes	59 (61.5%)	41 (62.1%)	18 (60.0%)	
O2:				0.233
No	23 (24.0%)	13 (19.7%)	10 (33.3%)	
Yes	73 (76.0%)	53 (80.3%)	20 (66.7%)	

Variable	OVERALL <i>N</i> = 96	No-Alopecia <i>n</i> = 66	Alopecia <i>n</i> = 30	<i>p</i> -Value
Steroids:				0.611
No	72 (75.0%)	48 (72.7%)	24 (80.0%)	
Yes	24 (25.0%)	18 (27.3%)	6 (20.0%)	
Pulmonary Embolism prophylaxis:				0.049
No	65 (67.7%)	40 (60.6%)	25 (83.3%)	
Yes	31 (32.3%)	26 (39.4%)	5 (16.7%)	

2.2. Post-COVID Alopecia Characteristics

Alopecia was assessed in 30 of the 96 patients (31.3%) (**Figure 1**), of whom 22 (73.3%) were females and 8 (26.7%) males, with a significant difference in gender. The average time elapsed from the onset of the first symptom (fever) to that of alopecia was 68.43 days, with a difference between females (72.36) and males (54.00). Eight patients (26.6%) reported trichodynia as the initial symptom of telogen effluvium.

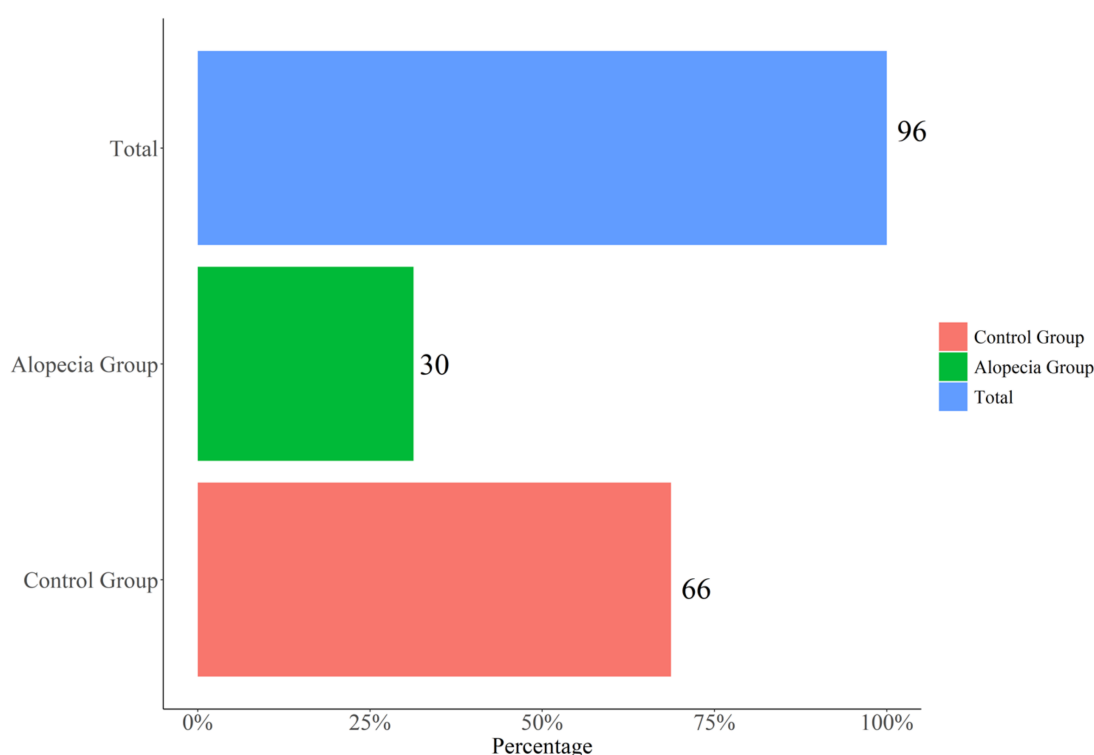


Figure 1. Alopecia frequency in SARS-CoV-2 pneumonia patients.

Telogen effluvium (TE) involved the whole scalp, with a gradual loss of hair volume in all patients reporting increased hair loss. (**Figure 2**). Women, in particular, reported difficulty in bending their hair. Dermoscopy (trichoscopy) was useful for the purpose of making a good assessment of the rarefaction and concentration of vellus hair, in order to differentiate TE from androgenic alopecia (**Figure 3**). Images of the vertex were collected

and compared to those of the occipital and the supra-auricular areas. At trichoscopy, most of the hair had a normal appearance. In addition, follicular openings with only one hair predominated. Dermoscopy showed no significant changes between the vertex area, the parietal zone, and the occipital zone, with no miniaturization, and vellus hair allowed to exclude the diagnosis of androgenetic alopecia in all patients.



Figure 2. Macroscopic photo showing diffuse alopecia. The arrows indicate typical areas of alopecia.



Figure 3. The predominance of single-hair follicular units, with perifollicular discoloration and generalized tiny hair (red circle). Note the presence of upright regrowing hairs (blue circle).

2.3. COVID-19 Characteristics and Alopecia

Overall, there was no association between COVID-19-related characteristics (days of hospitalization, days of COVID-2 positivity, days with fever, and TE (**Table 1**). The disease was not associated with any COVID-directed therapy (**Table 1**).

2.4. Laboratory and Alopecia

Overall, there was no association between the laboratory test outcomes of the control group and the patients with TE. In particular, the levels of iron ($p = 0.371$), ferritin ($p = 0.194$), transferrin ($p = 0.890$), and zinc ($p = 0.375$) were similar in patients with and without TE.

3. Current Insights

The rate of post-SARS-CoV2 TE appeared to be significantly higher in females, although in males the onset of alopecia was more premature. This occurrence could be linked to the evidence that men infected with CoV-2 have an increased risk of severe COVID-19 disease compared to women [4]. A large number of other factors have been associated with this gender disparity. There is evidence that supports the role of androgens in the COVID-19 severity [5][6], to the extent that androgenic alopecia has been hypothesized as a predicting factor for more severe SARS-CoV-2 cases [7]. In the research, TE is not reported as a causative factor, but as the consequence of the disease. Physiological stress, such as childbirth, surgical trauma, high fever, chronic systemic illness or infections, and hemorrhage have been associated with TE. However, the relationship between TE and emotional stress is uncertain and ambiguous [8]. TE has also been linked to severe protein, fatty acid and zinc deficiency, chronic starvation, and caloric restriction [8]. Numerous drugs can cause TE, starting after Week 12 of dosage [9][10]. Iatrogenic causes of TE include oral contraceptive pills, androgens, retinoids, beta-blockers, angiotensin-converting enzyme inhibitors, anticonvulsants, antidepressants, and anticoagulants (heparin) [11]. The relation between TE and anticoagulant therapy is strongly controversial in the literature [12]; however, no association was manifest here. The onset of hair loss in the sample started just over 2 months from the beginning of the fever but, at the same time, it showed no link with any significant laboratory abnormalities. In particular, zinc and iron deficiencies were not related to the onset of alopecia. In the context of these considerations, ATE following SARS-CoV infection is to be considered as a foreseeable complication directly related to the disease. The report on the absence of any association with the severity of infection and treatments has major implications on the number of patients potentially affected. The absence of a nutritional deficiency, combined with trichodynia, may suggest that the inflammatory condition inherent to COVID-19 may be a principal cause of ATE. Interestingly, the prevalence of trichodynia—a distinctive symptom of TE—is reported in only about 20% of TE patients [13], whereas in this sample, it affected almost one-quarter of subjects.

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