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Clinical and epidemiological features of post COVID-19 telogen effluvium

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ABSTRACT

Introduction: During the COVID-19 pandemic, there has been an increase in the incidence of telogen effluvium (TE)–alopecia characterized by diffuse, non-scarring, and self-limiting hair loss, caused by a trigger–generating a negative impact on the self-esteem of those affected. Thus, understanding the epidemiology and clinical aspects of post-COVID-19 alopecia helps guide treatment towards reducing physical and psychological adverse effects. **Objective:** To evaluate the clinical and epidemiological characteristics of individuals with post-COVID-19 TE. **Method:** Retrospective cohort study using the non-discriminative exponential sampling technique "Snowball" with 204 volunteers who answered an online questionnaire, with subsequent statistical analysis of the data. **Results:** The sample consisted of 204 volunteers, of which 127 met the inclusion criteria for the study. Of this group, 41% reported post-COVID-19 alopecia, with 25% seeking medical assistance and 44% stating that it negatively impacted their self-esteem. At a significance level of 0.05, there was an association between post-COVID-19 hair loss and the use of Azithromycin, as well as with female sex and the presence of symptoms such as fatigue, memory impairment, and skin irritation post-COVID-19. **Conclusion:** There has been a noticeable increase in TE cases after COVID-19, and it is important to consider the association of this disease with the use of Azithromycin, female sex, and other post-COVID-19 symptoms. However, further studies are needed to understand the true mechanisms of this TE infection to propose new treatments and guidelines.

Keywords: Alopecia; COVID-19; Hair.

INTRODUCTION

In late 2019, the novel coronavirus, SARS-CoV-2, began to spread, later giving rise to the COVID-19 pandemic, whose symptoms include fever, headaches, dry cough, extreme fatigue, muscle aches, disorders in smell and taste, in addition to its impact on the cardiorespiratory system. However, alongside these symptoms, a significant increase in certain dermatological conditions has been reported, such as herpes zoster, pityriasis rosea, urticaria, cold sores, and alopecia–the absence, thinning, or transient loss of hair–with telogen effluvium (TE) being predominantly the alopecia most associated with COVID-19.

TE is characterized by diffuse and non-scarring hair loss, presenting as transient or chronic hair loss. This loss occurs due to an abnormal change in the follicular cycle, where the transition of hair follicles from the anagen phase–the growth phase–to the telogen phase–the resting phase–is increased, leading to premature hair shed-

ding. This transition typically occurs between 60 to 90 days after the triggering factor and lasts for up to six months, therefore being self-limiting.

The cause of TE correlates with a wide variety of endogenous and exogenous factors, such as protein or caloric malnutrition, medications, prolonged stress, systemic diseases, childbirth, among others. However, in up to 30% of cases, the triggering factor of TE remains unknown.

Unfortunately, individuals with TE tend to experience higher levels of emotional stress compared to those without it. This is because they are constantly concerned about the causes, duration, and resolution of hair loss, as well as the stress related to aesthetics. Thus, TE presents a direct negative association with psychological well-being, interfering with quality of life.

Therefore, the aim of the research is to understand the epidemiology and clinical aspects of TE after COVID-19. This understanding will facilitate the management and treatment, ultimately reducing the adverse physical and psychological effects experienced by patients with TE following COVID-19.

METHOD

This was a retrospective cohort study conducted using the non-discriminatory exponential sampling technique "Snowball," through an 18-question questionnaire distributed on social networks. Data collection began after the research project was approved by the Research Ethics Committee of the institution (CAAE No. 64583222.6.0000.5134–opinion No. 121345/2022), and was only answered by those who agreed to the Free and Informed Consent Forms (FICF), with ethical principles being respected according to Resolution 466/12 of the National Health Council. The collected information was used solely for research purposes.

The sample consisted of 204 volunteers, with individuals who did not present COVID-19 with at least one positive PCR test between January 2020 and April 2022 being subsequently excluded, resulting in a group of 127 participants. Individuals who were pregnant or in the postpartum period during the presentation of COVID-19 and post COVID-19; those using immunosuppressant, immunocompromised for other reasons; who had recent surgery; participants who had dengue or another infectious disease, were using antibiotics, started or stopped using oral contraceptives at the time, suffered a severe physical accident, were hospitalized during this period, or were minors under 18 years of age were also excluded.

To obtain clinical and epidemiological information on post-COVID-19 alopecia, the following variables were collected:

- Age at which COVID-19 test was positive
- Gender
- Race
- Comorbidities
- Use of continuous medications at the time
- Duration of COVID-19 symptom manifestation
- Medications used in an attempt to treat COVID-19
- Severe complications with hospitalizations
- Increased hair loss up to six months post COVID-19
- When the hair loss began
- How long it lasted
- Whether medical help was sought for the resolution of alopecia and the approach taken
- Whether there were self-esteem issues related to alopecia
- Other post-COVID-19 symptoms presented."

Regarding statistical analysis, Descriptive Statistics and Inferential Statistics methodologies wereapplied. In Descriptive Statistics, simple frequencies and percentages, medians, and interquartile range were used. In the application of Inferential Statistics, Fisher's Exact Test and the chi-square test of independence were performed on qualitative variables to determine the degree of association between variables, and for quantitative variables, the Wilcoxon rank sum test was used to determine the difference between groups. The significance level was set at 0.05.

RESULTS

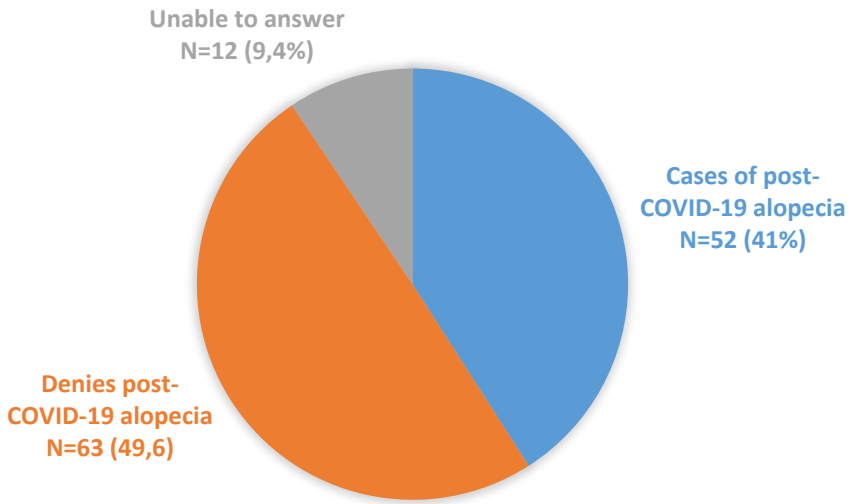
The sample consisted of 204 participants, of whom 127 had COVID-19 with at least one positive PCR test between January 2020 and April 2022 and did not meet any of the exclusion criteria. The median age was 47 years, and 89 (70%) were female. Additionally, 108 (85%) were white, and 15 (12%) were of mixed race.

Regarding comorbidities, 29 (23%) had Systemic Arterial Hypertension; 19 (15%) had Depressive Disorder; 6 (4.7%) had Hypothyroidism; 5 (3.9%) had Type 2 Diabetes Mellitus. Considering the continuous medications used at the time, 29 (23%) were using antihypertensive; 19 (15%) antidepressants; 10 (7.9%) thyroid hormone.

Regarding the duration of acute COVID-19 symptoms, 78 (61%) reported a duration of approximately 1 to 7 days, while 25 (20%) experienced the prolongation of symptoms for 8 to 14 days. As an attempt to improve symptoms, 22 (17%) individuals used Azithromycin; 9 (7.1%) Hydroxychloroquine; 2 (1.6%) Ivermectin. Regarding severe complications, 4 (3.1%) of the sample required hospitalization.

Considering alopecia up to six months post COVID-19, 52 (41%) participants reported experiencing hair loss, and 12 (9.4%) were unsure (Graph 01).

Graph 01–Incidence of post-COVID-19 alopecia in the studied population.



Source: Own dataset

Analyzing the participants who presented alopecia, 18 (35%) reported onset one month after infection; 13 (25%) did not know; 8 (15%) after two months; 5 (9.6%) after one week; 4 (7.7%) after three months. Regarding the duration of hair loss, 11 (21%) reported it lasting more than six months; 11 (21%) did not know; 9 (17%) lasted three months; 8 (15%) lasted two months; 6 (12%) lasted six months; 3 (5.8%) lasted four months. Additionally, 13 (25%) of these individuals sought medical assistance, and 23 (44%) stated that it influenced their self-esteem or caused other negative concerns.

Furthermore, other post-COVID-19 symptoms were investigated in the group of 127 individuals who met the inclusion and exclusion criteria. It was observed that 74 (58%) of the participants experienced fatigue; 46 (36%) reported memory impairment; 34 (27%) reported headaches; 33 (26%) reported anhedonia; 26 (20%) reported sleep disturbances; 14 (11%) reported skin irritation.

A cross-referencing was conducted between the variable "Did you notice increased hair loss within six months after having COVID-19?" and other variables under study. Thus, it can be affirmed at a significance level of 0.05 that there was a significant association between the group consisting of female individuals and those who reported post-COVID-19 alopecia. Additionally, it was observed that individuals who used Azithromycin in the treatment of COVID-19 had a higher rate of alopecia. There was also a statistically significant association between post-COVID-19 symptoms of fatigue, memory impairment, and skin irritation with post-COVID-19 alopecia (**Table 01**).

Table 01–"Cross-referencing between the variable 'Did you notice increased hair loss within six months after having COVID-19?' and variables that showed statistical significance at the significance level of 0.05."

"Did you notice increased hair loss within six months after having COVID-19?"

Characteristic	Total, N =1271	No N = 631	Unable to answer, N= 121	Yes, N = 521	P value2
Female	89 (70%)	37 (59%)	8 (67%)	44 (85%)	0,008
Male	38 (30%)	26 (41%)	4 (33%)	8 (15%)	
Medications used for the treatment of COVID-19					
Azithromycin–no	105 (83%)	57 (90%)	7 (58%)	41 (79%)	0,019
Azithromycin–yes	22 (17%)	6 (9,5%)	5 (42%)	11 (21%)	
Other post-COVID-19 symptoms					
Fatigue–yes	74 (58%)	30 (48%)	7 (58%)	37 (71%)	0,039
Fatigue–no	53 (42%)	33 (52%)	5 (42%)	15 (29%)	
Memory impairment–no	81 (64%)	48 (76%)	7 (58%)	26 (50%)	0,014
Memory impairment–yes	46 (36%)	15 (24%)	5 (42%)	26 (50%)	
Skin irritation–no	113 (89%)	61 (97%)	9 (75%)	43 (83%)	0,009
Skin irritation–yes	14 (11%)	2 (3,2%)	3 (25%)	9 (17%)	

n (%): Number and percentage representation; Median (IQR): Median and Interquartile Range; 2 Kruskal-Wallis Test; Fisher's Exact Test; Chi-square Test for Independence.

The remaining cross-tabulations were not statistically significant at the 0.05 significance level, including age, race, comorbidities, medications in continuous use, and other medications used as attempted COVID-19 treatments, duration of acute illness symptoms, and complications leading to hospitalization.

DISCUSSION

TE is known to be a multifactorial disease, and therefore, when aggressive factors overlap, exacerbation of alopecia occurs. This occurrence is linked to the fact that hair is a unique structure, composed mainly of proteins, with the hair follicle embryological derived from the ectoderm and its muscles and blood vessels from the mesoderm. The lower segment, called the hair bulb, is abundantly irrigated and innervated. The hair structure is extremely sensitive to external factors such as pollution, stress, nutritional imbalance, medication use, endocrinopathies, and fungi, with some of these factors related to COVID-19.

According to the results presented, there was a significant incidence of post-COVID-19 hair loss, reported by 41% of the participants. It was expected to observe a high number of cases, as some reports on COVID-19, such as those by Xiong et al. and Starace et al., indicated an important relationship between the infection and hair loss. In the study by Xiong et al., conducted with 538 post-COVID-19 participants, Starace et al. observed in 28.6% of the sample and in the study alopecia with a sample composed of 128 post-COVID-19 participants, 66.3% presented TE.

Physiologically, COVID-19 infection results in a systemic state favorable to inflammation, precipitating the pro-inflammatory cascade that affects not only the infected site but also other tissues. However, the pathophysiology that justifies post-COVID-19 TE is still poorly understood, with some hypotheses in the literature that may explain this hair loss.

One theory heavily supported suggests that SARS-CoV-2 infection leads to an inflammatory state that releases metalloproteinase 1 and 3 and interleukin-1β, proteins that can trigger TE, as they are highly potent inhibitors of human hair follicle growth. In addition to interleukin-1β, individuals with COVID-19 may experience increased interleukin-6, and according to the literature, this interleukin inhibits hair shaft elongation and proliferation of matrix cells in cultured hair follicles, indicating a possible connection between COVID-19 pathophysiology and TE manifestation.

TE can also be justified by the activation of the interferon pathway that the SARS-CoV-2 virus and other viruses are capable of causing. In this antiviral response, interferons are released, which are molecules potentially capable of causing hair loss. Tosti et al.'s study demonstrates that a significant portion of individuals using interferon alpha-2β experience TE.

Another mechanism to consider is direct damage to hair follicles by the SARS-CoV-2 virus. Additionally, COVID-19 triggers the activation of the coagulation cascade in response to infection, a scenario conducive to the formation of microthrombi that can occlude the vascular supply of the follicles, justifying possible TE.

In addition to the probable pathophysiological mechanisms causing TE that the SARS-CoV-2 virus can generate, the literature warns of the possible association of this alopecia with drugs administered in the treatment of COVID-19. Thus, medications used, such as Hydroxychloroquine and Azithromycin, should be considered responsible for TE.

However, as it is a topic lacking clarity, the literature is contradictory in this regard, with Rizzetto et al. believing that the drugs administered in the treatment of COVID-19 do not influence TE, as they are drugs used for a short period.

Due to the lack of sufficient information explaining the biological mechanisms of Azithromycin that result in TE, current data corroborate the possible association of post-COVID-19 TE with the use of Azithromycin, also observed in the current research. Thus, a better understanding of the topic could guide doctors' choice of drugs in order to reduce the incidence of TE, requiring more studies to establish such a relationship.

Finally, the considerable psychosocial burden, resulting from a unique situation such as a pandemic, can also play a central role in exacerbating underlying diseases. In Rivetti et al.'s study, the recurrence of TE during the pandemic in individuals who had a previous history of TE was analyzed. All participants reported a higher level of stress than usual, with a mean value of 8.2 on a scale of 1 to 10, indicating that the stress generated by the pandemic can affect the increased incidence of TE. This is because the isolation and uncertainties surrounding hospitalizations due to COVID-19 lead to intense distress among those infected, significantly impacting their mental health. Thus, the entire context poses a significant limitation, not only on existing literature but also for future research investigating the relationship between TE and COVID-19, ideally requiring the separation of underlying factors for better understanding of the relationship.

Apart from COVID-19, there are other factors that frequently trigger TE, such as postpartum and pregnancy.

CONCLUSION

The significant incidence of post-COVID-19 TE found in this study is consistent with the incidence found in similar studies, being consensually caused by inflammatory and debilitating events of the infection, combined with psychological stressors arising from the disease and the pandemic. Furthermore, it is important to consider the predominant frequency of post-COVID-19 TE cases in female individuals and in those who used Azithromycin in the treatment of the infection, however, the mechanism by which this occurs is not clearly described in the literature, requiring further studies for a deeper understanding of the issue. Additionally, other post-COVID-19 symptoms, such as fatigue, memory impairment, and skin irritation, were also found to be associated with post-COVID-19 TE.

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THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS IN RELATION TO THIS ARTICLE.