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Original Article

Clinical and trichoscopic features of post-COVID-19 telogen effluvium

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Abstract

Objective Telogen effluvium is the most common, self-limiting cause of alopecia. An association between telogen effluvium and COVID-19 has recently been reported.

Methods This cross-sectional study included 75 patients at dermatology outpatient clinic. The patients were classified according to their COVID-19 history as mild, moderate, or severe. History was taken to assess the onset of hair loss. All patients were examined by hair pull test and assessed trichoscopically for the presence of follicles with a single hair, yellow dots, decreased hair density, peri pilar sign, empty hair follicles, and upright regrowing hair.

Results The mean duration of hair loss in the current study was 8.55 weeks. Patients with higher severity of COVID-19 reported significantly earlier onset of hair loss. Pain and dystrophic anagen hair on pull test was observed in association with hair shedding in all patients with severe COVID-19 infection.

Conclusion Post-COVID-19 telogen effluvium has a significant positive correlation with the severity of COVID-19 infection with earlier onset of hair loss, increased frequency of trichodynia, and dystrophic anagen hair.

Key words
Telogen effluvium; Covid-19; Hair loss; Trichoscopy.

Introduction

Telogen effluvium (TE) is a self-limited, diffuse non-scarring hair loss that affects less than 50% of the scalp, and occurs within two to three months after the onset of the triggering event.[1] TE was described by "Kligman" who mentioned that the increase in hair loss might be reactive to several underlying causes.[2] It represents the most common cause of diffuse hair loss[3] and the majority of individuals have experienced a "subclinical" TE episode at some point in their lives.[4]

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The disease has no known racial predilection and affects both sexes, though women are more likely to seek medical attention for hair loss. Although the relationship between TE and age is unclear, older women are more prone to developing acute TE after experiencing a fever, trauma, hemorrhage, or psychological stress.[5] About 40-50 percent of new mothers experience hair loss after childbirth.[6]

Many causes and triggers are associated with TE, making it a challenging disorder. Among the list of etiological factors are the physiological factors, infections, stresses, drugs**,** endocrine disorders, organ dysfunction, disorder of the hair cycle, nutritional deficiencies, autoimmune and local scalp diseases.[5,6]

Patients present with significant hair loss, worry

and anxiety that they might go bald and do not connect these incidents to their recent illness.[7] Other hairy regions of the body (e.g., pubic and axillary hair) may be affected especially in those with diffuse thinning involving the entire scalp.[8] Patients suffering from acute TE experience ‘‘trichodynia’’ as opposed to scalp itching.[9]

Hair usually appears normal in thickness on examination, with shorter regrowing hair in the frontal and bitemporal areas.[10] Many diagnostic procedures are available to diagnose TE and to assess its severity. Among these are the Hair Pull Test, Modified Wash Test, Trichoscopy, Trichogram, Trichoscan, and phototrichogram.

Trichoscopy plays an important role in TE diagnosis. The presence of empty hair follicles, a predominance of follicular units with only one hair, perifollicular discoloration (the peripilar sign), and upright regrowing hairs represent frequent, but not specific findings.[6,10]

Recently, many studies emphasized the association between TE and COVID-19. Although skin involvement in COVID-19, was initially regarded as insignificant, it has been proven to be important. Post COVID-19 hair loss, mostly in the form of acute TE, is becoming a prominent and common manifestation.[11,12]

The pathophysiology of COVID-19 induced TE is not yet known. However, researchers have brought a few hypotheses regarding the higher levels of pro-inflammatory cytokines, including factors such as hypoxia, inflammation, and metabolic abnormalities, the immediate harm of the virus to the hair follicles,[13] the formation of microthrombi that could stop the blood flow to the hair follicles,[12] and finally COVID-19 medications.

Trichoscopy of post COVID-19 TE is pretty comparable to that of conventional TE, revealing empty hair follicles, upright regrowing hairs, follicular units with one hair, and yellow dots.[13]

The association of telogen effluvium with COVID-19 infection is relatively new phenomenon and the present study was designed to evaluate the clinical and dermoscopic features of this entity in Iraqi patients.

Methods

This cross-sectional study was performed dermatology outpatient clinic in a tertiary referral hospital from 1st July 2021 to 1st of July 2022. The study incorporated seventy-five patients with post-COVID-19 hair loss that were diagnosed by PCR test.

All patients with post-COVID-19 TE diagnosed clinically assisted by the hair pull test were invited to participate in the study, whereas patients with any conditions that cause acute TE-like physiological stress such as high fever other than COVID-19 infection, acute starvation, or hemorrhage three months prior to presentation was excluded from the study.

Additionally, patients with a drug history, surgical history, and childbirth in the past 6 months, patients with acute medical or autoimmune diseases, patients suffering from hair loss due to other causes like androgenic alopecia, and patients with any type of hair loss before COVID-19 infection are all precluded from participating.

Clinical classification of COVID-19 was done according to the severity spectrum released by the National Institutes of Health.[14]

The hair pulls test was performed by grasping 50-60 hairs between the thumb, index, and middle fingers in the frontal, occipital, and both temporal areas of the scalp. When the telogen phase represented 10% of hair pulled away from

the scalp, the test was considered positive.

Clinical and trichoscopic photos of hair loss were performed with a polarized light non-contact dermoscopy [3 Gen Dermlite DL 200] at 10 X magnification and photographed with iPhone 11 Pro max.

Trichoscopic features included the presence of: follicles with a single hair, yellow dots, decreased hair density, peri pilar sign, empty hair follicles, and upright regrowing hair.

Verbal consent was obtained from patients, and confidentiality was assured. Ethical approval was obtained from the IRB of the Arabic board study in the Ministry of Health.

Microsoft Excel 2019 was used for data entry. The SPSS-V26 program was used to analyze the data. Fischer's exact test was used for statistical analyses. Data was presented as frequencies and percentages. Significances of variables were considered when the P value was <0.05.

Results

The sociodemographic characteristics of the 75 patients of the study are shown in **Table 1**, and COVID-19 severity is illustrated in **Table 2**.

Table 1 Sociodemographic characteristics of the study sample.

		Frequency	*Percentage*
Age group	<40 years	46	61.3
	≥40 years	29	38.7
Gender	Female	73	97.3
	Male	2	2.7

Table 2 Covid-19 characteristics of the studied sample.

		Frequency	*Percentage*
Disease severity	Mild	38	50.7
	Moderate	26	34.7
	Severe	11	14.7
Hospitalization	Yes	11	14.7
	No	64	85.3

The duration of hair loss after COVID-19 infection ranged from (3-12 weeks) with a mean of 8.55±2.71 weeks. 64 (85.3%) patients had increased hair shedding, whereas 11 (14.7%) patients had increased hair shedding associated with pain. Regarding the pull test result, 64 (85.3%) patients had telogen club hair, while 11 (14.7%) patients had telogen club hair associated with dystrophic anagen hair as illustrated in **Table 3**.

Follicles with single hair and decreased hair density were found on Trichoscopic examination in all the patients. However, 65 (86.7%) patients showed peripilar sign, 64 (85.3%) showed empty hair follicles, 57 (76.0%) showed upright regrown hair, and 9 (12.0%) showed yellow dots **(Table 4)**.

A statistically significant association was detected between COVID-19 severity and the clinical features of hair loss and pull test results **(Table 5)**.

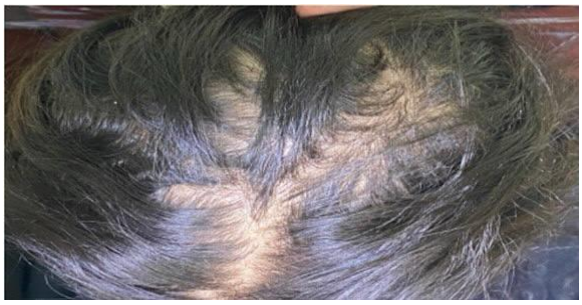

Figure 1 38 years old female with diffuse hair loss after 4 weeks from COVID 19 infection.

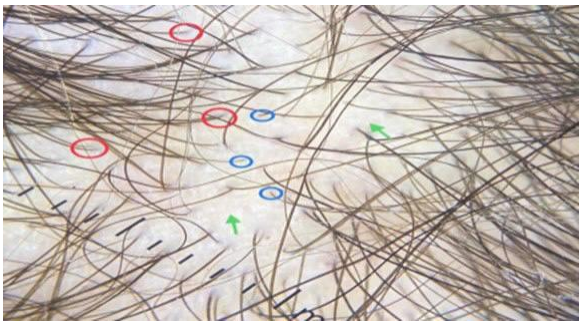

Figure 2 Trichoscopy findings. Red circles show peripilar sign. Green arrows show empty hair follicles. Blue circles show follicles with single hair.

Table 3 Clinical characteristics of post-COVID-19 TE.

		Frequency	*Percentage*
Clinical features of hair loss	Increased hair shedding	64	85.3
	Increased hair shedding and pain	11	14.7
Pull test result	Tellogen club hair	64	85.3
	Tellogen club hair with dystrophic anagen	11	14.7

Table 4 Trichoscopic characteristics of post-COVID-19 TE.

		Frequency	*%*
Follicles with single hair	Present	75	100
	Absent	0	0.0
Decreased hair density	Present	75	100
	Absent	0	0.0
Peri pilar sign	Present	65	86.7
	Absent	10	13.3
Empty hair follicles	Present	64	85.3
	Absent	11	14.7
Upright regrowing hair	Present	57	76.0
	Absent	18	24.0
Yellow dots	Present	9	12.0
	Absent	66	88.0

Table 5 Association between COVID-19 infection severity and time of hair loss after infection.

	Frequency	*Time of hair loss after infection (mean ± SD)*
Covid severity		
Mild	38	10.82 weeks ± 1.01
Moderate	26	7.23 weeks ± 0.76
Severe	11	3.82 weeks ± 0.75
P value: <0.001		

Pain and dystrophic anagen hair on the pull test were observed in association with hair shedding in all patients with severe COVID-19, while no patient with mild or moderate COVID-19 showed associated pain on the scalp or dystrophic anagen on the pull test **(Table 6)**.

A non-significant association was shown between COVID-19 severity and the presence of empty hair follicles, peri pilar sign, upright regrowing hair, and yellow dots **(Table 7)**.

Discussion

The present work shows that the mean age of the involved patients was 36.96 years, which is slightly higher than Arjel *et al*. and Babaei *et al*. studies, which reported mean ages of 31.0 and 30.9; respectively.[15,16]

The predominant patients were females (97.3%), in line with the female frequency in Sharquie (92.3%) and Wei (96.4%) studies.[17,18] However, this is not surprising, as females are more prone to stress, are more concerned about hair loss, and are more inclined to seek medical help. Moreover, TE is more easily noticed in females because of their long hair.[1]

The mean time interval of hair loss after COVID-19 infection in the current study was 8.55 weeks (60 days), which is in agreement with the studies of Moreno-Arrones (57.1 days)[19] and Hussain (74 days).[20] In a study by Olds, hair shedding began 50 days after the first symptom of COVID-19.[12] Whereas in Sharquie's study, hair loss began within 2-3 months after infection,[17] while Hussain *et al*. reported a mean of 74 days.[20]

Table 6 Association between COVID severity and clinical characteristics of TE.

		Covid severity			*P*
		Mild	*Moderate*	*Severe*	*value*
Clinical features of hair loss	Increased hair shedding	38	26	0	<0.001
	Increased hair shedding associated with pain on the scalp	0	0	11	
Pull test result	Tellogen club hair	38	26	0	<0.001
	Tellogen club hair and dystrophic anagen	0	0	11	
Total		38	26	11	

Table 7 Association between COVID severity and trichoscopic features of TE.

		Covid severity			*P value*
		Mild	*Moderate*	*Severe*	
Empty hair follicle	Present	32	23	9	0.823
	Absent	6	3	2	
Peri pilar sign	Present	33	21	11	0.417
	Absent	5	5	0	
Upright regrowing hair	Present	29	19	9	0.873
	Absent	9	7	2	
Yellow dots	Present	5	1	3	0.122
	Absent	33	25	8	
Total		38	26	11	

The severity of COVID-19 in our study was significantly linked to a shorter TE onset after COVID-19. This finding is in concordance with that of Arjel *et al*; in which hair loss started substantially sooner in the post-COVID-19 period in patients with severe forms of infection.[15] Similarly, Babaei reported that patients with severe COVID-19 presented with significantly earlier onset of hair loss.[16] This can be attributed to the high levels of proinflammatory cytokines and an inflammatory state that may follow severe COVID-19 infection which may trigger a coagulation cascade and decrease the blood flow of anticoagulant agents.

These factors may be linked to occlusion and microthrombi in the hair follicle microvessels. Furthermore, severe COVID-19 is associated with more risk factors for TE (such as heparin administration), which may lead to rapid development of hair loss.[21]

Another noticeable finding in the present study was that trichodynia was associated with TE in 11 (14.6%) patients, and the cases were exclusively found in the severe COVID-19 group. Arjel *et al*. also reported that the frequency of trichodynia increased in higher severity COVID-19 groups.[15] Identically, Starace found an association between trichodynia and TE in 42.4% of cases and TE was significantly associated with trichodynia in higher severity COVID-19 groups.[22] Whereas An Italian study by Di Landro *et al*. reported trichodynia in 17.9% of patients with post-COVID-19 TE.[23]

When trichodynia and TE occur together, it raises the question of whether they are the result of the same neuropathology that causes COVID-19-induced anosmia and ageusia. Hair follicles on the human scalp contain functioning olfactory receptors, which must be continuously stimulated by an unidentified endogenous ligand to remain in the anagen phase and continue producing insulin-like growth factor.[24] This raises the fascinating issue of whether COVID-19, which causes significant olfactory damage,[25] also decreases the expression of hair follicle-specific olfactory receptors that promote hair growth; thus, interfering with anagen. In addition, angiotensin-converting enzyme 2 receptors, which are utilized by the virus to enter human cells, are highly expressed in keratinocytes and sebaceous glands, although their functional role in hair follicle biology has not been fully explained.[23]

Another interesting result of this study is that all severe cases were associated with fractured roots and misshapen bulb, which support the diagnosis of dystrophic anagen. Miola *et al*. proposed that COVID-19-induced effluvium can be severe, and is characterized some telogen but numerous anagen dystrophic hairs at the trichogram.[26] This suggests that COVID-19 may cause direct changes in hair physiology.

The research by Mazeto *et al*. went further and concluded that the early onset post-COVID-19 effluvium may be distinguished from TE, is often found after severe infections by the high incidence of dystrophic anagen hair in the trichogram.[27]

It has been hypothesized that viral insult induces TE by immediate anagen release in post-COVID-19 TE. Postinfectious hair loss is usually regarded as acute TE, although, it can be caused by various pathogenetic pathways and manifest in a variety of clinical patterns.

Depending on the type and severity of the damage, hair follicles may react to infection in one of two ways: dystrophic anagen effluvium or TE. Therefore, patients with severe infection due COVID-19 virus may present with early-onset telogen phase, i.e. dystrophic anagen effluvium, indicating a greater effect of the levels of proinflammatory cytokines on the matrix cells of the hair follicle.[20]

Concerning trichoscopic features of hair loss, follicles with single hair and decreased hair density were found in all patients; after which peripilar sign was the most common, as it was detected in 86.7%.

Bains *et al*. assessed 33 patients with TE regardless of a history of COVID-19 infection and found peripilar sign in 30.3% of patients, which is considerably less than the present study.[28] Perifollicular brown coloration ("peripilar sign") is thought to be associated with the presence of perifollicular lymphocytic infiltrates.[29]

Hussain *et al*. reported that empty follicles, decreased hair density, and upright regrowing hairs were the most common trichoscopic findings, which is somewhat in line with the present study, as these features were very common.[20] Roda *et al*. reported a decreased hair density with the presence of empty follicles and short regrown hair.[30]

Rossi *et al*. reported follicular units with single hair, regrown hair, and empty hair follicles.[13] It is noteworthy that the present study found no significant difference in trichoscopic features between the different severity groups of COVID-19. However, this has not been assessed in previous studies.

Further research is needed to identify the exact cause of TE after COVID-19 infection. A consistent increase in proinflammatory cytokines, (Interleukin 1b, Interleukin 6, tumor necrosis factor α and type 1, and 2 interferon) was shown in patients with long hospital admission for severe COVID-19 infection.[31] Cytokine-storm can induce TE by damaging hair-producing matrix cells, keeping in mind that high levels of interferons have been previously shown to be associated with acute TE.[17]

Moreover, the potential role of enoxaparin in the development of TE cannot be disregarded. Anticoagulants such as enoxaparin have recently been emphasized by Watras *et al*. for their involvement in triggering TE.[32]

The main limitation of this study is that it was a single center study with no follow up for the study group to evaluate the natural progression of the condition.

Conclusion

In post-COVID-19 TE, the higher severity of COVID-19 infection correlated significantly with earlier onset of hair loss, increased frequency of trichodynia and dystrophic anagen hair. The trichoscopic features of post-COVID-TE include: follicles with a single hair, decreased hair density, peripilar sign, empty hair

follicles, upright regrowing hair, and yellow dots. The presence of any of these features was not associated with infection severity.

Limitations Single center study with less than expected sample size.

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