Received: 14 November 2021 | Accepted: 19 December 2021

DOI: 10.1002/jmv.27534

REVIEW

JOURNAL OF MEDICAL VIROLOGY WILEY

A systematic review of acute telogen effluvium, a harrowing post-COVID-19 manifestation

Nabeel Hussain[1] | Preeti Agarwala[2] | Kinza Iqbal[3] | Hanaa Mohamed Sheikh Omar[4] | Gurusha Jangid[5] | Vraj Patel[6] | Sawai Singh Rathore[5] | Chandani Kumari[7] | Felipe Velasquez-Botero[8,9] | Guadalupe Abigail Benítez López[9] | Yogesh Vishwakarma[7] | Airin Parvin Nipu[10] | Noman Khurshid Ahmed[3]

[1]Saba University School of Medicine, The Bottom, The Netherlands

[2]Rajshahi Medical College and Hospital, Rajshahi, Bangladesh

[3]Department of Internal Medicine, Dow Medical College, Dow University of Health Sciences, Karachi, Pakistan

[4]Zamzam University of Science & Technology, Mogadishu, Somalia

[5]Dr. Sampurnanand Medical College, Jodhpur, Rajasthan, India

[6]Smt NHL Municipal Medical College, Ahmedabad, Gujarat, India

[7]American University of Barbados, Wildey, St. Michael, Barbados

[8]Universidad CES, Medellin, Colombia

[9]Larkin Community Hospital, Miami, Florida, USA

[10]University of Arkansas at Pine Bluff, Pine Bluff, Arkansas, USA

Correspondence
Sawai Singh Rathore, Dr Sampurnanand Medical College, Jodhpur, Rajasthan 342003, India.
Email: sawais.rathore77@gmail.com

Abstract

This systematic review focuses on the clinical features, physical examination findings, outcomes, and underlying pathology of acute telogen effluvium (TE), a type of diffuse hair loss, occurring in coronavirus disease 2019 (COVID-19) recovered patients. MEDLINE/PubMed and Embase databases were queried till October 2021 to identify studies reporting acute TE occurring after COVID-19 recovery. Data were obtained from 19 studies, which included 465 patients who were diagnosed with acute TE. The median age of these patients was 44 years and 67.5% were females. The most common trichoscopic findings were decreased hair density, the presence of empty follicles, or short regrowing hair. The mean duration from COVID-19 symptom onset to the appearance of acute TE was 74 days, which is earlier than classic acute TE. Most patients recovered from hair loss, while a few patients had persistent hair fall. Our results highlight the need to consider the possibility of post-COVID-19 acute TE in patients presenting with hair fall, with a history of COVID-19 infection, in the context of COVID-19 pandemic. Despite being a self-limiting condition, hair loss post-COVID-19 is a stressful manifestation. Identifying COVID-19 infection as a potential cause of acute TE will help the clinicians counsel the patients, relieving them from undue stress.

KEYWORDS
hair loss, post-COVID-19, TE, telogen effluvium, trichoscopy

1 | INTRODUCTION

At the end of the year 2019, a new infectious pathogen severe acute respiratory syndrome (SARS-CoV-2) associated with an unexplained cause of pneumonia arose in China, which was later coined as coronavirus disease 2019 (COVID-19).[1] The clinical manifestation of COVID-19 is quite diversified, ranging from mild symptoms to life-threatening respiratory failure, septic shock, and eventually multiorgan failure.[2,3] The most frequently encountered clinical manifestations of COVID-19 infection include fever, dry cough, fatigue, sore throat, dyspnea, headache, vomiting, diarrhea, anosmia, and ageusia.[4–6]

The dermatological manifestations of COVID-19, which were initially considered to be of little significance, have proven to be varied and sophisticated. According to published literature, the incidence of dermatological lesions in COVID-19 ranges from 0.6% to 20.4%.[7] Hair loss after recovery from COVID-19 is becoming a prominent dermal manifestation, with acute telogen

effluvium (TE) being a common occurrence. TE is defined as diffuse hair loss that occurs 2–3 months after a stressful event like febrile states, drugs, and postpartum period. The precipitating event induces hair loss by prematurely terminating the anagen phase and conversion to the catagen and telogen phases.[8,9] The body responds to infection with COVID-19 by establishing a proinflammatory state that causes tissue damage and associated sequelae. proinflammatory cytokines are produced and the process of anticoagulation is disrupted, which might cause TE in hair follicles through a systemic inflammatory response.[8]

This systematic review aims to compile and illustrate the clinical characteristics, physical examination findings, outcomes, and possible pathology behind acute TE occurring in COVID-19 recovered patients.

2 | METHODS

This systematic review was performed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[10]

2.1 | Search strategy

A literature search was carried out using MEDLINE/PubMed and Embase databases for studies published from December, 2019 till 5th of October, 2021. The search terms used included "Coronavirus," "Covid-19," "SARS-CoV-2," "Telogen effluvium," "TE," "Hair loss," "Hair fall," "Scalp," and "late manifestation." Studies were included from all over the world without any language restriction. Titles and abstracts of the articles retrieved from the literature search were screened by two authors (P. A. and C. K.). These authors ascertained the relevance of the studies based on predetermined eligibility criteria. Additional relevant studies were identified by manually inspecting the reference lists of the included studies. PRISMA flow diagram is illustrated in Figure 1.

2.2 | Eligibility criteria

Only those articles that met our predefined eligibility criteria were included in the analysis. Inclusion criteria consisted of (1) adult participants ≥18 years of age, (2) observational studies, case reports, and case series, and (3) studies reporting patients recovered from laboratory-confirmed SARS-CoV-2 infection presenting with hair loss

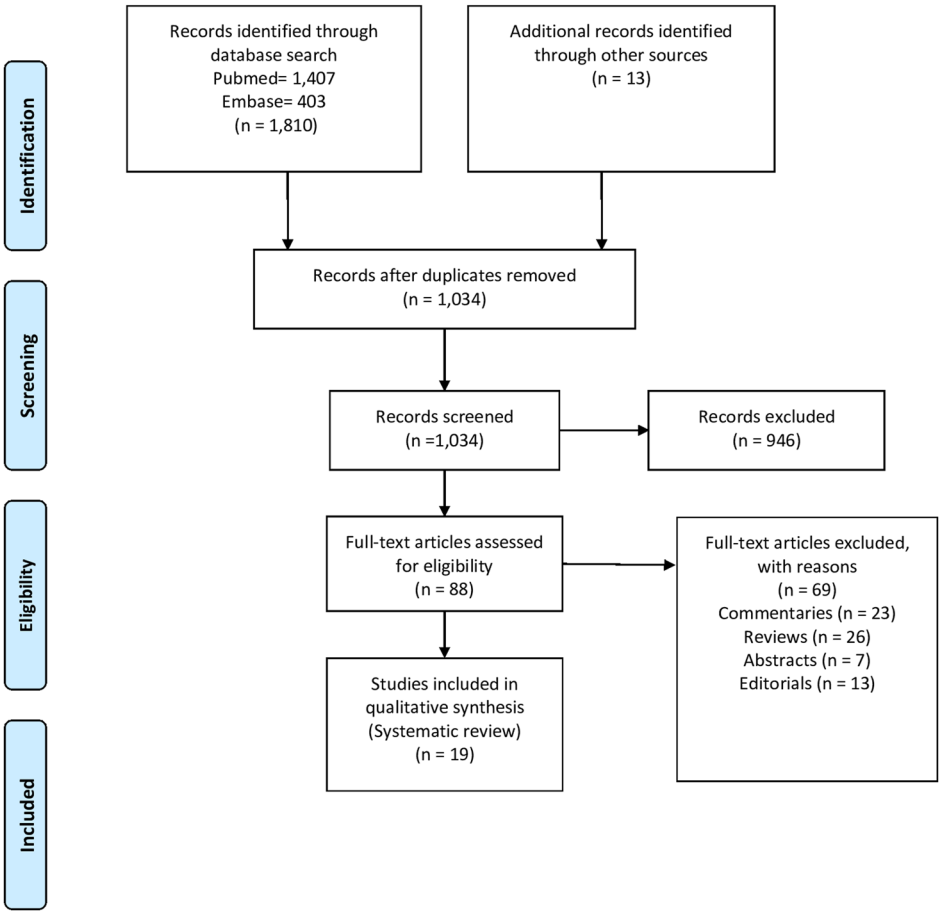

FIGURE 1 PRISMA flow diagram: representation of systematic literature search and study selection process. PRISMA, Reporting Items for Systematic Reviews and Meta-analyses. *Source*: Moher et al.[11]

weeks to months after infection. Review articles, posters, and duplicate publications were excluded.

2.3 | Quality assessment

The risk of bias assessment and quality appraisal of observational studies was done with the help of the Newcastle-Ottawa Scale.[12] Two investigators (Y. V. and V. P.) independently employed the Newcastle-Ottawa Scale for evaluating the quality of each included study. Quality appraisal for included case reports and case series was done using a tool established by Murad et al.[13] With the aid of this tool, three authors (K. I., N. K. A., and G. J.) analyzed all articles on four domains, including election, ascertainment, causality, and reporting. Studies were graded as good, fair, or poor quality.

2.4 | Data extraction

For each study, the following details were obtained: author, country of origin, study design, sample size, mean age, previous history of hair loss, physical exam findings, duration after recovery from COVID-19, duration from COVID-19 symptoms to the onset of acute TE, treatment of COVID-19, treatment of acute TE, and outcomes of acute TE.

3 | RESULTS

Of the 1810 articles obtained from the initial database search, 1034 articles remained after the removal of duplicate articles. After screening these articles for eligibility, 946 articles were removed as they focused on dermatologic manifestations of COVID-19 other than TE. Subsequently, 88 full-text articles pertaining to the objective of the manuscript were reviewed. A total of 19 articles met our priori inclusion criteria and were included in this systematic review (Figure 1).

A total of 632 patients with a history of COVID-19 infection were included from 19 studies.[8,9,14–30] Out of these 632 patients, 465 patients reported hair loss after recovery from COVID-19 and were subsequently diagnosed with acute TE. The median age of these patients was 44 years (which ranged from 34 to 64 years), with 67.5% of them being female. Most of the included studies were from the United States (four studies), followed by Italy (three studies), Spain (two studies), and one study each from France, China, Thailand, Pakistan, Colombia, Turkey, and Portugal. The data of two studies (97 patients) were from multinational registries (Table 1).

3.1 | Clinical characteristics of patients during COVID-19 infection

At the time of COVID-19 infection, the most prevalent symptoms in these patients were fever (59%), cough (23.6%), dyspnea (16.5%), anosmia (15%), ageusia (13.5%), and fatigue (12%). Other COVID-19 symptoms included diarrhea (6.4%), myalgia (5.5%), headache (4.26%), chest pain (2.84%), and coryza (1.2%). The most prevalent comorbidities in these patients were hypertension (27%), diabetes mellitus (17%), and dyslipidemia (6%). Other less frequently documented comorbidities included asthma (2.7%), anxiety disorder (0.75%), and major depressive disorder (0.38%). During the phase of COVID-19 infection, about 39% of patients had a history of hospitalization with an average hospital length of stay of 12 days. Medications used for the management of COVID-19 varied and the most frequently used medications were paracetamol, antibiotics, anticoagulant, steroids, tocilizumab, and hydroxychloroquine. Clinical features at the time of COVID-19 infection are summed up in Table 2.

3.1.1 | Clinical features of TE in COVID-19 recovered patients

COVID-19 recovered patients presented with hair loss, which was later diagnosed as acute TE on an average of 67 days after recovery from infection, with 34 days being the earliest. Similarly, the mean duration from COVID-19 symptom onset to the appearance of acute TE was 74 days. Table 3 illustrates the clinical findings of acute TE observed in COVID-19 recovered patients.

3.2 | Physical examination findings

Physical examination of the scalp depicted a positive telogen hair pull test in about 79% of patients. Telogen hair pull test is based on the concept of "gentle" hair pulling to induce telogen hair shedding. It aids in determining the extent and location of hair loss. Trichoscopic findings most commonly included decreased hair density with the presence of empty follicles and short regrowing hair, as shown in Table 4.

3.3 | Management and outcomes of acute TE

Medications used for the management of acute TE varied from patient to patient as well as across different studies. Most drugs used were targeted at hair regrowth. Minoxidil was the most common medication used in about 40% of patients, followed by steroids (26%), and sulfur amino acid/vitamin B6 (12.2%). Less frequently vitamin D (5%), platelet-rich plasma injections (2.5%), biotin (5%), and iron supplements (4.68%) were also prescribed. Most patients recovered from hair loss, while a few patients had active persistent hair fall.[27]

4 | DISCUSSION

While extensive research has been carried out to guide the diagnosis, treatment, and prevention of COVID-19, the growing evidence of post-recovery symptoms has prompted researchers to delve more

TABLE 1 Study characteristics and patient demographics

First author	Study design	Country of origin	Sample size	Mean age (years) and sex (female %)	Patients with telogen effluvium, *N* (%)	Comorbidities, *N* (%)	Previous history of hair loss	Quality assessment
Mieczkowska et al.	Case series	United States of America	10	55/100%	10 (100)	Asthma—2 (20), breast cancer–1 (10), chronic kidney disease Stage 3–1 (10), depression–1 (10), emphysema–1 (10), hyperlipidemia– 3 (30), PCOS–2 (20), type 2 diabetes mellitus–3 (30)	None—100%	Good
Garrigues et al.	Case series	France	120	63.2/37.5%	24 (20)	Diabetes—26 (21.7), hypertension—56 (46.7)	-	Fair
Rizzetto et al.	Case series	Italy	3	64.67/100%	3 (100)	Autoimmune thrombocytopenia—1 (33.34), osteoporosis—1 (33.34), diabetes mellitus—1 (33.34), systemic hypertension—1 (33.34), dyslipidemia—1(33.34)	AGA—1/3	Fair
Olds et al.	Retrospective study	United States of America	10	48.5/90%	10 (100)	-	-	8 (NCOS)
Moreno-Arrones et al.	Prospective study	Spain	191	47.4/78.5%	191 (100)	-	-	7 (NCOS)
Lv et al.	Case report	China	1	38/100%	1 (100)	-	-	Fair
Thuangtong et al.	Retrospective study	Thailand	93	40.8/41.9%	22 (23.6)	Hypertension—13 (13.97), diabetes—12 (12.90), dyslipidemia—6 (6.45), allergic rhinitis—3 (3.225), old pulmonary tuberculosis—2 (2.15), cancer—2 (2.15), stroke—2 (2.15),		8 (NCOS)
Abrantes et al.	Retrospective study	Multinational	30	40.5/70%	30 (100)	Hypertension—1 (3.34), anxiety disorder—2 (6.67), obesity—2 (6.67), major depressive disorder—1 (3.34), arterial hypertension—1 (3.34), hypothyroidism—2 (6.67), dyslipidemia—1 (3.34).	AGA—8(27)	7 (NCOS)
Cline et al.	Retrospective study	United States of America	10	-/100%	10 (100)	Obesity—4(40), diabetes mellitus type 1—1 (10), hyperlipidemia 4 (40), asthma 4 (40), diabetes mellitus type 2—3 (30)	-	7 (NCOS)
Rossi et al.	Case series	Italy	14	47.57/78.57%	14 (100)	-	AGA—3 (21.4), scalp psoriasis 1 (7.14)	Fair
Saeed et al.	Case series	Pakistan	4	39.75/100%	4 (100)	None	-	Fair
Di Landro et al.	Case series	Italy	39	64.6/76.9%	39 (100)	-	-	Fair

TABLE 1 (Continued)

First author	Study design	Country of origin	Sample size	Mean age (years) and sex (female %)	Patients with telogen effluvium, *N* (%)	Comorbidities, *N* (%)	Previous history of hair loss	Quality assessment
Starace et al.	Survey-based	Multinational	67	47.5/92%	67 (66.3)	-	-	-
Domínguez-Santás et al.	Case report	Spain	1	42/100%	1 (100)	-	-	Fair
Deng et al.	Case report	United States of America	1	41/100%	1 (100)	Allergic rhinitis, diabetes mellitus, hyperlipidemia	-	Fair
Temiz et al.	Case series	Turkey	8	37.25/75%	8 (100)	-	-	Fair
Arenas Soto et al.	Case reports	Colombia	2	36/100%	2 (100)	-	-	Fair
Roda et al.	Case series	Portugal	27	45/89%	27 (100)	-	-	Good
de Oliveira Izumi et al.	Case study	Brazil	1	34/100%	1 (100)	None	No	Fair

Abbreviations: AGA, androgenetic alopecia; NCOS, newcastle ottawa scale; PCOS, polycystic ovarian syndrome.

into this crucial aspect. Post-COVID-19 manifestations have been described in the literature; a recent meta-analysis reported the five most common post-recovery symptoms, including fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%).[31] Hair loss after recovery from COVID-19 is a harrowing manifestation. The current literature on acute TE occurring after recovery from COVID-19 is limited to underpowered studies, which have not been systematically appraised. We sought to fill this gap by compiling the characteristics of 465 patients, who were diagnosed with acute TE post-recovery, from 19 studies originating from 10 different countries.

In alignment with our findings, acute TE was also reported during the life-threatening influenza pandemic of 1918–1919 (commonly known as Spanish flu), with hair loss developing 2–6 weeks after the onset of fever.[24,32] Moreover, we observed that acute TE occurred around a mean duration of 74 days after the onset of COVID-19 symptoms. This is earlier than classic acute TE, which occurs approximately 3–4 months after a triggering event. However, the trichoscopic and trichogram findings did not differ from classic acute TE.[25] As shown in our results, the detailed trichoscopic findings reported across the studies most commonly included reduced hair density,[19,24,30] empty hair follicles,[9,24,25,30] short regrowing hair,[24,25] and/or hair in the telogen phase.[16,19]

Similar to the findings of classic acute TE, there was a female preponderance (67.5%) in the patients diagnosed with acute TE post-COVID-19. This can be explained by the higher vulnerability of female hair follicles, easier identification of hair loss in females owing to longer hair, and under-reporting in males due to the higher psychological effects of hair loss in women.[24,33] Stress during COVID-19 infection has been implicated as a potential contributor to hair shedding.[26,27]

Hypertension (27%), diabetes mellitus (17%), and dyslipidemia (6%) were the most prevalent comorbidities in the COVID-19 recovered individuals who subsequently developed acute TE. The presence of comorbidities has been shown to increase the risk of developing post-COVID-19 acute TE. In a case series of 10 patients with COVID-19-associated acute TE, 9 of them had underlying comorbidities.[28] Similarly, Mieczkowska et al.[14] found that most (8 out of 10) acute TE patients had pre-existing medical conditions. However, observational studies with a larger sample size are needed to confirm this association. Interestingly, the presence of comorbidities increases the risk of severe COVID-19 infection,[34] and both the presence of comorbidities and severe COVID-19 infection have been associated with post-COVID-19 acute TE.[14,18] Our results demonstrated that more than one-fourth (39%) of the patients diagnosed with acute TE post-recovery were hospitalized during the phase of COVID-19 infection. Olds et al.[8] reported that 70% of the patients with post-COVID-19 acute TE required hospitalization for COVID-19 infection. Similarly, Di Landro et al.[18] noted that 16 of the 39 patients who presented with COVID-19-associated acute TE had a severe COVID-19 infection and required hospitalization and continuous positive airway pressure therapy. This can be attributed to the suggested correlation between COVID-19 severity and the increased

TABLE 2 Clinical features at the time of COVID-19 infection

First author	Symptoms during COVID-19 infection, *N* (%)	No. of patients hospitalized, *N* (%)	Hospital length of stay	Treatment for COVID-19
Mieczkowska et al.	-	4 (40)	2.8 days	Azithromycin—2, doxycycline—2, ceftriaxone—2, hydroxychloroquine—2
Garrigues et al.	Confusion—7 (5.8), cough—87 (72.5), dyspnea—88 (73.3), myalgia—19 (15.8), diarrhea—29 (24.2), cough—20 (16.7), chest pain—13 (10.8), fatigue—66 (55.0), dyspnea—50 (41.7), ageusia—13 (10.8), anosmia—16 (13.3), hair loss—24 (20.0), attention disorder—32 (26.7), memory loss—41 (34.2), sleep disorder—37 (30.8)	24 (100)	11.2 days	-
Rizzetto et al.	Bilateral interstitial pneumonia—(100), distress respiratory syndrome—(66.7), diarrhea—(33.34), diffuse itching and flushing—(33.34), weight loss—(33.34)	3 (100)	27 days	Enoxaparin—3, ceftriaxone—1, tocilizumab—1, lopinavir/ritonavir—2, gliclazide—1, acarbose—1, ezetimibe/simvastatin—1, sitagliptin—1, chlorphenamine maleate—1
Olds et al.	-	10 (100)	-	Azithromycin—4/10 (49), antibiotics—2/10 (20), ceftriaxone—1/10 (10), hydroxychloroquine—4/10 (40), methylprednisolone—3/10 (30), supportive—2/10(20), prednisone—1/10 (10)
Moreno-Arrones et al.	Fever—165 (86.4), dermatologic manifestations—23 (12)	55 (28.8)	-	Paracetamol—144 (75.4), NSAIDs—28 (14.7), oral corticosteroids—50 (26.2), oral antibiotics—82 (42.9), lopinavir/ritonavir—38 (19.9), remdesivir—10 (5.2), tocilizumab—26 (13.54), enoxaparin—97 (50.5)
Lv et al.	Trichodynia, oily scalp		13 days	-
Thuangtong et al.	Asymptomatic—1/93 (1.0), upper respiratory tract—66/93 (71.0), lower respiratory tract—26/93 (28.0), urticaria—2/93(2.15), maculopapular rash—2/93 (2.15)	93 (100)	6 days	-
Abrantes et al.	-	1 (3.34)	-	-
Cline et al.	-	-	-	-
Rossi et al.	Defluvium—14/14 (100), itching—2/14(14.28), eyelid edema—1/14 (7.14)	4 (28.57)	-	Tocilizumab—2/14 (14.28), paracetamol—7/14 (50), hydroxychloroquine—2/14 (14.28), other antibiotics—3/14 (21.43), azithromycin—3/14 (21.428), steroids—1/14 (7.14), levofloxacin—1/14 (7.14), darunavir + cobicistat—1/14 (7.142), pantoprazole—1/14 (7.142)
Saeed et al.	Diarrhea—2 (50), loss of taste and smell—1 (25)	0	0	Zinc—1 (25), vitamin C—1 (25), calcium—1 (25), vitamin D—1 (25)
Di Landro et al.	Trichodynia (18), anosmia aguesia (66.6)	16 (41)	-	Paracetamol—39 (100), systemic steroids—25 (64), anticoagulants—16 (41)

TABLE 2 (Continued)

First author	Symptoms during COVID-19 infection, N (%)	No. of patients hospitalized, N (%)	Hospital length of stay	Treatment for COVID-19
Starace et al.	Fever−(75.2), cough−(53.5), ageusia−(41.6), anosmia−(57.4), diarrhea−(5.9), myalgia−(10.9), ooryza−(9.9), headache−(23.8), dyspnea−(7.9), asthenia−(28.7)	-	-	-
Domínguez-Santás et al.	Coughing, fever	0	0	-
Deng et al.	Acral desquamation of fingers and palms, perniosis, beau lines on fingers	0	0	Ibuprofen−1 (100), antitussive−1 (100)
Temiz et al.	-	-	-	-
Arenas Soto et al.	None	0	0	-
Roda et al.	Trichodynia−5 (18.5), fever−17 (63), ageusia−8 (30), cough−6(22), myalgia−5 (18.5), anosmia−4 (15), thoracalgia−3 (11), asymptomatic−4 (15), pernio lesions−1 (3.7), maculopapular eruption−1 (3.7)	3 (11)	-	-
de Oliveira Izumi et al.	-	-	-	-

risk of subsequent acute TE, as patients with severe COVID-19 infection have higher levels of pro-inflammatory cytokines.[8] However, this does not imply that acute TE does not occur in patients with subclinical COVID-19 infection. In a multicenter study of 214 cases of COVID-19 associated acute TE, Moreno-Arrones et al.[29] observed that approximately 1 out of 10 patients had subclinical COVID-19 infection. Therefore, it is imperative for clinicians to consider a prior history of COVID-19 infection, regardless of the severity, as a differential diagnosis in every patient consulting for acute TE in the context of the pandemic.[9,29] The correlation between the severity of COVID-19 infection and the intensity of acute TE remains unclear. According to Rossi et al.,[25] all four patients who required hospitalization during COVID-19 infection had a regression in acute TE around 3–5 months after the onset of hair fall, suggesting no association between the severity of COVID-19 infection and the severity of subsequent acute TE.

In COVID-19 patients, the pathophysiology behind acute TE is poorly understood, with numerous suggested mechanisms. According to the existing literature, the following pathological pathways have been proposed:

1. Elevated levels of interleukin-6, a pro-inflammatory cytokine, were observed in COVID-19 patients.[25] Interleukin-6 inhibits the elongation of the hair shaft by suppressing the proliferation of matrix cells in cultured hair follicles.[9]

2. Interferon is well-recognized to induce acute TE. Elevated levels of interferon are documented in COVID-19 and other viral illnesses as a part of the body's antiviral response.[25]

3. Metalloproteinases 1 and 3 and interleukin-1β may inhibit the growth of hair follicles.[25]

4. COVID-19 infection causes the activation of the coagulation cascade, which subsequently decreases the concentration of anticoagulation proteins due to diminished production and increased consumption. Moreover, these factors may result in microthrombi formation, which may occlude the blood supply of hair follicles.[8,27]

5. In COVID-19 patients, non-neutralizing virus-specific antibodies interact with Fcγ and/or complement receptors, facilitating the entry of the virus into the host cells. This may lead to direct damage to the hair follicles by the virus. The entry of the pathogen into the host cells via this antibody-dependent enhancement, which led to hair fall, was documented in some infected patients in the 2014–2015 dengue epidemic.[25]

6. Medications used during COVID-19 treatment may have contributed to acute TE.[8,27] However, there is conflicting evidence regarding their potential pathways. According to Rossi et al.[25] and Rizzetto et al.,[30] drug-induced acute TE in COVID-19 patients was quite unlikely due to the early onset of acute TE and the short duration of treatment for COVID-19, respectively.

The management of acute TE associated with COVID-19 varied across the studies. Lv et al.[16] described the case of a 38-year-old female with post-COVID-19 acute TE who was successfully treated with topical 5% minoxidil mixed with halcinonide solution as well as selenium sulfide lotion mixed with shampoo. In a case series of

TABLE 3 Clinical findings of TE observed in COVID-19 recovered patients

First author	Duration after recovery	Mean time from COVID-19 symptom onset	Physical exam findings	Treatment of TE, *N* (%)	Outcome of alopecia
Mieczkowska et al.	-	114 days	Positive hair pull test with many telogen hair, pronounced thinning—1 patient; global loss of hair volume—1 patient, areas of lower hair density with many vellus hair on bilateral frontotemporal regions—1 patient	-	Resolution
Garrigues et al.	110 days	110.9 days	-	-	Resolution
Rizzetto et al.	57 days	90 days	Positive pull test positive—3 patients	Oral supplementation with sulfur amino acid/vitamin B6—3 (100), peptide mimicking hair growth factor lotion—3 (100), minoxidil 5% lotion—1 (33.34%)	-
Olds et al.	-	50 days	Positive telogen hair pull test—4 (40%), negative telogen hair pull test—2 (20%), diffuse hair thinning—4 (40%), postinflammatory hyperpigmentation—1(10%), thinning of frontal scalp and vertex—1 (10%), miniaturization at crown—1 (10%)	Triamcinolone lotion for itching—1 (10), minoxidil 5% solution—4 (40), minoxidil 5% foam—1 (10), biotin supplementation—1 (10), iron supplementation—1 (10), dandruff shampoo—1 (10), clobetasol solution—1 (10)	Resolution
Moreno-Arrones et al.	-	57.1 days	Absence of anisotrichosis and presence of regrowing hair	2% topical minoxidil—32 (26.8), 5% topical minoxidil—45 (23.6), oral minoxidil—18 (9.3), oral nutricosmetics—70 (36.4), PRP injections—8 (4), no treatment—18 (9.4)	-
Lv et al.	72 days	83 days	Positive pull test (whole head)	Topical 5% minoxidil, halcinonide lotion, selenium sulfide lotion	Resolution
Thuangtong et al.	42 days	12 days	Increased hair shedding	-	Resolution
Abrantes	34 days	45 days	Positive hair pull test grading—1, grading—1 (3.34%), 2—13 (43.34%), 3—826.67%), 4—8 (26.67%)	-	Resolution
Cline et al.	-	-	-	-	-
Rossi et al.	-	60 days	Hair pull test positive—(50)	Alpha-lipoic acid, calcium pantothenate (vitamin B5), vitamin D3, ferrous gluconate, clobetasol propionate 0.05% foam—14 (100)	Resolution
Saeed et al.	-	-	Positive hair pull test—4 (100)	-	-
Di Landro et al.	72 days	63 days	Positive hair pull test—39 (100), empty follicular ostia and telogen club hair—3 (16.67)	N/m	Resolution

TABLE 3 (Continued)

First author	Duration after recovery	Mean time from COVID-19 symptom onset	Physical exam findings	Treatment of TE, N (%)	Outcome of alopecia
Starace et al.	-	84 days	-	High-potency topical steroids—(50), supplements with amino acids and vitamin B complex—(27), topical minoxidil—(15), pain relief lotions or hair growth promoters—(10)	Resolution—91 (90), active persistent—10 (10)
Domínguez-Santás et al.	-	120 days	Positive hair pull test	Reassurance	-
Deng et al.	81 days	60 days	-	-	Resolution
Temiz et al.	-	81.9 days	-	-	Resolution
Arenas Soto et al.	-	-	Positive hair pull test—2 (100), increase in the percentage of villous hair—(50)	Oral sulfur amino acids—1 (50), Vitamin B6—1 (50), topical 5% minoxidil—1 (50), 0.5% biotin—1 (50)	-
Roda et al.	-	70 days	Positive pull test	-	Resolution—16 (59%)
de Oliveira Izumi et al.	-	90 days	Positive hair pull test, area of diffuse capillary thinning	Topical 5% minoxidil	Partial resolution

Abbreviations: PRP, platelet-rich plasma; TE, telogen effluvium.

10 patients conducted by Olds et al.,[8] topical minoxidil was prescribed in half of the patients, while no treatment was provided to three patients. In all three cases of post-COVID-19 acute TE presented by Rizzetto et al.,[30] oral supplementation with sulfur amino acid/vitamin B6 as well as peptide mimicking hair growth factor lotion were used to treat acute TE, while topical minoxidil was given to only one patient who was suffering from androgenetic alopecia. Minoxidil was not given to the rest of the two acute TE patients as it could have increased the hair fall initially, due to the reduced telogen phase and the early entry of the resting follicles into the anagen phase. The efficacy of minoxidil for treating post-COVID-19 acute TE has not been established.[8] This warrants randomized controlled trials and prospective studies to fill this gap.

Acute TE is self-limited and undergoes remission within 3–6 months of onset unless associated with androgenetic alopecia.[27] In concordance with the findings of acute TE caused by other etiologies, post-COVID-19 acute TE also resolved in most patients, as shown in Table 3. Through this article, we highlight the importance of an increased familiarity of clinicians with post-COVID-19 acute TE to provide appropriate counseling and treatment. It is imperative to recognize that TE is a stressful situation for most patients, especially females. Identifying COVID-19 infection as a potential cause of acute TE will help the clinicians counsel the patients that after recovery from COVID-19, the factor triggering acute TE has been resolved. Educating the patients about the transient nature of the condition is essential to alleviate their stress. Patients should be advised to ensure a healthy diet and informed that it may take up to 18 months for the hair thickness to return to the baseline.[8]

4.1 | Limitations

There are a few limitations in this systematic review that must be taken into account. First, these reports are underpowered as many cases of acute TE go unreported, and hence, the findings may not be decisive and relevant to the entire population. This calls for further large-scale studies addressing the clinical characteristics and possible pathological mechanisms of post-COVID-19 acute TE. Second, most of the studies were case series that described patients selected for inclusion because they had acute TE and therefore the incidence and prevalence of this complication post-COVID-19 cannot be determined. Evaluation of the incidence of acute TE in COVID-19 survivors mandates large prospective studies. Third, although COVID-19 has been established as the main trigger for acute TE, other factors, including poor nutrition, deteriorating scalp health, infrequent shampooing, and medications such as anticoagulants, may be potential contributors. Moreover, the emotional toll of the COVID-19 pandemic on the mental health, of even the noninfected individuals, may be an inciting factor for acute TE. Last, another limitation was that we could not register the review. We tried to prospectively register our review, but decided to go against it as it was taking an unreasonably longer time than expected due to the increased pool of COVID-19-related articles.

TABLE 4 Detailed trichoscopic findings reported across all studies

First author	Trichoscopic findings
Mieczkowska et al.	Areas of lower hair density with many vellus hair on bilateral frontotemporal regions
Rizzetto et al.	Reduction in hair density, some empty follicles, with the integrity of the stem and absence of miniaturized hair
Lv et al.	Scalp inflammation, capillary ectasia, dandruff, increased density of telogen hair, and relatively uniform diameter of the terminal hair shaft, clubbed end of hair root
Rossi et al.	Regrowing hair, follicular units with hair, empty hair follicles, and thin terminal hair
Saeed et al.	Telogen hair having a white bulb
Di Landro et al.	Empty follicles and a telogen root on the scalp surface
Domínguez-Santás et al.	Numerous follicular units of only one hair and without anisotrichosis
Arenas Soto et al.	Reduction of hair density in the temporoparietal region, hair in the telogen phase
Roda et al.	Decreased hair density with the presence of empty follicles and short regrowing hair

5 | CONCLUSIONS

In this article, we systematically reviewed the existing literature on acute TE occurring after recovery from COVID-19. Post-COVID-19 acute TE occurred earlier than classic acute TE, but showed similar trichogram and trichoscopic findings, including reduced hair density, empty hair follicles, and/or short regrowing hair. Although our results did not suggest COVID-19 to be the absolute cause of acute TE, they highlight the need to consider the possibility of post-COVID-19 acute TE in a patient presenting with hair fall, with a history of COVID-19 infection, in the context of COVID-19 pandemic. Although acute TE is a transient condition, it can negatively impact the mental health of individuals who have already suffered from the debilitating COVID-19 illness. Identifying COVID-19 infection as a potential cause of acute TE will help the clinicians counsel the patients, relieving them from undue stress.

ACKNOWLEDGMENT

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Conceptualization, writing—reviewing and editing: Nabeel Hussain. *Conceptualization, writing—original draft*: Preeti Agarwala. *Conceptualization, writing—reviewing and editing*: Kinza Iqbal. *Data curation, writing—reviewing and editing*: Hanaa Mohamed Sheikh Omar. *Data curation, formal analysis*: Gurusha Jangid. *Data curation, writing—original draft*: Vraj Patel. *Writing—original draft, writing—reviewing and editing*: Sawai Singh Rathore. *Data curation, methodology*: Chandani Kumari. *Writing—original draft*: Felipe Velasquez-Botero. *Formal analysis, supervision*: Guadalupe Abigail Benítez López. *Data curation, methodology*: Yogesh Vishwakarma. *Formal analysis, supervision*: Airin Parvin Nipu. *Data curation, supervision*: Noman Khurshid Ahmed.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Sawai Singh Rathore http://orcid.org/0000-0003-1954-094X

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-733. doi:10.1056/NEJMoa2001017
2. Rathore SS, Rojas GA, Sondhi M, et al. Myocarditis associated with Covid-19 disease: a systematic review of published case reports and case. *Int J Clin Pract*. 2021;75:e14470. doi:10.1111/ijcp.14470
3. Drake TM, Riad AM, Fairfield CJ, et al. Characterisation of in-hospital complications associated with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol UK: a prospective, multicentre cohort study [published correction appears in *Lancet*. 2021;398(10298):390]. *Lancet*. 2021;398(10296):223-237. doi:10.1016/S0140-6736(21)00799-6
4. Menon T, Sharma R, Kataria S, et al. The association of acute kidney injury with disease severity and mortality in COVID-19: a systematic review and meta-analysis. *Cureus*. 2021;13(3):e13894. doi:10.7759/cureus.13894
5. Gulati A, Pomeranz C, Qamar Z, et al. A comprehensive review of manifestations of novel coronaviruses in the context of deadly COVID-19 global pandemic. *Am J Med Sci*. 2020;360(1):5-34. doi:10.1016/j.amjms.2020.05.006
6. Rathore SS, Hussain N, Manju AH, et al. Prevalence and clinical outcomes of pleural effusion in COVID-19 patients: a systematic review and meta-analysis. *J Med Virol*. 2021;94:229-239. doi:10.1002/jmv.27301
7. Shams S, Rathore SS, Anvekar P, et al. Maculopapular skin eruptions associated with Covid-19: a systematic review. *Dermatol Ther*. 2021;34(2):e14788. doi:10.1111/dth.14788
8. Olds H, Liu J, Luk K, Lim HW, Ozog D, Rambhatla PV. Telogen effluvium associated with COVID-19 infection. *Dermatol Ther*. 2021;34(2):e14761. doi:10.1111/dth.14761

9. Abrantes TF, Artounian KA, Falsey R, et al. Time of onset and duration of post-COVID-19 acute telogen effluvium. *J Am Acad Dermatol*. 2021; S0190-9622(21):02149-6. doi:10.1016/j.jaad.2021.07.021
10. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535. doi:10.1136/bmj.b2535
11. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097
12. Lo CK, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC Med Res Methodol*. 2014;14: 45. doi:10.1186/1471-2288-14-45
13. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med*. 2018;23:60-63. doi:10.1136/bmjebm-2017-110853
14. Mieczkowska K, Deutsch A, Borok J, et al. Telogen effluvium: a sequela of COVID-19. *Int J Dermatol*. 2021;60(1):122-124. doi:10.1111/ijd.15313
15. Garrigues E, Janvier P, Kherabi Y, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J Infect*. 2020;81(6):e4-e6. doi:10.1016/j.jinf.2020.08.029
16. Lv S, Wang L, Zou X, et al. A case of acute telogen effluvium after SARS-CoV-2 infection. *Clin Cosmet Investig Dermatol*. 2021;14: 385-387. doi:10.2147/CCID.S307982
17. Thuangtong R, Angkasekwinai N, Leeyaphan C, et al. Patient recovery from COVID-19 infections: follow-up of hair, nail, and cutaneous manifestations. *BioMed Res Int*. 2021;2021:5595016. doi:10.1155/2021/5595016
18. Di Landro A, Naldi L, Glaser E, Paus R, Tosti A. Pathobiology questions raised by telogen effluvium and trichodynia in COVID-19 patients. *Exp Dermatol*. 2021;30(7):999-1000. doi:10.1111/exd.14352
19. Arenas Soto CM, Diaz Mestre MP. Efluvio telógeno: una manifestación del síndrome Post-COVID-19 [Telogen effluvium: a manifestation of the post-COVID-19 syndrome]. *Piel*. 2021. doi:10.1016/j.piel.2021.06.013
20. Deng J, Ngo T, Zhu TH, Halverstam C. Telogen effluvium, beau lines, and acral peeling associated with COVID-19 infection. *JAAD Case Rep*. 2021;13:138-140. doi:10.1016/j.jdcr.2021.05.026
21. Temiz SA, Kutlu Ö. The development of dermatologic diseases in patients recovered from COVID-19. *Dermatol Ther*. 2021;34(2): e14791. doi:10.1111/dth.14791
22. Domínguez-Santás M, Haya-Martínez L, Fernández-Nieto D, Jiménez-Cauhé J, Suárez-Valle A, Díaz-Guimaraens B. Acute telogen effluvium associated with SARS-CoV-2 infection. *Aust J Gen Pract*. 2020;49:49. doi:10.31128/AJGP-COVID-32
23. de Oliveira Izumi M, Figueiredo Brandão BJ. Tratamento do eflúvio telógeno pós-Covid 19. *BWS J*. 2021;4:1-8.
24. Roda Â, Oliveira-Soares R. Acute telogen effluvium in patients recently infected with SARS-CoV-2. *J Port Soc Dermatol Venereol*. 2021;79(1):21-25. doi:10.29021/spdv.79.1.1299
25. Rossi A, Magri F, Sernicola A, et al. Telogen effluvium after SARS-CoV-2 Infection: a series of cases and possible pathogenetic mechanisms. *Skin Appendage Disord*. 2021;21:1-5. doi:10.1159/000517223
26. Saeed W, Hussain I, Altaf F. Telogen effluvium: long term Covid-19 symptom. *J Pak Assoc Dermatol*. 2020;30(4):695-698.
27. Starace M, Iorizzo M, Sechi A, et al. Trichodynia and telogen effluvium in COVID-19 patients: results of an international expert opinion survey on diagnosis and management. *JAAD Int*. 2021;5: 11-18. doi:10.1016/j.jdin.2021.07.006
28. Cline A, Jacobs AK, Fonseca M, et al. Race, ethnicity, and comorbidities are critical factors in the diagnosis of telogen effluvium during the COVID-19 pandemic. *J Am Acad Dermatol*. 2021;85(1): 209-211. doi:10.1016/j.jaad.2021.03.099
29. Moreno-Arrones OM, Lobato-Berezo A, Gomez-Zubiaur A, et al. SARS-CoV-2-induced telogen effluvium: a multicentric study. *J Eur Acad Dermatol Venereol*. 2021;35(3):e181-e183. doi:10.1111/jdv.17045
30. Rizzetto G, Diotallevi F, Campanati A, et al. Telogen effluvium related to post severe Sars-Cov-2 infection: clinical aspects and our management experience. *Dermatol Ther*. 2021;34(1):e14547. doi:10.1111/dth.14547
31. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Sci Rep*. 2021;11(1):16144. doi:10.1038/s41598-021-95565-8
32. Shors T, McFadden SH. 1918 influenza: a Winnebago county, Wisconsin perspective. *Clin Med Res*. 2009;7(4):147-156. doi:10.3121/cmr.2009.863
33. Grover C, Khurana A. Telogen effluvium. *Indian J Dermatol Venereol Leprol*. 2013;79(5):591-603. doi:10.4103/0378-6323.116731
34. Honardoost M, Janani L, Aghili R, Emami Z, Khamseh ME. The association between presence of comorbidities and COVID-19 severity: a systematic review and meta-analysis. *Cerebrovasc Dis*. 2021; 50(2):132-140. doi:10.1159/00051328

How to cite this article: Hussain N, Agarwala P, Iqbal K, et al. A systematic review of acute telogen effluvium, a harrowing post-COVID-19 manifestation. *J Med Virol*. 2021;1-11. doi:10.1002/jmv.27534