Dermatology Practical & Conceptual

Relationship Between Anemia and Telogen Effluvium in Post-COVID-19 Survivors

Canan Emiroglu[1], Murat Dicle[1], Süleyman Görpelioglu[1], Cenk Aypak[1]

1 Department of Family Medicine, University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

Key words: COVID-19, Anemia, Iron deficiency anemia, Hair shedding, Inflammation

Citation: Emiroglu C, Dicle M, Görpelioglu S, Aypak C. Relationship Between Anemia, and Telogen Effluvium in Post-COVID-19 Survivors. *Dermatol Pract Concept*. 2025;15(1):4234. DOI: https://doi.org/10.5826/dpc.1501a4234

Accepted: August 27, 2024; **Published:** January 2025

Copyright: ©2024 Emiroglu et al. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (BY-NC-4.0), https://creativecommons.org/licenses/by-nc/4.0/, which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Canan Emiroğlu, Medical Doctor, Specialist of Family Medicine, University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Family Medicine, Ziraat Mahallesi, Şehit Ömer Halisdemir Cad. No:20, Dışkapı Altındağ Ankara Turkey. Phone: 90 535 336 6038; E-mail address: cananmemiroglu@gmail.com

ABSTRACT

Introduction: There are insufficient studies in the literature on the relationship between the acute severity of disease and the occurrence of anemia and telogen effluvium (TE) in the post-coronavirus disease 2019 (COVID-19) period.

Objectives: The purpose of this study was to investigate the relationship between anemia and TE in individuals who had experienced COVID-19 during the post-COVID period.

Method: The study has a retrospective cross-sectional design and was conducted on patients presenting to a tertiary care hospital for COVID-19 follow-up. Patient data, including demographic parameters, data regarding smoking history, comorbidities, symptoms, and laboratory panel at presentation, were evaluated.

Results: Out of 672 patients, 249 had TE complaints. TE was more common in females, those under the average age of this patient group, and those with a body mass index of under 25. Anemia was identified in 80 patients. Among individuals with anemia, TE was observed in 47.3%, whereas among those without anemia, the occurrence of TE was noted at a rate of 35.5%. When the severity of infection in the acute phase was examined in relation to the presence of TE in the post-COVID period, TE was observed in 45.1% of those receiving outpatient treatment, 37.0% of those hospitalized, and 30.7% of those in intensive care.

Conclusion: The results obtained in this study group indicate that TE complaints after COVID-19 are more common in those with anemia, but the fact that they did not correlate with the acute disease's severity requires consideration of other causes besides the virus effect.

Introduction

The disease terminologically referred to as "novel coronavirus disease" occurs due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and primarily manifests as a respiratory tract infection. Several studies have demonstrated that it should be considered a multisystemic disease including cardiovascular impairment, respiratory illness, gastrointestinal disorders, neurological symptoms as well as hematopoietic and immune system dysregulation [1-3]. Iron dyshomeostasis and anemia may play an important role in multiple organ dysfunction syndrome in COVID-19. Both anemia of inflammation (AI) and iron deficiency (IDA) are frequently found in severe COVID-19 and contribute to the mortality and morbidity of the acute disease [4]. Inflammation causes typical changes in iron homeostasis, characterized by increased iron uptake and storage in macrophages and decreased intestinal iron absorption. This leads to decreased circulating iron levels and reduced availability of the metal for erythropoiesis, resulting in the development of inflammatory anemia with cytokine-mediated inhibition, shortened erythrocyte lifespan, and reduced biological activity of the red cell hormone erythropoietin [5].

In patients admitted to the intensive care unit at a tertiary hospital in London, UK, a rapid and significant decrease in hemoglobin levels was observed, accompanied by an increase in white blood cell and platelet counts during this period. Importantly, it was noted that anemia was not concomitant with myelosuppression. In a study conducted there, it was shown that SARS-CoV-2 could infect and amplify its genome in erythroid progenitors (ERP), named as ERP-S2 ($CD71^{+}CD235A^{-}$) and ERP-S3 ($CD71^{+}CD235a^{+}$), but was not able to bind and infect hematopoietic stem/progenitor cells (HSPCs) from the bone marrow [6]. Interestingly, the authors found that SARS-CoV-2 remained in ERP-S2 after 14 days of the initial infection.

Telogen effluvium (TE) is characterized by diffuse hair shedding 2–3 months after a triggering event [7]. The precipitating event causes premature termination of the anagen phase and subsequent transition to the catagen and telogen phases, resulting in hair shedding. TE is usually self-limited; acute TE typically resolves within six months from onset and is not a scarring alopecia [7,8]. Triggering factors for TE include pregnancy, drugs, illness, psychological trauma, febrile states, malnutrition, hospitalization, and surgery [7,8]. SARS-CoV-2 infection has previously been linked to TE. In several reports, TE developed 2–12 weeks after the SARS-CoV-2 infection [9,10]. However, to date, no studies have been conducted on the relationship between TE and anemia in the patients who have recovered from COVID-19. In addition, no similar study has been found in the literature regarding the severity of COVID-19 in the acute phase and its relationship with the incidence of anemia and TE in the post-COVID-19 period.

Objective

The purpose of this study was to investigate the relationship between anemia and TE in individuals who experienced COVID-19 during the post-COVID period. Simultaneously, our objective was to discern whether there are differences between patients who underwent hospitalization for a more severe course of the disease and those who received outpatient treatment.

Methods

Study Design and Population

This retrospective cross-sectional study was conducted on patients who presented to the COVID-19 follow-up clinic of our tertiary care hospital between 01 December 2020 and 30 November 2021. Adult (age ≥18) patients diagnosed with COVID-19 by a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test result and discharged from the hospital at least six weeks previously constituted the target population of this study. **Individuals with a history of complaints related to hair loss were excluded from the study.** A total of 672 patients with complete laboratory results were included in the evaluation.

Patient data, including demographic parameters, data regarding smoking history, and comorbidities, and symptoms at presentation, were retrospectively reviewed. Laboratory panels determined by the Ministry of Health were obtained from all patients (complete blood test (CBC), ferritin, vitamin B12, folic acid levels, serum iron, iron binding capacity, C-reactive-protein (CRP), thyroid-stimulating hormone (TSH), total protein, albumin.). The hemogram parameters were measured with the Beckman Coulter LH 700 Hematology Analyzer (Beckman Coulter Inc., Brea, CA, USA). Levels of TSH were assayed by chemiluminescence immunoassay method (Beckman Coulter, Access 2, USA). Other biochemical parameters were examined by Beckman Coulter AU5800 (Beckman Coulter Inc., Brea, CA, USA) autoanalyzer.

Participants were divided into two groups using WHO criteria, which define anemia as Hb<13 mg/dl for males and Hb<12 mg/dl for females [11]; anemic individuals with serum ferritin levels <30 ng/ml are labeled as "absolute iron deficiency anemia" (IDA). For those with ferritin >30 ng/ml, serum iron, iron binding capacity, and transferrin saturation values were examined. Anemia patients with normal serum iron (>60 µ/dL), normal or decreased (250-450 µg/dL) total iron binding capacity (TIBC), and normal (>20%) transferrin saturation (TSAT) were categorized as "Unknown Anemia". Individuals with ferritin levels above 100 ng/ml,

decreased transferrin saturation, and decreased TIBC were categorized as having "Anemia of Inflammation" or "Anemia of Chronic Disease" [11]. Vitamin B12 deficiency has been detected in those with serum levels below 200 ng/ml and folic acid deficiency in those with serum levels below 4 ng/ml [12]. Glomerular filtration rate (GFR) was measured using the modification of diet in renal disease (MDRD) formula (186 x (plasma creatinine (mg/dl))-1,154 x (age)(year)-0.203 for males; for females, the results were multiplied by 0.742. Glomerular filtration rate was expressed in ml/min/1.73 m2.

This study was done in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants for the use of their data for study purposes. The study was approved by our institutional ethics review board (Number:132/12 Date:07.03.2022).

Statistical Analysis

IBM SPSS Statistics 11.5 software version (Chicago, ILL, USA) was used for data analysis. Descriptive parameters, including demographic data, are given as frequencies, percentages, and means±standard deviation (SD). Quantitative variables are expressed as means±SD and medians [min-max], while categorical variables are expressed as numbers (N) and percentages (%). Normal distribution analysis was performed with Kolmogorov-Smirnov. In the comparison of two-category groups regarding quantitative measurements, the Student *t*-test was used when the assumption of normal distribution was met, and the Mann-Whitney U test was used when it was not met. For the variables which were determined as not suitable for the normal distribution, the Mann-Whitney U Test was used in the comparison between two independent groups and the Kruskal-Wallis test was used as a statistical method among three independent groups. Chi-squared test was used to examine the relationships between categorical variables. Significance was set at $P < 0.05$.

Results

Baseline sociodemographic and hospital-based characteristics of the 672 patients analyzed are presented in Table 1. These variables were compared between patients with and those without TE, and it was attempted to determine whether there was a statistically significant difference. The presence of TE in patients showed a statistically significant difference according to their sex ($x^2=121.009$; $P < .001$). While the majority of males did not have TE (82.9%), the majority of females did (58.1%). Whether the complaint of TE showed a significant difference according to age was examined with the *t*-test, and the average age of patients with TE (Mean age=51.74) was found to be significantly lower than those without TE (Mean age=55.29) ($t=3.484$; $P < .001$). It was examined whether there was a statistically significant difference between different groups of body mass indexes in those with and without complaints of TE. According to their body mass index (BMI), individuals were mostly in the non-TE group. It was found that the absence of TE complaints was highest in the group with a BMI 25.0–29.9, followed by the groups with a body mass index of 30.0–34.9 and of 35.0–44.9, respectively.

Out of 672 patients, 249 had TE complaints. Hematological and biochemical tests were performed in all patients; the values of the parameters of these tests in the groups with and without TE are shown in Table 2. While hemoglobin (Hgb), mean corpuscular volume (MCV), ferritin, serum iron, and iron binding capacity were found to be statistically significantly lower in those with TE, platelet count, transferrin saturation, thyroid stimulating hormone (TSH), and C-reactive protein (CRP) values were found to be higher in the same group.

Anemia was identified in 80 out of 672 patients. When comparing the hematological and biochemical parameters between the groups with and without anemia, statistically significant differences were observed in all values, with the exception of folic acid, total protein, and TSH (Table 3). In the anemia group, in addition to the findings of iron deficiency and vitamin B12 deficiency, albumin values were observed to be lower, and CRP and leukocyte values were statistically significantly higher.

When the groups with and without anemia were compared with the groups with and without TE using the chi-squared test, a statistically significant relationship was identified ($x^2=4.694$; $P < 0.05$). Among individuals with anemia, TE was observed in 47.3%, whereas among those without anemia, the occurrence of TE was noted at a rate of 35.5%.

The laboratory parameters of the group that experienced the acute phase of COVID-19 infection as an outpatient were compared with those of the group that received inpatient treatment in the hospital and/or intensive care (Table 4). While there was no significant relationship between disease severity and the whole parameters of complete blood count, statistically significant results were found for the elevation of acute phase reactants such as ferritin and CRP, leukocyte count, and the decrease in total protein and albumin values. The inpatient population exhibited the highest mean ferritin, serum iron, transferrin saturation, CRP, and total protein levels, whereas outpatients demonstrated the lowest mean in this regard. Furthermore, patients admitted to intensive care during hospitalization displayed the lowest mean albumin levels.

When the severity of infection in the acute phase was examined in relation to the occurrence of TE in the post-COVID period, statistically significant results were found ($P=0.031$). TE was observed in 45.1% of those receiving

Table 1. Sociodemographic and Hospital-Based Characteristics of 672 Post-COVID-19 Patients.

Characteristics		Total	With Alopecia	Without Alopecia	*P* Value
Sex n (%)	Male	345(%51.3)	59(%17.1)	286(%82.9)	<0.001[a]
	Female	327(%48.7)	190(%58.1)	137(%41.9)	
Age	Mean±SD	53.98±12.88	51.74±12.90	55.29±12.70	<0.001[b]
	Med.(Min-Max.)	55(18-87)	52(22-87)	56(18-87)	
Marital Status, n (%)	Married	566(84.2%)	204(%36.0)	362(%64.0)	0.210[a]
	Single	106(15.8%)	45(%42.5)	61(%57.5)	
People living with, N (%)	Alone	36(5.4%)	17(%47.2)	19(%52.8)	0.327[a]
	Parents&children	570(84.9%)	210(%36.8)	360(%63.2)	
	Extended family	65(9.7%)	21(%32.3)	44(%67.7)	
Working status, N (%)	Working	242(36.0%)	85(%35.1)	157(%64.9)	<0.001[a]
	Not working	254(37.8%)	134 (%52.8)	120(%47.2)	
	Retired	176(26.2%)	30(%17.0)	146(%83.0)	
Smoking, N (%)	No	620(92.3%)	228(%36.8)	392(%63.2)	0.605[c]
	Yes	52(7.7%)	21(%40.4)	31(%59.6)	
BMI, N (%)	<18.5	11(1.6%)	5(%45.5)	6(%54.5)	0.028[a]
	18.5–24.9	88(13.2%)	36(%40.9)	52(%59.1)	
	25.0–29.9	261(39.0%)	76(%29.1)	185(%70.9)	
	30.0–34.9	188(28.1%)	83(%44.1)	105(%55.9)	
	35.0–44.9	112(16.7%)	45(%40.2)	67(%59.8)	
	≥45.0	9(1.3%)	3(%33.3)	6(%66.7)	
Post-Covid-19 period, N (%)	6–11 weeks	463(68.9%)	170(%36.7)	293(%63.3)	0.866[a]
	12–23 weeks	118(17.6%)	43(%36.4)	75(%63.6)	
	≥24 weeks	91(13.5%)	36(%39.6)	55(%60.4)	
Intensive care, N (%)	No	496(73.8%)	195(%39.3)	301(%60,7)	0.042[a]
	Yes	176(26.2%)	54(%30.7)	122(%69,3)	
Intubation, N (%)	No	663(98.7%)	246 (%37.1)	417(%62,9)	0.816[a]
	Yes	9(1.3%)	3(%33.3)	6(%66.7)	
Hospitalization, N (%)	No	142(22.0%)	64(%45.1)	78(%54.9)	0.000[a]
	Yes	530(78.0%)	185(%34.9)	345(%65.1)	
Pneumonia, N (%)	No	139(20.7%)	60(%43.2)	79(%56.8)	0.094[a]
	Yes	533(79.3%)	189(%35.5)	344(%64.5)	
Previous comorbidities, N (%)*	No	262(39.0%)	98(%37.4)	164(%62.6)	0.593[a]
	1 chronic disease	187(27.8%)	63(%33.7)	124(%66.3)	
	2 CD	103(15.3%)	43(%41.7)	60(%58.3)	
	3 or more CD	120(17.9%)	45(%37.5)	75(%62.5)	

a: Chi-square test, b: Independent sample *t*-test; c: continuity correction. Abbreviations: Max: maximum; Min: minimum; SD: standard deviation; CD: chronic disease

Table 2. Hematological and Biochemical Parameters of All Patients and Group Values for Telogen Effluvium.

Variables	All Patients (N=672)		Those without TE (N=423)		Those with TE (N=249)		P Value
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	
Hemoglobin	14.06±1.70	14.00 (8.00-19.00)	14.38±1.64	14.50 (8.00-19.00)	13.53±1.66	13.50 (8.90-17.00)	**<0.001**[a]
MCV	86.09±5.30	86.40 (60.70-99.50)	86.40±4.87	86.70 (62.80-99.50)	85.56±5.93	85.90 (60.70-99.30)	0.058[a]
MCH	28.30±2.34	28.65 (17.10-33.90)	28.57±2.15	28.90 (18.80-33.30)	27.84±2.56	28.10 (17.10-33.90)	**<0.001**[a]
Platelet	261.07±73.57	254.00 (22.00-650.00)	254.04±73.44	247.00 (22.00-650.00)	273.00±72.38	269.00 (89.00-604.00)	**<0.001**[b]
Leukocyte	6.83±2.68	6.55 (1.38-57.70)	6.95±3.09	6.59 (3.10-57.70)	6.63±1.76	6.43 (1.38-16.09)	0.213[b]
Ferritin	113.24±223.34	69.85 (2.38-4749.00)	136.47±269.98	83.30 (4.65-4749.00)	73.77±91.88	48.30 (2.38-775.00)	**<0.001**[b]
Serum iron	288.28±375.11	94.25 (16.40-2753.00)	305.39±394.44	97.60 (16.40-2753.00)	259.22±338.56	89.30 (17.30-1557.00)	**0.011**[b]
Iron Binding capacity	277.25±135.69	267.25 (91.90-3299.00)	264.01±67.76	257.80 (91.90-580.40)	299.63±202.72	278.50 (126.70-3299.00)	**<0.001**[b]
Transferrin saturation	118.44±168.04	38.92 (3.27-1162.55)	129.62±178.01	40.67 (3.27-1162.55)	99.56±148.13	35.68 (4.11-907.54)	**0.001**[b]
Vitamin B12	375.93±196.12	335.00 (123.00-1849.00)	372.41±200.14	332.00 (123.00-1849.00)	381.92±189.34	347.00 (123.00-1433.00)	0.193[b]
Folic acid	8.72±3.80	8.20 (1.97-20.00)	8.55±3.61	8.17 (2.12-20.00)	9.01±4.10	8.33 (1.97-20.00)	0.273[b]
TSH	2.14±3.93	1.65 (0.01-96.90)	2.16±4.84	1.58 (0.01-96.90)	2.10±1.39	1.76 (0.01-8.99)	**0.034**[b]
CRP	4.71±8.83	2.33 (0.14-134.12)	4.84±10.43	2.06 (0.16-134.12)	4.47±5.05	2.77 (0.14-32.87)	**0.018**[b]
T. Protein	71.34±4.17	71.40 (58.90-88.30)	71.06±4.34	70.90 (58.90-88.30)	71.83±3.82	72.10 (59.60-80.80)	**0.023**[a]
Albumin	45.94±2.83	46.15 (30.70-53.90)	45.95±2.90	46.20 (32.70-53.90)	45.93±2.71	46.00 (30.70-52.50)	0.924[a]

a: Student *t*-test; b: Mann-Whitney U test. Abbreviations: CRP: C-reactive protein; MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume, TE: telogen effluvium; TSH: thyroid stimulating hormone; T. Protein: total protein; SD: standard deviation.

Table 3. Hematological and Biochemical Parameters of All Patients and Group Values Divided According to Hemoglobin.

Variables	All Patients (N=672)		Those Without Anemia (N=592)		Those With Anemia (N=80)		P Value
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	
Hemoglobin	14.06±1.70	14.00 (8.00-19.00)	14.46±1.32	14.30 (12.00-19.00)	11.10±1.12	11.30 (8.00-12.90)	**<0.001**[a]
MCV	86.09±5.30	86.40 (60.70-99.50)	86.74±4.27	86.80 (63.10-99.30)	81.27±8.67	81.70 (60.70-99.50)	**<0.001**[a]
MCH	28.30±2.34	28.65 (17.10-33.90)	28.72±1.79	28.90 (19.00-33.90)	25.20±3.39	25.60 (17.10-32.20)	**<0.001**[a]
Platelet	261.07±73.57	254.00 (22.00-650.00)	256.17±65.05	251.00 (75.00-527.00)	297.29±113.19	280.50 (22.00-650.00)	**0.001**[b]
Leukocyte	6.83±2.68	6.55 (1.38-57.70)	6.69±1.77	6.46 (3.10-21.10)	7.88±6.03	7.34 (1.38-57.70)	**0.006**[b]
Ferritin	113.24±223.34	69.85 (23.8-74.900)	110.88±131.77	75.10 (5.9-1939.00)	130.71±541.67	17.65 (2.38-4749.00)	**<0.001**[b]
Serum iron	288.28±375.11	94.25 (16.40-2753.00)	297.81±375.40	96.65 (26.20-1695.00)	217.78±367.62	64.45 (16.40-2753.00)	**<0.001**[b]
Iron binding capacity	277.25±135.69	267.25 (91.90-3299.00)	268.70±138.83	261.45 (91.90-3299.00)	340.30±87.51	357.90 (139.10-580.40)	**<0.001**[b]
Transferrin Saturation	118.44±168.04	38.92 (3.27-1162.55)	124.13±171.76	40.05 (6.64-1162.55)	76.50±130.95	21.41 (3.27-750.75)	**<0.001**[b]
Vitamin B12	375.93±196.12	335.00 (123.00-1849.00)	374.10±177.72	338.00 (123.00-1849.00)	389.50±300.31	302.50 (131.00-1792.00)	**0.041**[b]
Folic acid	8.72±3.80	8.20 (1.97-20.00)	8.77±3.77	8.21 (1.97-20.00)	8.32±4.01	7.89 (2.15-20.00)	0.257[b]
TSH	2.14±3.93	1.65 (00.1-96.90)	2.15±4.16	1.66 (00.1-96.90)	2.01±1.42	1.55 (00.5-8.29)	0.801[b]
CRP	4.71±8.83	2.33 (0.14-134.12)	4.22±7.79	2.21 (0.14-134.12)	8.33±13.86	3.92 (0.42-103.67)	**<0.001**[b]
T. Protein	71.34±4.17	71.40 (58.90-88.30)	71.45±4.17	71.40 (58.90-88.30)	70.56±4.14	70.80 (60.70-79.10)	0.078[a]
Albumin	45.94±.2.83	46.15 (30.70-53.90)	46.19±2.71	46.40 (30.70-53.90)	44.14±3.03	44.85 (34.00-50.00)	**<0.001**[a]
GFR	127.98±136.02	118.32 (13.12-3461.11)	130.17±143.80	119.83 (39.76-3461.11)	111.74±46.70	106.94 (13.12-239.65)	**0.017**[b]

a: Student *t*-test b: Mann-Whitney U test. Abbreviations: CRP: C-reactive protein; MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume, TSH: thyroid stimulating hormone; T. Protein: total protein; SD: standard deviation.

Table 4. Comparison of Some Hematological and Biochemical Parameters Between Groups Separated According to Severity of COVID-19 Infection in the Acute Phase.

Variables	Outpatient (N=142)		Inpatient (N=354)		Intensive Care Patients (N=176)		P Values
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	
Hemoglobin	14.14±1.56	14.00 (8.90-17.40)	14.00±1.73	13.95 (8.00-18.40)	14.12±1.74	14.30 (9.20-19.00)	0.641[a]
MCV	86.28±4.94	86.55 (63.10-97.70)	86.21±5.29	86.95 (60.70-98.80)	85.69±5.59	85.80 (62.80-99.50)	0.234[a]
MCH	28.37±2.20	28.60 (19.00-32.30)	28.43±2.29	28.85 (17.80-33.90)	27.97±2.51	28.45 (17.10-33.30)	0.065[a]
Platelet	268.87±71.43	258.50 (128.00-586.00)	257.21±74.50	252.00 (22.00-650.00)	262.53±73.26	252.00 (109.00-604.00)	0.294[a]
Leukocyte	6.34±1.68	6.15 (3.10-10.95)	6.84±3.29	6.45 (1.38-57.70)	7.22±1.74	6.87 (4.05-15.95)	**<0.001**[a]
Ferritin	81.97±81.44	51.75 (2.38-463.00)	125.85±276.43	71.45 (2.58-4749.00)	113.10±175.08	77.15 (4.65-1939.00)	**0.038**[a]
Serum iron	116.41±156.79	86.00 (16.40-1230.00)	372.23±418.25	105.65 (23.30-2753.00)	258.11±357.36	89.55 (17.30-1582.00)	**<0.001**[a]
Iron binding capacity	269.62±63.70	269.20 (126.70-439.90)	277.56±174.89	262.10 (91.90-3299.00)	282.73±74.48	275.65 (125.70-580.40)	0.171[a]
Transferrin saturation	47.95±64.52	32.62 (4.11-529.94)	153.78±190.52	45.40 (5.13-1162.55)	104.06±157.75	34.59 (3.27-843.05)	**<0.001**[a]
Vitamin B12	389.72±170.21	352.50 (157.00-1219.00)	371.37±185.32	332.50 (123.00-1576.00)	373.99±233.79	326.50 (128.00-1849.00)	0.110[a]
Folic acid	8.65±3.92	8.11 (1.97-20.00)	8.49±3.43	8.17 (2.18-20.00)	9.23±4.36	8.41 (2.15-20.00)	0.400[a]
TSH	2.06±1.33	1.76 (0.01-8.99)	1.92±1.34	1.58 (0.01-11.80)	2.64±7.34	1.68 (0.01-96.90)	0.216[a]
CRP	3.01±4.39	1.44 (0.14-28.73)	5.28±10.90	2.38 (0.19-134.12)	4.92±6.37	2.88 (0.36-54.31)	**<0.001**[a]
T. protein	72.67±3.70	72.70 (62.70-80.80)	70.92±3.98	71.00 (59.30-82.50)	71.10±4.67	71.00 (58.90-88.30)	**<0.001**[a]
Albumin	46.77±2.44	46.70 (41.10-53.90)	45.73±2.82	46.00 (32.70-51.80)	45.71±3.03	45.90 (30.70-51.50)	**0.005**[a]

a: Kruskal-Wallis H test. Abbreviations: CRP: C-reactive protein; MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume, TSH: thyroid stimulating hormone; T. Protein: total protein; SD: standard deviation.

outpatient treatment, 37.0% of those hospitalized, and 30.7% of those in intensive care.

Absolute iron deficiency anemia (IDA) (ferritin ≤ 30 µg/L and TSAT <20%) was found in 35.0% (N=28) of patients. Functional iron deficiency (ferritin > 100 µg/L and TSAT <20% or serum ferritin 30-100 µg/L and sTFRF index<1) was identified in the remainder of the patients. Three of the remaining 52 anemia patients were defined as anemia of unknown cause because their ferritin was >100, TSAT was >20, TIBC was within normal limits, and vitamin B12, folic acid, and MCV values were normal. Since we could not determine the soluble transferrin receptor/log serum ferritin (sTFRF) index values, it could not be determined whether the other 49 patients had inflammation anemia (IA) or IA+IDA.

Discussion

In this study, we evaluated the incidence of anemia and TE in our patient group in the post-COVID period and the relationship between these two conditions. TE was detected in 37% of the patients admitted to our follow-up outpatient clinic. There have been a few studies investigating the development of TE as a consequence of COVID-19. In a study conducted on a similar patient group, the incidence of TE was found to be 36.7% [9]. This result is similar to the result of our study. In another study of 128 post-COVID-19 patients who presented to hair clinics with hair loss, TE was observed in 66.3% [10]. However, since this study was conducted specifically on patients who applied to a dermatology outpatient clinic due to post-COVID hair shedding, it is thought that the incidence of TE was found to be higher. In our study, a significant relationship was found between TE and variables such as age and BMI, while in a similar study conducted by Aksoy et al., a significant relationship was not found [9].

In our study results, TE was detected at a higher rate in females than in males. Other studies in the literature show that COVID-19-associated TE is more common in females [7-10].

It is known that anemia is one of the causes of TE. It is also suggested that post-infection hair shedding, apart from the traditionally known acute TE, may also lead to dystrophic anagen effluvium due to the release of proinflammatory cytokines, depending on the severity of the disease [10]. However, in our study, TE was detected at a higher rate in those receiving outpatient treatment because their disease was milder. This finding can be related to a previous study we conducted; in that study, it was found that in the same patient group, symptoms of depression, anxiety, panic disorder, and post-traumatic stress disorder (PTSD) were more common in individuals receiving outpatient treatment [13]. Outpatients tend to experience more psychological difficulties in the post-COVID-19 period. It is conceivable that hospitalization may make individuals feel safer because it provides a safe environment where hospital staff can detect and treat the potentially fatal consequences of the disease early. On the other hand, being infected and staying at home can make people feel vulnerable, lonely, and abandoned by the disease.

COVID-19 is associated with iron metabolism dysregulation. Although there are many studies on anemia and iron metabolism in the acute phase of COVID-19 infection, studies examining the same issue in the post-COVID period are limited [4,14,15]. In one of the few studies in the literature conducted in the post-COVID period, pathophysiological mechanisms were examined, and in another, the prevalence and phenotypes of anemia, iron deficiency, and hyperferritinemia were evaluated [5,16]. It was shown that the prevalence of anemia was 9%, iron deficiency was 30%, and hyperferritinemia was 35% at 60 days post-COVID-19 follow-up [16]. The prevalence of anemia detected in our study group (11.9%) is similar to the results of that study. The rate of absolute iron deficiency observed in those with anemia was determined to be 35%, which also shows similarity. Due to the fact that the admission dates of our post-COVID-19 follow-up patient group mostly fall between 6-8 weeks and 12 weeks after infection, the elapsed time since infection is also similar to that of the post-COVID group in that study, which was conducted on the 60th day post-infection.

We found the incidence of TE to be higher in the group with anemia. Although there are few studies in the literature that examine the relationship between TE and serum hemoglobin and ferritin values, we have not come across a study that examines the relationship between TE and anemia in COVID-19 survivors [17-20]. A study was conducted in which the effect of monocytes was investigated in patients with TE complaints after COVID-19 which stated that the causes leading to TE are not fully known, but the effect of monocytes on hair follicles may be only one of the mechanisms leading to TE [21]. Although the presence of anemia in patients with TE is statistically significant, the fact that 35.5% of patients did not have anemia and this complaint began after COVID-19 infection requires investigating different causes.

This study revealed those who had the severe acute phase of COVID-19 infection were not associated with the risk of subsequent occurrence of anemia and TE. However, it was found to be more common among outpatients. In addition to all the strengths of this study, it also has some limitations. It is a study conducted in a single center and with a limited number of participants. Second, not all potentially eligible participants were enrolled. From our tertiary hospital, all patients discharged after recovery from COVID-19 were called and invited; however, only those who participated voluntarily were included and followed up. Third, there was no

control group in the study, consisting of those who had not had COVID-19 but who do and do not have TE complaints. Fourth, since we could not determine the soluble transferrin receptor values, IF and IF+IDA could not be distinguished.

Conclusion

Current study data show that those who had the typical acute TE, which occurs 3–4 months after a COVID-19 infection, might be associated with iron deficiency anemia and/or inflammation anemia. The fact that TE was detected more in outpatients than in those who received inpatient treatment in hospitals and intensive care suggests that psychological causes such as stress should be taken into consideration, as should the effect of the virus itself and organic causes such as anemia.

Acknowledgments

We would like to thank all our colleagues who worked with us at the COVID-19 follow-up outpatient clinic and contributed to our article.

References

1. 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 Aug 9;11(1):16144. DOI: 10.1038/s41598-021-95565-8.
2. Seeßle J, Waterboer T, Hippchen T, et al. Persistent Symptoms in Adult Patients 1 Year After Coronavirus Disease 2019 (COVID-19): A Prospective Cohort Study. *Clin Infect Dis*. 2022 Apr 9;74(7):1191-1198. DOI: 10.1093/cid/ciab611.
3. Lippi G, Sanchis-Gomar F, Henry BM. COVID-19 and its long-term sequelae: what do we know in 2023? *Pol Arch Intern Med*. 2023 Apr 19;133(4):16402. DOI: 10.20452/pamw.16402.
4. Taneri PE, Gómez-Ochoa SA, Llanaj E, et al. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. *Eur J Epidemiol*. 2020 Aug;35(8):763-773. DOI: 10.1007/s10654-020-00678-5.
5. Abu-Ismail L, Taha MJJ, Abuawwad MT, et al. COVID-19 and Anemia: What Do We Know So Far? *Hemoglobin*. 2023 May;47(3):122-129. DOI: 10.1080/03630269.2023.2236546.
6. Huerga Encabo H, Grey W, Garcia-Albornoz M, et al. Human Erythroid Progenitors Are Directly Infected by SARS-CoV-2: Implications for Emerging Erythropoiesis in Severe COVID-19 Patients. *Stem Cell Reports*. 2021 Mar 9;16(3):428-436. DOI: 10.1016/j.stemcr.2021.02.001.
7. Olds H, Liu J, Luk K, Lim HW, Ozog D, Rambhatla PV. Telogen effluvium associated with COVID-19 infection. *Dermatol Ther*. 2021 Mar;34(2):e14761. DOI: 10.1111/dth.14761.
8. 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 Jan;34(1):e14547. DOI: 10.1111/dth.14547.
9. Aksoy H, Yıldırım UM, Ergen P, Gürel MS. COVID-19 induced telogen effluvium. *Dermatol Ther*. 2021 Nov;34(6): e15175. DOI: 10.1111/dth.15175.
10. 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 Dec; 5:11-18. DOI: 10.1016/j.jdin.2021.07.006.
11. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. *BMJ Open Gastroenterol*. 2022;9(1):e000759. DOI: 10.1136/bmjgast-2021-000759.
12. Green R. Vitamin B_{12} deficiency from the perspective of a practicing hematologist. *Blood*. 2017;129(19):2603-2611. DOI: 10.1182/blood-2016-10-569186.
13. Emiroglu C, Gorpelioglu S, Ozagar SD, Demir P, Aypak C. Prevalence and risk factors of psychological symptoms and quality of life in COVID-19 survivors: A cross-sectional study of three different populations. *Int J Nurs Pract*. 2023 Sep 28:e13202. DOI: 10.1111/ijn.13202.
14. Bergamaschi G, Borrelli de Andreis F, Aronico N, et al; Internal Medicine Covid-19 Collaborators. Anemia in patients with Covid-19: pathogenesis and clinical significance. *Clin Exp Med*. 2021 May;21(2):239-246. DOI: 10.1007/s10238-020-00679-4.
15. Tao Z, Xu J, Chen W, et al. Anemia is associated with severe illness in COVID-19: A retrospective cohort study. *J Med Virol*. 2021 Mar;93(3):1478-1488. DOI: 10.1002/jmv.26444.
16. Sonnweber T, Grubwieser P, Sahanic S, et al. The Impact of Iron Dyshomeostasis and Anaemia on Long-Term Pulmonary Recovery and Persisting Symptom Burden after COVID-19: A Prospective Observational Cohort Study. *Metabolites*. 2022 Jun 14;12(6):546. DOI: 10.3390/metabo12060546.
17. Kakpovbia E, Ogbechie-Godec OA, Shapiro J, Lo Sicco KI. Laboratory Testing in Telogen Effluvium. *J Drugs Dermatol*. 2021 Jan 1;20(1):110-111. DOI: 10.36849/JDD.5771.
18. İbiş S, Aksoy Saraç G, Akdağ T. Evaluation of MCV/RDW Ratio and Correlations With Ferritin in Telogen Effluvium Patients. *Dermatol Pract Concept*. 2022 Jul 1;12(3):e2022151. DOI: 10.5826/dpc.1203a151
19. Yorulmaz A, Hayran Y, Ozdemir AK, et al. Telogen effluvium in daily practice: Patient characteristics, laboratory parameters, and treatment modalities of 3028 patients with telogen effluvium. *J Cosmet Dermatol*. 2022 Jun;21(6):2610-2617. DOI: 10.1111/jocd.14413.
20. Arslan H, Gündüz Ö. Micronutrient Deficiencies and Digital Computerized Phototrichogram Analysis in Telogen Effluvium: a Retrospective Correlation Study in a Tertiary Medical Center. *Dermatol Pract Concept*. 2023 Jul 1;13(3):e2023202. DOI: 10.5826/dpc.1303a202.
21. Koç Yıldırım S, Erbağcı E, Demirel Öğüt N. Evaluation of patients with telogen effluvium during the pandemic: May the monocytes be responsible for post COVID-19 telogen effluvium? *J Cosmet Dermatol*. 2022 May;21(5):1809-1815. DOI: 10.1111/jocd.14883.