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Investigating Biochemical Biomarkers in Telogen Effluvium Post-COVID-19 Patients: A Retrospective Cohort Study

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Abstract:

Acute telogen effluvium (TE) represents a non-scaring form of hair loss that manifests approximately 3-months after a stressful incident. Notably, it relates to post-COVID-19 infections. This study aims to investigate the biochemical biomarkers associated with telogen effluvium in recovered COVID-19 patients. The study encompassed 108 participants, categorized by sex (64 male and 44 female) and age groups. Biochemical biomarkers were assessed, including complete blood count, liver enzymes, ferritin, D-dimer, and C-reactive protein (CRP) levels.

Significant differences were revealed between males and females in terms of Hb levels, RBC, WBC, platelet, ESR, and CRP levels (p-value < 0.05). In addition to significant differences in D-dimer levels between age groups; lower mean values in age group 26-35 years and higher values observed at ≥ 46 years (p-value < 0.05). Additionally, significant correlations were found between D-dimer levels with LDH, CRP, and ferritin.

The available evidence concludes that COVID-19 may lead to TE, a type of hair shedding, attributed to the stress induced by the infection. Sex disparities were noted in blood characteristics, with males exhibiting alterations in several parameters. D-dimer levels varied across different age groups. Persistently elevated D-dimer levels following a COVID-19 infection may be correlated with inflammatory markers.

Keywords: Biochemical Biomarkers, Hair Loss**,** Telogen Effluvium (TE)**,** COVID-19.

Introduction:

While COVID-19 is mainly a respiratory disorder, it can also cause dermatologic symptoms such as hair loss and herpetic lesions (1,2). Although there are relatively few descriptions of the cutaneous manifestations of COVID-19, it is worth noting that it could serve as an initial sign of the disease (3,4). Moreover, COVID-19 has been observed to impact various alopecia-related ailments, this is due to the virus's disruption of stress and physiological factors, which can lead to hair loss (5,6). In addition to other conditions (7).

Telogen effluvium (TE) is a form of hair loss that manifests several weeks after experiencing a stressful event (8). The disease affects both males and females, although females are more susceptible. Elderly women are more prone to acute TE following fever, trauma, or psychological stress (9).

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Emerging research has revealed a correlation between COVID-19 and hair loss (10,11). Specifically, the estimated prevalence of this phenomenon is up to 20.4% (1). A previous study investigating the clinical sequelae of COVID-19 found that approximately 28% of patients experienced alopecia (12). Furthermore, recent research indicates that COVID-19 could exacerbate alopecia by impacting the transmembrane protease, serine 2 (TMPRSS2) gene, which plays an important role in androgen pathways (13).Increased psychosocial stress can also worsen many common stress-responsive skin conditions, including TE, which is often triggered by stressful events (14-16). Consequently, hair loss has become a standard consequence of COVID-19 that has a considerable impact on the psychosocial status of patients recovering from COVID-19. The precise underlying causes of TE remain elusive, albeit autoimmune disorders, immunological problems, and persistent infection of hair follicles are believed to play a contributory role (2).

Numerous studies have been conducted to study the potential correlation between COVID-19 infections and TE development. Nonetheless, the current evidence concerning the association between COVID-19 infections and the development of TE among recovered COVID-19 patients in Iraq remains limited. In light of this, our study seeks to delve into the possible impact of COVID-19 on hair and identify any associated factors.

Methods:

The study is a retrospective cohort analysis that was performed from September to December 2021 to investigate 108 individuals diagnosed with COVID-19 who experienced increased hair shedding within 4 months of contracting the virus. Biochemical biomarkers were evaluated in Alnokhba Medical Lab as part of the study after having ethical approval, categorized by sex: 64 male and 44 female participants; and age (23) individuals aged 15-25, (36) were 26-35, (22) were 36-45, and (24) were ≥ 46. The study gathered data on various demographic variables such as age and sex.

Sampling technique and sample preparation

COVID-19 infection was confirmed through positive results from antigen test kits and/or polymerase chain reaction (PCR) tests. A 7 ml blood sample was collected by venipuncture from each participant. Two milliliters were in an EDTA tube for complete blood picture measurement; five milliliters withdrawn in a gel tube were left on the bench for 15 minutes at room temperature, after coagulation, blood was centrifuged at 3000 rpm for 10 minutes for measurement of liver enzymes, serum ferritin, D-dimer, and CRP (17).

Chemicals, apparatus, and instruments

This encompassed the assessment of a complete blood picture using an auto-hematology analyzer apparatus for the measurement of complete blood counts, and platelet counts (PLT). Serum ferritin, D-dimer, CRP, LDH, ALT, and AST were tested using Roche kits and apparatus/ Germany origin/ model Cobas C311 apparatus. The erythrocyte sedimentation rate (ESR) was analyzed by the Westergren method.

Statistical Analysis:

The study utilized SPSS version 22 to perform appropriate statistical tests, comparing the mean ± standard deviation of each parameter. Continuous variables were evaluated using independent t-tests. Categorical variables were analyzed using chi-square tests or Fisher's exact tests. A p-value of < 0.05 was judged statistically significant.

RESULTS:

In this study, 108 individuals who had tested positive for COVID-19 and experienced increased hair shedding within 4 months were examined. The participants' mean age was 36.1 ± 12.6 years old. Among them, 64 individuals (59.3%) were male, and 44 individuals (40.7%) were female. The age distribution was as follows: 23 individuals (21.3%)

were aged 15-25, 36 individuals (33.3%) were aged 26-35, 22 individuals (20.4%) were aged 36-45, and 24 individuals (22.2%) were 46 or older.

According to the findings, males and females have significant differences in terms of Hb, RBC, WBC, platelet counts, ESR, and CRP levels, p-value < 0.05. However, there were no significant differences observed between males and females in terms of age, ALT, AST, D-dimer, LDH, and ferritin levels, p-value > 0.05 (Table 1).

Table 2 indicates the paraclinical biomarkers of individuals in different age groups along with their respective mean values and standard deviations. Based on the provided data, there are no notable differences shown in the age groups of the assessed biomarkers (Hb, RBC, WBC, PLT, ESR, ALT, AST, LDH, CRP, and ferritin). However, there are significant differences in D-dimer levels between the age groups, with lower mean values observed in the 26-35 years and higher mean values observed in ≥ 46 years age groups compared to the other groups, p-value < 0.05.

Table 3 displays Pearson correlation coefficients and corresponding p-values that demonstrate the relationships between different paraclinical characteristics in all the study samples. Key findings include a significant positive correlation between D-dimer levels and LDH, CRP levels, and ferritin, p-value less than 0.05.

Table 1: Sociodemographic and laboratory parameters.

Demographic and Para -clinical characteristics	Male 64 (59.3%) Mean±Std.D	Female 44 (40.7%) Mean±Std.D	P-value
Age (yr)	35.9±12.7	36.4±12.7	0.835
Hb gm/dl	15.7±8.0	12.2±1.9	**0.001****
RBC	5.22±1.5	4.51±1.4	**0.011***
WBC	9.61±5.2	7.84±3.6	**0.039***
PLT	223.9±82	272.6±109	**0.010****
ESR	19.8±22.8	23.1±20	**0.043***
ALT	45.6±47	41.03±64	0.674
AST	39.8±43	40.0±66	0.98
D-DIMER	895.5±1727	609.0±844	0.256
LDH	221.1±139	201.8±105	0.439
CRP	64.6±79	33.48±57	**0.020***
FERRITIN	488.1±1142	268.9±1001	0.30

* **The p-value ≤ 0.05 is statistically significant**
** **The p-value ≤ 0.01 is highly significant**

Table 2: Biochemical Biomarkers of individuals in different age groups

Clinical Biomarkers	15–25 years (Mean ± Std.D) No = 23	26–35 years (Mean ± Std.D) No = 39	36–45 years (Mean ± Std.D) No = 22	≥ 46 years (Mean ± Std.D) No = 24	P-value
Hb	14. 35±4.3	15. 36±10.12	13.52 ±1.84	13.13 ±1.74	0.549
RBC	4.98 ±2.3	4.74 ±0.84	4.89 ±0.63	5.22 ±1.79	0.652
WBC	8.59 ±5.12	9.25 ±4.79	8.30 ±3.48	9.12 ±5.13	0.866
PLT	238.58 ±88.74	262.09 ±104.97	223.62 ±91.33	237.18 ±96.61	0.477
ESR	12.04 ±9.32	15.15 ±10.62	16.41 ±10.39	17.54 ±10.26	0.296
ALT	32.60 ±35.93	57.57 ±73.23	38.8 7±40.36	36.3 3±42.68	0.257
AST	27.43 ±17.80	52.0 2±74.60	28.88 ±16.77	42.2 3±57.03	0.246
D-dimer	626.13 ±1087.91	434.38±720.065 *	850.57±1716.21	1418.94±2066.02*	**0.008***
LDH	202.11±95.38	203.61±102.71	204.32±102.68	247.70±192.34	0.519
CRP	43.4 7±64.09	56.99 ±83.85	31.27±33.95	70.77±84.5 8	0.277
Ferritin	414.55±1374.03	209.16±281.79	688.50 ±1798.75	426.31±684.2 2	0.434

*** The p-value ≤ 0.05 is statistically significant**
**** The p-value ≤ 0.01 is highly significant**

Table 3: Correlations among D-dimer in all the study samples:

Para-clinical characteristics	Pearson correlations	Significance (2-tails)
D-dimer * LDH	**.0544**	**0.001****
D-dimer * CRP	**0.242**	**0.012***
D-dimer * Ferritin	**0.428**	**0.001****
*** p-value ≤0.05 level indicates significant correlations** **** p-value ≤0.01 level indicates significant correlations**		

DISCUSSION:

The available evidence strongly indicates that COVID-19 infection is a notable trigger for TE, leading to excessive hair loss. This shedding might be linked to psychosocial or physiological stress associated with the infection (18).

In the conducted study, 108 patients diagnosed with acute TE (ATE) were examined. All participants reported a prior history of COVID-19 infection and reported experiencing significant loss of hair within 4 months following SARS-CoV-2 infection, characterized by substantial shedding of hair. Similarly, existing studies and clinical experience have indicated a higher incidence of TE in the 3 months following SARS-CoV-2 infection as a trigger event (19,20). A study found that 28% of patients developed significant TE as a result of SARS-CoV-2 infection (20). Other studies have suggested that pro-inflammatory cytokines released during the infection may trigger loss of hair (22,23). Furthermore, another study reported that the presence of SARS-CoV-2 in the sweat glands of

infected patients (24). The exacerbation of various skin conditions may be influenced by heightened psychosocial stress, impacting the progression of the disease (15,19,25).

The study findings indicate significant variances in hematological parameters between males and females, specifically in terms of Hb, RBC, WBC, platelet counts, ESR, and CRP levels, $p < 0.05$. There were observed alterations in the average Hb, RBC, WBC, platelet counts, ferritin, and CRP levels, with the levels in males exceeding the reference values. This suggests that inflammatory markers released during the infection may initiate TE. Additionally, a recent study demonstrated higher CRP levels in patients with long-term symptoms, including hair loss (26,27,28). The results of the current study indicate no notable differences between both sexes in terms of age, AST levels, ALT levels, D-dimer levels, LDH levels, and ferritin levels. Furthermore, a study revealed a higher incidence of anemia and lower ferritin values among predominantly female patients (2)(29). Another study reported iron deficiency anemia and elevated ESR levels in their patients (26). Males are at a higher risk of experiencing factors associated with hair shedding, particularly due to the physiological processes of childbirth and lactation. It is important to note that previous research has produced conflicting results regarding ferritin [26,30], and the disparity in liver enzymes (ALT) and (AST) may linked to the time of biomarker tests concerning the early stages of the disease (27).

According to the provided data, we did not find any substantial variances among the age groups concerning the assessed parameters (Hb, RBC, WBC, PLT, ESR, ALT, AST, LDH, CRP, and ferritin). Our findings are consistent with a study that identified elevated AST levels in patients aged over 60 years (27). Significant variations exist in D-dimer levels across different age groups. The mean values are notably lower in the 26-35 age group and higher in the 46-year-old and above group compared to the other age groups, with a p-value exceeding 0.05.

Moreover, our findings reveal a meaningful positive correlation between D-dimer levels and LDH, CRP levels, and ferritin. Consistent with our results, prior investigations have documented elevated D-dimer levels persisting for up to four months following acute infection (31,32). Following a recent study, it was observed that elevated D-dimer levels were present in 15% of patients approximately eight months post-mild COVID-19 infection (33). Observation of elevated D-dimer levels post-COVID-19 infection is associated with markers of inflammation.

CONCLUSION

The available evidence indicates that COVID-19 may lead to telogen effluvium (TE), a type of hair shedding, attributed to the stress induced by the infection. Sex disparities were noted in blood characteristics, with males exhibiting alterations in several parameters. D-dimer levels varied across different age groups. Persistently elevated D-dimer levels following a COVID-19 infection may be correlated with inflammation markers.

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Conflicts of interest

No conflicts of interest to disclose.

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