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Unraveling Dermatological Manifestations after COVID-19: Insights from Skin Pigmentation and Hair Loss Patterns

Faranak Salajegheh[1], Mohammad Rahimi[2], Fatemeh Rezaei[1,3], Niloofar Farsiu[4], Reza Sinaei[3] and Mohsen Nakhaie[4,3,*]

[1]*Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran*
[2]*Department of Microbiology, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran*
[3]*Clinical Research Development Unit, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran*
[4]*Gastroenterology and Hepatology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran*

Abstract:

Introduction: In addition to respiratory symptoms, COVID-19 has been linked to many clinical manifestations, such as changes in skin pigmentation and hair loss. The objective of this research was to examine these manifestations.

Methods: Cross-sectional research was performed at Afzalipour Hospital in Kerman, Iran, between June and August 2021. COVID-19-recovered patients were included in the study, and data were obtained *via* medical records, verbal interviews, and self-administered questionnaires. Statistical investigations evaluated the relationships between manifestations, demographic factors, and clinical indications.

Results: Among the 190-study population, 76.3% encountered alopecia, while 15.3% indicated changes in skin pigmentation. The prevalence of hair loss was considerably higher among females (P=0.002). The hair loss patterns exhibited characteristics similar to telogen effluvium (TE), with a higher occurrence in the frontal region of the head. There was a relationship between hair loss and the level of arterial oxygen saturation.

Conclusion: This research emphasizes a significant prevalence of alopecia after the recovery from COVID-19, especially among females. It is crucial to provide proactive care and support to people who have recovered from COVID-19, including customized therapies that specifically target post-COVID-19 problems.

Keywords: COVID-19, Female alopecia, Hair loss, Post-inflammatory hyperpigmentation, Telogen effluvium, Female.

*Address correspondence to this author at the Gastroenterology and Hepatology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran and Clinical Research Development Unit, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran; Tel: +983433257470, +989133426824; Fax: +983433257470, E-mail: mohsennakhaee1367@gmail.com

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1. INTRODUCTION

At the end of December 2019, the city of Wuhan, which is located in China, was confronted with a cluster of severe respiratory disorders that are now known as COVID-19 [1]. The SARS-CoV-2 virus, which rapidly spread from China to become a global pandemic, is what causes the illness. The latest data indicate that there have been more than 775 million reported cases and over seven million fatalities globally. Specifically, Iran has recorded over 7.6 million confirmed cases and more than 147,000 deaths [2].

COVID-19 presents with a diverse range of symptoms, including fever, cough, asthma, myalgia, weariness, and exhaustion. In extreme instances, it may result in life-threatening complications, such as shock, acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), and myocardial infarction (MI) [3]. Moreover, the psychological consequences of COVID-19, such as stress, depression, anxiety, insomnia, and posttraumatic stress disorder (PTSD), can have a detrimental effect on the overall well-being of patients [4-6].

Significantly, COVID-19 has been associated with alopecia (hair loss) and alterations in skin pigmentation, which are likely worsened by increased levels of stress and mental strain. Patients who have experienced stressful events may develop stress-induced diseases, such as telogen effluvium (TE), which is characterized by widespread hair loss [7, 8]. TE usually occurs between one and six months after the triggering event, causing roughly 70% of actively growing hair (anagen hair) to transition into the resting phase (telogen phase) and subsequently shed. Thankfully, TE is limited in duration and does not need any more therapy after the conditions that caused it are eliminated [9, 10].

According to reports from Wuhan Central Hospital, several COVID-19 patients had skin hyperpigmentation, which suggests the possibility of post-inflammatory hyperpigmentation (PIH). PIH is a kind of reactive melanosis that often occurs after irritation or inflammation [11]. Acne and allergic or irritating contact dermatitis are examples of common inflammatory skin diseases that may result in PIH [12, 13]. The occurrence of skin presentations was documented in 1% of Chinese epidemiological reports and over 20% of Italian reports. However, the exact causes of these manifestations are still unclear owing to limited paraclinical tests and the temporary nature of marks [14-16].

The COVID-19 epidemic has had a profound effect on the physical and emotional well-being of people and communities. The necessity for comprehensive investigation is emphasized when considering health in its multidimensional aspect, which includes physical, mental, and social well-being. Although several studies have examined the non-respiratory impacts of COVID-19, there is a lack of particular research on the prevalence of psychiatric problems and other non-respiratory manifestations in people who have recovered from the virus. With the intention of addressing this gap, our research sought to observe and record the occurrence rate of skin and hair diseases among individuals who have recovered from COVID-19 at Afzalipour Hospital in Kerman, Iran, in 2021.

2. METHODS AND MATERIALS

2.1. Study Design and Participants

This cross-sectional study was carried out on patients admitted to Afzalipour Hospital (Kerman University of Medical Sciences) from June 2021 to August 2021.

2.2. Inclusion and Exclusion Criteria

Patients were enrolled in the study if they had the following criteria:

- Positive RT-PCR results for SARS-CoV-2
- Full consciousness

Patients were rolled out of the study if they had the following criteria:

- History of skin pigmentation or hair loss
- History of cancer, chronic inflammatory diseases, or auto-immune diseases
- Pregnancy
- Hormonal disorders
- Consumption of hormonal, contraceptive, and immunosuppressive medications
- Consumption of substance drugs or addiction history
- Radiotherapy or chemotherapy
- Consumption of sedative derivatives
- Dissatisfaction with participation in the study
- Occurrence of death during hospitalization

2.3. Data Collection

This research used a simple sampling method for its benefit of having a more general appeal. The medical records of patients who tested positive for SARS-CoV-2 were examined, and several mentioned inclusion and exclusion criteria were taken into account to regulate the panel of participants.

Patients were verbally asked a series of questions on skin pigmentation and hair loss three months after their discharge from the hospital. Demographic data were collected by a questionnaire sent to individuals *via* social media applications because of quarantine precautions. Participants were instructed to provide very careful responses to these questions.

In order to assess skin hyperpigmentation, a series of questions were asked of the individuals. For hair loss, patients were directed to do a self-administered hair-pull test (HPT). This test included grasping around 50–60 hairs between the thumb, index, and middle fingers and applying a mild but firm pulling force to three specific locations of the head (top/vertex, occiput, and frontal area). Extracting five or fewer hairs in HPT was considered normal; however, extracting six or more hairs was indicative of a positive test and significant hair loss [17].

In order to accurately assess the severity of the illness, the clinical results were evaluated and assigned scores. The variables measured in this study were the initial oxygen saturation level, the levels of lactate dehydrogenase (LDH), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) at admission, and the duration of the hospital stay. In addition, the hospital information system (HIS) was used to verify the frequency of transfers to the intensive care unit (ICU), and this information was included in the research checklist.

2.4. Statistical Analysis

The collected data were examined using SPSS (version 21). The study consisted of descriptive statistics, including measures, such as the mean and standard deviation (SD), to describe the data. Additionally, a frequency distribution table was utilized to organize and provide an overview of the results. The Chi-squared test and T-test were used to show inferential statistics based on aims, and variation analyses were conducted. A *P value* less than 0.05 was deemed statistically significant for the performed tests.

3. RESULTS

This research included a study group of 190 people who tested positive for COVID-19 and were confirmed using RT-PCR. The participants were admitted to the hospital and subsequently released in healthy condition from June to August 2021. Due to the large sample size, parametric testing was utilized despite the lack of normal distribution among tested parameters.

The average age of individuals was 46.04 ± 13.05 years. The age range of the people spanned from 17 to 75. Among the 190 participants in the study, 92 (48.4%) were male and 98 (51.6%) were female.

Based on the data presented in Table **1**, there was no significant disparity in skin pigmentation across genders. Nevertheless, there was a significant alteration in hair loss based on the results of HPT (P=0.002). There was no statistically significant variation in the prevalence of skin pigmentation and hair loss across various age groups, as shown in Table **2**. There was no significant difference in the patients' outcomes when comparing those who were admitted to ICU with those who were not, as shown in Table **3**.

The research also examined alterations in other crucial inflammatory markers (Tables **4** and **5**). There was a significant difference in the average ESR level between men and females (P = 0.014); however, there were no statistically significant variations detected between other inflammatory variables based on gender or age group.

Table 1. Frequency distribution of skin pigmentation and hair loss based on gender in recovered COVID-19 patients.

Manifestations	Absolute Frequency	Relative Frequency	Sex		*P.value*
			Male	Female	
Skin pigmentation	29	15.3%	13	16	0.692
Hair loss	145	76.3%	61	84	0.002

Table 2. Frequency distribution of skin pigmentation and hair loss based on age groups in recovered COVID-19 patients.

Manifestations	Age Groups				*P.value*
	≤18	19-35	36-60	>60	
Skin Pigmentation	1	4	22	2	0.140
Hair Loss	2	30	92	21	0.683

Table 3. Frequency distribution of skin pigmentation and hair loss among recovered COVID-19 patients based on intensive care unit (ICU) admission status.

Manifestations	Admission to ICU		*P.value*
	Yes	No	
Skin Pigmentation	5	24	0.417
Hair Loss	18	127	0.871

Table 4. Average inflammatory factor serum levels based on gender in recovered COVID-19 patients.

Inflammatory Factors	Sex				*P.value*
	Male		Female		
	Mean	SD	Mean	SD	
CRP (mg/dL)	46.19	30.35	43.89	32.81	0.619
LDH (U/L)	762.70	292.40	757.7	411.31	0.934
ESR (mm/h)	43.04	23.93	52.57	28.26	0.014

CRP: C-reactive protein; LDH: lactate dehydrogenase; ESR: erythrocyte sedimentation rate; SD: standard deviation.

Table 5. Average inflammatory factors serum levels based on age groups in recovered COVID-19 patients.

Inflammatory Factors	Age group	Mean ± SD	*P.value*
CRP (mg/dL)	≤18	9.8	0.069
	19-35	35.94±31.23	
	36-60	46.15±30.93	
	60<	54.14±32.37	
LDH (U/L)	≤18	464	0.337
	19-35	669.25±284.51	
	36-60	789.55±357.89	
	60<	724.95±424.88	
ESR (mm/h)	≤18	38	0.124
	19-35	39.43±24.44	
	36-60	50.98±27.14	
	60<	48.36±26.37	

CRP: C-reactive protein; LDH: lactate dehydrogenase; ESR: erythrocyte sedimentation rate; SD: standard deviation.

Additional metrics, such as arterial oxygen saturation and duration of hospital stay, did not exhibit a noteworthy variation across various genders and age categories (Tables **6** and **7**).

The correlation between hair loss and skin pigmentation, as well as the clinical findings indicated above, was evaluated using Pearson and Spearman coefficient tests (Table **8**). The only illness and clinical manifestation that showed a noteworthy connection was alopecia with arterial oxygen saturation level ($P < 0.05$).

Table 6. Average levels of other clinical findings based on gender in recovered COVID-19 patients.

Parameters	Sex				*P.value*
	Male		Female		
	Mean	SD	Mean	SD	
Arterial oxygen saturation level (%)	86.81	6.91	87.67	5.66	0.349
Hospitalization duration (day)	4.41	4.90	6.01	4.70	0.564

SD= standard deviation.

Table 7. Average levels of other clinical findings based on age group in recovered COVID-19 patients.

Inflammatory Factors	Age Group	Mean ± SD	*P.value*
Arterial oxygen saturation level (%)	**≤18**	92.50±4.94	0.079
	19-35	89.15±6.65	
	36-60	86.85±6.29	
	60<	85.96±5.37	
Hospitalization duration (day)	**≤18**	30.50±0.70	0.722
	19-35	5.67±5.60	
	36-60	6.36±4.73	
	60<	6.46±3.98	

SD= standard deviation.

Table 8. Correlation analysis: skin pigmentation and hair loss with average inflammatory factors serum levels and other clinical findings in recovered COVID-19 patients.

Parameters	Correlation Coefficient®	
	Skin Pigmentation	Hair Loss
Hospitalization duration (day)	0.070	0.052
Arterial oxygen saturation level (%)	-0.066	-0.147*
CRP (mg/dL)	0.025	-0.080
LDH (U/L)	0.127	0.141

(Table 8) contd.....

Parameters	Correlation Coefficient®	
	Skin Pigmentation	Hair Loss
ESR (mm/h)	-0.086	-0.059

CRP: C-reactive protein; LDH: lactate dehydrogenase; ESR: erythrocyte sedimentation rate; SD: standard deviation;
Note*: $P < 0.05$.

4. DISCUSSION

The great focus placed on preserving the lives of individuals afflicted with SARS-CoV-2 raised inquiries about the subsequent outcomes of those who had been successfully treated. Various rumors have circulated on social media and in the press about people who have had the disease and reported hair loss and changes in skin color. Many individuals in Iran reported having hair loss as a consequence. In an effort to clarify the correlation between COVID-19 and hair and skin pigmentation, this study was conducted from June to August 2021 at Afzalipour Hospital in Kerman in response to these concerns.

The research included a total of 190 participants, with an average age of 46.04 ± 13.05 years and a maximum age of 75 years. Significantly, women comprised the majority of the population, making up about 51.6%. In addition to 76.3% of the patients experiencing hair loss, 15.3% of the patients had skin pigmentation.

Our data confirm previous research findings that indicate a greater occurrence of hair loss among female participants, which has been further intensified during the COVID-19 pandemic [18, 19]. The significance of this discovery lies in the fact that it highlights the need for increased awareness of post-COVID-19 dermatological disorders. A multifactorial etiology is suggested by the observed pattern of hair loss, which is similar to TE. This etiology includes stress, malnutrition, and physiological changes that are connected with the condition.

Our data did not show a significant connection between skin pigmentation and gender or age group. A previous study also showed that there is no link between the appearance of skin manifestations and gender or age in patients with COVID-19 [20]. The lack of a significant connection between skin pigmentation alterations and gender or age emphasizes the complexities of dermatological symptoms after COVID-19. While the underlying processes remain unknown, further research into the pathophysiology of PIH and its possible link to COVID-19 is needed.

The observed disparity in ESR between males and females in this research may indicate distinct physiological or inflammatory responses to COVID-19 infection based on gender. The ESR is a biomarker that is not unique to any particular kind of inflammation, but it may indicate the existence of underlying inflammatory processes in the body [21]. However, since this inflammatory component is not gender specific and there is a chance that other variables like age, medical background, and hormonal impacts may affect the results, no conclusions can be drawn.

The challenges faced throughout the research, such as participant hesitancy and difficulties with accessibility, highlight the need for implementing well-planned recruiting techniques and extensive outreach initiatives. Undertaking longitudinal research on future pandemics or epidemics might provide crucial information. Consistent follow-up assessments and proactive communication with patients may help with continuous monitoring and assistance. Furthermore, researching several samples that exhibit distinct climatic or seasonal fluctuations may reveal novel aspects in this field of study.

Following these discoveries, it is critical to provide individuals undergoing treatment with comprehensive knowledge regarding possible negative consequences and offer suggestions for mitigating these concerns. If patients believe that everything is under control and that there are some plans in place to meet their needs, they may feel more at ease, which should keep them from being concerned about their post-COVID condition and from overthinking about other conditions with which they may interact later. However, it is crucial to highlight that this study has limitations, such as a small sample size and a lack of investigation into factors, such as stress, dietary patterns, and other confounding variables that may impact the findings. Furthermore, this research only included previously hospitalized patients and patients were not followed up; therefore, the outcomes may change in a more diversified study group and a longitudinal investigation. As a result, further research should be undertaken to address these concerns and get a more certain conclusion about the impact of COVID-19 on skin and hair.

As we move beyond the COVID-19 pandemic, there are many possibilities to investigate the many aspects of SARS-CoV-2 infections and their consequences. Through the use of acquired knowledge and the implementation of a proactive strategy, we may enhance our readiness for forthcoming public health emergencies and reduce their consequences for individuals and communities.

CONCLUSION

Finally, our work clarifies the complex connection between the COVID-19 infection and the changes in skin and hair color that have been seen in those who have recovered. Through a thorough study of a diverse participant group, we discovered a significant incidence of hair loss after recovery, especially in female participants. These results stress the need to provide COVID-19 survivors with proactive care and support, as well as the need for customized therapies to deal with the various impacts of the virus. Longitudinal studies and ongoing monitoring are crucial to improve our knowledge of the long-term effects of COVID-19 and to create focused

treatments that will improve the quality of life of people and communities long after the epidemic has ended. Table **T1**. Frequency distribution of skin pigmentation and hair loss based on gender in recovered COVID-19 patients.

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

LIST OF ABBREVIATIONS

ARDS	=	Acute respiratory distress syndrome
AKI	=	Acute kidney injury
PTSD	=	Posttraumatic stress disorder
TE	=	Telogen Effluvium
PIH	=	Post-inflammatory hyperpigmentation
PIH	=	Post-inflammatory hyperpigmentation
HPT	=	Hair-pull test
LDH	=	Lactate Dehydrogenase
CRP	=	C-reactive protein
ESR	=	Erythrocyte Sedimentation Rate
HIS	=	Hospital Information System
ICU	=	Intensive Care Unit

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Our study received approval from the Ethics Committee of Kerman University of Medical Sciences, Iran (Reference Number: IR.KMU.AH.REC.1400.172, Date: 10.25.2021).

HUMAN AND ANIMAL RIGHTS

All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Prior to their inclusion in the study, all participants provided verbal informed consent.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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