Short Communication

The Role of Vitamin D and Testosterone Levels with Hair Loss among Females with Coronavirus Disease

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Abstract

Background: Coronavirus disease (COVID-19) is a respiratory illness that has been found to affect various body systems, leading to unpredicted symptoms such as hair loss. **Objective:** This study investigates the potential relationship between hair loss and hormonal factors, specifically testosterone and Vit-D, in female COVID-19 patients. **Materials and Methods:** This is a cross-sectional case-control study involving 100 participants, including 50 female COVID-19 cases experiencing hair loss after infection and healthy volunteers without post-COVID-19 hair loss. Blood samples were taken to determine testosterone and Vit-D3 measures. Anthropometric variables including age and Body Mass Index, and hematological tests, were also evaluated. Statistical analyses, including receiver operating characteristic (ROC) curve analysis, were performed to assess the diagnostic accuracy of testosterone and Vit-D. **Results:** The study exposed COVID-19 females with hair loss exhibited raised serum testosterone measures (P = 0.001) and reduced Vit-D values (P = 0.001) compared to controls. Significant correlations were observed between testosterone and Vit-D levels (r = 0.317, P = 0.001), as well as between testosterone and age (r = 0.219, P = 0.027). ROC analysis demonstrated a good predictive value of testosterone for hair loss (area under the curve [AUC] = 0.888) compared to Vit-D (AUC = 0.262). **Conclusion:** The results emphasize the importance of considering nutritional and hormonal aspects to understand the mechanisms underlying COVID-19-associated hair loss.

Keywords: Alopecia areata, androgenic alopecia, COVID-19, hair loss, testosterone, Vit-D

Introduction

Coronavirus (COVID-19) is a positive-sense RNA virus that affects various systems and a wide range of promiscuous natural hosts. COVID-19 was previously thought to be a respiratory condition, but as time went on, it was discovered that other organs and systems may also be affected.[1-3]

Numerous research publications have been published since the onset of this global pandemic to describe the long-term health impacts of COVID-19 in humans,[4] with hair loss being one of the prevalent outcomes. The condition is known as telogen effluvium (TE), which is characterized by diffuse hair loss brought on by a disruption in the cycle of hair development. In the first two to three months following the infection, 25% of COVID-19 patients experience acute classic TE, with women being more susceptible than men.[5]

The enzyme 5-alpha-reductase converts testosterone to dihydrotestosterone (DHT) in target tissues, resulting in the production of active androgenic steroid form. While androgens expand hair follicles in androgen-dependent areas, they can later in life cause the miniaturization of scalp follicles and contribute to androgenic alopecia (AGA).[6]

Vit-D has multifaceted effects including metabolic and immunoregulatory functions.[7-12] Testing for 25-hydroxy Vit-D levels is advised when examining patients with post-COVID-19 hair loss because research has linked TE

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to low serum Vit-D levels. Hair follicle cells carry Vit-D receptors, which can control keratinocyte proliferation and hair development cycles.[13]

Nevertheless, after COVID-19 infection, alopecia aerates (AA), a different non-scarring hair loss, have also been seen in small sample size investigations. It is thought that the condition is immune-mediated and results from the inflammatory process that damages anagen hair follicles. In the control of the innate and adaptive immune systems, sex hormones have a significant and heterogeneous function. A recent research revealed that a severe course of COVID-19 could be caused by both high and low testosterone levels.[14]

In our governorate (Babylon), there are nearly inadequate studies on hair loss in general or exactly how testosterone and Vit-D may affect hair loss in COVID-19 patients. As a result, the goal of this study was to determine how much hair loss among girls with COVID-19 in Babylon province was correlated with levels of Vit-D and testosterone.

Materials and Methods

Sample collection and study design

This study was done in the Biochemistry Department laboratory at the University of Babylon, Colleges of Medicine and Pharmacy (because the laboratories of both colleges are included in the practical work). In this cross-sectional case-control study, there were 100 individuals in total. The patient group consisted of 50 participants who had COVID-19and developed hair loss as a result of their COVID-19 infection. The control group was made up of healthy volunteers who had previously contracted COVID-19 but had no prior history of abnormal hair loss either during or after the illness.

The samples were obtained between November 20, 2022, and May 20, 2023. Patients were gathered from individuals visiting Merjan Medical City and A-Imam Al-Sadiq Teaching Hospital's outpatient clinics. Specialist doctors and dermatologists chose the control groups based on selection criteria and made the patient diagnoses. The history, clinical examination, radiological studies, serology, positive polymerase chain reaction (PCR) during the infection from the patient's archive, or positive antibody (IgG, IgM) post-infection were all used to confirm the diagnosis of COVID-19.

The patient group consists of any girl between the ages of 17 and 45 who has had hair loss after contracting the COVID-19 virus. Any female between the ages of 17 and 45 who had never had hair loss after contracting COVID-19 was enrolled in the control group. Any subjects who met even one of the conditions listed below were disqualified from the study. In addition to pressure-induced alopecia areata, other well-known conditions that can cause hair loss include chronic illness, immune disorders, hereditary hair loss, and recognized cases of hormonal imbalance.

Venous blood samples were taken, and then, biochemical assays were conducted on their sera. With the use of Fluorescence Immuno Assay Technology (FIAT) from Finecare® (China), Vit-D and testosterone hormone levels were assessed. Enzyme-Linked Immuno Sorbent Assay (ELISA) from Elabscience® (Houston, TX, USA) was used to measure the COVID-19 serological test (IgG, IgM). Blood tests were completed using a Fully Automated Hematology Analyzer DYMIND®-DH-36 (3 part) to perform a complete blood count from whole blood.

Age, weight, height, the length of hair loss following COVID-19 infection, a history of any chronic conditions, and medications were all included in the study questionnaire.

Statistical analysis

SPSS IBM (Chicago, IL, USA), version 24.0, was used to conduct the analysis. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to check the normality of the data distribution. Continuous data that are normally distributed are reported as mean ± standard deviation (SD). To compare the means between groups for non-normal and regularly distributed data, respectively, the Mann-Whitney *U* test and Student's *t* test were used. Binary correlations utilized partial coefficients. The receiver operating characteristic (ROC) curve was performed in an attempt to identify the diagnostic performance and to classify a patient's illness status as either positive or negative based on test findings. Statistical significance was defined as a *P* value of 0.05.

Ethical approval

Before collecting samples, all study participants were informed and allowed to verbally consent. A local college and hospital ethics committee examined and approved the study protocol, subject information, and permission form by the document number (IRB: 5-25, October 18, 2022).

Results

An overview of various variables and their respective values in a given population is demonstrated in Tables 1 and 2. The mean values and standard deviations are provided for each variable, along with the minimum and maximum values observed, allowing for an understanding of the distribution and ranges of the variables.

Table 3 compares several factors between patients and controls. The patients' mean age is noticeably lower than that of the control group. In comparison to the controls, the patients also have higher testosterone levels and lower Vit-D3 levels.

Table 1: The characteristic demographic of the studied participants

Variables	Total Mean ± SD	Min-Max
Age (years)	29.7 ± 8.7	17–45
BMI (kg/m^2)	25.7 ± 3.5	19–35
Age categories No (%)		
17–24	34	33.3%
25–35	40	39.9%
36–45	28	27.4%
Duration/months since		
Infection	8.2 ± 3.3	3–15
Hair loss	5.6 ± 3.3	1–12
Hair loss after infection	2.6 ± 1.2	1–7
Marital state No (%)		
Married	52	51%
Unmarried	50	50%
Menstrual regularity		
Regular	86	84.3%
Irregular	16	15.7%

BMI: Body Mass Index

Table 2: Biochemical and hematological variables of the study participants

Variables	Total Mean ± SD	Min-Max
Testosterone (ng/mL)	0.31 ± 0.20	0.10–0.96
D3 (ng/mL)	22.2 ± 1.5	4.2–62.9
WBCs (10^3/μL)	7.3 ± 2.2	2.5–13.9
Hb (10^6/μL)	12.4 ± 1.2	9.9–14.7
Platelets (10^3/μL)	296.2 ± 3.2	103–661

Table 3: Comparison of study variables between patients and control

Variables	Patients Mean ± SD	Control Mean ± SD	*P*-value
Age/years	27.6 ± 8.6	31.9 ± 8.3	0.01
D3 (ng/mL)	17.7 ± 7.7	26.9 ± 11.5	0.001
BMI (kg/m^2)	25.7 ± 3.2	25.8 ± 3.9	0.83
Testosterone (ng/mL)	0.435 ± 0.190	0.177 ± 0.106	0.001
Hb (10^6/μL)	12.06 ± 1.1	12.4 ± 1.2	0.12
Platelets (10^3/μL)	270.2 ± 6.4	296.2 ± 3.2	0.087

BMI: Body Mass Index

Both the testosterone hormone and Vit-D have positive significant correlations (r = 0.317 and P = 0.001), as do the testosterone hormone and age (r = 0.219 and P = 0.027). A weak relationship between the testosterone hormone and Body Mass Index (BMI). In this study, there was a positive significant association between age and BMI (r = 0.309 and P = 0.002), as well as a negative non-significant correlation between Vit-D and age and Vit-D and BMI [Table 4].

Tables 5 and 6 present the diagnostic accuracy of testosterone and Vit-D. Overall, the table provides valuable insights into the variables being studied and their relevance to the patient population. Testosterone shows higher values for area under the curve, sensitivity, and specificity compared to Vit-D. The significant *P*-values for both variables indicate a strong association.

Table 4: Relationships between the study's variables

Person correlation		Testosterone	Vit-D	Age	BMI
Testosterone	*r*	-			
	p	-			
Vit-D	*r*	-0.032	-		
	p	0.001	-		
Age	*r*	-0.219	-0.219	-	
	p	0.027	0.027	-	
BMI	*r*	-0.075	0.085	0.309	-
	p	0.454	0.398	0.002	-

BMI: Body Mass Index

Table 5: ROC curve analyses of testosterone and vitamin D to predict patients with hair loss from those without hair loss

Variable	AUC	Sensitivity	Specificity	*P*-value	95% CI
Vitamin D	0.262	50.4%	30.5%	0.001	0.167–0.357

AUC: area under the curve, ROC: receiver operating characteristic

Table 6: ROC curve analyses of testosterone to predict patients with hair loss from those without hair loss

Variable	AUC	Sensitivity	Specificity	*P*-value	95% CI
Testosterone	0.888	95.2%	72.7%	0.001	0.820–0.956

AUC: area under the curve, ROC: receiver operating characteristic

Discussion

In this study, women with COVID-19 in Babylon province were investigated to estimate the relationship between Vit-D and testosterone hormone and hair loss. The patients in this study had high levels of testosterone and low levels of Vit-D2, which were the main findings. Another important finding is the inverse relationship between testosterone and Vit-D2. COVID-19 patients with hair loss had high testosterone levels, while those without hair loss had low Vit-D levels [Figure 1].

Similar findings were reported in another study,[15] supporting recent studies that suggest hair loss often begins 50 days after the first sign of COVID-19 infection and may last 12-100 days.[16] Rasheed *et al.*'s[17] study in Egypt found that women with female pattern hair loss and chronic TE had significantly lower levels of Vit-D in their serum compared to the controls and the severity of alopecia correlated with decreasing Vit-D levels. In cases of Vit-D deficiency, a prescription for it can aid in hair growth.

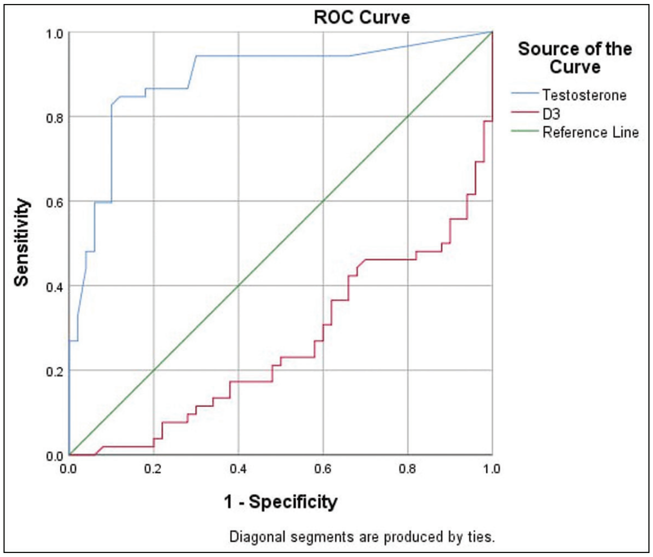

Figure 1: ROC curve analyses of testosterone and vitamin D to predict patients with hair loss from those without hair loss. ROC, receiver operating characteristic

Because of the quarantine during the COVID-19 period, individual factors including age, skin phototype, and sun exposure can have an impact on Vit-D levels in the body. Weather, season, location, exposure to the outdoors, and air pollution are among the environmental and seasonal elements that might impact serum Vit-D levels.[1]

Vit-D plays a significant role in autoimmune conditions such as AA, which specifically targets hair follicles. Extensive research has established a clear connection between Vit-D deficiency and AA. Moreover, this deficiency proved to be a crucial diagnostic indicator, as it was frequently observed in individuals with AA, and telogen effluvium.[6,17]

The role of Vit-D in hair loss and its various functions, such as regulating keratinocyte differentiation and proliferation was a subject of many previous studies. Vit-D's anti-inflammatory and immunomodulatory effects are highlighted,[7] along with its significance in maintaining the hair cycle.[6,17] However, because of the COVID-19 virus's ability to reduce Vit-D receptors supplementing with Vit-D might not be effective for treating long-term COVID-19.

Harmonious to several recent data, the current study showed that testosterone levels were significantly higher in COVID-19 patients enough to distinguish those with hair loss from those without with a high degree of ROC metrics. Likewise, 5/6 investigations have indicated a higher frequency of AGA in patients with severe COVID-19,[18] although it was unknown whether AGA had become worse or stayed the same after COVID-19. AGA is listed as a risk factor for, rather than a sequela of, COVID-19. Additionally, a German study found that COVID-19 females had high testosterone positively correlated with pro-inflammatory cytokines.[19] Progesterone can reduce DHT, curbing hair loss. Estradiol influences hair growth via receptors. COVID-19 may lower systemic estrogen and progesterone in females due to viral shock from the viral infection.

Additionally, the pneumocytes and keratinocyte cells contain the angiotensin-converting enzyme 2 (ACE2) receptor, a critical receptor for COVID-19 pathogenicity, that is also influenced by androgens. Thus, the virus penetrates host cells through the damaged ACE2 receptor.[20]

One explanation of the negative correlation of serum testosterone with low Vit-D levels is that Vit-D controls several enzymes involved in the synthesis/signaling of steroids, such as sex and adrenal hormones. Furthermore, all trace minerals and vitamins, including Vit-D, were found to be insufficient in patients with high circulating levels of DHT who had AGA. Blood and lesional scalp biopsies were obtained from patients with AGA and AA and investigated for vitamin D receptors (VDR) levels which were found to be considerably reduced, and Vit-D may contribute to the early onset of AGA.[21]

The results of the current investigation showed a strong relationship between age and the incidence of hair loss after COVID-19. In a related study, participants aged 46 and older had a considerably decreased rate of hair loss.[22] Because children are less commonly infected with COVID-19 and have less severe symptoms than adults with COVID-19, most hair loss cases appear at older ages.

BMI was not significantly different between groups in this study. Similar results were also demonstrated by Turkish researchers.[23] However, another study found a greater BMI in patients than in controls. It's well known that obesity has a documented immunoregulatory role, as well, obesity might impair the homeostasis of minerals such as zinc and copper in the hair.[24]

Nearly half of the study's participants were married, and irregular periods were also observed among the females. An investigation in Jordan and Iraq revealed similar menstrual irregularities. Psychological disorders (especially stress and depression) can typically alter these fluctuations in the menstrual cycle.[25]

Conclusion

This study demonstrated the intricate interplay between serum testosterone hormone levels, serum vitamin levels, and hair loss in individuals affected by COVID-19. The findings underscored the importance of considering hormonal and nutritional factors in understanding hair loss dynamics post-COVID-19 infection.

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Conflicts of interest

There are no conflicts of interest.

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