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THE RELATIONSHIP BETWEEN ANDROGENETIC ALOPECIA AND SERUM VITAMIN D3 LEVEL

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ABSTRACT

Background: Androgenetic alopecia is a common dermatological condition that can significantly affect patients' quality of life. A potential role of serum vitamin D3 levels in various hair disorders has been proposed, which may pave the way for expanded therapeutic options. **Aim:** To investigate the relationship between androgenetic alopecia and serum vitamin D3 levels, and the correlation of these levels with each of the following: age, sex, age of onset, duration of alopecia, and alopecia severity. **Materials and Methods:** This study (case – control study) was conducted in the dermatology clinic at Latakia University Hospital, Syria. It included 50 patients diagnosed with androgenetic alopecia and 50 healthy controls, matched for sex and age. Serum vitamin D3 levels were measured in both cases and controls. The severity of androgenetic alopecia was assessed using the Hamilton-Norwood scale for males and the Ludwig scale for females. **Results:** The mean serum vitamin D3 level in patients was 28.38 ng/mL, compared to 32.84 ng/mL in the control group (p-value = 0.002). A deficiency and insufficiency of vitamin D3 was observed in 60% of the cases compared to 40% of the controls (p-value = 0.03). The mean serum vitamin D3 level was significantly lower in patients with a disease duration of less than or equal to 10 years (p-value = 0.001). A significant decrease in vitamin D3 levels was also observed with increased severity of alopecia in both males and females (p-value less than 0.05). No significant correlation was found between vitamin D3 levels and sex, age, age of onset, or duration of alopecia within the cases group (p-value more than 0.05). **Conclusion**: A relationship was observed between low serum vitamin D3 levels (deficiency or insufficiency) and the presence of androgenetic alopecia. In addition, a correlation was found between these decreased levels and both the duration and severity of alopecia.

KEYWORDS: Androgenetic alopecia, vitamin D3.

INTRODUCTION

Androgenetic alopecia is a hereditary, non-scarring type of hair loss that affects both males and females. It is primarily mediated by androgenic activity and is characterized by the gradual miniaturization of terminal hair follicles into vellus-like follicles. This transformation is influenced by a multifactorial interplay of etiological and pathological mechanisms, including hormonal imbalances, abnormalities in the hair growth cycle, genetic predisposition, aging, and variations in end-organ sensitivity.[27]

Clinically, androgenetic alopecia is classified into male and female pattern hair loss, each representing the most common type of alopecia in their respective sexes. In men, it typically presents with bitemporal recession and thinning at the vertex. In contrast, women often exhibit diffuse thinning over the mid-frontal scalp, usually accompanied by frontal accentuation.[26]

The Hamilton–Norwood scale is widely employed to grade the severity of hair loss in males[7], whereas the Ludwig scale is commonly used to evaluate the extent of hair loss in females.[4]

Vitamin D plays an essential and irreplaceable role in maintaining human health. As a fat-soluble vitamin, it can be obtained exogenously from dietary sources or synthesized endogenously in the skin. Cutaneous production involves the conversion of ergosterol into vitamin D_2 and 7-dehydrocholesterol into previtamin D_3 upon ultraviolet (UV) exposure in epidermal keratinocytes. These precursors subsequently undergo α- and β-hydroxylation steps to produce the biologically active form, 1, 25-dihydroxyvitamin D_3, the final product of the synthesis pathway.

The most reliable method for assessing vitamin D status is measuring serum levels of 25-OH-vitamin D_3.[24]

Recently, vitamin D has gained attention for its involvement in the pathophysiology of various autoimmune, neurological, reproductive, cardiovascular, and infectious disorders. Notably, vitamin D receptors (VDRs) have been recognized as key regulators in hair follicle cycling, particularly in initiating the anagen (growth) phase. Reduced expression of VDRs in hair follicles and keratinocytes has been associated with impaired epidermal differentiation and inhibited hair growth. As a result, maintaining adequate vitamin D levels is increasingly considered essential in preventing hair loss and managing hair aging.[24,25]

This study proposes a potential association between decreased Vitamin D levels and androgenetic alopecia. Demonstrating this relationship may pave the way for novel therapeutic approaches to manage the condition and enhance the quality of life and self-confidence of those affected.

MATERIALS AND METHODS

This case control study was conducted on 50 cases of androgenetic alopecia, between the ages of 18 to 60 years and 50 controls, matched for age and sex. cases and controls both were selected from the Dermatology Clinic of Latakia University Hospital during the period from November 2023 to November 2024. An informed consent was obtained from all cases and controls prior to their participation in the study. **Inclusion Criteria**: patients of androgenetic alopecia with age between 18 and 60 years.

Exclusion Criteria: Patients suffering from other causes of alopecia, including: Cicatricial alopecia and non-cicatricial alopecia, Patients with clinical or laboratory evidence of hyperandrogenemia, Patients suffering from malnutrition or malabsorption disorders, Patients with chronic liver or kidney disease, Pregnant or lactating women and Participants taking any drugs that could alter serum vitamin D levels, such as: (Systemic corticosteroids, Antiepileptic drugs, Cholesterol-lowering drugs ,Calcium and vitamin D supplements)

The demographic profile and clinical details of all participants were recorded, including the duration and severity of androgenetic alopecia, as well as any treatment received.

The diagnosis of androgenetic alopecia was based on clinical findings. Male patients were graded from stage I to VII according to the Hamilton-Norwood scale, while female patients were graded from stage I to III according to the Ludwig scale.

A venous blood sample was obtained from all cases and controls, and serum vitamin D levels were measured using the radioimmunoassay technique.

Vitamin D Level Interpretation:
Deficient: 20 ng/mL
Insufficient: more than20 ng/ml and less than 30 ng/mL
Sufficient: ≥ 30 ng/mL

Statistical analysis

The chi-square or Fisher exact test was used to study the relationships between categorical variables. The Independent T student test was employed to compare the mean differences between the two groups. All variables were tested using univariate regression, and the statistically significant variables were then entered into a multivariate analysis equation. Results were considered significant if the p-value was less than 5%. IBM SPSS Statistics software was used to compute the statistical parameters and analyze the results.

RESULTS

A total of 50 cases and 50 controls were regulated and analyzed. In cases, there were 36 (72%) males and 14 (28%) females, while in controls there were 33 (66 %) males and 17 (34%) females. (**Table 1**)

The mean age of participants was 33.11± 11.6 years. Among both cases and controls, the largest proportion of participants fell within the (18–28) years age group. **(Table 2)**

72% of cases had a disease duration of ≤ 10 years. **(Table 3)**

Regarding the severity of AGA, 27.8% of males were graded as Stage 4, followed by 25% in Stage 2 on the Hamilton–Norwood scale. **(Table 4)**

Among females, 42.8% were graded as Stage 2 on the Ludwig scale. **(Table 5)**

The mean serum vitamin D_3 level was significantly lower in cases compared to controls (28.38±6.7 ng/mL vs. 32.84±6.9 ng/mL). Additionally, 14% of cases had vitamin D_3 deficiency compared with 2% of controls. (**Table 6**)

No Statistically significant correlation was found between serum vitamin D_3 levels and gender, age, or age at AGA onset. **(Tables 7, 8, and 10)**

90% of vitamin D3 sufficiency were in cases with alopecia duration ≤10 years with p-value =0.03. **(Table 9)**

Vitamin D3 levels decreased progressively across AGA grades in both males and females, with an association showing a statistically significant p-value of less than 0.05. **(Table 11,12)**

Table 1: Distribution of research sample according to Gender.

Gender	Cases	Controls	P-value
Males	36(72%)	33(66%)	0.5
Females	14(28%)	17(34%)	

Table 2: Distribution of research sample according to Age.

Age	Cases	Controls	P-value
18 – 28	24(48%)	34(68%)	0.2
29 – 39	11(22%)	7(14%)	
40 – 49	5(10%)	3(6%)	
50 – 60	10(20%)	6(12%)	

Table 3: Distribution of cases according to Alopecia duration.

Alopecia duration	Number	Percentage
More than 10 years	36	72%
Less than 10 years	14	28%

Table 4: Distribution of male cases according to Alopecia severity.

Alopecia severity Hamilton- Norrword scale	Number	Percentage
II	9	25%
III	8	22.2%
IV	10	27.8%
V	4	11.1%
VI	5	13.9%

Table 5: Distribution of male cases according to Alopecia severity.

Alopecia severity Ludwig scale	Number	Percentage
I	4	28.6%
II	6	42.8%
III	4	28.6%

Table 6: Distribution of cases according to Vit D3 Level.

Vit D3 Level	Cases	Controls	P-value
Deficient	7(14%)	1(2%)	0.03
Insufficient	23(46%)	19(38%)	
Sufficient	20(40%)	30(60%)	
Mean ± SD	28.38±6.7	32.84±6.9	0.002

Table 7: The relationship between Gender and Vit D3 Level.

Vit D3 Level	Males	Females	P-value
Deficient	4(11.1%)	3(21.4%)	0.6
Insufficient	17(47.2%)	6(42.9%)	
Sufficient	15(41.7%)	5(35.7%)	
Mean ± SD	28.19±5.6	28.88 ± 9.2	0.7

Table 8: The relationship between Age and Vit D3 Level.

Vit D3 Level	Age				p-value
	18 - 28	29 – 39	40 – 49	50 – 60	
Deficient	4(57.1%)	1(14.3%)	0(0%)	2(28.6%)	0.06
Insufficient	8(34.8%)	8(34.8%)	4(17.4%)	3(13%)	
Sufficient	12(60%)	2(10%)	1(5%)	5(25%)	
Mean ± SD	29.4 ± 6.64	25.77 ± 4.7	25.73 ± 3.6	26.7 ±9.46	0.3

Table 9: The relationship between Alopecia duration and Vit D3 Level.

Vitamin D3 Level	Alopecia duration		P-value
	≤10	>10	
Deficient	4(57.1%)	3(42.9%)	0.03
Insufficient	14(60.9%)	9(39.1%)	

Sufficient	18(90%)	2(10%)	
Mean ± SD	30.20 ± 6.8	23.72 ± 3.8	0.001

Table 10: The relationship between age of alopecia onset and Vit D3 Level.

Vitamin D3 level	Age of Alopecia On Set Mean ± SD	P-value
Defincient	24.28 ±7.2	0.4
Insufficient	24.08±7.6	
Sufficient	27.20±8.9	

Table 11: The relationship between alopecia severity and Vit D3 Level in males.

Vitamin D3 Level	Alopecia severity Hamilton-Norrword scale					P-value
	II	III	IV	V	VI	
Deficient	0(0%)	0(0%)	2(50%)	1(25%)	1(25%)	0.02
Insufficient	2(11.8%)	4(23.5%)	4(23.5%)	3(17.6%)	4(23.5%)	
Sufficient	7(46.7%)	4(26.7%)	4(26.7%)	0(0%)	0(0%)	
Mean ± SD	31.89 ±2.61	31.65 ±4.53	27.20 ±6.68	25.10± 5.56	21.92± 2.3	0.01

Table 12: The relationship between alopecia severity and Vit D3 Level in females.

Vitamin D3 Level	Alopecia severity Ludwig scale			P-value
	I	II	III	
Deficient	0(0%)	2(66.7%)	1(33.3%)	0.03
Insufficient	0(0%)	3(50%)	3(50%)	
Sufficient	4(80%)	1(20%)	0(0%)	
Mean ± SD	38.81 ±5.42	26.84±8.73	22.02±3.71	0.01

DISCUSSION

Vitamin D influences hair growth in humans through multiple suggested pathways. The involvement of the Vitamin D receptor (VDR) in hair cycle regulation was first proposed based on observations in Alopecia Universalis, which is a symptom seen in Type IIA Vitamin D-dependent rickets (VDDR IIA). Infants affected by VDDR IIA are born with normal hair but begin experiencing hair loss between one to three months of age, coinciding with the shedding of embryonic hair and the onset of the initial postnatal hair cycle. This evidence underscores the critical role of a properly functioning VDR for the timely initiation and continued maintenance of the hair growth cycle. Another research indicates that the VDR gene and the hairless gene belong to a shared genetic signaling pathway and function together to regulate the hair growth cycle. This conclusion is drawn from the pathogenesis of Generalized Atrichia caused by mutations in the hairless gene, a condition that exhibits clinical and histological features resembling those seen in VDR Type IIA deficiency.

Research has demonstrated that Vitamin D3 promotes the terminal differentiation of hair follicles in humans. This process holds particular significance, as androgenetic alopecia is marked by the miniaturization of hair follicles, leading to a higher proportion of fine, vellus hairs compared to terminal hairs.[24,25]

Our study findings reinforce the hypothesis that hair loss in androgenetic alopecia correlates with decreased serum levels of 25-hydroxy vitamin D3. This conclusion is supported by a statistically significant difference in Vitamin D3 levels between the affected individuals and the control group. This suggests that decreased vitamin D levels may contribute to the development of androgenetic alopecia (AGA).

Similar results were also reported by Jun Zhao et al, Sarita Sanke et al, Amna Saeed et al, Raj Kumar et al and Rehana Batool et al, their findings indicated significantly lower levels of vitamin D in cases compared to matched controls[24,25,26,27,28]

In the current study, we identified a correlation between vitamin D3 levels and the severity of androgenetic alopecia (AGA). These results are consistent with the findings of Sanke et al and Rehana Batool et al, who similarly reported an association between serum vitamin D concentrations and AGA severity patients in males.[25,27]

Our study revealed a correlation between the duration of alopecia and vitamin D3 levels, consistent with the findings reported by Rehana Batool et al.[25]

Our study found no significant correlation between the age of disease onset and vitamin D3 levels (p-value = 0.04). This contrasts with the findings of Rehana Batool et al., who reported a significant association between these variables.[25]

These results indicate that vitamin D deficiency is a contributing factor in androgenetic alopecia (AGA). Further research is warranted for better understanding the role of Vitamin D receptors (VDRs) in the regulation of the hair cycle and hair growth. Additionally, regular

assessment of serum vitamin D levels should be considered following an AGA diagnosis to identify and correct any deficiencies. Future studies should also evaluate the potential therapeutic benefits of vitamin D supplementation in managing AGA, including its efficacy in slowing or preventing disease progression.

Limitations

The sample size is relatively small, Lack of objective (immunological or laboratory) measures to determine the severity of androgenic alopecia, thus relying on clinical assessments based on the examiner's judgment and Possible variation in vitamin D3 levels depending on occupation, season, and the method used to measure vitamin D.

CONCLUSIONS

Our study supports the existence of a relationship between low levels of vitamin D (deficiency and insufficiency) and the occurrence of androgenic alopecia, in addition to a correlation between this deficiency and both the duration and severity of the alopecia.

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