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Original Research Article

The evaluation of serum vitamin D3 in androgenetic alopecia: a case-control study

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ABSTRACT

Background: Androgenetic alopecia (AGA) is a common hereditary condition characterized by progressive hair loss influenced by androgens. Vitamin D has been implicated in various hair disorders, yet its association with AGA, particularly in South Asian populations, remains inconclusive.
Methods: We conducted a case-control study involving 100 male subjects from eastern Uttar Pradesh, India, comprising 50 AGA cases and 50 age-matched controls. Serum vitamin D levels were measured, and participants underwent clinical evaluations. Statistical analyses were performed using unpaired t tests and chi-square tests.
Results: Vitamin D deficiency (<20 ng/ml) was significantly more prevalent in AGA cases (56%) compared to controls (24%) (p<0.001), with an odds ratio of 4.0303. Mean serum vitamin D levels were significantly lower in cases (33.1±10.6 ng/ml) than controls (40.3±9.51 ng/ml) (p=0.0005). Severe AGA cases exhibited lower vitamin D levels compared to mild to moderate cases, although the difference was not statistically significant (p=0.32).
Conclusions: This study highlights the importance of vitamin D in AGA pathogenesis and suggests the need for routine monitoring of serum vitamin D levels in AGA patients. Further large-scale studies are warranted to confirm these findings and investigate the efficacy of vitamin D supplementation as a therapeutic intervention for AGA.

Keywords: Vitamin D, AGA, Non-scarring alopecia, Alopecia

INTRODUCTION

Androgenetic alopecia (AGA), a hereditary condition influenced by androgens, causes progressive hair loss in both men and women by converting terminal hair follicles into miniaturized ones.[1] This transformation is driven by various factors such as hormonal shifts, genetic predispositions, and aging. While men typically experience a receding hairline and bitemporal thinning, women often face diffuse hair thinning in the mid-frontal scalp area followed by frontal accentuation.[2,3]

The severity of AGA is often assessed using the Norwood Hamilton scale.[2] Although onset usually occurs in one's thirties or forties, there's a concerning trend of younger individuals experiencing hair loss, leading to significant emotional distress and self-esteem challenges.[4] Research indicates that a substantial portion of males aged 18-49 suffer from moderate to extensive hair loss, highlighting the psychological impact of premature alopecia.[5,6] Ultimately, the underlying cause of hair thinning stems from the influence of dihydrotestosterone, a by-product of testosterone, on susceptible hair follicles.[7]

Vitamin D plays a crucial role in human health, obtained through dietary sources or synthesized in the skin upon exposure to UV radiation.[8] Its active form, 1,25-dihydroxyvitamin D3, regulates immune function, cell growth, and the hair cycle. Monitoring serum levels of 25-hydroxy vitamin D3 is key, with normal levels considered above 30 ng/ml and deficiency below 20 ng/ml, while insufficiency ranges from 21 to 29 ng/ml.[9]

Research indicates vitamin D's involvement in various hair disorders like telogen effluvium, alopecia areata, and female pattern hair loss.[10-12] Recent studies also link vitamin D deficiency to autoimmune, neurological, cardiac, and infectious diseases. Reduced expression of vitamin D receptors (VDR) in hair follicles correlates with decreased hair growth and epidermal differentiation, suggesting its vital role in hair health.[6,13]

Despite extensive research, the relationship between vitamin D levels and AGA remains inconclusive, especially in South Asian populations. Our study aims to fill this gap by investigating the correlation between reduced vitamin D levels and AGA. Establishing such a link could pave the way for novel treatment strategies, offering hope to those affected by this challenging condition and enhancing their quality of life.

METHODS

This case-control study, conducted at a dermatology department of BRD medical college in Uttar Pradesh, India, involved 100 male subjects divided into two groups: 50 with AGA and 50 healthy age-matched individuals. Each participant underwent a thorough evaluation, including full medical history, clinical examination, and measurement of serum vitamin D levels.

The study was carried out over a four-month period from August 2023 to December 2023 and included patients aged 16 to 50 years. The study was approved by the institutional ethics committee. Patients and controls were selected from the outpatient department of the hospital, ensuring matched characteristics such as age, skin type, sun exposure, and socioeconomic status. Exclusion criteria comprised individuals with other types of alopecia, hyperandrogenemia, malnutrition, malabsorption disorders, chronic liver or the kidney disease.

Diagnosis of AGA was established based on clinical examination using the Norwood-Hamilton scale to assess hair loss patterns, along with positive hair pull tests and dermoscopy examinations. Male pattern AGA ranging from Norwood-Hamilton grades I to III was categorized as mild to moderate, while grades IV and higher were classified as severe.

To rule out hyperandrogenism, all participants underwent testing for dehydroepiandrosterone sulphate and free testosterone levels. Serum levels of 25-hydroxy vitamin D3 were measured and values below 20 ng/ml considered deficient.

The study utilized Microsoft excel and SPSS version 11 to analyse data, reporting quantitative variables as mean ± standard deviation and qualitative variables as proportions Statistical comparisons between groups were conducted using unpaired t tests for mean values, and Chi-square tests for qualitative data. $P \leq 0.05$ is considered significant.

RESULTS

The study included 50 cases and 50 age and skin type matched controls. Characteristics of participants in the case and control groups have been shown in Table 1. The mean age for cases was 33.44±7.92 years, while for controls it was 32.10±11.13 years. Among the cases, the highest number fell within the 21-30 age group (n=19, 38%), followed by 31-40 years (n=14, 28%), 41-50 years (n=10, 20%), and 16-20 years (n=7, 14%). Regarding the severity of AGA based on the Hamilton-Norwood classification, 22 cases (44%) were classified as grade II, 10 cases (20%) as grade III, 9 cases (18%) as grade IV, 6 cases (12%) as grade V, and 3 cases (6%) as grade VI. When assessing severity, 32 cases (64%) were categorized as mild to moderate AGA, while 18 cases (36%) were deemed severe.

Table 1: Characteristics of participants in the case and control groups.

Variables	Case, n=50 (%)	Control, n=50 (%)
Age (in year)	33.44±7.92	32.10±11.13
Skin phototype		
3	19 (38)	15 (30)
4	25 (50)	31 (62)
5	6 (12)	4 (8)
Age group (in years)		
16-20	7 (14)	5 (10)
21-30	19 (38)	16 (32)
31-40	14 (28)	18 (36)
41-50	10 (20)	11 (22)

Vitamin D levels showed a significant decrease in cases compared to controls, with 28 individuals affected in cases out of a total of 50 cases (56%), versus 12 in controls out of a total of 50 controls (24%). The difference was statistically significant ($p<0.001$). The odds ratio of 4.0303 indicates a 4.0303-fold increased likelihood of androgenetic alopecia among individuals with low levels of 25-hydroxy vitamin D3. Mean serum vitamin D levels for cases were 33.1±10.6 ng/ml, while controls averaged 40.3±9.51 ng/ml, indicating a highly significant difference ($p=0.0005$) (Table 2).

The study noted that vitamin D deficiency was statistically significantly more prevalent in patients with severe AGA compared to those with mild to moderate AGA (Table 2). serum vitamin D levels in patients with mild to moderate AGA were 31.2±10.31 ng/ml, while mean serum vitamin D levels in patients with severe AGA averaged 28.3±9.31 ng/ml. The difference was not significant with a p=0.32 (Table 3).

Table 2: Comparisons of vitamin D level in study groups.

Variables		Case, (n=50) (%)	Control, (n=50) (%)	P value
Vitamin D level (ng/ml)	Mean±SD#	33.1±10.6	40.3±9.51	0.0005*
Vitamin D level	Deficient	28 (56)	12 (24)	<0.001*
	Normal	22 (44)	38 (76)	

#SD: Standard deviation, *Significant.

Table 3: Association of grade of alopecia with vitamin D level.

Variables		Mild-moderate AGA**, (n=32) (%)	Severe AGA**, (n=18) (%)	P value
Vitamin D level (ng/ml)	Mean±SD#	31.2±10.31	28.3±9.31	0.32
Vitamin D level	Deficient	13 (40.6)	15 (83.33)	0.0035*
	Normal	19 (59.37)	3 (16.66)	

**AGA: Androgenetic alopecia, #SD: Standard deviation, *Significant.

DISCUSSION

Vitamin D is believed to exert various effects on hair growth through a range of proposed mechanisms. Maintaining an optimal level of vitamin D is thought to be crucial in staving off aging-related phenomena, such as hair loss, indicating its significance in hair health. Additionally, extensive research in animal models underscores the pivotal role of VDR activation in kickstarting the hair follicle cycle, particularly in initiating the growth phase known as anagen.[14]

Moreover, there's evidence suggesting that the VDR directly or indirectly governs the expression of genes essential for regulating the hair follicle cycle. Investigations into the relationship between vitamin D and different hair disorders have yielded mixed findings. Some studies have observed lower levels of serum vitamin D in women experiencing chronic telogen effluvium, female pattern hair loss, and alopecia areata.[15,16] Conversely, other studies found no significant correlation between serum vitamin D levels and the extent or severity of male AGA.[17,18]

The critical role of the VDR in hair cycle regulation was first postulated in cases of type IIA vitamin D dependent rickets (VDDR IIA), where alopecia universalises emerged as one of the symptoms. Infants with VDDR IIA typically exhibit normal hair at birth but experience hair loss within the first few months of life, coinciding with the initiation of the post-natal hair cycle. This underscores the indispensable role of a properly functioning VDR in orchestrating the timely onset and upkeep of the hair cycle.[19]

Furthermore, studies suggest a genetic interplay between the VDR gene and the hairless gene, both integral to regulating the hair cycle. This insight stems from the pathogenesis of generalized atrichia associated with mutations in the hairless gene, which bears clinical and histological resemblance to VDDR IIA.[20] Additionally, research indicates that vitamin D3 promotes the final differentiation of hair follicles, a crucial process given that AGA involves the miniaturization of follicles, leading to an increased proportion of fine, non-terminal hair.[21]

Our study suggests that hair loss associated with AGA may be related to lower levels of serum 25-hydroxy vitamin D3. We found a significant difference in vitamin D levels between those affected and the control group, with most cases falling into the category of vitamin D deficiency. This indicates that low vitamin D levels might play a role in contributing to AGA. These findings are consistent with the outcomes of a study led by Tahlawy et al where they noted a mean vitamin D level of 37.1 ng/ml in cases, contrasting with a mean of 44.2 ng/ml in controls.[22] The study revealed significantly lower Vitamin D levels in cases compared to controls, with a p=0.02. Similar results were also reported by Hagag et al, Moneib et al, Rasheed et al, and Banihashemi et al their findings indicated significantly lower levels of vitamin D in cases compared to matched controls.[12,15,16,23] However, it's important to note that all of these studies exclusively focused on female patients with female pattern hair loss.

In our present study, we discovered a substantial correlation between the level of vitamin D and the extent of hair loss. These findings align with those of Sanke et al who also observed a correlation between serum vitamin D levels and the degree of hair loss in patients with AGA.[1]

Conversely, the findings of this study contradict those of Bolland et al and Iyanda, who reported that the degree of

AGA does not seem to impact serum vitamin D levels in individuals with male pattern hair loss.[17,18]

Conic et al discovered lower serum vitamin D levels among individuals with AGA compared to controls.[24] Meanwhile, Sarac et al conducted a study in Turkey which found a correlation between AGA, telogen effluvium, and reduced serum vitamin D levels.[25] Additionally, Jun Zhao et al conducted a case-control study in China, revealing a significant association between male AGA and low serum vitamin D levels (p=0.0005).[3]

In our study, we discovered that 56% of the cases had lower serum vitamin D levels compared to only 24% of controls. This difference was found to be statistically significant, with a p<0.001. Moreover, our analysis revealed an odds ratio of 4.0303, indicating that individuals deficient in vitamin D had a fourfold higher risk of developing AGA.

These findings suggest that vitamin D deficiency is indeed one of the factors associated with AGA. It is important to conduct further investigations into the role of VDRs in regulating the hair cycle and hair growth. Moreover, routine monitoring of serum vitamin D levels should be considered following the diagnosis of AGA.[26] This would provide an opportunity to address any measurable deficiencies in vitamin D among patients. Furthermore, studies should explore the potential of vitamin D supplementation as a therapeutic intervention for AGA, including its effectiveness in halting the progression of the disease.

The limitation of our study is its relatively small sample size. A small sample size can affect the generalizability of study findings. Moreover, vitamin D levels in the body can be influenced by various individual factors, including age, skin phototype, and exposure to sunlight. Given that our cases and controls were carefully matched for these variables, such as age, skin type, and sun exposure, the potential confounding effects of these factors on the study results and their interpretation were minimized. Hence, it's clear that more extensive studies involving larger participant groups are necessary so that we get a more comprehensive understanding of the relationship between vitamin D levels and hair loss.

CONCLUSION

In our current investigation, we observed a higher prevalence of lower vitamin D levels among individuals with AGA compared to the control group. This difference was statistically significant, particularly among those with severe AGA in contrast to those with mild to moderate cases. These findings suggest that AGA may be influenced by multiple factors.

Our study provides supporting evidence for a correlation between AGA and vitamin D deficiency. However, to establish this association conclusively, further large-scale studies are warranted. Additionally, there remains an unanswered question regarding whether vitamin D supplementation could potentially prevent the onset or delay the progression of AGA in susceptible individuals. This underscores the importance of future research endeavours aimed at elucidating the role of vitamin D in the pathogenesis and management of AGA.

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