Study of vitamin D deficiency in patients with alopecia areata attending a dermatology center in Iran

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Received: 28 May 2020
Accepted: 14 June 2020

Background: Alopecia areata (AA) is an autoimmune disease involving the inflammation of hair follicles. In many autoimmune diseases, inadequate levels of vitamin D have been reported. We aimed to determine the association between vitamin D levels and AA.

Methods: In this case-control study, 50 AA patients and 50 controls were assessed regarding serum levels of 25-hydroxy vitamin D [25-(OH)-D_3]. The levels of 25-(OH)-D_3 were classified as deficient (< 20 ng/ml), insufficient (20 to 30 ng/ml), and sufficient (> 30 ng/dl). The severity of the disease was scored according to the Severity of Alopecia Tool (SALT).

Results: The serum level of 25-(OH)-D_3 was significantly lower in AA cases compared with the control group. Patients with the totalis or universalis pattern of hair loss had lower levels of 25-(OH)-D_3 relative to patients with the patchy or ophiasis type of AA. Moreover, severe cases showed significantly lower levels of vitamin D relative to mild and moderate cases. We found a significant inverse association between 25-(OH)-D_3 level and age. We found no association between serum levels of 25-(OH)-D_3 and gender, disease duration, disease recurrence, nail involvement, or positive family history of AA.

Conclusion: AA patients had lower serum levels of vitamin D, though this did not contribute to the severity or duration of disease or pattern of hair loss. More studies are required to evaluate the role of vitamin D supplementation in the pathophysiology of AA.

Keywords: vitamin D_3, alopecia areata, autoimmune disease, hair loss

Iran J Dermatol 2021; 24: 97-101

DOI: 10.22034/ijd.2021.132456

INTRODUCTION

Alopecia areata (AA) is a form of non-scarring hair loss. This condition usually appears as round or oval patches of sudden hair loss in any hairy area of the body. It can manifest in different patterns from patchy hair loss to alopecia totalis and universalis [1]. Despite being a benign disease and although most patients remain asymptomatic, it can cause emotional and psychosocial anxiety. AA has been reported in all races, and it affects men and women in the same ratio. The reported prevalence of AA is between 0.1 and 0.2% [2], and the risk of disease in the lifetime is 1.7% [3].

AA is an autoimmune disease caused by T-cells in patients with a genetic predisposition, though the exact pathophysiology of AA is still unknown. The disease is a chronic condition caused by immune system impairment that targets the hair follicles [4], leading to the early transfer of the anagen hair follicle to the catagen and telogen phases [5].

AA is also associated with different autoimmune

disorders, including thyroiditis and vitiligo [6]. Various micronutrients such as iron, zinc, amino acids, and vitamins are known to regulate hair growth [7]. Interestingly, the role of vitamin D and 1, 25 vitamin D receptors in keratinocytes is crucial for the normal hair cycle and hair regeneration [8,9]. The activity of vitamin D has been shown to increase the anagen phase velocity. Accordingly, the regeneration and anagen phases are not initiated when there is a lack of vitamin D [10]. Moreover, calcium and vitamin D have immunomodulatory activity, and vitamin D deficiency is seen in several autoimmune diseases including systemic lupus erythematosus, vitiligo, and psoriasis [11]. There are also controversial data on the link between vitamin D deficiency and AA [12].

Thus, in this study, we aimed to investigate the relationship between serum levels of 25-hydroxy vitamin D [25-(OH)-D3] and the severity of AA in patients referring to a dermatology center in Iran.

PARTICIPANTS AND METHODS

We conducted a case-control study that included patients with a definite diagnosis of AA who had visited the alopecia clinic at Razi Hospital affiliated to Tehran University of Medical Sciences (TUMS) during a period of 12 months from October 2016 to December 2017. The control group comprised fifty healthy volunteers matched in terms of age, sex, and body mass index (BMI) who presented with cosmetic complaints. The study was approved by the Ethics Committee of TUMS, and informed consent was obtained from all participants.

The inclusion criteria of cases were an age of above 10 years and a confirmed diagnosis of AA by a dermatologist. The exclusion criteria were as follows: a history of intralesional steroids' injection within the last month; use of systemic corticosteroids within the last year; use of immunosuppressive drugs within the last three months; calcium and vitamin D supplementation; consumption of bisphosphonates or cholesterol-lowering drugs; phototherapy treatment; pregnancy or lactation; and any coexisting inflammatory disease other than AA, diabetes, or smoking.

Clinical and demographic data including the disease duration, family history of AA, atopy, nail involvement, eyebrow and eyelash hair loss, the pull test result, and the hair loss pattern (patchy, ophiasis, totalis, and universalis) were recorded. The hair loss severity was also measured according to the Severity of the Alopecia Tool (SALT) score [13].

Blood samples (4 ml) were taken from all subjects. After centrifugation, vitamin D levels were measured in the endocrine laboratory. The serum 25-(OH)- D_3 concentration was measured using commercial Enzyme-Linked Immunosorbent Assay (ELISA) kits (LIAISON, Italy), which quantitatively determine the 25-(OH)-D_3 level via chemiluminescent immunoassay (CLIA) technology. Based on the 25-(OH)-D_3 level, the patients were divided into sufficient (> 30 ng/ml), insufficient (20-30 ng/ml), and deficient (<20 ng/ml) groups.

Data were analyzed using version 22 of the SPSS program (SPSS Inc., Chicago, Illinois, USA). Quantitative data were reported as mean ± standard deviation (SD), while qualitative data were reported using frequency and percentage. We used the independent t-test, analysis of variance (ANOVA), and chi-squared test to investigate the relationship between the variables. P-values below 0.05 were considered statistically significant.

RESULTS

The study included 50 patients with AA and 50 healthy controls of which 46% were female (P = 0.57). The mean age of the AA patients was 32.48 ± 12.61 years, which was statistically similar to the control group (32.26 ± 12.32 years; P = 0.34). The BMI of the patients and controls were 25.75 ± 4.58 and 25.79 ± 4.35, respectively (P>0.05) (Table 1).

Among the AA patients, 16 had positive pull test results, 35 had eyebrow involvement, 20 had beard involvement, 12 had nail involvement, 28 had a positive history of atopy, and 8 had a family history of AA. In terms of disease activity, 19 patients were in the stage of hair loss, 4 in the stage of hair regrowth, and 27 were in a stable condition. The pattern of hair loss in the AA patients included 18 cases of universalis, 9 cases of ophiasis, 6 cases of totalis, and 17 cases of the patchy pattern. The mean SALT score of patients was 67.9 ± 35.47 (3-100) percent, and the mean duration of disease was 76.32 months (Table 1).

Fifteen patients in the AA group and 28 individuals in the control group had a history of atopy, indicating a significant difference between cases and controls (P = 0.009). The serum

Table 1. Demographic information of alopecia areata (AA) patients and controls

Variable	AA patients	Controls	*P*-value
Sex, n (%)			
Female	23 (46)	23 (46)	0.579
Male	27 (54)	27 (54)	
Age (mean ± SD)	32.48 ± 12.61	32.26 ± 12.32	0.344
BMI (mean ± SD)	25.75 ± 4.58	25.79 ± 4.35	0.965
Vitamin D level (ng/ml) (mean ± SD)	18.32 ± 8.55	23.21 ± 8.71	0.03
Deficient (≤ 20 ng/ml)	28 (56%)	23 (46%)	0.01
Normal (≥ 30 ng/ml)	6 (12%)	13 (26%)	0.323
Type of AA			
Patchy	17	-	-
Ophyasis	6	-	
Totalis	9	-	
Universalis	18	-	
Disease duration (months)	76.32 ± 94.13	-	-
SALT score	67.96 ± 35.47	-	-
Family history of AA	8	-	-
History of atopy	15	28	0.009
Nail involvement	28	-	-
Eyebrow hair loss	35	-	-
Eyelash hair loss	25	-	-
Beard hair loss	20	-	-
Pull test	16	-	-

25-(OH)-D_3 levels were significantly lower in the AA (18.32 ± 8.55 ng/ml) patients compared with the controls (23.21 ± 8.71 ng/ml; P = 0.006). Although both groups had a deficiency of vitamin D, the severity of vitamin D deficiency in the AA patients was higher relative to the controls. In the AA group, 43.9% of females and 56.1% of males had a deficiency of vitamin D. The difference between the genders was not statistically significant (P>0.05) (Table 2).

We found no significant association between the serum concentration of vitamin D and the type of AA or the involvement of eyelashes, eyebrows, beard, or nails (P > 0.05) (Figure 1). Besides, there was no significant association between vitamin D levels and BMI, age, SALT score, and disease activity and duration (P > 0.05) (Table 2).

Table 2. Relationship of 25-hydroxy vitamin D levels with various parameters among patients with AA

Patients with AA	Mean ± SD	*P*-value
Sex		
Female	21.53 ± 15.94	0.452
Male	18.81 ± 8.03	
Age (years)	32.48 ± 12.61	0.660
BMI (kg/m^2)	25.75 ± 4.58	0.756
Disease duration (months)	76.32 ± 94.13	0.583
SALT score (0-100)	67.96 ± 35.47	0.181
Eyelash hair loss		
Positive	16.83 ± 7.83	0.059
Negative	23.36 ± 14.93	
Eyebrow hair loss		
Positive	20.87 ± 11.50	0.501
Negative	18.29 ± 14.11	
Beard hair loss		
Positive	18.10 ± 8.19	0.353
Negative	21.43 ± 14.32	
Nail involvement		
Positive	18.37 ± 7.98	0.581
Negative	20.64 ± 13.36	
Type of AA		
Patchy	20.53 ± 12.39	0.100
Ophiasis	28.20 ± 18.26	
Totalis	13.91 ± 5.99	
Universalis	17.70 ± 8.13	

DISCUSSION

This study indicated that the mean level of vitamin D was remarkably lower in patients with AA than healthy controls. However, we found no relationship between vitamin D level and disease activity, severity, or type of hair loss. In this study, seasonal variations of vitamin D levels were also considered and all patients were selected within

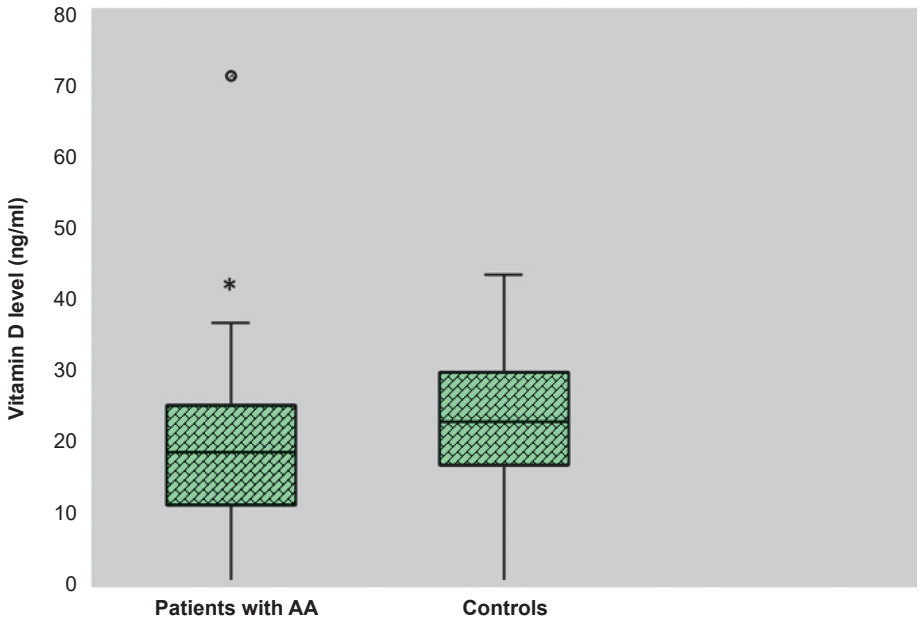

Figure 1. Serum levels of vitamin D in patients with alopecia areata (AA) and controls

a similar interval.

Vitamin D is found in certain foods and is also synthesized in the skin in a process that is induced by ultraviolet B light. The active form is 1,25-dihydroxy-vitamin D, but due to its short half-life (about 4 hours), the level of the 25-(OH)-D_3 form (half-life of approximately two weeks) was measured [14]. According to prior research, the active form of vitamin D influences the expression of genes contributing to the natural differentiation of epidermal cells and hair follicles, including the *DKKL* (Soggy), *HR* (Hairless), and *SOSTDC* (Wise) genes [15]. Vitamin D receptors are present in the outer pod of cortical hair and papillary dermal cells [16,17] and fulfill an active role in hair growth, with their absence being associated with alopecia [18].

Additionally, vitamin D_3 had a modulatory role in innate and acquired immunization, which is carried out via the expression of vitamin D receptors on B and T lymphocytes, dendritic cells, and macrophages. The association between vitamin D deficiency and autoimmune diseases such as diabetes mellitus type 1 (DM I), rheumatoid arthritis (RA), vitiligo, psoriasis, and irritable bowel syndrome has been reported in previous studies [19]. These findings propose that vitamin D deficiency may be a stimulator for the initiation of autoimmunity [20]. A number of studies have highlighted the anti-inflammatory role of vitamin D in vitiligo and AA [14,21-23]. In another study, cases of vitamin D deficiency rickets in patients with AA were presented [24].

Two recent systemic reviews showed significantly lower levels of vitamin D in AA patients than healthy controls [25,26]. In a study by Darwish *et al.* that included 50 patients and 20 controls from Egypt, the serum vitamin D concentration was significantly lower in the AA group compared with the controls. They found lower levels of vitamin D in males than females. However, in other studies, the prevalence of vitamin D deficiency was significantly more in women with AA compared with males [14,22,27-28]. This is reflective of the lower exposure of women to sunshine due to their religious beliefs and the customs of their communities. In our study, there was no significant difference between males and females in terms of serum vitamin D levels.

CONCLUSION

In conclusion, we showed serum 25-(OH)-D_3 levels to be depleted in AA patients. However, this depletion was not correlated with the severity, duration, or activity phase of the disease or the type of hair loss. Thus, nutritional supplementation of vitamin D might be reasonable for all AA patients. However, further studies are needed to define the

therapeutic effect of restoring sufficient vitamin D levels on the AA disease.

Conflict of Interest: None declared.

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