

Evaluation of Serum Vitamin-D Levels in Patients with Alopecia Areata

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ABSTRACT

Objective: To evaluate serum vitamin-D levels in patients with Alopecia areata compared to healthy controls.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Dermatology Outpatient Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from Nov 2019 to Apr 2020.

Methodology: The study included 70 patients with Alopecia areata (Group-1) and 70 healthy controls (Group-2). Complete blood count, TSH, urea and creatinine, fasting plasma glucose, liver function tests, serum Calcium and vitamin-D levels were performed.

Results: The mean vitamin-D levels of Group-1 were 38.28 ± 22.07 ng/mL, and the mean vitamin-D levels of Group-2 were 39.61 ± 18.36 ng/mL. In Group-1, deficient vitamin-D levels were seen in 14(20.0%) of Group-1, and insufficient in 19(27.1%) and 37(52.9%) had normal levels. In Group-2, 10(14.3%) had deficient levels, 16(25.0%) had insufficient levels and 44(62.9%) had normal levels. No statistically significant difference seen between Group-1 and Group-2.

Conclusion: There is no association between vitamin D level and Alopecia Areata.

Keywords: Alopecia areata, Autoimmune diseases, Vitamin-D deficiency

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INTRODUCTION

Alopecia areata (AA) is an autoimmune disorder with a remitting-relapsing course with a reported worldwide incidence of 2%.¹ It has a clinically heterogeneous presentation and can involve hair-bearing sites like eyebrows, eyelashes, beard, scalp and body. It appears as a well-defined oval-to-round hairless patch with no atrophy. However, it can manifest as total scalp hair loss, termed Alopecia totalis, and in some cases, hair loss from the entire body, called Alopecia universalis.^{2,3}

Vitamin-D is either obtained through dietary sources or most of it is synthesized in the skin upon exposure to sunlight. Vitamin-D plays multiple functions in the human body and acts on different cell types. Vitamin-D acts through its specific receptors known as vitamin-D receptors (VDRs) in target tissues. VDRs are also present in keratinocytes, playing a role in cell growth, differentiation or programmed cell death and thus acting as a regulator of cutaneous immune response.^{4,5} Various studies have reported an association of vitamin-D in the pathogenesis of certain autoimmune diseases like type-1 diabetes, psoriasis, ichthyosis, vitiligo, atopic dermatitis, systemic lupus erythematosus and hidradenitis suppurativa.^{6,7}

Vitamin-D also treats autoimmune diseases like vitiligo and psoriasis.^{8,9} Some literature showed that serum vitamin-D deficiency could be associated with alopecia areata.¹⁰ However, most of it is international and limited regional data is available, so if the relationship between vitamin-D deficiency and alopecia areata could be established, there is potential that supplementing vitamin-D in patients with alopecia areata could improve or even treat Alopecia areata. Therefore, the objective of this study was to evaluate vitamin-D levels in patients with alopecia areata and to compare them with healthy controls.

METHODOLOGY

The comparative cross-sectional study was carried out at the Dermatology Outpatient Department of Fauji Foundation, Hospital, Rawalpindi Pakistan, from November 2019 to April 2020. The sampling technique used was non-probability consecutive sampling. The sample size was calculated using WHO sample size calculator, taking level of significance=5%, power of test=90%, anticipated population proportion P1=0.64 and anticipated population proportion P2=0.38.¹¹ Ethical Approval was taken from the Hospital Ethical Review Board.

Inclusion Criteria: For Group-1, patients of either gender and any age group with no previous history of hepatobiliary, cardiovascular, renal or gastrointestinal disorder, no history of parathyroid or metabolic bone

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disorders and no history of taking topical or systemic treatment for Alopecia Areata at least one month before testing were included in the study. Patients with no history of taking drugs that can affect vitamin-D and calcium metabolisms like corticosteroids, bisphosphonates, phototherapy and no vitamin-D or calcium supplements were also included in the study. Patients presenting with skin diseases other than Alopecia Areata, such as eczema, acne, melasma, fungal infections etc., were included as Control Group in study.

Exclusion Criteria: Patients taking drugs that may affect calcium metabolism, patients taking Alopecia Areata treatment, patients with inflammatory and autoimmune conditions, pregnant, lactating women and smokers were excluded from the study.

Seventy patients presenting with Alopecia areata in skin OPD were enrolled for the study and labelled as Group-1. Other parameters recorded for both groups were Fitzpatrick skin phenotype, percentage of the area involved (by SALT score), sunscreen usage, disease duration, comorbid autoimmune conditions and family history. Both groups were enrolled after taking informed consent from participants. The researcher examined and diagnosed all the patients based on clinical presentation.

Alopecia areata patients were also classified based on the duration of disease: <6-months (D1), 7-months 12-months (D2), 13-months 18-months (D3), 19-months 24-months (D4) and > two years (D5). "Severity of Alopecia Tool (SALT) score was used to estimate the area of scalp involvement. The scalp was divided into four quadrants, right and left side (18%-0.18) each, top (40%-0.4) and posterior area (24%-0.24).¹² The extent of the area involved was calculated and then multiplied with the factor mentioned respectively.⁹(Figure).

Patients were further sub-grouped into the following SALT subclasses: SS1≤25%, SS2=25%-49%, SS3=50%-74%, SS4=75%-99% and SS5=100%. Investigations performed in both groups were: Serum Calcium, complete blood count, TSH, LFTs, RFTs, fasting plasma glucose and 25(OH) vitamin-D levels. We divided 25(OH)D levels into three categories: 'deficient' (≤20ng/ml), 'insufficient' (21-29.9ng/ml), and 'sufficient' (≥30ng/ml).¹³

Data were analysed using Statistical Package for the social sciences (SPSS) version 23.00. The percentage was calculated for categorical data. Mean and standard deviation were also calculated for age and serum vitamin-D levels. The Chi-square test was applied to

qualitative data. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

The study included 70 patients with Alopecia areata (Group-1) and 70 healthy controls (Group-2). The mean serum vitamin-D level of Group-1 was 38.28±22.07ng/mL, and the mean serum vitamin-D level of Group-2 was 39.61±18.36ng/mL (Table). 43 (61.4%) patients had scalp involvement <25%. 18 (25.7%) patients had between 25%-49% scalp involved, and 9(12.9%) patients had >50% scalp involvement, of which two patients had Alopecia universalis, and 1 had Alopecia totalis. The duration of lesions was also variable with 25(35.7%) patients categorized as D1, 32(45.7%) patients a D2, 2(2.9%) as D3 and 11(15.7%) patients as D4. No patient had a family history of alopecia areata. Eight patients also had comorbidities; 6 patients had diabetes mellitus, and 2 had thyroid disorders. No patient gave a history of sunscreen usage. All the patients belonged to Fitzpatrick skin phenotype III or IV.

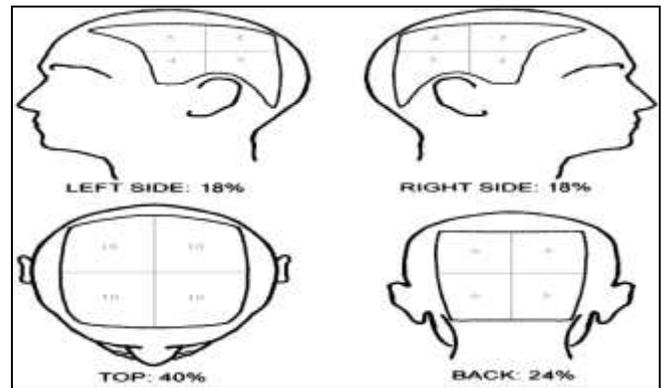


Figure: Olsen/Canfield tool for scalp hair loss percentage

Table: Characteristics of Study and Vitamin D Levels (n=140)

Characteristics	Group-1 (Patients)	Group-2 (Controls)	p-value
Age (years)	26.89±18.12	40.4±17.96	
Gender			
Male	14(20.0%)	14(20.0%)	
Females	56(80.0%)	56(80.0%)	
Vitamin D (ng/ml)			
Deficient	14(20.0%)	10(14.3%)	0.466
Insufficient	19(27.1%)	16(25.0%)	
Normal	37(52.9%)	44(62.9%)	

DISCUSSION

Alopecia areata is a common cause of non-scarring hair loss that has a controversial association with vitamin-D deficiency. Our study showed that 33

patients with alopecia areata had lower vitamin-D levels than 26 controls, but this difference was not statistically significant (p -value=0.466). Various studies have been done in different countries which have evaluated serum 25(OH)D levels and their association with AA with varying results.

A case-control study done in India on 60 patients and 60 controls concluded that patients with alopecia areata had significantly lower serum 25(OH)D levels ($p < 0.001$).^{13,14} A cross-sectional study on 50 patients and 35 controls were carried out in India. They showed serum 25(OH)D levels were low in alopecia areata patients compared to healthy controls, and there was a significant negative correlation between serum Vitamin-D levels and the severity of alopecia areata.¹⁵ Our study showed different results as compared to the studies mentioned above. Thirty-three patients in Group-1 had lower vitamin-D levels than 26 in Group-2, but this difference was not statistically significant (p -value=0.466).

In Pakistan, a case-control study was done on 30 patients of alopecia areata and 30 controls. The median vitamin-D level of Group-1 was 13.5(18.6)ng/dl, and healthy controls were 22.5(16.25) and the study concluded significantly lower vitamin-D levels in patients with alopecia areata than healthy controls, though the sample size was small.¹⁶ Our study had a larger sample size, and the results also differed, with the mean vitamin-D levels of Group-1 being 38.28±22.07 and the mean vitamin-D levels of controls being 39.61±18.36. However, the p -value was also not found to be statistically significant.

Like our study, some studies show no positive correlation between lower Vitamin-D levels and alopecia areata, as discussed: A study conducted in Italy on 156 patients with alopecia areata and 148 controls, d'Ovidio *et al.* found that 42.4% of patients and 29.5% of controls had low vitamin-D levels, but the difference was not statistically significant.¹⁷ The study also revealed that seasonal variation could be a causative factor in the incidence or relapse of alopecia areata, as higher relapse rates were observed by the end of the winter season. A study in Turkey on 41 alopecia areata patients and 32 controls found no statistically significant difference in the serum 25(OH)D levels between alopecia areata and controls.¹⁸

Our results also reveal that vitamin-D levels were low in both patients (47.1%) and controls. However, the p -value was not significant, which may indicate vitamin-D deficiency in the general population. The

study by Jadoon *et al.* on 202 people showed a high prevalence of vitamin-D deficiency in Pakistan. It has become a public health problem, significantly affecting our population irrespective of age and gender.¹⁹

Other environmental factors such as seasonal variation (sample collected in a particular season), degree of air pollution, latitude and cultural differences can also affect vitamin-D synthesis.²⁰

The study was conducted to determine the relationship between serum vitamin-D levels and alopecia areata. If vitamin-D levels are found deficient, vitamin-D supplementation could improve alopecia areata, as vitamin-D supplementation is therapeutically effective in various other autoimmune conditions. The results showed that Vitamin-D levels were relatively lower in the Patients Group compared to the Control Group though the difference was insignificant. Therefore, Further studies are needed from different areas of Pakistan to clarify the association. It is unknown at present whether Vitamin-D supplementation would be effective in the therapy of AA.

LIMITATIONS OF STUDY

Firstly, the controls were not related to patients. If controls belong to a similar geographical area and have the same level of sun exposure and similar dietary habits, it would ensure good comparison. Secondly, the male population was under-represented, and the majority of patients included in the study were female. In addition, the clothing style of most female patients reporting to the outpatient department and included in the study was such that it covers most of the body, allowing for limited sun exposure and thus can affect vitamin D status. Finally, the sample was collected from November to April. The sample should be collected throughout the year to study for seasonal variation, as seasonal variation of vitamin D is well established.

CONCLUSION

No positive correlation between vitamin D deficiency and alopecia areata could be established. However, patients with alopecia areata had lower vitamin D levels than healthy controls.

Conflict of Interest: None.

Author's Contribution:

Following authors have made substantial contributions to the manuscript as under:

AK: Conception, drafting the manuscript, approval of the final version to be published.

FR: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AJ: Critical review, drafting the manuscript, approval of the final version to be published.

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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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