

## Original Research Article

# A case control study of serum vitamin D levels in alopecia areata

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### ABSTRACT

**Background:** Alopecia areata is an autoimmune disorder of anagen hair follicle leading to distressing and relapsing non-scarring hair loss. Vitamin D is an immunomodulator and plays a role in regulating normal hair cycle. Recent evidence suggests inconsistent association between vitamin D deficiency and alopecia areata.

**Methods:** This case control study included 70 newly diagnosed cases of alopecia areata and 70 healthy controls. Competitive chemiluminescence immunoassay was used to determine and compare the serum vitamin D (25-hydroxyvitamin D) levels between these groups. Also, the serum vitamin D levels correlation with severity of the disease was studied. ANOVA test and student t test were used for the statistical analysis.

**Results:** Serum Vitamin D levels were significantly decreased in alopecia areata patients than in controls ( $p < 0.05$ ). There was no statistically significant relationship between serum 25-OH Vitamin D levels and severity of the disease ( $p = 0.06$ ).

**Conclusions:** Prevalence of serum 25 (OH) deficiency was significantly higher in alopecia areata group. However no significant relation was found with disease severity.

**Keywords:** Alopecia areata, Vitamin D, 25-Hydroxyvitamin D, Severity of alopecia tool score

### INTRODUCTION

Alopecia areata is a hair follicle restricted autoimmune disease that causes non scarring hair loss affecting the scalp/ any hair bearing area consequent to loss of immune privilege in hair follicle. It affects 0.1-0.2% of population with a lifetime risk of 2%.<sup>1</sup> The immune mediated destruction is triggered by environmental factors in genetically susceptible by T cell infiltrates (CD4+ and CD8+) and Th1 cytokine production around anagen stage hair follicles.<sup>2</sup> There is also an increased overall risk of other autoimmune disorders in patients of alopecia areata.<sup>3,4,5</sup>

Vitamin D (vit D) is an important secosteroid hormone which is vital for maintenance of calcium homeostasis, immune regulation, and cell growth and differentiation.<sup>6</sup> The active form of vitamin D (1,25-dihydroxyvitamin D) plays a crucial role in cutaneous immune modulation targeting T lymphocytes and B lymphocytes, monocytes, dendritic cells and macrophages.<sup>7</sup> 25-dihydroxyvitamin D plays an important role in the development of hair follicle and regulation of hair cycle via the vit D receptors (VDR) expressed in dermal papillae and in the epidermis of the hair follicles.<sup>8</sup> Studies have proposed a connection between few autoimmune diseases and vit D deficiency, suggesting vit D deficiency might be an environmental stimulus for induction of autoimmunity.<sup>9</sup> Also alopecia is

an important finding of the patients with vit D dependent rickets type II.<sup>10</sup>

In view of the discrepant results documented in earlier literature, this study was undertaken to evaluate the serum levels of vit D in patients with alopecia areata, to determine its possible role in the etiopathogenesis and affect on the severity of the disease

**METHODS**

This hospital based case - control study was conducted from June 2018 to May 2019. After obtaining Institutional ethical committee clearance, a total of 140 patients; 70 cases of alopecia areata and 70 age and gender matched healthy controls with no alopecia areata attending the outpatient department of dermatology of a teaching institute (Gayatri Medical College and Hospital, Visakhapatnam) in Southern India were recruited to participate in the study.

Seventy patients belonging to any age and both the genders who were confirmatively diagnosed as having alopecia areata based on clinical and trichoscopic findings and consenting to be a part of the study were included. In doubtful cases histopathological confirmation was done based on the characteristic peribulbar lymphocytic infiltration giving swarm of bees appearance and altered anagen:telogen ratio.

Alopecia due to other causes like chemotherapeutic agents, infections, scarring alopecia, trichotillomania, alopecia due to autoimmune, metabolic, nutritional deficiencies, hepatic and renal disorders were not included. Also pregnant, lactating mothers and patients on steroids and other immunosuppressive drugs, protein, calcium and vit D supplementation were excluded.

An elaborative history was elicited with respect to the site, pattern, duration and progression of alopecia areata. Relevant drug history and family history was taken. Patients were enquired about duration of sun exposure and sunscreen usage. Socio-demographic profile, clinical, and laboratory data were also noted. All details were recorded on prefixed performa.

Examination and assessment of alopecia lesions were made on the basis of number of active lesions, site of involvement as well as pattern and extent of alopecia. The severity of AA was scored by severity of alopecia tool score (SALT score), and patients were further sub-grouped into following SALT subclasses: S0 =no hair loss; S1= <25; S2=26-50; S3=51-75; S4=76-99; and S5=100.<sup>11</sup>

A venous blood sample was taken from all the cases and controls, and their serum vit D levels were measured by the radioimmunoassay technique. The values were interpreted as follows as follows: sufficient (>30 ng/ml), insufficient (20-30 ng/ml), and deficient (<20 ng/ml).

Correlation was done between SALT scores and serum vit D levels.

Since the half-life of 1,25-dihydroxy vit D is less than 4 hours, the circulating concentrations sometimes seem to appear normal in subjects, who are vit D deficient. Therefore, the free circulating concentration of 25-hydroxy vit D is taken into account as its half-life is 2 weeks and is clinically the best predictor of vit D status.

**Statistical analysis**

The results were analyzed using the statistical package for social science- SPSS 24 for Windows. Descriptive data were expressed as mean, standard deviation and percentages. Student's t-test and ANOVA test were used for the analysis of the difference between two study group means. P<0.05 was considered statistically significant.

**RESULTS**

A total of 70 cases and 70 controls satisfying the inclusion and exclusion criteria were included in the study. Male to female ratio was 2.48:1 in patients with alopecia areata and 1.18:1 in the control group. The youngest case was a 3 yr old and the eldest 57. Most cases presented with scalp involvement followed by beard and eyebrows. Time duration of alopecia areata ranged from <3 months to 5 years.

**Table 1: Vitamin D levels in case and control group.**

Group (n=70)	Mean±SD	P value
Case	17.481±5.87	<0.05
Control	32.03±4.83	

**Table 2: Vitamin-D deficiency in case and control group.**

Group (n=70)	Vitamin D deficiency (%)	P value
Case	42	<0.05
Control	71	

**Table 3: Classification of cases according to alopecia areata severity.**

SALT subclass (n=70)	N (%)
S1	46 (66)
S2	18 (26)
S3-S5	6 (9)

The mean serum vit D levels in the case group was stastically significantly lower than that of controls (17.481±5.87 ng/ml vs. 32.03±4.83 ng/ml; p<0.05) (Table 1). Significantly more no of patients among cases (71%) had vitamin D deficiency than in controls (42%)

(Table 2). Out of the 70 alopecia areata cases, 46 belonged to Subclass 1 (S1), 18 to S2 and 6 to 9 (S3- S5) (Table 3). The SALT scores in the cases when compared with serum vit D levels showed slightly lower levels of vit D in severe group than in mild cases, however the difference is not statistically significant (0.06) (Table 4).

**Table 4: Association of SALT scores with vitamin D.**

SALT subclass (n=70)	N	Mean±SD	P value
S1	46	18.99±4.4	0.06
S2	18	16.23±4.8	
S3-S5	6	15.82±5.9	

## DISCUSSION

Alopecia areata (AA) is a type of non-scarring, recurrent unslightly and distressing patchy loss of hair in hair-bearing areas and is mostly of autoimmune origin.<sup>11</sup> vit D deficiency was considered as a risk factor for the development of AA but the relationship between vit D deficiency and alopecia areata in patients was reported with conflicting results.<sup>12</sup> Moreover, there is dearth of literature in South India in this area where vit D deficiency is high.<sup>13</sup> Herein, we comprehensively evaluated association of vit D levels with alopecia areata and its severity.

Major histocompatibility complex (MHC) class I and II molecules are not expressed in the region of hair follicle as it is an immune privileged site. This immune privilege is collapsed in AA by the presence of increased MHC I and II complexes, decreased immunosuppressive molecules, and higher expression of adhesion molecules (ICAM-2 and ELAM-1) in the perivascular and peribulbar hair follicular epithelium, leading to perifollicular inflammation which causes thin dystrophic hair with miniaturization. Epidermal differentiation and hair follicle growth have been found to decrease with lack of vit D receptors in human hair follicles.<sup>14</sup> Vitamin D deficiency has been hypothesized to play a role in various autoimmune disorders and alopecia areata by inhibiting the expression of various inflammatory markers such as tumour necrosis factor; TNF- $\alpha$ , interleukin (IL)-6, IL-8 and TNF- $\gamma$ .<sup>15</sup> In such conditions deficient vit D levels acts as an environmental trigger for the induction of abnormal autoimmunity.<sup>16</sup> The beneficial effect of vitamin D3 is mediated through the prevention of strong Th1 cell responses via the action on Antigen presenting cells while simultaneously tilting the T cell response towards Th2 dominance.<sup>15,17</sup>

Our study showed that Mean serum vit D levels were statically significantly lower in cases in comparison to controls; 17.481±5.87 ng/ml and 32.03±4.83 ng/ml respectively. Similar results with decreased levels in diseased subjects were obtained by Mahamid et al, Cerman et al, El-Mongy et al and Attawa et al.<sup>18-21</sup> In

contrast, Nassiri et al and Erpolat et al in their studies failed to establish the association between deficiency of vit D between case and control groups.<sup>12,22</sup>

During this study, we found that the vit D levels were much lower in more severe cases or SALT scores. However this was not statistically insignificant. Vitamin D level was found to be low; 18.99±4.4 in S1 subclass. Levels of vit D further dropped to 16.23±4.8 ng/ml in S2 and 15.82±5.9 ng/ml in S3-S5 subclasses. Attawa et al, as in our study failed to prove significant correlation with disease activity.<sup>21</sup> The results of our study were also in concordance with results obtained by Aksu et al.<sup>23</sup> Studies by Siddappa et al, Bakry et al, showed significant negative correlation between alopecia areata severity and serum vit D.<sup>24,25</sup>

## CONCLUSION

The study results, with significantly decreased serum 25-hydroxy vit D levels suggest a causal role of vit D in pathogenesis of alopecia areata and hence a possible role of vit D supplementation as a reasonable and specific treatment strategy in future.

### Limitations

The sample size was less. Furthermore, the dietary intake of vit D in patients was not assessed and no therapeutic trial of vit D was given.

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