



## Original Research Article

## A case-control study evaluating association of serum vitamin D level with alopecia areata



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## ABSTRACT

**Introduction:** Evidence has suggested that Vitamin D may play a vital role in the pathogenesis of alopecia areata (AA). Vitamin D may prove as a game changer in the management of alopecia patients.

**Aim:** To study find the correlation, if any, between Alopecia areata and levels of Vitamin D.

**Materials and Methods:** This investigation included 100 cases of alopecia areata with age- and sex-matched healthy persons. Study subjects were grouped as per extent, pattern and severity of alopecia. Levels of vitamin D were evaluated and group wise comparison was made between cases and controls. Correlations were derived after analyzing the collected data.

**Results:** Mean serum Vitamin D levels was found to be  $22.87 \pm 10.03$  ng/ml among cases. Serum Vitamin D level was found to be  $26.04 \pm 10.06$  ng/mL where scalp involvement was between 0%–24%. Levels dropped to  $24.63 \pm 9.82$  ng/mL when scalp involvement was 25%–49%. Levels of Vitamin D further dropped to  $11.91 \pm 4.18$  ng/mL and  $11.91 \pm 4.18$  ng/mL where scalp involvement was graded as S4 and S5 respectively. Negative correlation ( $r = -0.264$ ) was noted between extent of Alopecia Areata and Vitamin D levels. Serum Vitamin D level was found to be  $25.58 \pm 9.82$  ng/mL among subjects graded as having alopecia circumscripta. Levels of Vitamin D further dropped to  $12.28 \pm 5.06$  ng/mL and  $11.27 \pm 5.90$  ng/mL where extent of scalp involvement was graded as alopecia totalis and alopecia universalis respectively.

**Conclusion-** Vitamin D levels were unsatisfactory in the study subjects of group 1(cases) in relation to subjects of group 2(controls). Vitamin D levels had inverse correlation with the pattern of alopecia in these patients. Such findings points towards a probable association between alopecia areata and Vitamin D deficient levels.

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### 1. Introduction

Alopecia areata (AA), an autoimmune disorder, is a type of non-scarring, recurrent patchy loss of hair in hair-bearing areas and is mostly of origin.<sup>1</sup> It is characterized by hair loss with no clinical signs of inflammation affecting scalp and/or any hair-bearing area of the body. Alopecia is an organ specific autoimmune disease characterized by T cell infiltrates and cytokine production around anagen stage hair follicle.<sup>2,3</sup> AA is a hair follicle specific autoimmune disease, triggered by environmental factors in genetically susceptible

individuals.<sup>4</sup>

Possible role of Vitamin D in the pathogenesis of AA remains a matter of interest since long. Evidence has accumulated from AA patients with hereditary Vitamin D resistant rickets.<sup>5</sup> This is supported by the research showing effect of Vitamin D on protecting hair follicles from chemotherapy induced alopecia.<sup>6</sup> Vitamin D is a secosteroid hormone that plays an important role in calcium homeostasis and bone health. Vitamin D has been hypothesized as a risk factor for the development of AA.<sup>7</sup>

Vitamin D may prove as a game changer in the management of AA, if one can provide evidence about relation between AA and Vitamin D. Keeping above facts

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in mind, we conducted this study with the aim of finding the correlation, if any, between Alopecia areata and Vitamin D levels for better management of this chronic autoimmune disorder.

## 2. Materials and Methods

This investigation was planned and executed at the department of dermatology of a northern India based medical college. This hospital based study was rolled out on 100 patients of AA, attending our outpatient department (OPD) in year 2017-18. Cases were termed as Group 1 subjects whereas controls were named as Group 2 subjects. Clinical features and trichoscopy were the basis of final diagnosis in this study. Group 2 was comprised of equal number of subjects matched with respect to age and sex (Case to control ratio 1:1). Group 2 subjects were selected randomly from our OPD with no history of alopecia areata.

Inclusion criteria used for this study were, subjects with confirmed diagnosis of alopecia areata belonging to any age and gender and subjects willing and consenting to become a part of this clinical investigation. Exclusion criteria were devised very cautiously and it contained subjects having body mass index (BMI)  $\geq 25$  (as per recent report pointing towards a connection between obesity and Vitamin D deficiency<sup>8</sup>), individuals having scarring and androgenic types of alopecia (as these are other causes of AA), telogen effluvium. Individuals showing female pattern of hair loss were kept away from this study. Individuals revealing history of receipt of certain medications like steroids, immunosuppressants, Vitamin D supplements in any form in past four weeks, were also excluded. Subjects having known dermatological problems or any systemic or autoimmune disorders were not included. Apart from these, lactating and pregnant women were also excluded from this study. Anelaborative history was also elicited that included information about disease itself, any other systemic or autoimmune disorder, relevant drug history and family history. A few questions were shot about pattern and duration of sun exposure and sunscreen usage by them. Socio-geographic profile, clinical, and laboratory data were also noted. 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. Criteria of SALT scoring (National Alopecia Areata Foundation<sup>9</sup>) were used to assess the extent of scalp involvement. Those patients who had only scalp involvement, they were classified on the SALT sub classes which is as follows: S0–S1 = 0%–24%, S2 = 25%–49%, S3 = 50%–74%, S4 = 75%–99% and S5 = 100%.

Anthropometry was done. Height, weight and BMI of study subjects were recorded. Relevant lab investigations were performed viz. blood investigations, function tests of liver and kidney. Serum calcium and Vitamin D levels were done. Fasting samples were collected and processed

quickly. Levels of 25-hydroxyvitamin D (25(OH)D) were also assessed. Categorization was done as per standard classification viz.  $<20$  ng/mL: Deficient, 20–29.99 ng/mL: Insufficient and  $\geq 30$  ng/mL: Normal.

Data from study participants was obtained only after taking consent from them. Ethical issues involved in the study were reviewed by Ethics and Research Board of the medical college. Data collected in the proforma was entered in the excel sheet. Analysis of data was performed by the computer software Statistical Package for Social Sciences (SPSS), version 20 (IBM, Chicago, USA). Results were expressed after applying appropriate statistical tests and drawing conclusions.

## 3. Results

In this study, data of two hundred subjects (one hundred cases and one hundred matched controls) was included and analyzed. Mean age of subjects in Group 1 and Group 2 was found to be  $23.7 \pm 8.2$  years and  $26.1 \pm 10.3$  years respectively. Most (36%) of subjects in Group 1 were found to be in the age group of 21–30 years, followed by 31–40 years (22%). Male subjects were more than females clearly in excess in both Group 1 and Group 2. Time duration of Alopecia Areata was  $<3$  months in 25%, 3 months - 1 year in 50% of subjects and 2–5 years in twelve percent cases. Mean value for duration of disease was found to be  $1.5 \pm 3.26$  years with a range of 20 days to 18 years. Difference was not statistically significant for dietary habits of study participants, occupation, daily exposure to sunlight, and sunscreen usage between Group 1 and Group 2 subjects.

Of total 100 cases, 16% cases had relapse of Alopecia as compared to 84% presenting with the first time. The disease was active in 64% of subjects, presenting with new alopecic areas. Among cases, scalp was most commonly (88%) affected, followed by beard and eyebrows. In a few cases axillary, pubic, and body hair involvement was also noted. Nail changes were seen in 9% subjects.

Mean serum Vitamin D levels of subjects in Group 1 and Group 2 was found to be  $22.87 \pm 10.03$  ng/ml and  $27.34 \pm 10.54$  ng/ml respectively. This difference was observed to be statistically significant ( $P < 0.001$ ). Mean Body mass index of Group 1 subjects was  $20.96 \pm 1.91$  with range of 14.36 to 25.08 whereas Group 2 subjects had mean BMI of  $21.37 \pm 1.70$  with a range of 15.84 to 26.11. This difference was observed to be statistically non-significant ( $P > 0.05$ ). Mean serum calcium levels of subjects in Group 1 and Group 2 was found to be  $8.3 \pm 0.3$  ng/ml and  $8.5 \pm 0.5$  ng/ml respectively. Mean fasting blood sugar level were  $82.11 \pm 8.39$  mg/dL among Group 1 subjects whereas  $79.81 \pm 11.26$  mg/dL among Group 2 subjects. (Table 1)

Serum Vitamin D levels was assessed as per various pattern and presentations of the disease like extent, severity and site. Study subjects involving scalp, were graded as per SALT scoring system to assess severity of Alopecia Areata.

**Table 1: Comparison of mean serum Vitamin D levels along with other important parameters in cases and controls**

Parameter	Cases/ Group 1	Controls/ Group 2	Level of significance
Vitamin D level (ng/ml)	22.87 ± 10.03	27.34 ± 10.54	<0.001
Body mass index	20.96±1.91	21.37±1.70	>0.05
Mean Serum calcium (ng/mL)	8.3±0.3	8.5±0.5	>0.05
Mean fasting blood sugar level (mg/dL)	82.11 ± 8.39	79.81 ± 11.26	>0.05

Most subjects (44%) scored S1 grade, followed by 27%, S2 grade; 14%, S3; 10%, S4; and 5% cases scored S5 grade.

Serum Vitamin D level was found to be  $26.04 \pm 10.06$  ng/mL where scalp involvement was between 0%–24%. Levels dropped to  $24.63 \pm 9.82$  ng/mL when scalp involvement was 25%–49%. Levels of Vitamin D further dropped to  $11.91 \pm 4.18$  ng/mL and  $11.91 \pm 4.18$  ng/mL where scalp involvement was graded as S4 and S5 respectively. This was a statistically significant observation. Negative correlation ( $r = -0.463$ ) was noted between severity of Alopecia Areata and Vitamin D levels. (Table 2 )

As per extent of involvement, 67% subjects had alopecia circumscripta, 28% had alopecia subtotalis, 4% had alopecia totalis, and 1% had alopecia universalis.

A constant drop was noted in serum Vitamin D levels when correlated with extent of alopecia areata. Serum Vitamin D level was found to be  $25.58 \pm 9.82$  ng/mL among subjects graded as having alopecia circumscripta. Levels of Vitamin D further dropped to  $12.28 \pm 5.06$  ng/mL and  $11.27 \pm 5.90$  ng/mL where extent of scalp involvement was graded as alopecia totalis and alopecia universalis respectively. This was a statistically significant observation. Negative correlation ( $r = -0.264$ ) was noted between extent of Alopecia Areata and Vitamin D levels. (Table 3 )

#### 4. Discussion

Alopecia was first described by Cornelius Censur, and the term “alopecia areata” was coined by Savages in 1760. It is an autoimmune disease wherein immune response is directed towards self-antigens in a particular organ, primarily mediated by the T lymphocytes causing inflammation around growing hair follicles and characterized by production of cytokines.<sup>10</sup> It has been reported to be associated with human leukocyte antigen class (HLA) I and II and with rheumatoid arthritis (RA), vitiligo, pemphigus and other autoimmune disorders.<sup>11</sup> The histological finding is the accumulation of CD4 + T cells, and a few CD8 + T c ells around the growing hair.<sup>12</sup> Previous reports state that vitamin D receptors are present in human hair follicles, an organ which consists of epidermal keratinocytes as well as mes odermal dermal papilla cells.<sup>13</sup> Most importantly, the expression of VDRs in keratino- cytes has a vital role in epidermal equilibrium<sup>14</sup> , and the absence of VDRs decreases the growth of hair follicle and epidermal differentiation leading to alopecia.<sup>15</sup>

In this study, data of two hundred subjects (one hundred cases and one hundred matched controls) was included and analyzed. Mean age of subjects in Group 1 and Group 2 was found to be  $23.7 \pm 8.2$  years and  $26.1 \pm 10.3$  years respectively. Most (36%) of subjects in Group 1 were found to be in the age group of 21–30 years, followed by 31–40 years (22%). Findings of this study was quite similar to another study from Odisha.<sup>16</sup> In that study, sample size was 72 cases of alopecia. Most (44.44%) cases were in the age group of 21 – 30 years whereas 29.16% were in the age group of 31 – 40 years. In both the studies males were more than females in both the groups. Similar type of observations were noted by Sharma et al.<sup>17</sup> In that study, out of total subjects 64.09% were males and remaining were females.

In this study, study subjects involving scalp, were graded as per SALT scoring system to assess severity of Alopecia Areata. Most subjects (44%) scored S1 grade, followed by 27%, S2 grade; 14%, S3; 10%, S4; and 5% cases scored S5 grade. Yilmaz et al.<sup>18</sup> in his study observed that severity of AA showed a decreasing trend : 71.4% cases were in S1 grade, then 14.2% in S2, 7.4% in S3 4.7 in S4, and 2.3% in S5 grade.

Our study showed that Mean serum Vitamin D levels of subjects in Group 1 and Group 2 was found to be  $22.87 \pm 10.03$  ng/ml and  $27.34 \pm 10.54$  ng/ml respectively. This difference was observed to be statistically significant. Various other authors (Mahamid et al., Aksu Cerman et al. and Attawa et al.<sup>19–21</sup> ) had conducted studies with similar objectives. Findings of Nassiri et al.<sup>22</sup> are a bit different from ours. That study failed to establish the association between deficiency of Vitamin D and AA. Similarly Erpolat et al.<sup>23</sup> could not find any relation between serum Vitamin D levels and alopecia.

We observed a constant drop in serum Vitamin D levels when correlated with extent of alopecia areata. Serum Vitamin D level was found to be  $25.58 \pm 9.82$  ng/mL among subjects graded as having alopecia circumscripta. Levels of Vitamin D further dropped to  $12.28 \pm 5.06$  ng/mL and  $11.27 \pm 5.90$  ng/mL where extent of scalp involvement was graded as alopecia totalis and alopecia universalis respectively. This was a statistically significant observation. Bakry et al.<sup>24</sup> noted that 25(OH)- Vitamin D gradually declined from patchy to alopecia totalis/universalis group and were negatively correlated with the pattern of AA but Attawa<sup>21</sup> failed to prove any such correlation.

**Table 2: Mean serum Vitamin D levels with scalp involvement and severity of alopecia areata among study subjects**

Scalp involvement	SALT Scoring	Vitamin D level (ng/ml)	Level of significance	Correlation coefficient
0%–24%	S0–S1	26.04 ± 10.06		
25%–49%	S2	24.63 ± 9.82		
50%–74%	S3	21.27 ± 7.26	P < 0.001	r = –0.463
75%–99%	S4	14.65 ± 4.15		
100%	S5	11.91 ± 4.18		

**Table 3: Mean serum Vitamin D levels with extent of alopecia areata among study subjects**

Extent of alopecia areata	Vitamin D level (ng/ml)	Level of significance	Correlation coefficient
Alopecia Circumscripta	25.58 ± 9.82		
Alopecia Subtotalis	21.34 ± 9.65	P < 0.05	r = –0.264
Alopecia Totalis	12.28 ± 5.06		
Alopecia Universalis	11.27 ± 5.90		

## 5. Conclusion

This study observed that Vitamin D levels were unsatisfactory in the study subjects of group 1 (cases) in relation to subjects of group 2 (controls). Vitamin D levels had inverse correlation with the pattern of alopecia in these patients. Such findings points towards a probable association between alopecia areata and Vitamin D deficient levels. Further controlled trials should be rolled out to support our findings.

## 6. Funding

None.

## 7. Conflict of Interest

None.

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