# Serum 25-Hydroxy Vitamin D Level in Patients with Alopecia Areata and Its Relationship with Severity of the Disease

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**Abstract**

***Background:*** *Alopecia areata (AA) is a common autoimmune disease in which autoantigens play an important role in activating T lymphocytes. Vitamin D is associated with various autoimmune diseases and Vitamin D receptors are strongly expressed in hair follicles and their expression in keratinocytes is necessary for the maintenance of the normal hair cycle. Several studies showed that there is an influence of vitamin D on patients with AA.*

***Aims and Objectives:*** *To find out serum 25-Hydroxy vitamin D level in patients with AA and its relationship with severity of the disease in a tertiary care hospital.*

***Method:*** *This cross-sectional study was conducted at the Department of Dermatology and Venereology in Dhaka Medical College Hospital (DMCH), Dhaka, from January 2019 to December 2019. A total of sixty-four subjects were enrolled. Among them thirty-two patients were with clinically diagnosed AA cases (Group A) and thirty-two healthy age and gender matched controls without AA (Group B). Serum 25-Hydroxy vitamin D was analyzed by the automated analyzer. The levels of serum 25-Hydroxy vitamin D were categorized as deficient (<20 ng/ml), insufficient (20 to 29.9 ng/ml) and normal (e"30 ng/ml) and the Severity of Alopecia Tool (SALT) score was used to assess the severity of the disease. p-value <0.05 was taken as significant. Statistical analyses were performed with SPSS version 25.0.*

***Results:*** *The mean age of Group A was 30.56 ± 13.52 years and Group B was 34.97 ± 13.03 years. The mean serum 25-Hydroxy vitamin D level was significantly lower in patients with alopecia areata (13.38± 7.36 ng/mL) as compared to the healthy group (23.16 ± 10.36 ng/mL) (p < 0.0004). Deficient, insufficient and normal Vitamin D levels among Group A vs Group B were (88% vs 44%), (9% vs 41%) and (3% vs 16%) respectively with significant difference (p-value 0.001) between the groups. There was a significant negative correlation between serum 25-Hydroxy vitamin D level and SALT score (r=-.509, p=0.003).*

***Conclusions:*** *This study revealed that the prevalence of serum 25-Hydroxy vitamin D deficiency was significantly higher in alopecia areata group compared to healthy group. There was a significant inverse correlation between its level and alopecia areata disease severity.*

***Keywords****: Serum 25-Hydroxy Vitamin D, Alopecia areata, Vitamin D, Severity of Alopecia Tool (SALT).*

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**Introduction**

Alopecia areata (AA) is a common nonscarring alopecia which can affect the scalp and/or any hair bearing area of body without any clinical sign of inflammation.[1] There are significant variations in clinical presentation ranging from small well demarcated patches to complete loss of scalp and/or body hair.[2] Nail changes are a common feature of AA, with an average prevalence of 30%. Pitting, trachyonychia, red spotted lunulae, onycholysis, and punctate leukonychia are the reported findings.[3] The prevalence of AA was estimated 0.1 -0.2% and a lifetime risk of 2%.[4] Alopecia areata can begin at any age. Both sexes are equally affected.[5] The histological feature of AA is lymphocyte infiltration, macrophages and langerhans cells around and within affected hair follicles.[6]

Exact etiology is incompletely understood. However, immunological factor is one of the most powerful explanations.[7] The proximal hair follicle constitutes an immune privileged site. This immune privilege is disrupted in alopecia areata.[2] There is an increase in major histocompatibility complex (MHC) I and II molecules and adhesion molecules and correlate with increased leukocyte trafficking into dermis leading to perifollicular inflammation. This peribulbar inflammation adversely affects hair follicle activity resulting in thin dystrophic hair with miniaturization.[8]

Autoimmune etiology has been proposed on the basis of its association with various autoimmune diseases, the presence of autoantibodies, the presence of inflammatory lymphocytes around and within the affected hair follicles, and the ability to promote hair regrowth with the use of immunosuppressive agents.[9] There is increased susceptibility in individuals with HLA DQ3 and increased concordance in monozygotic twins and positive family history.[10] Thus, alopecia areata is considered as a hair follicle-specific autoimmune disease which is triggered by environmental factor in genetically susceptible individual.[8]

Vitamin D is a fat-soluble steroid prohormone mainly produced photochemically in the skin from 7 dehydrocholesterol. Vitamin D consists of two bioequivalent forms: Vitamin D2, also known as ergocalciferol, is obtained from dietary vegetable sources and oral supplements and Vitamin D3, also known as cholecalciferol, is obtained primarily from skin exposure to ultraviolet B (UVB) radiation in sunlight as well as ingestion of food sources.[11]

Vitamin D mediates its effect through vitamin D receptors, which are strongly expressed in the vital structures of hair follicles and its expression is necessary for the maintenance of normal hair cycle.[12] In the immune system, vitamin D suppresses dendritic cell maturation and antigen presentation. If vitamin D level is reduced, regulation of the immune system theoretically can be disrupted possibly by promoting an autoimmune process.[13]

Several studies suggest the role of Vitamin D in pathogenesis of AA and hence a possible role of Vitamin D supplementation in treatment.[1] So, this study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Dhaka to evaluate serum vitamin D level in patients with AA and its relationship with severity of the disease.

**Materials and Methods:**

This cross-sectional study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Dhaka from January 2019 to December 2019 after taking ethical clearance from Ethical Review Committee of Dhaka Medical College, Dhaka. The study was a hospital-based cross-sectional comparative study involving a series of 32 patients of AA (as Group A) and age and gender matched 32 non-alopecic subjects (as Group B). After fulfilling all inclusion and exclusion criteria, an informed consent was taken from all patients. Patients, who were pregnant and lactating, alcoholic, smoker were excluded. Patients with malignancy, diabetes mellitus, chronic kidney disease, parathyroid disorders, bone metabolic disorders, other autoimmune diseases, and who received therapeutic intervention that might influence vitamin D status including bisphosphonates, systemic corticosteroid, calcium supplements, phototherapy, antitubercular drugs and systemic biologics were also excluded. All

characteristics recorded on a standard proforma. Relevant history was taken regarding present illness, duration of the disease, onset, extension, family history. Then complete dermatological examination was done to ascertain the extent of involvement of the disease. Disease severity of each and every patient were measured by using the severity assessment tools namely the Severity of Alopecia Tool (SALT). The scalp was divided into four areas, namely: Vertex: 40% (0.4) of scalp surface area, Right profile of scalp: 18% (0.18) of scalp surface area, Left profile of scalp: 18% (0.18) of scalp surface area, Posterior aspect of scalp: 24% (0.24) of scalp surface area. Percentage of hair loss in any of these areas was multiplied by the percentage surface area of the scalp in that area. SALT score was the sum of the percentage of hair loss in all the above-mentioned areas. Subgrouping of patients into SALT subclasses was done as follows: Scalp (S): S0, no hair loss; S1, <25% hair loss; S2, 25–49% hair loss; S3, 50–74% hair loss; S4, 75–99% hair loss, and S5, 100% hair loss. Body hair loss was assessed as: B0, no body hair loss; B1, some body hair loss; and B2, 100% body (Excluding scalp) hair loss.

Blood samples were taken from subjects at Department of Biochemistry, BSMMU. Serum 25-hydroxyvitamin D was analyzed by the automated analyzer: Architect Plus ci4100. After collecting all data, association of serum vitamin D level with Alopecia areata was find out by statistical analyses. Statistical analyses were performed with SPSS (statistical package for social science) version 25.0. Continuous parameters were expressed as mean ± SD and com pared with unpaired student's t test or ANOVA test. Categorical parameters were expressed as frequency and percentage and compared by Chi-Square test. Correlation coefficient test was done by Pearson's correlation coefficient test. Statistical significance was set < 0.05 level at 95% confidence interval (CI).

**Results:**

The mean age of Group A was 30.56 ± 13.52 years and Group B was 34.97 ± 13.03 years. Majority of the study subjects were female both in Group A (72%) and Group B (66%).

**Table-I**

*Comparison of demographic and clinical characteristics of patients and healthy group*

| Variables | Group A (n=32) | Group B (n= 32) |
|---|---|---|
| Age (years) | | |
| Mean ± SD | 30.56 ± 13.52 years | 34.97 ± 13.03 years |
| Range | 14-65 | 15-57 |
| Gender | | |
| Female | 23 (72%) | 21 (66%) |
| Male | 9 (28%) | 11 (34%) |
| Duration of disease | | |
| Mean ± SD | 2.09±1.14 (years) | |
| Range | 3 months-7 years | |
| Pattern of AA | | |
| Single patch | 9 (28%) | |
| Multiple patches | 16 (50%) | |
| Alopecia Totalis | 3 (9%) | |
| Alopecia Universalis | 4 (13%) | |
| Site of involvement | | |
| Scalp | 26 (81%) | |
| Body hair | 1 (3%) | |
| Both Scalp and Body hair | 5 (16%) | |

**Table-II**

*Disease severity and extension according to SALT scoring (n=32)*

| SALT | Frequency | Percentage (%) |
|---|---|---|
| S1 (<25%) | 13 | 41% |
| S2 (25-49%) | 7 | 22% |
| S3 (50-74%) | 4 | 12% |
| S4 (75-99%) | 1 | 3% |
| S5 (100%) | 7 | 22% |

Table II showed According to SALT scoring severity of AA, maximum 13(41%) patients had severity S1 (<25%), 7 (22%) patients had S2 (25-49%), 4 (12%) patients had S3 (50-74%), 1 (3%) patient had S4 (75-99%) and 7 (22%) patients had S5 (100%).

**Table-III**

*Comparison of serum 25-Hydroxy vitamin D between two groups (N=64)*

| Serum Vit D level (ng/ml) | Group A(n=32) | Group B(n=32) | p value |
|---|---|---|---|
| Mean | 13.38 ± 7.36 | 23.16 ± 10.36 | 0.0004* |
| Range | 5.0 – 39.40 | 7.30 – 61.70 | |

*Student's t- test

Results were expressed by mean ± SD & percentage.

Table III showed mean of Serum Vit D level in Group A (n=32) is 13.38 ± 7.36 and mean of Serum Vit D level in Group B (n=32) is 23.16 ±10.36 which is statistically highly significant (p value < 0.0004).

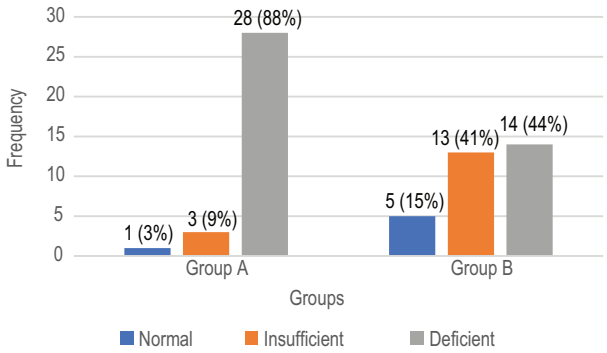


**Figure 1:** *Comparison of serum vitamin D between two groups (N=64)*

Figure 1 revealed deficient, insufficient and normal Vitamin D level among Group A vs Group B were (88% vs 44%), (9% vs 41%) and (3% vs 16%) respectively with significant difference (p-value 0.001) between the groups.

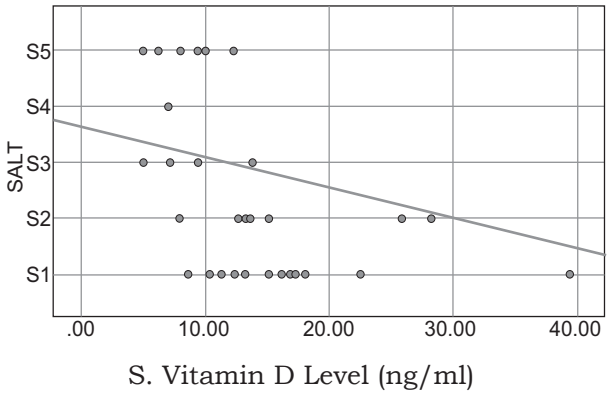


**Fig.-2:** *Correlation of serum vitamin D level with SALT score. (r=-.509, p=0.003)*

This Scatter diagram showed significant negative correlation (r=-.509, p=0.003) between serum vitamin D level (ng/ml) and SALT score.

**Discussion:**

In this study the mean age were 30.56 ± 13.52 years for case and 34.97 ± 13.03 years for control. This study included 71.9% female and 28.1% male in case and 65.6% female and 34.4% male in control. Both groups were age gender matched and male: female ratios were 2.5:1 in case and 1.9:1 in control. This result was consistent with the study of Ghafoor and Anwar (2017)[10]. Darwish et al. (2016) also found female predominance in their study.[7]

The present study showed mean duration of the disease is 2.09 ± 1.146 years. Study found that maximum patients 15(46.9%) had multiple alopecic patches followed by single AA patch 8(25.0%). 5(15.6%) patients had alopecia totalis and 4(12.5%) had A. Universalis. Ghafoor and Anwar (2017) in their study found highest patients with multiple pathches 15 (50%) followed by single patch in 6 (20%), a. Totalis in 4 (13.33%) and A. universalis in 2 (6.67%).

Area of highest involvement was scalp 26 (81.3%). Both scalp and body hair loss were involved in 5 (15.6%) and only body hair was involved 1 (3.1%). Dhillon (2013) found scalp to be affected in 38 (76%), beard 5 (10%) and total body hair 7 (14%).[14]

The present study measured the severity of alopecia areata in scalp of 32 patients by SALT scoring. Regarding severity of AA, maximum 13(41%) patients had severity S1(<25%), 7 (22%) patients had S2 (25-49%),4 (12%) patients had S3 (50-74% ), 1 (3%) patients had S4 (75-99%) and 7 (22%) patients had S5(100%).Ghafoor and Anwar (2017) found patients 4(13.33%) had S1

grade, 7 (23.33%) in S2 grade, 12 (40%) in S3, 1 (3.33%) in S4, and 6 (20%) cases in S5 grade.[10]

This study showed mean of Serum Vit D3 level in Group A (n=32) is 13.38 ± 7.36 ng/ml and mean of Serum Vit D3 level in Group B (n=32) is 23.16 ±10.36 ng/ml which is statistically highly significant (p value= 0.0004). In their study conducted in southern India, Siddappa, Kumar & Vivekananda (2019) found mean serum vitamin D level was significantly lower in cases as compared to controls (18.90 ± 8.32 vs 28.21 ± 18.32 ng/mL; p < 0.001).[13]

This study result was parallel to Attwa et al. (2016) who performed study on 23 patients with AA and 23 healthy controls to detect their serum 25(OH)D level in Egypt. This was also similar to study made by Bhat et al. (2017).[1] The mean serum 25(OH)D concentration of patients with AA was 16.6 ± 5.9 ng/ml, whereas in control group, the mean concentration was 25.49 ± 1.02. (p < 0.001).[1] On the other hand, Nassiri et al. (2013) and Erpolat et al (2017) differed with this result. They found no statistically significant difference in their study.[4,6] Lin et al. (2019 cited Erpolat et al. 2017) stated that this might be due to the uni-versal tendency toward lower values of 25(OH)D in their geographical area, and they noted that the blood samples were collected only once during the late fall and winter months.[17] Therefore, further studies are needed to confirm the association. There is a seasonal variation in vitamin D level and the effect of vitamin D deficiency on causation of AA seems to be associated mainly through its role in immune system regulation.[10]

This study showed deficient, insufficient and normal Vitamin D3 level among Group A vs Group B were (88% vs 44%), (9% vs 41%) and (3% vs 16%) respectively with significant difference (p-value 0.001) between the groups. In South Asia 80% of apparently healthy population is Vitamin D deficient and up to 40% of the population is severely deficient.[18]. Study showed that women in Bangladesh, were at risk of developing vitamin D deficiency, regardless of different age-groups, lifestyle and clothing.[19]

The study also showed that the mean serum vitamin D level was significantly associated with severity of alopecia areata (p=.041). Mean serum vitamin D level in S1 was 16.32 ± 7.86, S2 was 16.67 ± 7.43, S3 was 9.17 ± 4.33, S4 was 7.0, S5 was 7.98 ± 2.74. No relevant result or discussion was found elsewhere.

The study revealed statistically significant negative correlation (r=-.509, p=0.003) between serum vitamin D3 level (ng/ml) and SALT score. Such inverse correlation between serum vitamin D3 level and SALT score (p <0.05) also found by Siddappa, Kumar & Vivekananda (2018), Cerman et al. (2014), Mahamid et al. (2014), Attwa et al. (2016), Yilmaz et al. (2012), Bhat et al. (2017).[1,12,15,16,20,21] Cerman et al. (2014) reported a significant negative correlation between the degree of AA by (SALT) score and serum 25(OH)D level in AA patients (p <0.001)[20]. Conversely, D'Ovidio et al. (2013) found no correlation between the severity of AA and serum 25(OH)D level.[22] This may be because methodological data e.g. the scoring of AA was not available in this study.

Virtually all immune cells express the VDR, making them susceptible to 1,25(OH)2D3-mediated modulation. As autoimmune diseases are characterized by an overactive immune response, it seems logical that the beneficial effects of vitamin D on autoimmunity are due to effects on the immune system. [23] Promising results were obtained in a few clinical trials but there is still a lack of non-biased large-cohort studies that can sustain the proposed benefits of vitamin D supplementation for optimal immune function.[24]

**Limitations:**

Small sample size was selected from single tertiary center in Dhaka city, so that the results of the study may not reflect the exact picture of the country.

**Conclusion:**

Serum vitamin D level in patients with alopecia areata was significantly lower than in participants in the control group. There was a significant inverse correlation between level of serum vitamin D and severity of alopecia areata.

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