Original Research Article

Status of Serum Vitamin-D Level among the Patients with Alopecia Areata in a Tertiary Care Hospital, Bangladesh

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Abstract: *Background:* Alopecia areata is a common problem faced by many younger people, which has variety of risk factors. Vitamin D has emerged as a molecule with key role to play in various disorders. Recent evidences suggest inconsistent association between vitamin D deficiency and alopecia areata. We have very few research-oriented data regarding this issue. *Aim of the study*: The aim of this study was to assess the status of serum Vitamin-D level among the patients with alopecia areata. *Methods*: This was a prospective case control study which was conducted in the Department of Dermatology & Venereology, Anwer Khan Modern Medical College, Dhaka, Bangladesh during the period from January 2018 to December 2019. In total 30 patients with alopecia areata and 30 healthy people were finalized as the study population. Group of 30 alopecia areata (AA) was denoted as Group A (Case) and group of healthy people was denoted as Group B (Control). All patients were subjected to detailed history taking and examination to detect pattern, severity (SALT score) of AA. Blood samples were taken from all subjects to do complete blood count and to assess serum levels of vitamin-D3, random blood sugar, and calcium. All data were processed, analyzed and disseminated by MS Office and SPSS version 20 as per need. *Results:* The mean (±SD) vitamin level was found 8.63 ± 2.24 ng/mL among case group patients. On the other hand, it was found 30.26 ± 7.81 ng/mL among control group participants which was significantly higher than that of case group patients ($P<0.0001$). In analyzing the comparative status of Vitamin D level of several SALT score patients with control group we observed, in comparison with all the S1 patients, S2 patients, S3 patients and S4 patients the P values were found less than 0.0001. So, among all the above cases groups patients the level of vitamin D(ng/mL) were extremely significantly lower than that of control participants (In all comparison the P value were less than 0.0001). Besides among S5 patients, vitamin D level was also significantly lower than that of control group participants where P value was found 0.0002. *Conclusion*: Deficiency of vitamin D level is a potential factor of alopecia areata. Lower vitamin D levels were observed in patients with alopecia areata and significant inverse correlation exists between vitamin D levels and duration/severity of the disease. These findings may suggest a causal role of vitamin D deficiency in the pathogenesis and therapeutic role of vitamin D supplementation in the management of alopecia areata.
Keywords: Vitamin-D, Alopecia areata, Hair loss, SALT score.

I. INTRODUCTION

Hair loss which is known as 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% [1]. 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 [2]. There is also an increased overall risk of other autoimmune disorders in patients of alopecia areata [3]. Vitamin D is an important sec steroid hormone which is vital for maintenance of calcium homeostasis, immune regulation, and cell growth and differentiation [4]. 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 mcrophages [5]. 25-dihydroxyvitamin D plays an important role in the development of hair follicle and regulation of hair cycle via the Vitamin D receptors (VDR) expressed in dermal papillae and in the epidermis of the hair follicles [6]. Studies have proposed a connection between few autoimmune diseases and Vitamin D deficiency, suggesting Vitamin D deficiency might be an environmental stimulus for induction of autoimmunity [7]. Vitamin D is synthesized in the epidermal keratinocytes under effect of UV-B lights (290-315 nm) or ingested in diet and dietary supplements [8]. Vitamin D was found to have immune-regulatory effects. 1,25-Dihydroxy Vitamin D3 (1,25(OH)2 D3) which is the active form of Vitamin D, is one of the regulators of both innate and adaptive immune responses as it modulates immune functions and activities of both T-lymphocytes and B-lymphocytes [9]. Vita- min D receptors (VDR) expression in epidermal keratinocytes and the mesenchymal dermal papilla cells were detected [10]. Expression of the VDR in keratinocytes is necessary for preservation of the normal hair cycle [11]. Lack of the VDR is related with reduced epidermal differentiation and hair follicle growth. In addition, patients with 1, 25(OH) 2 D3-resistant rickets type II and VDR knockout mice exhibit phenotypes that include AT [12]. Assessment of Vitamin D level is not based on measurement of serum 1, 25 (OH) 2 D3 serum levels as they are relatively low and firmly regulated. Vitamin D status is evaluated by measurement of 25-hydroxy Vitamin (25(OH) D, which is an indicator of supply rather than function. It is the most stable and plentiful metabolite of Vitamin D in human serum and has a half-life of about 3 weeks, making it the most suitable indicator of the Vitamin D status [13].

Patients with AA showed significantly lower concentrations of both 25(OH) D and 1, 25(OH) 2 D3 with higher mean values of parathyroid hormone (PTH) than controls [14]. In addition, Vitamin D supplementation might have a preventive role in human autoimmune diseases such as AA [15].

II OBJECTIVES

General Objective
- To assess the status of serum Vitamin-D level among the patients with alopecia areata (Hair loss).

Specific Objective
- To collect information regarding the demographic status of patients with alopecia areata.
- To collect information regarding the disease duration of patients with alopecia areata.
- To collect information regarding the pattern of hair loss among patients with alopecia areata.
- To collect information regarding the comparative status of Vitamin. D level of several SALT score patients.

III METHODOLOGY & MATERIALS

This was a prospective case control study which was conducted in the Department of Dermatology & Venereology, Anwer Khan Modern Medical College, Dhaka, Bangladesh during the period from January 2018 to December 2019. In total 30 patients with alopecia areata attended to the hospital and 30 healthy people were finalized as the study population. Group of 30 alopecia areata (AA) was denoted as Group A (Case) and group of healthy people was denoted as Group B (control). All patients were subjected to detailed history taking and examination to detect pattern, severity (SALT score) of AA. Blood samples were taken from all subjects to do complete blood count and to assess serum levels of Vitamin-D3, random blood sugar, and calcium. This work was designed as prospective case control study and was approved by the ethical committee of the mentioned hospital. Informed written consents were obtained from all participants. According to the inclusion criteria patients with any type of AA not receiving any treatment for AA for at least 6 months were included in the study. On the other hand, according to the exclusion criteria patients taking Vitamin D supplementation, iron preparations, Vitamin B, folic acid or calcium (Ca) supplementations in the last 6 months, treated with topical vitamin D analog, with known to have a state of Vitamin D deficiency and with any associated disease that alter the blood 25 (OH) D level as vitiligo, psoriasis, SLE, renal disease, liver disease, cancers and autoimmune diseases

were excluded from this study. All participants were subjected to the full history taking, general examination to exclude associated systemic diseases that may affect the blood Vitamin D level, dermatological examination including skin, hair, nail and oral mucosa and clinical assessment of the degree of AA. The extent of scalp hair loss was determined by dividing the scalp into 4 quadrants and visually determining the percentage of scalp hair loss in each quadrant then adding the numbers together with a maximum score of 100%. This was determined according to the Severity of Alopecia Tool or SALT score [16]. It included assessment of scalp hair loss (S), Body hair loss (B) and Nail involvement (N). According to the SALT score scalp hair loss (S) were graded as: 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 (B) was graded as: B0 = No body hair loss, B1 = some body hair loss and B2 = 100% body (excluding scalp) hair loss. Nail involvement (N) were graded as: N0 = No nail involvement, N1 = some nail involvement and N2=20 nail dystrophy involvement.

Pattern of scalp hair loss were graded as: Patchy, Ophiasis and Totalis (100% scalp hair loss). Severity of hair loss were graded as, 'Mild AA': patients who showed <25% hair loss according to SALT score, 'Moderate AA': patients who showed 25-49% hair loss according to SALT score and 'Sever AA': patients who showed >50% hair loss according to SALT score, and they were 13 patients. All data were processed, analyzed and disseminated by MS Office and SPSS version 20.0 as per need.

IV. RESULT

In this study the mean (±SD) age of case group and control group patients were 27.67± 4.25 and 23.36 ± 3.94 years respectively. In group A (Case) 60% participants were male whereas 40% were female. On the other hand, in group B (Control)

3.330% participants were male whereas 36.67% were female. Among 30 case group patients 33% suffered from hair loss for less than 6 months' period of time whereas 67% suffered for more than 6 months period of time. In analyzing the patterns of hair loss among the case group participants we observed the highest number of patients were with patchy hair loss which was in 64%. Then 23% and 13% patients were with ophiasis and totalis types of hair loss respectively. In this study among patients with alopecia areata (hair loss, n=30) according to the SALT score the highest number of patients were with S1 score which was in 36.67%. Then 26.67%, 16.67%, 13.33% and 6.67% were with S2, S3, S4 and S5 SALT score respectively. In this current study the mean (±SD) vitamin level was found 8.63 ± 2.24 ng/mL among case group patients. On the other hand, it was found 30.26±7.81 ng/mL among control group participants which was significantly higher than that of case group patients (P<0.0001). In analyzing the comparative status of Vitamin D level of several SALT score patients with control group we observed, in comparison with all the S1 Patients, S2 Patients, S3 Patients and S4 Patients the P values were found less than 0.0001. So, among all the above cases groups patients the level of vitamin D (ng/mL) were extremely significantly lower than that of control participants (In all comparison the P value were less than 0.0001). Besides among S5 patients, vitamin D level was also significantly lower than that of control group participants where P value was found 0.0002.

Table-I: Demographic status of participants (N=60)

Variables	Group A (n=30)	Group B (n=30)
Age (years)		
Age (Mean ±SD)	27.67± 4.25	23.36 ± 3.94
Gender		
Males	18 (60.0)	19 (63.33)
Females	16 (40.0)	11 (36.67)
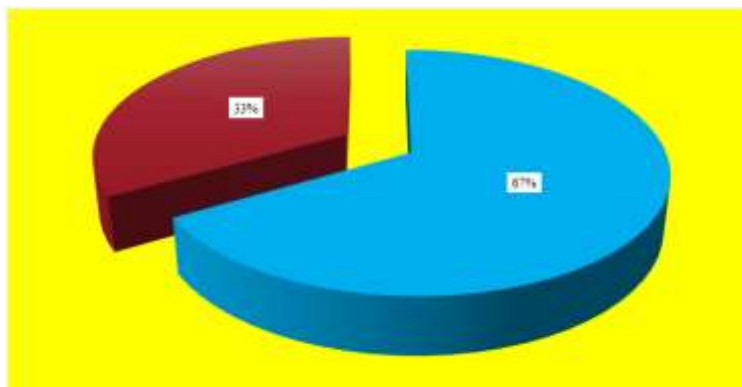
Fig-1: Distribution of disease duration among case group participants (n=30)
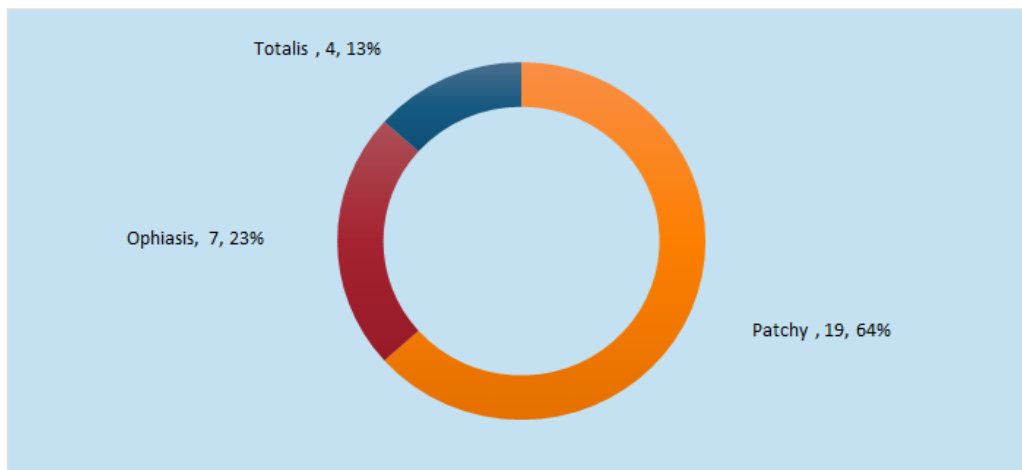
Fig-2: Distribution of pattern of hair loss among case group participants (n=30)

Table-II: SALT score distribution among case group participants (n=30)

SALT score		
S1	11	36.67
S2	8	26.67
S3	5	16.67
S4	4	13.33
S5	2	6.67

Table-III: Comparative status of Vitamin D level between case & control group (n=30)

Vitamin D Level	Case	Control	P- Value
	Mean ± SD	Mean ± SD	
Serum Vitamin D (ng/mL)	8.63 ± 2.24	30.26 ± 7.81	<0.0001

Table-IV: Comparative status of Vitamin D level of several SALT score patients with control group

Patient's SALT scores	Serum Vitamin D (ng/mL)		P- Value
	Case	Control	
S1 Patients	9.91 ± 3.34	30.26 ± 7.81	<0.0001
S2 Patients	9.75 ± 3.18	30.26 ± 7.81	<0.0001
S3 Patients	7.41 ± 2.96	30.26 ± 7.81	<0.0001
S4 Patients	6.76 ± 2.11	30.26 ± 7.81	<0.0001
S5 Patients	6.47 ± 2.09	30.26 ± 7.81	0.0002

V. DISCUSSION

The aim of this study was to assess the status of serum Vitamin-D level among the patients with alopecia areata. Alopecia areata (AA) is autoimmune disease characterized by T-cell infiltrates and cytokine production around anagen-stage hair follicles [17]. CD8+T cells act as the effector cells with help from CD4+T cells and a defect in regulatory/suppressor CD4+/CD25+ cells can explain the autoaggression of the disease [18]. The disease is known to occur with various autoimmune disorders, such as rheumatoid arthritis (RA), type I diabetes mellitus (DM), vitiligo, systemic lupus erythematosus (SLE), thyroiditis, pemphigus vulgaris (PV), pernicious anemia and celiac disease [19]. A connection between some autoimmune diseases, including type I DM, RA, SLE, vitiligo,

psoriasis, multiple sclerosis (MS), inflammatory bowel disease (IBD), and Vitamin D deficiency has been reported [20]. This finding suggests that vitamin D deficiency might be an environmental trigger for the induction of autoimmunity [21]. Vitamin D inhibits the synthesis of dendritic cells which in turn reduces the activation of T-cells and the T-cells mediated immune response. Vitamin D, also acts on T-cells themselves, regulating the differentiation and initiation of TH1 and TH2. It inhibits Th1 cells which produce interferon- and interleukin (IL)-2 and activates macrophages, and TH17 cells which produce IL17 and IL22 [22]. In this current study the mean (±SD) Vitamin level was found 8.63±2.24 ng/mL among case group patients. On the other hand, it was found 30.26 ± 7.81 ng/mL among control group participants which was

significantly higher than that of case group patients (P<0.0001). In our study, in analyzing the comparative status of Vitamin D level of several SALT score patients with control group we observed, in comparison with all the S1 Patients, S2 Patients, S3 Patients and S4 Patients the P values were found less than 0.0001. So, among all the above cases groups patients the level of Vitamin D (ng/mL) were extremely significantly lower than that of control participants (In all comparison the P value were less than 0.0001). Besides among S5 patients, vitamin D level was also significantly lower than that of control group participants where P value was found 0.0002. In contrary to our results, other studies reported that serum level of vitamin D were lower in female AA patients and controls, they explained this by the limited exposure of females to sunlight due to religious and social concerns [23, 24]. In this study, in analyzing the patterns of hair loss among the case group participants we observed the highest number of patients were with patchy hair loss which was in 64%. Then 23% and 13% patients were with ophiasis and totalis types of hair loss respectively. In this study among patients with alopecia areata (hair loss, n=30) according to the SALT score the highest number of patients were with S1 score which was in 36.67%. Then 26.67%, 16.67%, 13.33% and 6.67% were with S2, S3, S4 and S5 SALT score respectively. Another study also found no significant differences among the patients with different patterns of hair loss and their serum concentrations of 25(OH) D [23]. In the contrary a recent study by Cerman *et al*. [24] found a significant inverse correlation between low 25(OH) D levels and severity of AA according to SALT scores.

Limitations of the study

This was a single centered study with a small sized sample. So, the findings of this study may not reflect the exact scenario of the whole country.

VI. CONCLUSION AND RECOMMENDATIONS

Deficiency of Vitamin D level is a potential factor of alopecia areata. Lower Vitamin D levels were observed in patients with alopecia areata and significant inverse correlation exists between Vitamin D levels and duration/severity of the disease. These findings may suggest a causal role of Vitamin D deficiency in the pathogenesis and therapeutic role of Vitamin D supplementation in the management of alopecia areata. For getting more reliable information we would like to recommend for conducting more studies in several places with larger sample size.

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