ORIGINAL ARTICLE

Vitamin D Deficiency in Alopecia Areata

Rabia Ghafoor[1] and Muhammad Irfan Anwar[2]

Abstract

Objective: To compare the mean Vitamin D level in patients with alopecia areata (AA) with age and gender controlled matched healthy controls.

Study Design: Case-control study.

Place and Duration of Study: Dermatology OPD, JPMC, from October 2014 to March 2015.

Methodology: All the patients diagnosed of alopecia areata by a trained dermatologist were selected. Controls were age and gender matched healthy volunteers. Venous blood was drawn and sent to hospital laboratory for 25 (OH) vitamin D by enzyme immunoassay method on chemical analyser. Data was recorded on SPSS version 16. Mann-Whitney test was applied to compare vitamin D levels of cases and controls. P-value <0.05 was taken as significant.

Results: There are 30 cases of AA, and 30 age and gender matched controls. The mean age of our study group was 23.77 ±8.86 ng/dL in patients and 24.03 ±8.62 ng/dL in the control group. Fifteen (50%) patients presented between 3-12 months of onset of AA. Median (IQR) vitamin D level of cases was 13.5 (18.6) ng/dL and healthy controls was 22.5 (16.25) (p=0.001).

Conclusion: Serum Vitamin D levels were significantly lower in patients with alopecia areata compared to healthy controls.

Key Words: *Alopecia areata. Vitamin D deficiency. Vitamin D receptor.*

INTRODUCTION

Alopecia areata (AA) is an autoimmune disease affecting hair follicle causing non-scarring alopecia with incidence of 0.1 - 0.2%.[1] It can affect any hair bearing area; scalp, beard and body hair, causing mainly psychological morbidity.[2] Aetiology is unknown. Genetic and environmental factors are involved in its pathogenesis. There is increased susceptibility in individuals with HLA DQ3, increased concordance in monozygotic twins and positive family history. Histologically, peribulbar lymphocytic infiltrate predominantly composed of TH_1 cells is seen with high CD4 to CD8 ratio.[3] There is 16% increased life time risk of other autoimmune diseases like vitiligo, autoimmune thyroiditis, systemic lupus erythematosus (SLE) and lichen planus in patients with AA.[4] Recently, increased seasonality of autoimmune and diseases was noticed which is attributed to vitamin D deficiency.[5] Vitamin D is a secosteroid hormone involved primarily in maintaining calcium homeostasis and bone health. It is obtained from diet and also synthesized from skin under UV radiation. Its role in immune system regulation has been extensively studied. It has a role in both innate and adaptive immune response. Vitamin D deficiency predispose the patient to infections like influenza and mycoplasma pneumonia and to autoimmune diseases. The immunomodulatory action of Vitamin D is mediated via VDR (vitamin D receptors) present in cytosol and affect cytokine and chemokine production. The vitamin D deficiency causes loss of self tolerance and predispose individual to autoimmune diseases.[6]

Vitamin D deficiency was more common in autoimmune skin diseases like psoriatic patients and in vitiligo.[7] Only few studies have been done to find out association of vitamin D deficiency with AA.

The aim of present study was to compare the mean of Vitamin D level of alopecia areata patients to age and gender controlled matched healthy controls.

METHODOLOGY

This case control study was conducted in Dermatology Department of JPMC, from October 2014 to March 2015, after approval from the Ethical Review Committee of the Hospital. Sampling technique was non-probability purposive sampling. All the patients diagnosed of AA by a trained dermatologist meeting inclusion and exclusion criteria were selected for study. Controls were taken from healthy volunteers and patients coming to dermatology department for other disorders like acne, melasma etc. Those patients who have taken systemic steroids, calcium and vitamin D supplementations, bisphosphonates, immunosuppressive agents, received phototherapy during last one year, pregnant and lactating women, have autoimmune disorders, sarcoidosis,

[1] *Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi.*

[2] *Department of Dermatology, PNS Shifa, Karachi.*

Correspondence: Dr. Rabia Ghafoor, Assistant Professor, Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi.

E-mail: rabiaghafoordr@gmail.com

Received: October 29, 2015; Accepted: April 26, 2017.

renal disease, malignancy and malabsorption were excluded from study. After written informed consent, demographic data, history of disease, family history and history of atopy was taken. Pattern of hair loss as unifocal, multifocal, ophiasis, alopecia totalis and alopecia universalis was noted. Severity of alopecia tool (SALT) score was calculated for disease severity,[8] and recorded as S0, S1, S2, S3, S4 and S5. Five ml of venous blood was drawn and sent to hospital laboratory for 25 (OH) vitamin D by enzyme immunoassay method on chemical analyser by Hitachi (Roshe). Vitamin deficiency was defined as <20 ng/dl, insufficiency as 21-29 ng/dl and sufficiency as 30 ng/dl.

Data was recorded on SPSS version 16. Mean ±SD was calculated for continuous variables like age, number of patches and median with interquartile value for vitamin D levels. Non-parametric variables were checked by Kolmogorvsmirnov or Shapiro Wilks test. Frequencies and percentages were calculated for categorical variables like family history of disease, atopy, SALT score, duration of disease, and pattern of alopecia.

Table I: Clinical and demographic profile of patients.

	Diseased group N=30	Healthy controls N=30
Age (years)		
Mean ±SD	23.77 ±8.86	24.03 ±8.62
Min-max	15 - 45 years	15 - 45 years
Gender		
Male	12 (40%)	12 (40%)
Female	18 (60%)	18 (60%)
Duration of disease		
<3 months	3 (0.9%)	
3-12 months	10 (33.3%)	
12-24 months	6 (20%)	
2-5 years	6 (20%)	
>5 years	5 (16.66%)	
Total	30	
Pattern of alopecia		
Unifocal	6 (20%)	
Multifocal	15 (50%)	
Oophiasis	3 (0.9%)	
Alopecia universalis	2 (6.67%)	
Alopecia totalis	4 (13.33%)	
Total	30	
SALT score		
S1	4 (13.33%)	
S2	7 (23.33%)	
S3	12 (40%)	
S4	1 (3.33%)	
S5	6 (20%)	
Total	30	
Family history of disease		
Yes	8 (26.67%)	2 (6.67%)
No	22 (73.33%)	28 (93.33%)
Family history of atopy		
Yes	6 (20%)	4 (13.3%)
No	24 (80%)	26 (86.66%)

Mann-Whitney test was applied to compare median vitamin D levels of cases and controls. P-value <0.05 was taken as significant.

RESULTS

There were 30 cases of AA, and 30 age and gender matched healthy controls. Demographic and clinical profile is shown in Table I. The mean age was 23.77 ±8.86 years in patients, and 24.03 ±8.62 years in control group. There were 12 (40%) males and 18 (60%) females in each group. Stratification of patients was done according to duration of disease. Fifteen (50%) patients presented between 3-12 months of onset of AA. The most common pattern of AA was multifocal (>2 patches) which was seen in 15 (50%) of patients. Nail pitting was seen in 10 (33.3%) patients and none in controls. Severity of AA (SALT score) was calculated and shown in Table I.

Median (IQR) vitamin D level was 13.5 (18.6) ng/dL in cases, and 22.5 (16.25) nd/dL in controls. P-value was 0.001 which was statistically significant. Stratification of mean vitamin D levels were also calculated in patients having same SALT score (S1-S5). It was noted that vitamin D levels were lower in patients with higher SALT score, i.e. 24 ng/dl in S1 as compared to 8 ng/dl in S5.

DISCUSSION

Alopecia areata is a disease of young age and more common in females. In the present study, mean age of the study group was 23.77 ±8.86 years in the patients, and 24.03 ±8.62 years in the control group, which is similar to other studies.[4] Multifocal alopecia consisting of 2 or more patches is the most common type of AA in these patients. Most of the patients presented within one year of onset of symptoms. Family history of disease was positive in 8 patients as compared to only two healthy individuals. Family history of atopy was also found in higher number of AA patients than healthy controls.

This study showed that mean vitamin D levels were lower in patients of AA as compared to healthy controls; this difference was statistically significant (p-value <0.05). More severe deficiency of vitamin D was seen in more severe AA.[8-10] The seasonal variation in vitamin D levels is well established.[8] All the patients and controls were taken from same timeframe, i.e. from October to March. Patients taking agents which may affect calcium homeostasis were excluded and so were the patients suffering from the diseases which are known to have such associations with vitamin D and hypercalcemia.

Role of vitamin D in differentiation and function of keratinocytes is also a well known fact. Vitamin D receptors (VDR) are present in stem cells in bulge region of hair follicle and play an important role in hair cycle.[8,11] 1,25 dihydroxyvitamin D3 exerts its effect after binding to

VDRs which regulates the expression of vitamin D responsive genes; therefore, it controls the differentiation of keratinocytes and regulates hair follicle cell cycle.[12] There is increased incidence of AA in VDR receptor-knocked-out mice and hereditary vitamin D resistant rickets.[13] Calcipotriol, a vitamin D3 analogue, has been successfully used to treat alopecia associated with chemotherapeutic agents.[14] Few studies also show its effectiveness in AA.[15] However, studies conducted to detect VDR gene polymorphism and occurrence of AA failed to establish such an association.[16]

The effect of vitamin D deficiency on causation of AA seems to be associated mainly through its role in immune system regulation. Vitamin D causes shift of TH1 immune response to TH2 response. It also suppresses proinflammatory TH17 response, therefore decreasing the production of proinflammatory cytokines (IL-17 and IL-21). It may also suppress B cell proliferation. Therefore, vitamin D deficiency leads to loss of self-tolerance. AA is mainly TH1 response mediated disease, therefore vitamin D deficiency may play a causative role.[17] Studies have shown that vitamin D deficiency was more common in psoriatic patients and in vitiligo.[18] Another study has shown that disease severity of rheumatoid arthritis correlates with vitamin D deficiency.[19] Vitamin D replacement has improved SLE in another study.[19]

D' Ovidio showed seasonal variation in the new onset or relapse of AA; a high relapse rate was noted at the end of winter season corresponding to low vitamin D level in this season.[20] Vitamin D levels in this study groups (both patients and controls) were also found to be lower which may indicate vitamin D deficiency in general population. This may be due to inadequate dietary intake, period of sampling in winter season or genetic predisposition to vitamin D deficiency.

There are certain potential limitations of this study like small sample size, but it may be regarded as an index study. More studies on this subject with larger cohorts are certainly warranted. Secondly, patients may be followed up after replacement of vitamin D for their severity scores.

CONCLUSION

AA may be associated with vitamin D deficiency as mean levels of vitamin D of patients were found to be significantly lower than normal healthy controls.

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