

Comparing The Plasma Level Of Vitamin D In Patients With Tinea Versicolor And Healthy Individuals

Arash Pour Mohammad¹, Fatemeh Goodarzi², Mohammadreza Ghassemi^{3*}

¹Medical Student, Student Research Committee, Faculty of Medicine, Iran University of Medical Sciences (IUMS), Tehran, Iran.

²Faculty of Medicine, Iran University of Medical Sciences (IUMS), Tehran, Iran

^{3*}Department of Dermatology, Rasoul Akram Hospital, Iran University of Medical Sciences (IUMS), Tehran, Iran

^{3*}ghassemi.mr@iums.ac.ir

Abstract:

Introduction: The critical roles of vitamin D on regulation of immune system and protection of antimicrobial pathways have been revealed; however the protective role of this vital element in protecting body against fungal infections remains uncertain. The present study aimed to compare plasma level of vitamin D in patients with Tinea versicolor and healthy individuals.

Methods: This case-control study was conducted on 40 patients with the diagnosis of Tinea versicolor who referred to clinic of dermatology of Rasoul Akram hospital in Tehran between 2016 and 2017. Also, 40 healthy individuals were included as the control. The plasma level of vitamin D was measured by the ELISA technique in both groups.

Results: This study showed different frequency of vitamin D3 deficiency between two groups that this different was significant ($P = 0.030$). This means that frequency of vitamin D deficiency in Tinea versicolor group was higher than control group distribution but the mean plasma level of vitamin D was 17.77 in the group with Tinea versicolor and 21.93 in control group without a significant difference ($p = 0.152$). Using the multivariable linear regression model and with the presence of baseline variables, no difference was finally revealed in plasma level of vitamin D between those with Tinea versicolor and the healthy individuals ($p = 0.164$).

Conclusion: Vitamin D deficiency may not have a critical role in pathogenesis of Tinea versicolor.

Keywords: Vitamin D, Tinea Versicolor, Malassezia Species.

1. INTRODUCTION

Tinea versicolor is a benign skin fungal infection caused by a lipophilic *Malassezia species* which characterized by hyperpigmented or hypopigmented patches or macules on different areas of body, usually on the trunk, back and chest [1-3]. Both genetic and environmental factors (particularly warm and humid geographic conditions) predispose the affected patients to pathological feature of Tinea versicolor. Along with these two predisposing conditions, some other factors have been suggested to susceptible the individuals to this disorder such as that event led to immunosuppression, vital nutrients deficiency, and some metabolic condition. In this regard, the presence of diabetes mellitus, using corticosteroids or immunosuppressive medications, Cushing disease, and vitamins deficiency have been shown to increase the likelihood of this skin disease [4-6].

The critical roles of vitamin D on regulation of immune system and protection of antimicrobial pathways have been revealed [7, 8]. . Even, its protective role against viral and fungal species has been indicated. This vitamin has also a definitive anti-inflammatory role leading inhibition of pathways leading tissues destruction by infective conditions[9, 10]. Thus, lowering the level of vitamin D may predispose people to increase the risk for microbial disorders especially opportunistic

fungal infections [11-13]. In this regard, the protective role of this vital element in protecting body against fungal infections remains uncertain.

Because the main pathophysiological mechanisms of occurring fungal infections include immunosuppression as well as inflammatory systems activation and due to critical role of vitamin D as an anti-inflammatory and immunosupportive nutrient, we now hypothesized that some fungal infections such as Tinea versicolor may be linked to reducing the level or function of vitamin D. Hence, the present study was performed to test the hypothesis that the presence of Tinea versicolor may be associated with vitamin D deficiency.

2. MATERIALS AND METHODS

Study Design

This case-control study was conducted on patients with the diagnosis of Tinea versicolor who referred to clinic of dermatology of Rasoul Akram hospital in Tehran between 2016 and 2017. The exclusion criteria were history of corticosteroid use during the last month, history of using calcium or vitamin D supplements during the last month, history of receiving oral contraceptives, suffering simultaneous cutaneous disorders, or history of chronic hepatic or renal diseases. Eighty persons participated in this study in two groups (n = 40 for each group): The case group patients who suffered Tinea versicolor and the sex and age-matched control group. The control group included healthy individuals who went to the hospital for cosmetic procedures and did not meet the exclusion criteria.

Data Collection

To confirm or rule out the Tinea versicolor, all subjects were examined by a dermatologist in the clinic. After receiving written informed consent, a fasting blood sample (5cc of blood) was extracted from cubital vein in both groups to determine the serum level of vitamin D. The samples were first centrifuged at 3000g for 10 minutes and at temperature of 4°C and then the isolated plasma were transferred into -80 °C till the time of bio-analysis. Baseline information including demographic characteristics, laboratory results, medical history and history of medications were collected by interviewing. Data were recorded in a pre-designed information form and finally entered for statistical analysis.

Biochemical Assessment

The plasma level of vitamin D was measured by the ELISA (enzyme-linked immunosorbent assay) technique. When the vitamin D₃ serum level is higher than 30 ng/ml, it is defined as a normal level of vitamin D. Also, 20 ng/ml to 29 ng/ml level of vitamin D₃ was categorized as insufficient, 10 ng/ml to 19 ng/ml as moderately deficient and less than 10 ng/ml as severely deficient (18). The study endpoint was to compare the level of vitamin D between the case and control group adjusting for baseline variables.

Statistical Analysis

Results were presented as mean \pm standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with t test or Mann-Whitney U test. For the statistical analysis, the statistical software SPSS version 22.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

3. RESULTS

The results showed that 55% of Tinea versicolor group were female and the mean age of patients was 34.75 and in the control group, 50% were female and the mean age was 39.53 years. No significant difference was observed in terms of demographic variables.

As shown in Table 1, the two groups were similar in gender, mean age, mean body mass index, marital status and history of smoking.

Table 1: Comparing baseline characteristics between the case and control groups

Variable		Tinea versicolor group (n = 40)	Healthy people group (n = 40)	P-value
Gender	Male	18 (45.0)	20 (50.0)	0.654
	Female	22 (55.0)	20 (50.0)	
Age, year		34.75 ± 12.81	39.53 ± 23.59	0.264
BMI, kg/m ²		25.36 ± 4.60	25.09 ± 5.79	0.821
Marital status	Single	21 (52.5)	21 (52.5)	1.000
	Married	19 (47.5)	19 (47.5)	
History of smoking		4 (10.0)	3 (7.5)	0.999

The difference in plasma level of vitamin D between the case and control groups were completely independent to baseline characteristics as indicated in Table 2.

No significant relationship was observed between vitamin D levels and demographic variables. The plasma level of vitamin D was 17.77 ± 8.32 in the group with Tinea versicolor and 21.93 ± 14.23 in control group without a significant difference (p = 0.152).

Table 2: The difference in plasma level of vitamin D considering each baseline variables

Variable	Tinea versicolor group (n = 40)	Healthy people group (n = 40)	P-value
Gender			
Male	17.16 ± 11.83	20.97 ± 14.35	0.381
Female	18.27 ± 11.14	22.89 ± 14.41	0.250
Age group			
≤ 40 years	16.08 ± 9.53	17.88 ± 9.95	0.503
> 40 years	21.29 ± 14.14	29.44 ± 17.97	0.205
BMI group			
< 30 kg/m ²	17.80 ± 11.65	21.55 ± 14.54	0.240
≥ 30 kg/m ²	17.58 ± 10.20	25.33 ± 12.14	0.306
Cigarette smoking			
Yes	18.36 ± 11.74	22.22 ± 14.62	0.218
No	12.48 ± 14.20	18.30 ± 8.82	0.290
Vitamin.D level	17.77 ± 8.32	21.93 ± 14.23	0.152

Using the multivariable linear regression model and with the presence of baseline variables (Table 3), no difference was finally revealed in plasma level of vitamin D between those with Tinea versicolor and the healthy individuals (beta = 4.085, standard error = 2.907, p = 0.164).

Table 3: Multivariable linear regression model to determine difference in vitamin D level between case and control groups

	Unstandardized Coefficients		Standardized Coefficients	t	P-value
	B	Std. Error	Beta		
(Constant)	12.680	10.214		1.241	.219
group	4.085	2.907	.158	1.406	.164
sex	-3.385	3.117	-.131	-1.086	.281
age	.133	.146	.136	.907	.367
BMI	-.150	.370	-.051	-.406	.686

marriage	5.096	3.836	.197	1.328	.188
cigarette	-9.997	5.495	-.223	-1.819	.073

R² = 0.127

Chi-square test was used to compare the distribution frequency of vitamin D3 deficiency between two groups. The difference was significant (P = 0.030). The percentages of vitamin D3 levels less than 10 ng/ml were 42.5% in the Tinea versicolor and 20% in the control groups. Also, percentages of vitamin D3 levels in the range of 10 - 30 ng/ml within the Tinea group and control group were 32.5% and 57.5% respectively (Table 4).

Table 4: Frequency of vitamin D3 between case and control groups

		Vitamin D level (ng/ml)			Total
		< 10	10 - 30	> 30	
Tinea group	N	17	13	10	40
	%	42.5	32.5	25	100
Control group	N	8	23	9	40
	%	20	57.5	22.5	100
Total	N	25	36	19	80
	%	31.25	45	23.75	100

4. DISCUSSION

The present study showed different frequency of vitamin D3 deficiency between two groups that this difference was significant. This means that frequency of vitamin D deficiency in Tinea versicolor group was higher than control group distribution.

The basic pathophysiology of Tinea versicolor remains already unknown. Along with concomitant effects of genetic and environmental factors on increasing incidence of the disease, the effective role of other factors including inflammatory processes, immunosuppressive conditions, and malnutrition on occurring or extension of the disease has been recently evidenced. In recent years, it has been also suggested that the use of vitamin supplements as anti-inflammatory agents (Especially on skin health) or antioxidants may improve disease symptoms [14-17]. The antimicrobial and anti-inflammatory effects of vitamin D has been recently proposed. Its protective role against viral and fungal infections has been also shown in some studies. In this regard, we hypothesized that the level of vitamin D might be reduced in patients with fungal infections such as those who suffered Tinea versicolor.

The findings of our study showed that the frequency of vitamin D deficiency in patients with tinea versicolor was higher than healthy individuals, but the mean plasma levels of vitamin D were not significantly different between the two groups. Also, the plasma levels of vitamin D had no significant relationship with the studied variables. As a result it can be expressed that vitamin D deficiency may not have a central role in pathogenesis of Tinea versicolor. Therefore, it is not expected to improve disease symptoms by administering vitamin D supplement.

Although active metabolites of this vitamin have a regulatory role in a collection of the genes that regulate proliferation of keratinocytes[18]., but in our study this role was not revealed in relation to the pathophysiological process of Tinea versicolor. Moreover, although vitamin D is an important modulator for immune system leading regulation of antimicrobial resistance this role remains doubtful in relation to *Malassezia species* [19-23].

Studies have shown the effect of vitamin D on various skin diseases [24, 25]. A 2016 study by Matozi et al. Showed that vitamin D had a positive effect on lymphocytes in patients with psoriasis, but it was an autoimmune disease and not a fungal disease[26].

In general, the present study shows that vitamin D levels were not significantly different between the two groups, but the number of people with vitamin D deficiency was higher in Tinea versicolor group. This suggests that further studies should focus on more samples and differences in disease severity in people with vitamin D deficiency.

5. CONCLUSION

An important result of the present study was the frequent differences between the two groups in different levels of vitamin D. The number of people in the moderately deficient vitamin D in Tinea versicolor group was almost twice that of the healthy group. But the mean plasma levels of vitamin D in the two groups were not significantly different from each other. Vitamin D levels were also not associated with demographic variables. The present findings show that the need to pay attention to serum levels of vitamin D is important in patients with Tinea versicolor, but the main problem of them is not vitamin D deficiency.

6. ACKNOWLEDGEMENT

The authors would like to thank the Rasoul Akram Hospital Clinical Research Development Center (RCRDC) for its technical and editorial assist.

7. REFERENCES

- [1] Crespo-Erchiga V, Florencio VD. Malassezia yeasts and pityriasis versicolor. *Current opinion in infectious diseases*. 2006; 19(2): 139-147.
- [2] Gaitanis G, Velegriaki A, Alexopoulos E, Chasapi V, Tsigonia A, Katsambas A. Distribution of Malassezia species in pityriasis versicolor and seborrhoeic dermatitis in Greece. Typing of the major pityriasis versicolor isolate *M. globosa*. *British Journal of Dermatology*. 2006; 154(5): 854-859.
- [3] Morishita N, Sei Y, Sugita T. Molecular analysis of Malassezia microflora from patients with pityriasis versicolor. *Mycopathologia*. 2006; 161(2): 61-65.
- [4] Burkhart C, Dvorak N, Stockard H. An unusual case of tinea versicolor in an immunosuppressed patient. *Cutis*. 1981; 27(1): 56-58.
- [5] Güleç AT, Demirbilek M, Seçkin D, Can F, Saray Y, Sarifakioğlu E, Haberal M. Superficial fungal infections in 102 renal transplant recipients: a case-control study. *Journal of the American Academy of Dermatology*. 2003; 49(2): 187-192.
- [6] Mendez-Tovar LJ. Pathogenesis of dermatophytosis and tinea versicolor. *Clinics in dermatology*. 2010; 28(2): 185-189.
- [7] Aranow C. Vitamin D and the immune system. *Journal of investigative medicine*. 2011; 59(6): 881-886.
- [8] Mostafavi A, Jafarnejad S, Khavandi S, Tabatabaee SA. Effect of vitamin D deficiency on coronary artery stenosis. *Iranian Heart Journal*. 2015; 16(3): 38-44.
- [9] Bikle D. Nonclassic actions of vitamin D. *The Journal of Clinical Endocrinology & Metabolism*. 2009; 94(1): 26-34.
- [10] Van Etten E, Stoffels K, Gysemans C, Mathieu C, Overbergh L. Regulation of vitamin D homeostasis: implications for the immune system. *Nutrition reviews*. 2008; 66(suppl_2): S125-S134.
- [11] Yamshchikov A, Desai N, Blumberg H, Ziegler T, Tangpricha V. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. *Endocrine Practice*. 2009; 15(5): 438-449.
- [12] Kroner JDC, Sommer A, Fabri M. Vitamin D every day to keep the infection away? *Nutrients*. 2015;7(6):4170-4188.
- [13] Korf H, Decallonne B, Mathieu C. Vitamin D for infections. *Current Opinion in Endocrinology, Diabetes and Obesity*. 2014; 21(6): 431-436.
- [14] Goodarzi A, Behrangi E, Ghassemi M, Mehran G, Teymoori N, Ghahremani AP, Biglari Abhari M. Comparison of serum levels of calcium, vitamin-D, phosphorous and C-reactive protein in acne patients versus healthy subjects. *Iranian Journal of Dermatology*. 2020;23(1):16-20.
- [15] Goodarzi A, Roohaninasab M, Atefi NS, Sadeghzadeh Bazargan A, Ghassemi M, Ghahremani AP, Teymoori N, Biglari Abhari M. Determination of serum levels of zinc in acne vulgaris patients: a case control study. *Iranian Journal of Dermatology*. 2020;23(1):28-31.

- [16] Marcucci SB, Obeidat AZ. EBNA1, EBNA2, and EBNA3 link Epstein-Barr virus and hypovitaminosis D in multiple sclerosis pathogenesis. *Journal of Neuroimmunology*. 2020; 339: 577116.
- [17] Hupperts R, Smolders J, Vieth R, Holmøy T, Marhardt K, Schluep M, Killestein J, Barkhof F, Beelke M, Grimaldi LM. Randomized trial of daily high-dose vitamin D3 in patients with RRMS receiving subcutaneous interferon β -1a. *Neurology*. 2019; 93(20): e1906-e1916.
- [18] Lehmann B. Role of the vitamin D3 pathway in healthy and diseased skin—facts, contradictions and hypotheses. *Experimental dermatology*. 2009; 18(2): 97-108.
- [19] Wang T-T, Nestel FP, Bourdeau V, Nagai Y, Wang Q, Liao J, Tavera-Mendoza L, Lin R, Hanrahan JW, Mader S. Cutting edge: 1, 25-dihydroxyvitamin D3 is a direct inducer of antimicrobial peptide gene expression. *The Journal of Immunology*. 2004; 173(5): 2909-2912.
- [20] Peric M, Koglin S, Kim S-M, Morizane S, Besch R, Prinz JC, Ruzicka T, Gallo RL, Schaubert J. IL-17A enhances vitamin D3-induced expression of cathelicidin antimicrobial peptide in human keratinocytes. *The Journal of Immunology*. 2008; 181(12): 8504-8512.
- [21] Antal AS, Dombrowski Y, Koglin S, Ruzicka T, Schaubert J. Impact of vitamin D3 on cutaneous immunity and antimicrobial peptide expression. *Dermato-endocrinology*. 2011; 3(1):18-22.
- [22] Peric M, Koglin S, Dombrowski Y, Groß K, Bradac E, Büchau A, Steinmeyer A, Zügel U, Ruzicka T, Schaubert J. Vitamin D analogs differentially control antimicrobial peptide/“alarmin” expression in psoriasis. *PLoS ONE*. 2009;4(7):e6340.
- [23] Mohammad AP, Baba A, Ghassemi M. Comparison between serum levels of vitamin D and zinc in women with diffuse non-scarring hair loss (telogen effluvium) and healthy women. *Pakistan Journal of Medical and Health Sciences*. 2020;14(3):1400-1404.
- [24] Le P, Tu J, Gebauer K, Brown S. Serum 25-hydroxyvitamin D increases with NB-UVB and UVA/UVB phototherapy in patients with psoriasis and atopic dermatitis in Western Australia. *Australasian Journal of Dermatology*. 2016;57(2):115-121.
- [25] Fujiyama T, Ito T, Umayahara T, Ikeya S, Tatsuno K, Funakoshi A, Hashizume H, Tokura Y. Topical application of a vitamin D3 analogue and corticosteroid to psoriasis plaques decreases skin infiltration of TH17 cells and their ex vivo expansion. *Journal of Allergy and Clinical Immunology*. 2016; 138(2): 517-528. e515.
- [26] Mattozzi C, Paolino G, Salvi M, Macaluso L, Luci C, Morrone S, Calvieri S, Richetta A. Peripheral blood regulatory T cell measurements correlate with serum vitamin D level in patients with psoriasis. *Age (years)*. 2016; 56: 23-85.