Bosphorus Medical Journal
Boğaziçi Tıp Dergisi

Original Article

DOI: 10.14744/bmj.2022.96158

Bosphorus Med J 2022;9(1):40–45

Plasma Vitamin D levels in Patients with Vitiligo

Vitiligo Hastalarında Plazma Vitamin D Düzeyi

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ABSTRACT

Objectives: Vitiligo is an acquired skin disease characterized by depigmentation and characterized by loss of epidermal melanocytes in the skin. The low levels of Vitamin D have been observed in vitiligo patients and with other autoimmune diseases. This study aimed to investigate whether 25(OH) Vitamin D levels are associated with clinical types and features of vitiligo.

Methods: A total of 60 patients with vitiligo and 60 healthy volunteers were included in our study. The patients were divided into four groups; patients newly diagnosed with vitiligo in the winter season (W-VP), participants who visited the clinic in the winter season and were found to be healthy (W-HP), patients newly diagnosed with vitiligo in the summer season (S-VP), and participants who visited the clinic in the summer season and were found to be healthy (S-HP). Participants' age, sex, incidence of other autoimmune diseases among participants and their families, clinical type of vitiligo (localized (focal, segmental, or mucosal), common (acrofacial, vulgaris, or mixed), or universal), and 25(OH) Vitamin D levels were evaluated.

Results: Twenty-five (41.7%) of the patients and 33 (55%) of the control group were women. The mean age of vitiligo group was 42.2±13.29 years and the mean age of control group was 30.5±12.6 years. The groups were similar in terms of age and sex (p>0.05). About 45% of the patients were localized, 53.32% were widespread, and 1.6% were universal type vitiligo. Another autoimmune disease was accompanying in 55%. No significant difference was found between the W-VP and S-VP groups in terms of vitiligo types (p>0.05). The incidences of other autoimmune diseases among the families of patients with vitiligo did not differ between both the sexes (p>0.05). There was no statistically significant difference between the clinical types of vitiligo and incidence of autoimmune diseases (p>0.05). The 25(OH) Vitamin D levels of participants in the W-VP and S-VP groups were statistically lower than those of participants in the W-HP and S-HP groups (p<0.05). Comparison of the 25(OH) Vitamin D levels of the W-VH with S-VP groups and the W-HP with S-HP groups did not show any statistically significant difference (p>0.05). There was no statistically significant difference between patients with autoimmune disease in the W-VH and S-VP groups in terms of clinical type of vitiligo and 25(OH) Vitamin D levels (p>0.05).

Conclusion: Plasma 25 (OH) Vitamin D level is lower in vitiligo patients compared to the normal population. Vitamin D supplementation can be effective in the treatment and control of vitiligo.

Keywords: Autoimmunity; plasma 25(OH) vitamin D; vitiligo.

ÖZET

Amaç: Bu çalışmadaki amacımız 25 OH Vitamin D'nin, vitiligo tipi ve klinik özellikleriyle ilişkisi bulunup bulunmadığını ortaya koymak.

Yöntem: Çalışmamıza 60 vitiligo hastası ve 60 sağlıklı gönüllü dahil edildi. Hastalar 4 gruba ayrıldı; kış dönemi yeni vitiligo tanısı alanlar (K-VH), kış dönemi sağlıklı katılımcılar (K-SG), yaz dönemi yeni vitiligo tanısı alanlar (Y-VH) ve Y-SG yaz dönemi sağlıklı gönüllüler (Y-SG). Katılımcıların yaş cinsiyet, kendisinde veya ailesinde otoimmün hastalık varlığı, vitiligonun klinik tipi (lokalize (fokal, segmental, mukozal), yaygın (akrofasiyal, vulgaris, karışık tip) ve üniversal) ve 25 (OH) Vitamin D düzeyleri bakıldı.

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Cite this article as:
Akpolat ND, Metin A. Plasma Vitamin D levels in Patients with Vitiligo. Bosphorus Med J 2022;9(1):40–45.

Received: 08.08.2021
Accepted: 16.09.2021

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Bulgular: Çalışmada 62 (%51,7) erkek, 58 (%48,3)kadın katılımcı vardı. Vitiligo hastalarının yaş ortalamaları 42.2±13.29, kontrol grubunun yaş ortalamaları ise 30.5±12.6'ydı.. Grupların yaş ve cinsiyet bakımından benzer olduğu görüldü (p>0,05). Vitiligonun klinik tipleri ve otoimmun hastalıklarla arasında istatistiksel açıdan anlamlı bir fark tespit edimedi (p>0, 05). K-VH ve Y-VH hastaların 25 (OH) Vitamin D düzeyleri, K-SG ve Y-SG göre isttiksel olarak düşüktü (p < 0,05). K-VH ile Y-VH arasında ve K-SG ile Y-SG arasında 25 (OH) Vitamin D düzeyleri açısından istatistiksel fark saptanmadı (p>0,05) K-VH ve Y-VH'deki otoimmun hastalığı bulunan olguların 25 (OH) Vitamin D düzeylerinin ile klinik tipine göre 25 (OH) Vitamin D düzeylerinin arasında istatistiksel olarak anlamlı fark saptanmadı (p>0,05).

Sonuç: Vitiligo hastalarında ve vitiligoya eşlik eden başka otoimmun hastalık varlığında, normal populasyona göre plazma 25 (OH) vitamin D seviyesi daha düşük düzeyde bulunmaktadır. Vitiligo aktivasyonunun kontrolü ve ikincil otoimmun hastalıkların önlenmesinde, vitamin D desteğini etkili olabilir.

Anahtar sözcükler: Otoimmunite; plazma 25 (OH) vitamin D; vitiligo.

Vitiligo is an acquired skin disorder that progresses with depigmentation and is characterized by the loss of epidermal melanocytes in the skin.[1] Although the prevalence of the disease ranges from 0.14% to 8.8%, its incidence is 1–2%.[2–4] Moreover, despite the etiopathogenesis of vitiligo being unclear, vitiligo is classified as an autoimmune disease because of the identification of some specific autoantibodies against melanocytes. Vitiligo causes not only cosmetic problems but also serious psychological and social effects on the affected person.[5]

Vitamin D3, the active form of Vitamin D, is an essential vitamin for humans. Vitamin D, considered to be more of a hormone than a classic vitamin, has important effects on immunity, calcium regulation, brain functions, and melanin synthesis.[2–6] It also prevents the development of autoimmune diseases by inducing the activity of regulatory T-cells and increasing the modulation of antigen presenting cells and dendritic cells.[7,8]

Considering the association between low plasma Vitamin D levels and autoimmunity,[9–11] this study aimed to evaluate the relationship between clinical types and features of vitiligo and low plasma Vitamin D levels.

Methods

This prospective and single-center study was performed with the approval of the Institutional Review Board of Ankara Atatürk Education and Training Hospital and in line with the ethical principles of the Declaration of Helsinki. The study included 60 vitiligo patients and 60 health controls who applied to the dermatology clinic and met the study criteria.

The inclusion criterion was having been newly diagnosed with vitiligo. The exclusion criteria were as follows: Having a suspected diagnosis of vitiligo, not signing the voluntary informed consent form, taking oral Vitamin D supplements, being pregnant or breastfeeding, and not agreeing to undergo laboratory tests. The control group included healthy individuals who came to the dermatology outpatient clinic for other reasons and were not found to have any pathology on examination.

The patients were divided into four groups; patients who were newly diagnosed with vitiligo in the winter season (W-VP), healthy participants in the winter season (W-HP), patients newly diagnosed with vitiligo in the summer season (S-VP), and healthy participants in the summer season (S-HP).

Our study parameters were determined as participants' age, sex, incidence of other autoimmune diseases among participants and their families, clinical type of vitiligo (localized (focal, segmental, or mucosal), common (acrofacial, vulgaris, or mixed), or universal), and 25(OH) Vitamin D levels.

The 25(OH) Vitamin D levels were evaluated using the LC-MS/MS method (Applied Biosystems 3200, USA) and classified into the following categories: Deficiency: Levels<10 µg/L, insufficiency: Levels of 10–30 µg/L, and sufficiency: Levels>30 µg/L.

Statistical Analysis

Mean and standard deviation were used as descriptive statistics in data analysis using numerical variables. Categorical variables were indicated by the number of cases and their percentages. The relationship between categorical variables was examined using the Chi-square test. The statistical significance limit (p) was set at 0.05 and p<0.05 was considered as statistically significant. Statistical analyzes were performed using the SPSS 15.0 program.

Table 1. Demographic characteristics of the groups

Demographic characteristics	W-VP (n=30)	S-VP (n=30)	W-HP (n=30)	S-HP (n=30)	p
Age (years)	43±14.18	31.5±12.4	41.5±12.4	29.5±12.8	NS
Sex, n (%)					
Female	13 (43.3%)	12 (40%)	18 (60%)	15 (50%)	NS
Male	17 (57.6%)	18 (60%)	12 (40%)	15 (50%)	
25(OH) vitamin D (µg/L) Mean±SD	8.9±1.3	8.5±1.1	18.4±9.1	18.5±9.5	0.05*

W-VP: Vitiligo patients in the winter season; S-VP: Vitiligo patients in the summer season; W-HP: Healthy participants in the winter season; S-HP: Healthy participants in the summer season; *: Statistically significant; SD: Standard deviation; NS: Not significant.

Table 2. Distribution of clinical types of vitiligo in patients

Vitiligo type	W-VP (%)	S-VP (%)	p
Localized			
Focal	12 (40)	6 (20)	NS
Segmental	2 (6.7)	3 (10)	
Mucosal	0 (0)	4 (13.3)	
Common			
Vulgaris	13 (43.3)	15 (50)	NS
Acrofacial	2 (6.7)	0 (0)	
Mixed	0 (0)	2 (6.7)	
Universal	1 (3.3)	0 (0)	NS

W-VP: Vitiligo patients in the winter season; S-VP: Vitiligo patients in the summer season; NS: Not significant.

Results

The study included 35 (58.3%) male and 25 (41.6%) female in vitiligo group and 27 (45%) male and 33 (55%) female in control group. The mean age of vitiligo group was 42.2±13.29 years and the mean age of control group was 30.5±12.6 years. The groups were similar in terms of age and sex (p>0.05) (Table 1).

The patients in the W-VP and S-VP groups were classified according to the Fitzpatrick skin classification as follows: 6 (10%) patients were determined as having Type 2 skin, 49 (81.7%) patients were determined as having Type 3, and 5 (8.3%) patients were determined as having Type 4. Localized vitiligo was observed in 27 (45%) patients, common in 32 (53.3%), and universal in 1 (1.6%). Vitiligo covered 1–5% of the body surface area in 40 (66.7%) patients, 6–19% in 15 (25%), and more than 20% in 5 (8.3%). In addition, 31 (51.6%) patients had an autoimmune disease, whereas 16 (26.6%) patients reported a family history of autoimmune disease.

Clinical types of vitiligo in patients in the W-VP and S-VP groups are detailed in Table 2. On statistical evaluation, no significant difference was found in the vitiligo types between the groups (p>0.05) (Table 2).

When the patients were questioned in terms of the incidence of a familial autoimmune disease, at least one autoimmune disease was reported in the family in 5 (16.6%) of the patients in the W-VP and in 11 (36.6%) of the patients in the S-VH groups. A total of 7 (11.6%) female and 9 (15%) male patients reported a family history of autoimmune diseases. The incidence of other autoimmune disease in the families of patients with vitiligo did not differ between both the sexes (p>0.05).

One or more other autoimmune diseases were detected in 17 (56.7%) of the patients in the W-VP and in 14 (46.7%) of the patients in the S-VP groups. There was no statistically significant difference between clinical types of vitiligo and autoimmune diseases (p>0.05) (Table 3).

25(OH) Vitamin D levels of patients in the W-VP and S-VP groups were statistically lower than those in patients in the W-HP and S-HP groups (p<0.05). Comparison of the 25(OH) Vitamin D levels of the W-VH with S-VP groups and the W-HP with S-HP groups did not show any statistically significant difference (Table 1).

The distribution of 25(OH) Vitamin D levels in patients with autoimmune disease in W-VP and S-VP is given in table. There was no statistically significant difference between the groups (Table 4).

The distributions of 25(OH) Vitamin D levels of W-VP and S-VP according to the vitiligo clinical type are given in Table 5. There was no statistically significant difference between the groups (p>0.05).

Discussion

This study found that 25(OH) Vitamin D levels in all patients with vitiligo were lower independent of season, concomitant autoimmune disease, and clinical type of vitiligo.

The study results on the distribution of vitiligo types are conflicting. The results of a case series by Aktan et al.[12]

Table 3. Relationship between vitiligo type and autoimmune disease in patients

Vitiligo type	W-VP Autoimmune disease				S-VP Autoimmune disease				p
	Yes		No		Yes		No		
	n	%	n	%	n	%	n	%	
Localized									
Focal	7	58.3	5	41.7	3	20	3	20	
Segmental	2	11.1	0	0	2	13.4	1	6.6	
Mucosal	0	0	0	0	2	13.4	2	13.4	
Common									
Vulgaris	6	33.3	7	53.8	8	53.2	7	46.6	NS
Acrofacial	2	11.1	0	0	0	0	0	0	
Mixed	0	0	0	0	0	0	2	13.4	
Universal	1	5.6	0	0	0	0	0	0	
Total	18	30	12	20	15	25	15	25	

W-VP: Vitiligo patients in the winter season; S-VP: Vitiligo patients in the summer season; NS: Not significant.

Table 4. 25(OH) D levels of participants with autoimmune disease in addition to summer and winter period vitiligo disease

	W-VP (%)	S-VP (%)	p
Autoimmune patient (+) 25(OH)D levels			NS
<10 µg/L	14 (46.6)	13(43.3)	
10–30 µg/L	3 (30.0)	1 (3.3)	
>30 µg/L	13(43.3)	14 (46.6)	

W-VP: Vitiligo patients in the winter season; S-VP: Vitiligo patients in the summer season; NS: Not significant.

Table 5. Distribution of 25(OH) Vitamin D levels in summer and winter seasons among patients with vitiligo based on clinical type

Vitiligo type	W-VP (%)	S-VP (%)	p
Local			
<10 µg/L	11 (36.6)	11 (36.6)	
10–30 µg/L	3 (10)	2 (6.7)	
>30 µg/L	13 (43.4)	14 (46.6)	
Common			
<10 µg/L	13 (43.4)	15 (50)	
10–30 µg/L	2 (6.7)	2 (6.7)	NS
>30 µg/L	15 (50)	13 (43.4)	
Universal			
<10 µg/L	1 (3.4)	0 (0)	
10–30 µg/L	0 (0)	0 (0)	
>30 µg/L	29 (96.6)	30 (100)	

W-VP: Vitiligo patients in the winter season; S-VP: Vitiligo patients in the summer season; NS: Not significant.

that included 63 patients with vitiligo indicated that 22.2% of the cases had a localized type and 77.8% had a diffuse type of vitiligo. Firooz et al.[13] reported that vitiligo was localized in 71.3% of 80 cases and presented as common type in 28.7% of the cases. Onunu et al.[14] reported that 77% of a group of 351 cases showed localized type and that 10.5% showed a common type of the disease. In our study, we found that our patients mostly had the common type of vitiligo (53.3%).

Vitiligo is considered to be an autoimmune disease in terms of etiopathogenesis based on a hypothesis that has been supported since a long time.[15] The high incidence of other autoimmune diseases and the detection of certain autoantibodies on examination support this hypothesis.[16] Narita et al.[17] found that 20.3% of 133 patients with generalized vitiligo had at least one concomitant autoimmune disease. The data obtained in our study are consistent with these reports.

Both patients with vitiligo and their siblings in families with generalized vitiligo, where a large number of family members are affected, have a higher incidence of autoimmune/autoinflammatory diseases.[18] Spritz reported a marked increase in the incidence rates of familial autoimmune diseases in his research.[19] Vrijman et al.[20] reported a familial autoimmune disease history in 3.8% of patients with vitiligo in their study. In our study, we also observed a significant relationship between vitiligo and autoimmune diseases. In addition, we found that the familial autoimmune disease incidence rates among our participants were higher than those reported in

the literature. We believe that this may be because the studies were conducted in different geographical areas.

Vitamin D exerts an anti-inflammatory effect on the acquired immune system by suppressing immunoglobulin production and plasma cell differentiation. In addition, it prevents the development of autoimmune diseases by inducing regulatory T-cells and modulating antigen presenting cells and dendritic cells.[8,11,21] Cantorna, in his study, found a relationship between the incidence and severity of autoimmune diseases, such as multiple sclerosis and autoimmune bowel diseases, and Vitamin D levels.[9] Saleh et al.,[11] in their study on patients with vitiligo, found a relationship between vitiligo as well as autoimmune diseases and Vitamin D deficiency and suggested that Vitamin D deficiency may be a triggering factor in the development of autoimmunity.[10,11] In our study, it was observed that the 25(OH) Vitamin D levels of patients with vitiligo who were included in the study in both summer and winter seasons were low.

Silverberg et al.[6] evaluated 25(OH) Vitamin D levels in patients with vitiligo in their study and detected moderate and severe plasma 25(OH) Vitamin D deficiency in 55.6% and 13.3% of 45 patients with vitiligo, respectively; however, the control group was not evaluated in this study and seasonal variables were not considered. In our study, all patients with vitiligo demonstrated severely low 25(OH) Vitamin D levels irrespective of seasonal differences suggesting that excessive consumption of Vitamin D in the body may occur in patients with autoimmune diseases, such as vitiligo.

We found only one study in the literature evaluating the relationship between 25(OH) Vitamin D and vitiligo type. This study by Xu et al.[22] on 171 vitiligo cases in China reported that there was no significant difference in 25(OH) Vitamin D levels in cases with segmental vitiligo. In our study, although it was not statistically significant, severe plasma 25(OH) Vitamin D deficiency was found in patients with the common vitiligo type.

Severe Vitamin D deficiency has been reported in all studies evaluating 25(OH) Vitamin D deficiencies in vitiligo cases with concomitant autoimmune disease.[6,11] In our study, severe plasma 25(OH) Vitamin D deficiencies were detected in patients with vitiligo with concomitant autoimmune diseases, consistent with the literature. This result suggests that low plasma 25(OH) Vitamin D levels increase the risk of developing secondary autoimmune conditions or may be associated with excessive consumption of plasma 25(OH) Vitamin D in autoinflammatory processes.

The small number of patients in the study and control groups in our study was a study limitation. In addition, after obtaining adequate plasma levels with Vitamin D replacement, we could not evaluate disease activation, clinical types of vitiligo, and the presence of other concomitant autoimmune diseases. Moreover, assessing serum levels of 1, 25(OH)2 D3, which is the active form of Vitamin D, in further studies may be beneficial.

Conclusion

Plasma 25(OH) Vitamin D levels are lower in the patients with vitiligo than those in the normal population. Vitamin D supplementation may be effective in controlling the progression of vitiligo and the development of secondary autoimmune diseases.

Disclosures

Ethics Committee Approval: The Yıldırım Beyazıt University Clinical Research Ethics Committee granted approval for this study (date: 21.11.2012, number: 26379996/117).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – N.D.A.; Design – N.D.A., A.M.; Supervision – A.M.; Materials – N.D.A.; Data collection and/or processing – N.D.A.; Analysis and/or interpretation – N.D.A., A.M.; Literature search – N.D.A.; Writing – N.D.A.; Critical review – A.M.

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