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Research Thesis

# Correlation between Vitamin D and Interleukin - 21 in Patients with Vitiligo

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## Abstract

**Introduction:** Vitiligo is an acquired skin disease characterized by loss of functional melanocytes from the epidermis. Despite the several factors studied the pathogenesis of vitiligo remains unclear. Vitiligo could be associated with low vitamin D levels and high level of interleukin-21.

**Objective:** The aim of this study was to evaluate serum 25(OH) D levels, interleukin-21serumlevels and correlation between them in vitiligo patients in comparison of normal controls.

**Patients and Methods:** After meeting inclusion and exclusion criteria, serum 25 hydroxy vitamin D and interlukin-21 levels were assayed, in all subjects included in this case control study (21 patients and 21 age and sex matched healthy individuals).

Vitiligo disease activity index (VIDA), affected body surface area (BSA), site of lesion, age of patients and duration of vitiligo were evaluated in relation to vitamin Dand interleukin-21 level.

**Results:** A total of 42 participants were enrolled in our study, 21 patients with vitiligo and 21 who served as controls. The mean serum level of vitamin D were significantly decreased in the patients group as compared with the control group (17.3ng /ml ±5.3vs 25.8 ng/ml ±7.9, P < 0.05). There was non-significant correlation between vitamin D level with age, duration of vitiligo, and affected body surface area (P>0.05), but there was significant difference in 25(OH)D levels between different grades of VIDA.

The mean serum level of interleukin-21 were significantly increased in the patients group as compared with the control group (606.1ng/ L ± 549.1 vs 137.5ng/ L ± 182). There was non-significant correlation between interleukin-21 level with age, duration of vitiligo, &affected body surface area (P>0.05), but there was significant difference in interleukin-21 levels between different grades of VIDA (increase disease activity associated with higher interleukin-21 level).

**Conclusion:** In this study, we found a significant 25(OH)D deficiency and significant high level of interleukin-21 in patients with vitiligo, suggesting that vitamin D deficiency and high-level interleukin -21 may play a role in the pathogenesis of vitiligo.

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## Introduction

Vitiligo is a common autoimmune disease that progressively destroys melanocytes in the skin, resulting in the appearance of patchy depigmentation. This disfiguring condition frequently affects the face and other visible areas of the body, which can be psychologically devastating [1].

Vitiligo affects approximately 1% of the world's population both adults and children are affected with no predilection for sex or ethnicity. The average age at onset lies around the second to the third decade of life [2].

In recent years, vitamin D deficiency as a result of lifestyles with inadequate sun exposure, has received increased attention due to its association with the risk of serious chronic diseases. Since prolonged exposure to sunlight has been associated with risk for skin cancer, food fortification arises as an important option in obtaining vitamin D sufficiency [3].

Interleukin-21 regulates both innate and adaptive immune responses, and it not only has key roles in antitumor and antiviral responses but also exerts major effects on inflammatory responses that promote the development of autoimmune diseases and inflammatory disorders [4].

The aim of this study was to evaluate serum 25(OH)D levels, interleukin-21serum levels and correlation between them in vitiligo patients in comparison of normal controls.

## Patients and Methods

This case control study in which 42persons were enrolled at Dermatology Outpatient Clinics of Zagazig University Hospital during the period from March 2018 till October 2018, after the approval of the Research ethical committee of Faculty of medicine, Zagazig University and obtaining an informed consent. This study included 21clinically diagnosed patients of vitiligo (10 males and 11 females), their ages varied from 11 to 68 years. The control group included 21 age and sex matched healthy individuals, their ages varied from 4 to 54 years.

Patients suffering from any other skin or autoimmune disorders, patients who had taken treatment for vitiligo in the last three months, pregnant and lactating women had been excluded.

All subjects underwent a complete medical examination and laboratory tests. Laboratory tests were performed within 30 days of enrollment in the study and included vitamin D and interleukin-21 levels. In all case and control groups, serum level of 25(OH)D was measured by MINI VIDAS machine which is a compact automated immunoassay system based on the Enzyme Linked Fluorescent Assay (ELFA) principles. Made in France. The normal range ofvitamin D levels was 30-100 ng/ ml. We then defined vitamin D insufficiency as vitamin D < 30 ng/ml and vitamin D deficiency as < 10 ng/ml.

The degree of depigmentation was measured by Wallace role of nines. While the vitiligo activity measured by Vitiligo Disease Activity Score (VIDA).

## Results

A total of 42 participants were enrolled in our study, 21 patients with vitiligo and 21 who served as controls. The patients group comprised 10 males and 11 females with a mean age of 30.8 ± 19.1 years and mean duration of diagnosis 9.3 ± 6.9 years of the 21 participants in the control group, 10 were males and 11 were females with a mean age of 30.6 ±13.2 years. The mean serum level of vitamin D were significantly decreased in the patients group as compared with the control group ( 17.3ng/ml ± 5.3 vs 25.8 ng/ml ±7.9, P < 0.05). There was non-significant correlation between vitamin D level with age, duration of vitiligo, and affected body surface area (P>0.05), but there was significant difference in 25(OH)D levels between different grades of VIDA.

The mean serum level of interleukin-21 were significantly increased in the patients group as compared with the control group (606.1ng/ L ± 549.1 vs 137.5ng/ L ± 182). There was non-significant correlation between interleukin-21 level with age, duration of vitiligo, and affected body surface area (P>0.05), but there was significant difference in interleukin-21 levels between different grades of VIDA (increase disease activity associated with higher interleukin-21 level).

## Discussion

In the current case control study, the mean age of the case group was 30.8 ± 19.1 ranged from (11-68) years, 52.4 % of them female, while the mean age of the control group was 30.6 ± 13.2 ranged from (4-54) years, 52.4 % of them female.

Different mean of ages was found in another studies; 31.3 years and 28.11 years respectively Nunes and Esser, et al. and Nejad, et al. [5,6]. However in Bouayad, et al. studied group average age 36.7 years. These data reinforced that vitiligo is a disease that occurs at any age [7].

Our study showed there was a significant difference of serum levels of 25-(OH)D between patients (15.2 ng/ml) and their age and gender matched healthy controls (23.8 ng/ml.), (P = 0.006). In agreement with our study, Beheshti, et al. in their cross-sectional study included 100 patients with Vitiligo found that the mean level of serum 25(OH) D was 42 nmol/L which had a significance difference with a normal level; (P = 0.042) [8].

Also, Saleh, et al. in their case-control study on 40 vitiligo patients and 40 healthy, age, gender matched controls, found that 39 patients (97.5%) versus 5 controls (12.5%) have deficient 25(OH)D levels with significantly lower serum 25(OH)D levels in patients compared to controls. statistically highly significant lower serum 25(OH)D levels existed in patients compared to controls (P = 0.0001) [9].

Parallel to this Shalaby and Ibrahim, in their case control study included 40 vitiligo patients and 40 age and sex matched healthy individuals, reported that, there was a strong correlation between patients with vitiligo and 25(OH)D deficiency [10].

While, Xu, et al. in their case control study on 280 chines patients with vitiligo, found non-significant difference between vitiligo patients and controls in serum 25(OH)D, therefore they do not support a role for vitamin D in vitiligo pathogenesis [11].

On the other hand, our study demonstrated that was statistically significant negative correlation between patients serum level of 25(OH)D and disease activity assessed by (VIDA), ( p value = 0.003). While in a cross-sectional study conducted by Singla, et al. on 75 patients with vitiligo and 75 control, showed no significant correlation between serum 25(HO)D with VIDA, (P value = 0.518) [12].

On the contrary, Doss, et al. in their case control study included 30 vitiligo patients and 30 age, gender matched healthy control, find no relation between the level of 25(HO)D and the disease activity assessed by (VIDA) score [13].

In current study there was non-significant correlation existed between age, sex, affected body surface area, duration and family history of vitiligo with 25(HO)D level in case group.
Parallel to this, Saleh, et al. found no significant correlations existed between serum 25(OH)D with age, duration of vitiligo, family history of vitiligo and affected body surface area of the case group [9].

Consistent with our results, Ustun, et al. a total of 25 patients and 41 controls were included in the cross-sectional study, showed no correlation between 25(HO)D with age, affected body surface area and duration of the disease in the patients with vitiligo [14].

Alsosingla, et al. in their cross sectional study showed no significant correlation between serum 25 (HO)D with age, sex, affected body surface area and duration of disease in patients [12].

Inconsistent with our results, Doss, et al. showed that the affected body surface area was higher in patients with 25(OH) D level above 30 ng/ml compared to those with levels below 30 ng/ml, which means that the level of vitamin D could influence the extent of the disease [13].

In this study, the serum level of IL-21 in cases group was higher than controls group with highly significant value (P = 0.001), also there was significant correlations between IL-21 level and disease activity (P = 0.008). This result supported by Zhou, et al. who evaluated the potential role of IL-21in the pathogenesis of NSV in 45 patients with active NSV. They showed elevated serum IL-21 levels in patients with NSV [15].

Our study showed non-significant correlation between serum level of IL-21 with affected body surface area of vitiligo in case group, these findings were in disagreement with Zhou, et al. who reported

that the affected body surface area of lesions is positively correlated with elevated IL-21 levels [15].



Also in case group of this study there was significant positive correlation between IL-21 and disease activity assessed by (VIDA), ($p = 0.008$). But regarding age, sex, family history of autoimmune disease and disease duration there was no statistically significant correlation with IL-21 serum level. Finally in our study there was non-significant correlation between serum 25-(HO) D and IL-21 level in vitiligo patients.

## Conclusion

Based on the results obtained in the present study, we can conclude that vitamin D deficiency is present in vitiligo patients, suggesting that vitamin D deficiency may play a role in the pathogenesis of vitiligo. More studies with a large number of patients are needed to confirm this hypothesis.

Accordingly, screening for vitamin D deficiency seems of value in vitiligo patients. Moreover, the growing enthusiasm for vitamin D supplementation in autoimmune diseases emphasizes the need for timely and thorough testing of this hypothesis on a large sample size of vitiligo patients to assess the efficacy of oral vitamin D supplementation on controlling long-term disease activity and the possibility of prevention of disease onset in susceptible family members of vitiligo patients.

I was concluded that elevated serum IL-21 levels in patients with vitiligo suggested development and progression of vitiligo.

More studies are needed, to evaluate tissue levels of IL-21 in vitiligo patients, and inclusions of IL-21 as a prognostic value during examination of patients with vitiligo should be considered.

More studies are needed by pharmaceutical company with emphasis on therapeutic trials to determine the effect of lowering elevated IL-21 levels on the treatment of vitiligo.

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