

Evaluation of Serum Vitamin D Levels in Patients with Vitiligo

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ABSTRACT

Objective: To evaluate serum vitamin D levels in patients with vitiligo and compare them to the healthy controls.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Dermatology Outpatient Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from Nov 2019 to Apr 2020.

Methodology: The study included 75 patients with vitiligo (Group-1) and 75 healthy controls (Group-2). Complete blood count, urea and creatinine, liver function tests, TSH, fasting plasma glucose, vitamin B12 levels, serum calcium and vitamin D levels were performed. In addition, vitamin D levels were compared in both groups.

Results: The mean age of Group-1 was 32.81±20.59 years, and Group- 2 was 40.13±16.09 years. In Group-1, deficient vitamin D levels were seen in 17(22.7%) of cases, insufficient in 25(33.3%) and 33(44.0%) had normal levels. In Group-2, 10(13.3%) had deficient levels, 10(13.3%) had insufficient levels and 55(77.3%) had normal levels. Patients with vitiligo had low serum 25(OH)D levels compared to controls, and this difference was statistically significant ($p=0.001$).

Conclusion: Low serum vitamin D levels are seen in patients with vitiligo compared to controls.

Keywords: Autoimmune diseases vitamin-D, Vitiligo.

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INTRODUCTION

Vitiligo is an acquired cutaneous depigmenting disease that affects both genders and all skin phenotypes. The worldwide prevalence of vitiligo is estimated to be 0.5-2%.¹ Vitiligo has been associated with other autoimmune diseases like psoriasis, thyroid disorders, alopecia areata, pernicious anaemia, inflammatory bowel disease and lupus erythematosus.^{2,3}

Vitamin-D plays a dynamic role and acts on many cell types, including endothelial cells, immune cells, keratinocytes and osteoblasts. The major endocrinological function of vitamin-D includes regulating calcium homeostasis.⁴ Vitamin-D mediates its biological functions through specific receptors in target tissues known as nuclear vitamin D receptors (VDR). It also plays an important role in innate and adaptive immune response and mediation of cutaneous immune responses.^{5,6} Vitamin-D also increases tyrosinase activity and thus melanogenesis. On keratinocytes, it can induce cell proliferation and differentiation or apoptosis.^{7,8}

A wide array of autoimmune disorders are associated with vitamin-D deficiency like alopecia areata, psoriasis, atopic dermatitis, androgenetic alopecia, systemic lupus erythematosus, ichthyosis,

melanoma, and nonmelanoma skin malignancy, type 1 diabetes, inflammatory bowel disease and rheumatoid arthritis.⁹ Thus, Low vitamin-D levels could also be associated with vitiligo, an autoimmune disorder. Suppose the relationship between vitamin-D deficiency and vitiligo could be established. In that case, vitamin-D supplementation in patients with vitiligo could potentially improve vitiligo management. Some international literature shows that vitamin D deficiency could be associated with vitiligo.¹⁰

Therefore, the objective of this study was to evaluate vitamin D levels in patients with vitiligo and compare them with healthy controls.

METHODOLOGY

The comparative cross-sectional study was carried out at the Outpatient Department of Dermatology, Fauji Foundation Hospital, Rawalpindi Pakistan, from November 2019 to April 2020. Ethical approval was taken from the Hospital Ethical review board. The sampling technique used was non-probability consecutive sampling. WHO sample size calculator was used for estimating sample size taking level of significance=5%, power of test=80%, anticipated population proportion P1=0.97 and anticipated population proportion P2=0.12.¹⁰

Inclusion Criteria: For Group-1, patients of either gender and any age group with no previous history of hepatobiliary, cardiovascular, renal or gastrointestinal

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disorder, no history of parathyroid or metabolic bone disorders and no history of taking topical or systemic treatment for vitiligo at least one month before testing were included in the study. Patients with no history of taking drugs that can affect vitamin-D and calcium metabolisms like corticosteroids, bisphosphonates, phototherapy and no vitamin-D or calcium supplements were also included in the study. Patients presenting with skin diseases other than vitiligo, such as eczema, acne, melasma, fungal infections etc., were included as Control Group in the study.

Exclusion Criteria: Patients taking drugs that may affect calcium metabolism, patients taking vitiligo treatment, patients with inflammatory and autoimmune conditions, pregnant, lactating women and smokers were excluded from the study.

Both groups (patients and healthy controls) were enrolled after taking informed consent from participants. All the patients were examined and diagnosed based on clinical findings and wood's lamp examination, which showed chalky white fluorescence of depigmented areas, diagnosis of vitiligo was made. Seventy-five patients presenting with vitiligo were enrolled in the study and labelled as Group-1. Seventy-five healthy controls were also selected from patients coming to skin OPD.

Investigations performed in both groups were complete blood count, LFTs, fasting plasma glucose, TSH, Urea, creatinine, Serum vitamin B12 levels, Serum Calcium and vitamin-D levels. 25(OH) vitamin D levels were measured as this form is a better indicator of vitamin-D status. Other parameters recorded were Fitzpatrick skin phenotype, type of vitiligo and sunscreen usage, disease duration, comorbid autoimmune conditions and family history of vitiligo other labs were done to look for associations of vitiligo and rule out systemic diseases that could alter vitamin-D levels. We divided 25(OH)D levels into sufficient (≥ 30 ng/ml), insufficient (<30 - >20 ng/ml) and deficient (≤ 20 ng/ml).¹¹

Data were analysed using Statistical Package for the social sciences (SPSS) version 23.00. Quantitative variables were summarized as Mean \pm SD and qualitative variables were summarized as frequency and percentages. Chi-square test was applied to find out the association. The *p*-value of ≤ 0.05 was considered statistically significant.

RESULTS

The mean age of Group-1 was 32.81 \pm 20.59 years, and in Group-2 was 40.13 \pm 16.09 years. Vitamin-D

levels of Group-1 ranged from 9ng/ml to 75ng/ml while vitamin-D levels of Group-2 ranged from 9ng/ml to 139ng/ml.

Patients had lower vitamin D levels than controls, the difference being statistically significant (*p*=0.001), as shown in the Table.

Table: Comparison of vitamin D levels between the Study Groups (n=150)

Baseline Characteristics	Group-1 (Patients with vitiligo)	Group-2 (Healthy Controls)	p-value
Age (years)	32.81 \pm 20.59	40.13 \pm 16.90	0.53
Gender			
Male	11(14.7%)	15(20.0%)	0.388
Females	64(85.3%)	60(80.0%)	
Vitamin D (ng/ml)	31.81 \pm 14.53	46.22 \pm 26.44	0.001
Deficient	17(22.7%)	10(13.3%)	
Insufficient	25(33.3%)	10(13.3%)	
Normal	33(44.0%)	55(77.3%)	

In Group-1, 17(22.7%) patients had segmental vitiligo, 27(36.0%) had non-segmental with 5(6.7%) acrofacial, 10(13.3%) generalized, 8(10.7%) focal, 1 (1.3%) halo nevus, 2(2.7%) trichrome and 5(6.7%) had mixed vitiligo. The duration of the lesion varied from 2 months to 5 years or more. 36(48.0%) patients had lesions for <6 months. 33(44.0%) patients had lesions for ≤ 1 year. All the patients belonged to Fitzpatrick skin phenotype III or IV.

DISCUSSION

Vitiligo is a common cause of localized depigmentation caused by the loss of melanocytes. As melanocytes express VDRs, their function can be affected by vitamin-D status. The study showed that in Group-1, out of 75 patients, 17 patients were deficient, 25 patients were insufficient, and 33 patients had normal vitamin-D levels. In Group-2, 10 patients had deficient, ten had insufficient, and 55 had normal vitamin-D levels, and the difference between the two groups was statistically significant (*p* $<$ 0.001). Various studies in the literature from different countries show variable results. Some studies, like ours, show that low vitamin serum vitamin-D levels are associated with vitiligo. Like case-control study conducted in Egypt by Saleh *et al.* on 40 patients of vitiligo and 40 healthy controls concluded that a positive correlation exists between low serum vitamin-D levels and vitiligo patients.¹⁰ Another cross-sectional study conducted in Iran by Beheshti *et al.* on 100 vitiligo patients showed that mean serum vitamin-D levels were 42 \pm 24.1, and these values had a statistically significant difference

from normal values (p -value <0.04).¹¹ A meta-analysis was done on 17 studies by Upala and Sanguaneko, which showed a positive correlation between low vitamin-D levels and vitiligo. The study could not prove that low vitamin-D levels could cause vitiligo though the authors emphasized checking serum vitamin-D in vitiligo patients.¹² Another meta-analysis done in China by Zhang *et al.* included 17 studies and revealed that a significant relationship exists between vitamin D deficiency and the onset of vitiligo. Another Chinese case-control study by Zhang *et al.* on 114 vitiligo patients and 100 controls, showed that mean vitamin D levels in patients were 43.62 ± 19.23 and 67.87 ± 19.45 in controls, and this difference was statistically significant.¹⁴ Our study also revealed similar results to the earlier studies showing vitamin-D deficiency to be more prevalent in patients with vitiligo.

Contrary to the results of this study, some studies also concluded that no significant statistically significant difference was seen in serum vitamin-D levels of vitiligo patients and healthy controls, like the cross-sectional study by Ustun *et al.* conducted in Turkey.¹⁵ Other studies like the case-control study also conducted in Turkey by Karagun *et al.* on 50 vitiligo patients and 47 healthy controls. Serum vitamin-D levels were measured in both groups during winter months, and the data was assessed. The study concluded that although patients had relatively lower vitamin-D levels than controls, this difference was not statistically significant.¹⁶ Another case-control study conducted in Jordan by Alshiyab *et al.* found no significant differences in vitamin-D levels between the vitiligo patient and the controls.¹⁷ Our results, however, showed that vitamin-D deficiency is associated with vitiligo, as 42 patients in Group-1 had lower vitamin-D levels than as compared to 20 patients in Group-2.

The study conducted by Jadoon *et al.* on 202 people, showed that there is a high prevalence of vitamin-D deficiency in the Pakistani population and the study also concluded that vitamin-D deficiency has become a public health problem and significantly affecting our population irrespective of age & gender.¹⁸

Most patients reporting to the Outpatient Department and included in the study were females. Many of these patients had a conservative clothing style wearing the hijab that covers most of the body, allowing for limited sun exposure. In addition to clothing, other religious, behavioural and sociocultural factors such as time spent outdoors, skin pigmentation or insufficient playgrounds could also be other contributory factors

to low levels of vitamin-D. The results can also vary depending on sunscreen usage, sun exposure, dietary intake of vitamin-D, degree of skin pigmentation because darker skin is a known risk factor for vitamin-D deficiency as melanin filters UV radiation. Other environmental factors such as seasonal variation (sample collected in a particular season) degree of air pollution, latitude and cultural differences can also affect vitamin-D synthesis.¹⁹ Therefore, an important consideration should be provided to the pathogenesis of vitiligo which is complex and multifactorial.

Therefore, we recommend checking vitamin-D levels in all patients with vitiligo, and if deficient should be replaced. Though to establish the extent of the benefit of vitamin-D supplementation in vitiligo patients and management outcomes, further studies and clinical trials are required.

STUDY LIMITATIONS

The majority of patients included in the study were female because the hospital. There should be equal gender representation to ensure good comparison. Secondly, controls ideally should belong to a similar geographical area, so they have the same level of sun exposure and similar dietary habits. Third, the controls were not age-matched to vitiligo patients, which could also affect the study results.

CONCLUSION

Low serum vitamin-D levels are seen in patients with vitiligo compared to controls. Multicentric studies from different geographical areas around Pakistan are needed on a larger sample size, including both genders, to establish a strong correlation between serum vitamin-D levels and vitiligo. The study recommends screening for vitamin-D deficiency seems of value in vitiligo patients for the possibility of vitamin-D supplementation.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AK: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

FR: Conception, study design, drafting the manuscript, approval of the final version to be published.

AJ: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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