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Efficacy of Oral Vitamin D Supplementation on the Serum Vitamin D Levels and Disease Severity of Vitiligo Patients: A Systematic Review of Randomized Controlled Trials

Cadacio KAD, Rescober-Valencia C and King-Ismael D*

Department of Dermatology Resident Jose R. Reyes Memorial Medical Center, Manila, Philippines

***Address for Correspondence**
Karen Andrea D. Cadacio, Department of Dermatology Resident Jose R. Reyes Memorial Medical Center, Manila, Philippines Email Id: kdcadacio@gmail.com

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Abstract

Introduction: Vitiligo is an autoimmune skin condition where CD8+ T cells target and destroy melanocytes, leading to depigmented patches. Vitamin D has been found to play a key role in melanogenesis by stimulating melanocyte activity. Vitamin D deficiency is linked to autoimmune diseases like vitiligo, making vitamin D supplementation a potential therapeutic approach.

Objectives: This study aims to determine the efficacy of oral vitamin D supplementation on serum vitamin D levels and disease severity in vitiligo patients through an in-depth systematic review of randomized controlled trials.

Results: A total of five randomized controlled trials (RCTs) were included in the study. All five studies reported serum vitamin D levels, while only two provided data on Vitiligo Area Scoring Index (VASI) scores. The overall mean difference in serum vitamin D levels before and after vitamin D supplementation was found to be statistically significant, with a consistent increase across all studies. Similarly, the mean difference in VASI scores was also statistically significant, showing a notable decrease in vitiligo severity after supplementation in the two studies. Homogeneity tests based on the Q statistic indicated significant heterogeneity and publication bias was identified in studies related to changes in serum vitamin D levels, but not in those measuring VASI scores.

Conclusion: Oral vitamin D supplementation significantly increases serum vitamin D levels and may improve vitiligo severity. Studies with larger sample sizes and standardized methodologies are needed to further confirm these findings.

Introduction

Vitiligo is a skin condition where melanocytes progressively decrease, leading to well-defined milky-white macules and/or patches on the skin, which can sometimes be accompanied by the loss of pigmentation in hair, known as poliosis [1]. Varying prevalence rates in different populations may be attributed to genetic or environmental factors. Moreover, it is possible that social and cultural stigmas play a role in the prevalence of vitiligo. Given these complexities, it is often stated that the global prevalence of the disease is roughly consistent, estimated to be around 0.5% to 1%.[1]

Vitiligo usually starts before the third decade of life. It tends to occur early in the segmental variant of vitiligo, which affects only one side of the body. There is no gender predilection with regards to its demographics; however, it has been that females seek treatment more frequently than males.[1]

Vitiligo typically presents as painless, white patches with clear edges that glow under a Wood's lamp. These patches can appear anywhere on the body, often symmetrically. While the condition can begin in any areas, it frequently starts on the face, hands, feet, or genital regions. Several clinical patterns exist, such as acrofacial, mucosal, generalized, universal, mixed, and rare forms, but distinguishing between them can be challenging due to frequent overlaps or evolution. [1]

Vitiligo is a skin autoimmune condition where CD8+ T cells attack and destroy melanocytes, leading to areas with no pigment production. The cause is still a subject of debate however, it is now understood that melanocytes in vitiligo patients are abnormal and more susceptible to cellular stress processes, such as oxidative stress and abnormal melanogenesis. This leads to the release of reactive oxygen species and triggers the unfolded protein response, which, in turn, prompts melanocytes to release signaling molecules that act as danger signals, alerting the innate immune system. This, in turn, activates and attracts adaptive immune CD8+ T cells to the skin, where they identify and eliminate the abnormal melanocytes.[1]

Vitamin D is produced in the skin through a photochemical process when the skin is exposed to sunlight containing ultraviolet B (UVB) rays. During this reaction, previtamin D is transformed into vitamin D. Vitamin D exists in two primary forms: cholecalciferol and ergocalciferol. These forms can be acquired through dietary sources. Ergocalciferol, known as vitamin D2, is naturally found in fungi and yeast, while cholecalciferol, also known as vitamin D3, is present in animal-derived foods (herring and mackerel).[2]

Given the well-established fact that calciferols can be photochemically converted from ergosterol and 7-dehydrocholesterol (pro-vitamin D3) through exposure to ultraviolet B (UVB) irradiation, it was suggested that cholecalciferol could have a role in the natural process of melanogenesis induced by sunlight in human skin. [3] This was further proven by the Tomita et. al, saying that cholecalciferol, or vitamin D, has a stimulating impact on melanocytes, specifically in the context of photoinduced skin pigmentation. This includes the initiation of tyrosinase synthesis, enlargement of cell size, and the

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extension of cell dendrites, which facilitate the transfer of melanin granules to nearby keratinocytes in the skin.[4]

Low vitamin D levels have been linked to vitiligo, an autoimmune condition. Some experts believe that vitamin D deficiency might even trigger autoimmune diseases. Therefore, vitamin D supplements could potentially be used to treat vitiligo.

The synthesis of vitamin D occurs in epidermis from the precursor molecule 7-dehydrocholesterol (provitamin D3) to previtamin D3 by ultraviolet B (UVB) radiation [5]. Previtamin D3 next converted into vitamin D3 (cholecalciferol) through spontaneous, temperature-dependent isomerization. Once in the circulation, vitamin D is transformed into 25-hydroxyvitamin D (25- (OH)D3 by hepatic hydroxylase enzyme The amount of circulating 25(OH)D3 in the blood is a good indicator of overall vitamin D status and can help diagnose deficiency. Getting enough sunlight and consuming vitamin D-rich foods are key to maintaining healthy vitamin D levels. However, the effectiveness of vitamin D supplements depends on a person's initial vitamin D levels, so blood tests are recommended after starting treatment.

This study aims to determine the efficacy of oral vitamin D supplementation on serum vitamin D levels and disease severity in vitiligo patients. It reviewed randomized and non-randomized controlled trials assessing serum 25(OH)D3 levels and/or VASI scores in vitiligo patients to evaluate the potential benefits of vitamin D supplementation for this condition.

Objectives of the Study

The main objective of this study is to determine the efficacy of oral vitamin D supplementation on the serum vitamin D levels and disease severity of vitiligo patients.

The specific objectives are:

1. To conduct a thorough and in-depth review of the effectiveness in the treatment of vitiligo and in serum levels of vitamin D in response to oral vitamin D supplementation
2. To pool the mean differences and statistically compare serum vitamin D levels in vitiligo patients given oral vitamin D supplementation

Methodology

Study Design

This research is a quantitative systematic review on the efficacy of oral vitamin D supplementation in vitiligo patient. This study adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA).

Inclusion and Exclusion criteria

Inclusion Criteria

- Randomized and non-randomized clinical trials
- Study in patients diagnosed with vitiligo by any diagnostic methods
- Intervention of oral vitamin D supplementation with or without other treatment modalities, compared to without oral vitamin D supplementation in the treatment of vitiligo patients
- Study with at least one of the following outcome measurements: Vitiligo Area Severity Index (VASI score) and serum vitamin D levels

Exclusion Criteria

- Non-human research (i.e., animal or cell biology research)
- Duplicate publications
- Studies with insufficient data for pooling even after attempts of contacting the author/s
- Study published in languages the reviewers cannot translate

Data Sources and Strategy

Keywords used for the literature search include the following:

1. "vitiligo"
2. "oral vitamin D supplementation"
3. "serum 25(OH)D" or "serum 25-hydroxy vitamin D"
4. "VASI scoring" or "Vitiligo Area Severity Index scoring"
5. "trial" OR "clinical trial"

These terms were used into accessible electronic databases, including PubMed Central, Cochrane Library, Google Scholar, Embase, Science Direct, Clinical Key, eMedicine, Wiley Online Library, and Herdin. Additionally, the reference lists of all collected studies pertinent to the research were reviewed.

Data Collection

The primary investigator selected and screened articles by the information from the title and abstract, based on the abovementioned inclusion and exclusion criteria. The primary investigator then thoroughly read on the screened articles to gather data including the author, publication, patient characteristics, sample size, intervention, treatment protocol, outcome measures.

Outcome Measures

The primary outcomes collected in each journal article include: 1) serum vitamin D levels of vitiligo patients before and after intervention, and/or 2) disease extent and severity using VASI score. Serum 25-hydroxyvitamin D [25(OH)D] concentration is considered the gold standard biomarker for vitamin D status, widely used in clinical and epidemiologic research. An increase in serum 25(OH)D levels following supplementation represents improved systemic vitamin D status. VASI score, on the other hand, is a validated clinical tool that quantifies the extent and severity of vitiligo lesions, directly correlating with patient burden and repigmentation outcomes. Together, these outcome measures allow assessment of both biochemical efficacy and clinical impact of oral vitamin D supplementation.

Statistical Analysis Plan

All statistical analyses in this systematic review were performed using Revman 5.4.1, following the PRISMA guidelines. Difference

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between the serum vitamin D levels in response to the oral vitamin D supplementation were analyzed. The results of each RCT were plotted into Revman to create a forest plot to derive the resulting direct effects and the studies significance. To ensure quality of the RCT, publication bias analysis and test of heterogeneity were employed.

Quality Assessment

Studies were independently reviewed and assessed using the JBI Critical Appraisal Tool for Randomized Controlled Trials. The JBI Critical Appraisal Tool [6] for Randomized Controlled Trials is a 13-item checklist that provide a descriptive assessment of potential studies to be included or excluded in the systematic review or meta-analysis. Unlike traditional assessment tools, there is no threshold which determines whether a study is to be included; rather, the assessment lies on the judgement of the researchers.

Results

Study Characteristics

A total of 8 articles were collected by searching PubMed Central, Cochrane Library, Google Scholar, Embase, Science Direct, Clinical Key, eMedicine, Wiley Online Library, and Herdin. After removing 2 duplicate studies and 1 prospective cohort study, 5 articles remained for screening based on the titles and abstracts. All 5 studies were available and read in full. These 5 studies were included for the systematic review and meta-analysis. (Figure 1)

The selected studies were either randomized controlled trials (RCTs) or non-randomized controlled trials (nRCTs) conducted within the last 11 years. The sample sizes of these studies ranged from 8 to 24 participants, with age ranges from 25 to 51 years. These trials involved patients with either generalized or non-segmental vitiligo, without specifying the affected areas of the body. The studies were conducted in various countries: Indonesia, Brazil, Mexico, Iran, and Japan. Although all five studies reported serum vitamin D levels of the patients, only two included data on the Vitiligo Area Scoring Index (VASI) scores. The characteristics of the trials are summarized in (Table 1), and details on the experimental and control groups are summarized in (Table 2).

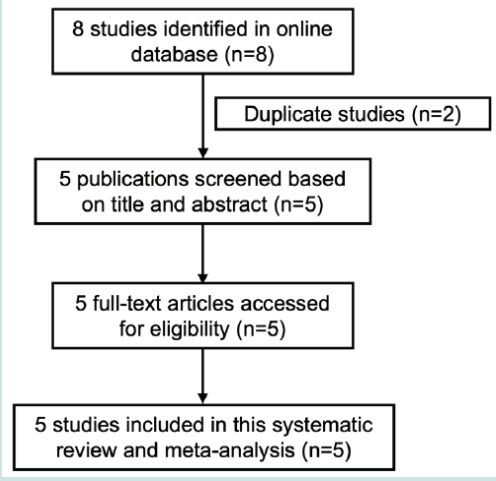

Figure 1: Protocol flowchart for study

Risk of Bias

The risk of bias assessment for randomized controlled trials (RCTs) was evaluated using the JBI Critical Appraisal Tool. Based on the researchers' assessments, the studies by Dwiyana et al. (2019) [5], Finamor et al. [7]. Garza-Davila et al. (2023) [8], Omidian et al. (2018) [9], and Watabe et al. (2018) [10] were included in the systematic review and meta-analysis. Four out of the five studies were randomized; however, only one detailed the randomization procedure and allocation concealment. One study lacked a control group, as all subjects underwent the intervention. Among the two studies that included the Vitiligo Area Scoring Index (VASI) as an outcome measure, only one specified that the assessment was conducted by three blinded board-certified dermatologists. Detailed information regarding the risk of bias is provided in (Table 3).

Response to Therapy

Serum 25(OH)D3 Levels

All five included RCTs involved vitamin D supplementation, administered orally at dosages of either 5,000 IU or 35,000 IU once daily, or 50,000 IU once every two weeks and measurement of serum 25(OH)D3 levels pre and post-intervention (Table 2). Additionally, three of these studies incorporated narrowband ultraviolet B (NB-UVB) therapy as part of the treatment. One study permitted patients to continue using their current topical glucocorticoids or topical tacrolimus.

Based on the result of the statistical test, we find that the overall mean difference in the serum vitamin D levels of the patients before and after the vitamin D supplementation to be statistically significant. As presented in the (Table 4), we find significant increase in the serum vitamin D levels of the patients after vitamin D supplementation across all studies. (Figure 2) shows the forest plot of the meta-analysis conducted on the changes in serum vitamin D levels of the patients.

Vitiligo Area Severity Index (VASI)

Only two of the five studies included in this review used the Vitiligo Area Scoring Index (VASI) as an outcome measure (Table 2). In these studies, the subjects underwent narrowband ultraviolet B (NB-UVB) therapy, while the intervention group received either 5,000 IU of vitamin D daily or 50,000 IU once every two weeks as supplementation. Table 5 summarizes the meta-analysis results on the changes in VASI scores of the patients after vitamin D supplementation.

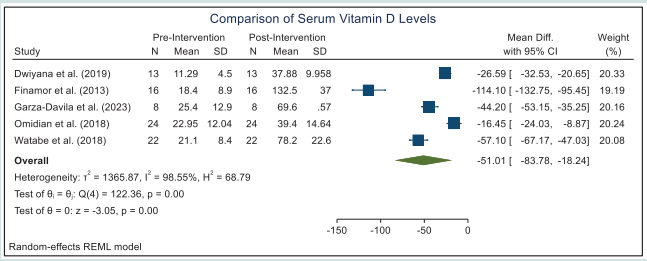

Figure 2: Comparison of serum vitamin D levels before and after vitamin D supplementation.

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Table 1: Baseline characteristics of included studies

Author (Year)	Type of Study	Age	Sex (M/F)	Vitiligo type	Treatment duration	Fitzpatrick skin type (n)	**Country**	Sample Size
Dwiyana et al. (2019)	RCT	39.61 ±15.91	4/9	NSV	8 weeks	N/A	Indonesia	13
Finamor et al. (2013)	nRCT	49.2 ±11.9	3/9	NSV	24 weeks	III – 11 IV – 4 V - 1	Brazil	16
Garza-Davila et al. (2023)	RCT	41.5 ±11.2	4/4	Generalized	24 weeks	III – 3 IV - 5	Mexico	8
Omidian et al. (2018)	RCT	25.54 ±14.9	12/12	NSV	8 weeks	N/A	Iran	24
Watabe et al. (2018)	RCT	51.2 ±10.3	0/22	NSV	20 weeks	N/A	Japan	22

RCT, randomized controlled trials; nRCT, non-randomized controlled trials; NSV, nonsegmental vitiligo; N/A,not available

Table 2: Summary of interventions and main outcome measures in the experimental and control groups

Author (Year)	**Experimental Group**		**Control Group**		**Main Outcome Measure**
	Vitamin D supplementation	**Other treatment modalities**	**Vitamin D supplementation**	**Other treatment modalities**	
Dwiyana et al. (2019)	5000 IU of Vitamin D per day per orem for 8 weeks	NB-UVB phototherapy twice a week	Placebo	NB-UVB phototherapy twice a week	Serum 25(OH)D3 levels
Finamor et al. (2013)	35,000 IU of vitamin D per day per orem for 24 weeks	N/A	N/A	N/A	Serum 25(OH)D3 levels
Garza-Davila et al. (2023)	5000 IU of Vitamin D per day per orem for 24 weeks	NB-UVB phototherapy	Placebo	NB-UVB phototherapy	Vitiligo Area Severity Index (VASI) and Serum 25(OH)D3 levels
Omidian et al. (2018)	50,000 units once every 2 weeks per orem for 8 weeks	NB-UVB phototherapy twice a week for 16 weeks	Placebo	NB-UVB phototherapy twice a week for 16 weeks	Vitiligo Area Severity Index (VASI) and Serum 25(OH)D3 levels
Watabe et al. (2018)	5000 IU of cholecalciferol per day per orem for 20 weeks	Topical glucocorticoid or topical tacrolimus	Placebo	Topical glucocorticoid and topical tacrolimus	Serum 25(OH)D3 levels

NB-UVB, narrowband-UVB; N/A, not available

Table 3: Risk of bias assessment using JBI Critical Appraisal Tool for Randomized Controlled Trials

Author (Year)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**Total**	**Assessment**[1]
Dwiyana et al. (2019)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	11/13	Include
Finamor et al. (2013)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	11/13	Include
Garza-Davila et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	12/13	Include
Omidian et al. (2018)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	11/13	Include
Watabe et al. (2018)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	11/13	Include

1 The JBI Critical Appraisal Tool for Randomized Controlled Trials is a 13-item checklist that provides a descriptive assessment of potential studies to be included or excluded in the systematic review or meta-analysis. Unlike the Newcastle-Ottawa Scale, there is no threshold which determines whether a study is to be included; rather, the assessment lies on the judgment of the researchers.

Table 4: Summary of meta-analysis results on changes in serum vitamin D levels

Studies	**Pre-intervention**	**Post-intervention**	**Mean Difference**
Dwiyana et al. (2019)	11.29 (± 4.50)	37.88 (± 9.96)	26.59 [-32.53, -20.65]
Finamor et al. (2013)	18.40 (± 8.90)	132.50 (± 37.00)	-114.10 [-132.75, -95.45]
Garza-Davila et al. (2023)	25.40 (± 12.90)	69.60 (± 0.57)	-44.20 [-53.15, -35.25]
Omidian et al. (2018)	22.95 (± 12.04)	39.40 (± 14.64)	-16.45 [-24.03, -8.87]
Watabe et al. (2018)	21.10 (± 8.40)	78.20 (± 22.60)	-57.10 [-67.17, -47.03]
Overall Mean Difference[1]			-51.01 [-83.78, -18.24]
p-value[2]			0.000**

1 The random-effects model based on inverse-variance weighting was used to conduct the meta-analyses. The Paule-Mandel specification was implemented to calculate for the between study variance (tau2).
2 A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. ** signifies that the p-value is statistically significant at the 1% level, while * signifies that the p-value is statistically significant at the 5% level.

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Table 5: Summary of meta-analysis results on changes in VASI scores

Studies	Pre-intervention	Post-intervention	Mean Difference
Garza-Davila et al. (2023)	21.90 (± 10.10)	8.10 (± 5.90)	13.80 [5.69, 21.91]
Omidian et al. (2018)	27.14 (± 19.45)	4.40 (± 6.40)	22.74 [14.55, 30.93]
Overall Mean Difference[1]			18.25 [9.49, 27.01]
p-value[2]			0.000**

1. The random-effects model based on inverse-variance weighting was used to conduct the meta-analyses. The Paule-Mandel specification was implemented to calculate for the between study variance (tau2).
2. A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. ** signifies that the p-value is statistically significant at the 1% level, while * signifies that the p-value is statistically significant at the 5% level.

Based on the result of the statistical test, we find that the overall mean difference in the VASI scores of the patients before and after the vitamin D supplementation to be statistically significant. As presented in the table, we find significant decrease in the VASI scores of the patients after vitamin D supplementation across the two studies. (Figure 3) shows the forest plot of the meta-analysis conducted on the changes in VASI scores of the patients.

Measures of Heterogeneity and Publication Bias

Measures of Heterogeneity

Based on the homogeneity tests based on the Q statistic indicated a statistically significant presence of heterogeneity in studies on changes in serum vitamin D levels but not in studies on changes in VASI scores. (Table 6) summarizes the different heterogeneity measures from the meta-analyses.

Publication Bias

We find a presence of publication bias for studies on changes in serum vitamin D levels but not in studies on changes in VASI scores. (Table 7) summarizes the results of Egger's test for publication bias.

Limitations of the Study

Clinical trials exhibit variability in outcome measures, follow-up periods, intervention periods. Fitzpatrick skin types, diets, sun exposure, and other factors that may affect the results of each study. Additionally, the clinical trials included in this study differ in the dosing regimens of vitamin D supplementation, and some incorporated additional interventions alongside oral vitamin D supplementation, which may further influence the results. Limitations of this study include small sample sizes, and the inclusion of non-randomized trials, all of which may impact the generalizability and reliability of the findings.

Discussion

Serum 25(OH)D3 Levels

This systematic review revealed a statistically significant increase in serum 25(OH)D levels and a concomitant improvement in VASI scores following oral vitamin D supplementation in patients with vitiligo. Forest plot analysis of serum 25(OH)D levels demonstrated a consistent post-intervention elevation across studies. However,

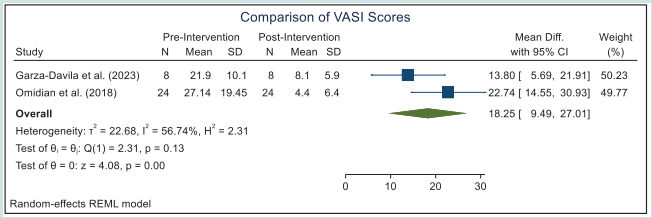

Figure 3: Comparison of VASI scores before and after vitamin D supplementation.

Table 6: Summary of measures of heterogeneity

Measures	T^2	I^2	H^2	p-values[1]
Changes in serum vitamin D levels	1365.87	98.55%	68.79	0.000**
Changes in VASI scores	22.68	56.74%	2.31	0.130

1 A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. ** signifies that the p-value is statistically significant at the 1% level, while * signifies that the p-value is statistically significant at the 5% level.

Table 7: Results of Egger's test for publication bias

Measures	Beta	Standard Error of Beta	p-values[1]
Changes in serum vitamin D levels	-14.74	2.552	0.000**
Changes in VASI scores	202.68	133.302	0.128

[1] A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. ** signifies that the p-value is statistically significant at the 1% level, while * signifies that the p-value is statistically significant at the 5% level.

substantial heterogeneity was observed, suggesting potential variations in treatment response among participants.

A closer examination of the included studies indicates that the heterogeneity might be attributed to differing intervention protocols. While Finamor et al [7]. Exclusively employed oral vitamin D supplementation, the remaining studies incorporated additional therapies such as topical glucocorticoids, tacrolimus, or narrowband ultraviolet B (NB-UVB). Furthermore, variations in vitamin D dosage and treatment duration across studies could also contribute to the observed heterogeneity. Across trials, supplementation was administered at 5,000 IU/day, 35,000 IU/day, or 50,000 IU once every two weeks. These high-dose protocols were designed for research purposes and differ from standard clinical recommendations. According to the Endocrine Society guidelines, adults at risk of deficiency typically require 1,500–2,000 IU/day for maintenance, with higher doses only under supervision. To ensure safety, serum 25(OH) D and calcium are generally monitored every 8-12 weeks, particularly with high-dose or bolus regimens. In the reviewed trials, laboratory testing was consistently performed at baseline and post-intervention, and some incorporated mid-treatment monitoring, ensuring both efficacy and safety surveillance.

Several studies have correlated the relationship between serum vitamin D levels and predisposition to or severity of vitiligo. A meta-analysis of observational studies conducted by Upala et al. has shown a correlation between lower serum levels of 25-hydroxyvitamin D and vitiligo [11] similar to our study's results. However, it remains

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uncertain whether this associated with vitiligo, similar to its role in other autoimmune diseases. Similarly, Saleh et al.'s study found that patients having both vitiligo and autoimmune diseases had lower serum levels of 25(OH)D compared to vitiligo patients without autoimmune conditions, although this difference was not statistically significant. [12] This study also concluded that age, duration of vitiligo, affected body surface area has no statistically significant correlations with the serum 25(OH)D levels of patients.

On the other hand, studies by Khurum et al [13] and Karaguzel et al [14] to determine the level of serum vitamin D in adult[13] and pediatric[14] vitiligo patients compared to control's reveal that there is no significant difference in vitamin D serum levels between individuals with vitiligo and those without. However, the deficiency in 25(OH)D levels within the various subgroups of vitiligo patients could be associated with factors such as younger age, male gender, a shorter duration of vitiligo, and the absence of phototherapy use.[13]

Environmental and Geographic Factors

Environmental and geographic factors also influenced baseline vitamin D levels. Endogenous synthesis varies depending on latitude, climate, and sun exposure. For example, patients in equatorial regions such as Indonesia and Brazil may start with higher vitamin D status compared to patients in Japan, were lower UV indices and seasonal variation limit synthesis. Dietary intake adds further variability. These environmental and nutritional differences should be accounted for in future trials to reduce confounding.

Vitiligo Area Severity Index

The forest plot analysis of VASI scores demonstrated a significant reduction in vitiligo severity following vitamin D supplementation across both included studies. Despite the clear overall benefit, moderate heterogeneity was observed, suggesting potential variations in treatment response among patient populations or study conditions. Although both studies incorporated NB-UVB therapy, differences in vitamin D dosage regimens may have influenced the observed heterogeneity. Moreover, it can be inferred that bolus dosing of vitamin D presented with better VASI scores.

The result of this study coincides with the In vitro studies done by Tomita et. al, showed that vitamin D3 increases the tyrosinase content of cultured melanocytes. [4] This was further elaborated by the study of Watabe et al. wherein they observed an increase in L-3,4-dihydroxyphenylalanine-positive (DOPA-positive) cells following treatment with 1,25(OH) 2D3 in primary neural crest cell cultures.[15] These results suggest that 1,25(OH) 2D3 may promote the maturation of early melanocyte precursors. Moreover, the study of Karaguzel et. al [14] demonstrated that combining oral vitamin D with topical tacrolimus in pediatric patients with vitiligo is more effective at achieving repigmentation compared to using topical tacrolimus alone. Collectively, these studies suggest that it is plausible to consider vitamin D supplementation as a potential therapy for autoimmune diseases like vitiligo.

Conclusion and Recommendations

In conclusion this systematic review suggests that oral vitamin D supplementation shows statistically significant increase in the serum vitamin D levels in vitiligo patients. It also shows improvement on vitiligo severity, as measured by the VASI scoring system. The high heterogeneity of the studies included in this review should be taken into consideration. Further comprehensive studies, including larger sample size, more high-quality RCTs with similar methodologies are needed to conduct a more objective analysis on the efficacy of oral vitamin D supplementation on the serum vitamin D levels and disease severity of vitiligo patients.

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