International Journal of Pharmaceutical and Clinical Research

ISSN Print: 2664-7591
ISSN Online: 2664-7605
Impact Factor: RJIF 5.2
IJPCR 2025; 7(1): 49-52
www.pharmaceuticaljournal.in
Received: 19-03-2025
Accepted: 23-04-2025

Christina Pritha Rozario
Ph.D., Scholar, Department of Food and Nutrition, Swami Vivekananda University, Barrackpore, Kolkata, West Bengal, India

Corresponding Author:
Christina Pritha Rozario
Ph.D., Scholar, Department of Food and Nutrition, Swami Vivekananda University, Barrackpore, Kolkata, West Bengal, India

An evidence-based study for assessment of the effects of Vitamin D in the treatment of vitiligo

Christina Pritha Rozario

DOI: https://www.doi.org/10.33545/26647591.2025.v7.i1a.124

Abstract
The active form of vitamin D, namely— 1,25-dihydroxy vitamin D acts as a steroid hormone that regulates a myriad of biological responses through its nuclear receptor (VDR). The VDR occupies 2,776 positions in the human genome; making up about 10% of the human genes directly and/or indirectly responsive to vitamin D. Similarly, a wide range of human cells like that of muscle, bone, skin, blood vessels, brain, colon, breast, prostate, and immune cells encode for the enzyme 25-hydroxyvitamin D-1 α-hydroxylase suggesting that the extra-renal intracrine and paracrine 1,25(OH)2D3 synthesis may critically affect the activities of many tissues and organs. Cumulative data originating from several in-vivo as well as clinical studies have associated low vitamin D status (as assessed by the levels of circulating 25-hydroxyvitamin D3 or 25(OH)D3) not only with bone-related disorders such as rickets and osteoporosis but also with several infectious diseases as well as cancer, secondary hyperparathyroidism and autoimmune diseases like multiple sclerosis, systemic lupus erythematosus, psoriasis, rheumatoid arthritis, and type 1 diabetes. Vitiligo is a pigmentary disorder of autoimmune origin that is characterized by anomalous loss of functional melanocytes from the epidermis. Although the exact etiological causes of vitiligo are yet to be known, numerous studies over the years have indicated an interrelationship of vitamin D with vitiligo. Vitamin D influences skin pigmentation by increasing tyrosinase activity and melanogenesis and its immunoregulatory functions, thereby exerting a positive response in the treatment of vitiligo. Therefore, this review article aims to discuss the various interventional studies that have been carried out so far to observe the effect of oral and topical administration of Vit D in the management and treatment of vitiligo. Understanding its mechanisms will facilitate the integration of genomic information into the workup of individualized patient care and make better clinical and nutritional decisions.

Keywords: Vitamin D, vitiligo, auto-immune disorder, oral administration, clinical studies

Introduction

Vitiligo is a long-term skin disorder identified by skin patches that lose their pigment. It occurs when the body's immune system destroys melanocytes (melanin-producing skin cells, the chemical that gives skin, eyes, or hair it's colour or pigmentation). It is a form of autoimmune disorder. Its pathogenesis begins with altered melanocytes that exhibit an elevated cellular response, resulting in the loss of melanocytes from the epidermis and clinically shows demarcated white patches on the body (Bishnoi and Parsad, 2018) [6]. The skin colour becomes lighter and shows patches. The exact reason these pigment cells get destroyed or die is still unclear. However, it is thought to be associated with an autoimmune disorder, hereditary, or trigger events such as stress, severe sunburn, or skin trauma (contact with chemical) (Nordlund *et al*., 1989) [14].

It has an estimated prevalence of 0.5-2% of the world’s population. Approximately, 25-50% of people with vitiligo have a parent with vitiligo, and around 6% have vitiligo siblings. The risk of vitiligo in the other family members is not predictable (Silverberg, 2015) [18]. The skin hair can also turn white as well as the inside of the mouth and nose.

Loss of skin colour, which primarily appears on the hands, face, and areas around body openings and the genitals. Getting a white or grey colour of the hair on the scalp at a very young age, eyelashes or eyebrows, or beard are a few common effects of this disease. Colour loss in the tissues inside of the mouth and nose may also be seen. There is no fixed age for vitiligo to develop, however it usually appears before age 30. There are mainly three types of vitiligo, segmental (an uncommon form of localized vitiligo, characterized by dermatomal distribution. It is often unilateral and asymmetrical that never crosses the midline of the body), non-segmental (This is a depigmented skin disorder showing acquired, progressive, and depigmented lesions of the skin, mucosa, and hair. Research believes it to be caused mainly by the autoimmune loss of melanocytes from the involved areas. It is often linked with other autoimmune diseases, particularly autoimmune thyroid diseases including Hashimoto's thyroiditis and Graves' disease, rheumatoid arthritis), and mixed vitiligo (a rare combination of both segmental vitiligo and non-segmental vitiligo) (Taylor *et al*., 2002) [19].

Recent studies demonstrate that a high dose of vitamin D therapy may be safe and effective in reducing vitiligo activity. Melanocytes express vitamin D receptors, and vitamin D status can affect their function. Reduced serum levels of vitamin D have been linked with this as well as other skin conditions. However, the effectiveness of vitamin D analogues is controversial with limited data (Finamor *et al*., 2013) [10].

The role of Vitamin D in skin pigmentation

1,25-(OH)2D3 and its chemical analogues regulate the function of cells mainly through the manipulation of their transcriptional machinery employing the vitamin D receptor (VDR). VDR is considered to be a 427-amino-acid containing protein with numerous functional regions, namely, a short activation function-1 (AF-1), a DNA binding domain (DBD), a multifunctional domain with the ligand-binding domain (LBD), the retinoid X receptor (RXR) heterodimerization motif, and a ligand-dependent transactivation function, activation function-2 (AF-2). VDR is the sole nuclear protein that binds vitamin D hormone with high affinity and belongs to the steroid/thyroid nuclear receptor superfamily (Birlea, Costin, and Norris, 2008) [5]. VDR is considered to be a ligand-activated transcription factor that binds to certain DNA sequences in vitamin D responsive genes (vitamin D responsive elements, VDREs) and hence regulates their transcription. Several genes in multiple tissues and organs including the skin consist of VDRE in their promoter region. Gene expression along with known inflammatory, proliferative, differentiation, and adhesive functions of these genes are modulated by the VDR-ligands (Nagpal, Na, and Rathnachalam, 2005) [13]. There are three ways in which VDRs regulate the expression of vitamin D-responsive genes— by binding to VDRE, the expression of specific genes can be actively regulated; by binding to negative VDRE (nVDRE), it negatively regulates the expression of other genes; or by inhibiting the action of specific transcription factors such as nuclear factor-activated T cells (NFAT) and nuclear factor-kB (NF-kB). Therefore, Vitamin D influences the transcriptional mechanisms of these genes and acts as the coordinator of growth factors and cytokine network of the skin as well as the cells associated with skin such as melanocytes, keratinocytes, macrophages, fibroblasts, and T cells. This implies that vitamin D compounds can target inflammation and proliferative activity associated with various skin diseases (Birlea, Costin, and Norris, 2008) [5]. Loss of melanocytes from the epidermis, resulting in skin depigmentation is a common phenomenon in vitiligo. Removal of melanocytes have been linked with cell apoptosis. De Haes *et al*., (2003) [9] observed that 1,25-(OH)2D3 diminishes apoptotic activity in UVB-induced keratinocytes and melanocytes. Vitamin D exerted protective effects on melanocytes by mitigating DNA damage (Brożyna *et al*., 2011) [7].

Table 1: Overall Outline of the Inflammatory Cytokines documented to being associated with vitiligo depigmentation and whose expression is determined by vitamin D ligands.

Cytokine	Principal Source	Primary Activity	References
IL-2	CD4 Th cells	• Assist T cell survival. • Promotes clonal T cell proliferation. • Promotes accretion of B cells. • Restores proliferation and activation of antigen-presenting cells (dendritic cells, macrophages) and activates cytokines and helper T cells, conducted to melanoma-associated antigens.	•
IL-6	Aroused Th2 cells APCs Monocytes Macrophages	• Induced ICAM expression. • Induced polyclonal B cell activation, increasing auto-antibody production, and causation of melanocyte damage in vitiligo.	•
IL-8	Macrophages Endothelial cells	• Able to draw polymorphonuclear neutrophils and T lymphocytes to the site of the lesions, raising inflammatory reactions and, therefore facilitating melanocytic cytotoxicity.	•
TNF-α	Macrophages Mast cells Natural killer cells.	• Elementary inflammatory mediator • Concerned in melanocyte programmed death.	•
IFN-γ	Th1 cells T cells natural killer cells	• Elementary inflammatory mediator • Concerned in melanocyte programmed death.	•

Interventional studies targeting the treatment of vitiligo with Vitamin D

In-vitro studies with the objective of elucidating the relationship between Vit D and melanocyte functions have provided promising results that make Vit D a potential therapeutic agent for the treatment of vitiligo. Watabe *et al*., (2002) [22] studied the role of vitamin D3 in melanocyte development and melanogenesis. They observed that 1,25(OH)2D3 treatment enhances the number of L-3,4-dihydroxyphenylalanine-positive (DOPA-positive) cells in primary neural crest cell cultures, thereby indicating the stimulatory effects of 1,25(OH)2D3 in the differentiation of immature melanocyte precursors. Oikawa, and Nakayasu, (1974) [15] treated murine B16 melanoma cells with vitamin D3 and observed a notable rise in melanogenesis as well as tyrosinase activity. Tomita *et al*., (1988) [20] made similar observations and demonstrated that vitamin D3 could increase the tyrosinase activity in cultured human melanocytes. Xu *et al*., (2004) [23], in their study, observed that vitamin D and UVB irradiation promoted the proliferation of melanocytes. This finding is crucial as it implies that this combination might be effectively used to treat vitiligo.

Silverberg *et al*., (2010) [17] in their prospective cohort study observed very low levels of 25 hydroxy vitamin D (<15 ng/mL) to be associated with auto-immunity in patients suffering with vitiligo. Karagüzel *et al*., (2016) [12], conducted a prospective study where he supplemented oral doses of Vit D along with topical tacrolimus to thirty patients aged 6-17 years, with vitiligo, for six months. Thirty sex- and age-matched apparently healthy controls were also included in this prospective study. They found that the lesion size reduced significantly in vitiligo patients being treated with both topical tacrolimus and Vit D oral supplementation in comparison to patients being treated with tacrolimus alone. A dosage of 1500 IU/day of vitamin D was administered to patients with the serum 25(OH)D levels <20 ng/ml and 3000 IU/day to patients having the levels <10 ng/ml, for a period of six months. The topical application of vitamin D yields significant results when used in combination with tacrolimus and vitamin D in treating this autoimmune disorder. Colucci *et al*., (2019) [8] conducted an observational study using medical records of 101 vitiligo patients. Their objective was to correlate baseline levels of 25(OH)D with the re-pigmentation of vitiligo macules, for a follow-up period of 6-months. They concluded that very low levels of 25(OH)D (≤20 ng/mL) and insufficient levels of 25(OH)D (21-29 ng/mL) was significantly associated with active vitiligo. On the other hand, stable disease was found to be significantly associated with sufficient 25(OH)D levels (30-100 ng/mL). After 6 months, vitiligo patients with sufficient 25(OH)D levels (30-100 ng/mL) had experienced a significantly higher degree of re-pigmentation, thereby highlighting the importance of serum Vit D levels (Ambagaspitiya *et al*., 2025) [3].

Upala *et al*., (2016) [21] in their meta-analysis observed a significant relationship between the levels of 25(OH)D and vitiligo. They concluded that lower 25(OH)D levels were associated with vitiligo. Zhang *et al*., (2018) [24] in their meta-analysis made similar observations corroborating the positive association of lower levels of serum 25(OH)D with the incidence of vitiligo. Ambad *et al*., (2020) [20] did not find any significant differences in the serum levels of Vit D among vitiligo patients and controls, and therefore suggest larger controlled investigations to demonstrate whether low levels of Vit D result in vitiligo.

Conclusion

Topical steroids and surgical techniques are popular therapy against vitiligo for most patients. Over the recent years accumulating evidence indicates an alternative mode of treatment for patients with vitiligo. As discussed throughout this article; Vit D gives positive outcomes, in addition to the vast array of genotypic determinants that influence this condition A person acquires a complete set of genes from each parent that donate both directly and indirectly to the pathogenesis of the disease. Vitamin D proves to decrease the expression of various cytokines that cause vitiligo. It increases melanogenesis and the tyrosinase content of cultured human melanocytes by its antiapoptotic effect. Studies show positive results when tacrolimus is combined with vitamin D or vitamin D alone is given to patients with vitiligo.

The results of the other recent studies, surveys, and statistical methods that are done yield significant results for most of the subjects but not for all. Therefore, larger controlled studies are required to come up with a strong and stable answer to whether or not vitamin D supplementation should be given for the treatment of vitiligo patients in the future.

References

1. Adorini L. Intervention in autoimmunity: the potential of vitamin D receptor agonists. Cell Immunol. 2005;233(2):115-124.
2. Ambad RS, Suryawanshi M, Jha RK, Mulchandani PD, Singh S. To assess the serum vitamin D in vitiligo patients: SMHRC and AVBR Hospital of Vidarbha Region. Indian J Forensic Med Toxicol. 2020;14(4).
3. Ambagaspitiya SS, Appuhamillage GA, Wimalawansa SJ. Impact of vitamin D on skin aging, and age-related dermatological conditions. Front Biosci (Landmark Ed). 2025;30(1):25463.
4. Amer MA, Khater GME, Marei MA, Firjani AAB. Evaluation of serum level of 25-hydroxy vitamin C in vitiligo patients. Zagazig Univ Med J. 2019;25(6):935-940.
5. Birlea SA, Costin GE, Norris DA. Cellular and molecular mechanisms involved in the action of vitamin D analogs targeting vitiligo depigmentation. Curr Drug Targets. 2008;9(4):345-359.
6. Bishnoi A, Parsad D. Clinical and molecular aspects of vitiligo treatments. Int J Mol Sci. 2018;19(5):1509.
7. Brożyna AA, Jozwicki W, Janjetovic Z, Slominski AT. Expression of vitamin D receptor decreases during progression of pigmented skin lesions. Hum Pathol. 2011;42(5):618-631.
8. Colucci R, Conti R, Dragoni F, Cammi A, Cianferotti L, Brandi ML, *et al*. Evidence of a possible therapeutic role of vitamin D in a cohort of adult Caucasian vitiligo patients. [Journal name missing - please provide for complete reference].
9. De Haes P, Garmyn M, Degreef H, Vantieghem K, Bouillon R, Segaert S. 1,25-Dihydroxyvitamin D_3 inhibits ultraviolet B-induced apoptosis, Jun kinase activation, and interleukin-6 production in primary human keratinocytes. J Cell Biochem. 2003;89(4):663-673.
10. Finamor DC, Sinigaglia-Coimbra R, Neves LC, Gutierrez M, Silva JJ, Torres LD, *et al*. A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of vitiligo and psoriasis. Dermatoendocrinol. 2013;5(1):222-234.
11. Karagun E, Ergin C, Ekiz O. The role of serum vitamin D levels in vitiligo. Adv Dermatol Allergol/Postepy Dermatol Alergol. 2016;33(4):300-302.
12. Karagüzel G, Sakarya NP, Bahadır S, Yaman S, Ökten A. Vitamin D status and the effects of oral vitamin D treatment in children with vitiligo: a prospective study. Clin Nutr ESPEN. 2016;15:28-31.
13. Nagpal S, Na S, Rathnachalam R. Noncalcemic actions of vitamin D receptor ligands. Endocr Rev. 2005;26(5):662-687.
14. Nordlund JJ, Abdel-Malek ZA, Boissy RE, Rheins LA. Pigment cell biology: an historical review. J Invest Dermatol. 1989;92(4 Suppl):S53-S60.

15. Oikawa A, Nakayasu M. Stimulation of melanogenesis in cultured melanoma cells by calciferols. FEBS Lett. 1974;42(1):32-35.
16. El Abd RA, Hamada MB, El-Sayed MT, Tolba N. Vitamin D and platelet rich plasma in the treatment of vitiligo. Fayoum Univ Med J. 2019;3(1):60-70.
17. Silverberg JI, Silverberg AI, Malka E, Silverberg NB. A pilot study assessing the role of 25 hydroxy vitamin D levels in patients with vitiligo vulgaris. J Am Acad Dermatol. 2010;62(6):937-941.
18. Silverberg NB. The epidemiology of vitiligo. Curr Dermatol Rep. 2015;4:36-43.
19. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease. J Am Acad Dermatol. 2002;46(2 Suppl):S41-S62.
20. Tomita Y, Torinuki W, Tagami H. Stimulation of human melanocytes by vitamin D_3 possibly mediates skin pigmentation after sun exposure. J Invest Dermatol. 1988;90(6).
21. Upala S, Sanguankeo A. Low 25-hydroxyvitamin D levels are associated with vitiligo: a systematic review and meta-analysis. Photodermatol Photoimmunol Photomed. 2016;32(4):181-190.
22. Watabe H, Soma Y, Kawa Y, Ito M, Ooka S, Ohsumi K, *et al*. Differentiation of murine melanocyte precursors induced by 1,25-dihydroxyvitamin D_3 is associated with the stimulation of endothelin B receptor expression. J Invest Dermatol. 2002;119(3):583-589.
23. Xu QX, Du J, He PY, Zhang JZ, Zhu TJ. Effects of 1α,25-dihydroxyvitamin D_3 and UVB on cell proliferation and melanin synthesis of cultured human melanocyte. J Peking Univ Health Sci. 2004;36(5):483-486.
24. Zhang JZ, Wang M, Ding Y, Gao F, Feng YY, Yakeya B, *et al*. Vitamin D receptor gene polymorphism, serum 25-hydroxyvitamin D levels, and risk of vitiligo: a meta-analysis. Medicine (Baltimore). 2018;97(29).