

# A Study to assess the association of vitamin D (serum 25 hydroxy vitamin D3) and vitiligo

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## Abstract

**Introduction:** Vitiligo is an acquired pigmentary anomaly of the skin. It is manifested via de-pigmentary white patches on the skin with normal border or surrounding hyperpigmentation. Over the recent years, vitD (vitamin D) is implicated in a wide variety of medical conditions. It functions like a hormone and is produced in the skin where it plays an important role in skin pigmentation, increase enzyme action of tyrosinase and thus also affects melanin production. It also displays various immunoregulatory functions. VitD is found to be reduced in autoimmune diseases, like SLE, DM, alopecia areata, RA and multiple sclerosis. There has been very few studies (over the past 10 years) to study the association of vitD (in blood samples) and vitiligo but their results were inconsistent and conflicting.

**Aim:** This study aimed to determine any association between serum vitamin D levels and vitiligo.

**Materials and Methodology:** In our study fifty diagnosed vitiligo patients and fifty healthy controls were included. VitD levels were measured from blood samples. Appropriate statistical methods were used for group comparisons.

**Results:** Serum vitD values were found to be less in cases than controls, but this difference was not statistically significant ( $p = 0.570$ ).

**Conclusion:** Since the role of vitD in pathogenesis of vitiligo is still unclear there is a need for larger controlled studies for establishing the association between lower circulating values of vitD and vitiligo.

**Keywords:** Vitiligo, Etiopathogenesis, Vitamin D, Autoimmune diseases.

## Introduction

Vitiligo, an autoimmune disorder, which is known to be due to the destruction of skin melanocytes, and is characterized by depigmented macules of different shapes.<sup>1</sup> Both genders have equal predilection and may also be associated with systemic autoimmune diseases such as lupus erythematosus, scleroderma, autoimmune thyroiditis and alopecia areata.<sup>2</sup> Reduced serum vitD (vitamin D) levels are found in many autoimmune diseases including systemic lupus erythematosus, diabetes mellitus, alopecia areata, multiple sclerosis and rheumatoid arthritis.<sup>1,3,4</sup>

VitD, originally associated with osteomalacia and rickets, has recently been revealed to have a role in a number of medical and dermatological diseases. The active form of vitD i.e vitamin D<sub>3</sub>, behaves as a hormone which has an imperative role in regulating bone and Ca<sup>++</sup> metabolism. This active form is also found to have certain immunoregulatory purposes and controlling cell proliferation.

It has been found that vitD receptors and the enzymatic reaction & machinery capable of converting the present 25-hydroxy vitD [25(OH)D] to its active form - vitamin D<sub>3</sub> [1,25(OH)D] and is present in majority of the cells in the body including the skin. There have now been found new roles for vitD in skin, such as immunomodulatory and anti-apoptotic effects thus raising a possibility of its use in conditions such as atopic dermatitis and infections.

VitD through receptors in B and T lymphocytes can affect both adaptive and innate immune system, and also in part by receptors in dendritic cells and macrophages.<sup>5</sup> Vitamin D<sub>3</sub> furthermore is also known to increase enzymatic activity of tyrosinase via a nuclear hormone receptor – the VDR (vitamin D receptor) in melanocytes and thus increase its production.<sup>1,6</sup>

There has been various epidemiological studies which investigated the association of vitD and autoimmune diseases including (but not limited to) vitiligo but all yielded conflicting and inconsistent results.

## Materials and Methodology

The study included 50 diagnosed vitiligo patients attending dermatology opd from 1<sup>st</sup> january 2018 to 31<sup>st</sup> april 2018. 50 healthy controls were also recruited after required matching was done based on demographics (age & sex) and skin phototype.

Through clinical history and physical/woods lamp examination, the expert dermatologist established/ refuted the diagnosis of vitiligo. None of the patients required biopsy for confirmation. Patients data were recorded, which included (but was not limited to) age, sex of the patient, skin phototype and sunscreen usage. Detailed history about the disease and family history were obtained.

Exclusion criteria included those with any liver or kidney disorders, thyroid disorders, metabolic bone disorders or inflammatory diseases, and even those taking medication (which included Ca<sup>++</sup> or vitD), and also those who within the past thirty days where on any treatment for vitiligo (both topical/oral/other form). To curtail any possible bias in study due to dietary intake of vitD, the control population (examined by previous said Dermatologist), were recruited from kin or the partners of patients who are not affected by vitiligo.

Our study was started only after obtaining the necessary clearance from ethics committee of our institute and informed consent was obtained from the entire study population (test and control).

After an overnight minimum fasting period of eight hours, in the morning samples were collected to measure

vitD. Other tests measured included serum free T3, free T4, TSH, anti-thyroglobulin antibodies, anti-thyroid peroxidase antibodies, fasting blood sugar, vitamin B<sub>12</sub> values.

### Statistical Analysis

Using a  $\chi^2$  test for categorical variables and Student's *t*-test for continuous variables all group comparisons were performed

SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc. was used for statistical analysis.

### Results

Out of fifty (50) patients included in our study population, there were 27 males (54%) and 23 females (46%). The control population comprised of twenty (40%) females and thirty (60%) males. The mean ages of the patient were  $30.96 \pm 10.57$  and that of control groups were  $31.45 \pm 8.33$  years. No statistically significant difference was established between the patient and control population in terms of gender ( $p = 0.43$ ) or age ( $p = 0.53$ ). However, sunscreen usage was not reported among the participants.

The entire disease group in our study had generalized vitiligo as established by bilateral symmetrically distribution of de-pigmented macules. The mean age at onset of vitiligo macules was  $18.84 \pm 8.84$  years with duration of the lesions ranging from two to twenty five years. Presence/diagnosed vitiligo was reported in the families of 3 of our patients. Vitamin B<sub>12</sub> deficiency or diabetes mellitus was not reported in any of our patients. In 12 (24%) of our patients autoimmune thyroid diseases was also picked up/diagnosed.

Investigations done (blood analysis) from all the patients enrolled in the study from January 2018 to April 2018 were analyzed for serum 25 hydroxy vitD<sub>3</sub>. The vitD values in patients' and in the control group ranged from 6 to 42 ng/ml (mean:  $12.04 \pm 8.84$  ng/ml) and from 8 to 39 ng/ml (mean:  $12.91 \pm 6.08$  ng/ml), respectively. The circulating vitD levels were less in patients compared to controls, however, the analysis did not show statistical significance ( $p = 0.570$ ).

### Discussion

Our present study was done to analyze the relationship between vitD values and vitiligo. Since both controls and patients had very low circulating vitD levels, the difference was not statistically significant.

Very few studies (over the past 5 years) which estimated blood vitD in vitiligo patients were found in our literature search. Ustun *et al.* observed in the majority of patients insufficient (< 30 ng/ml) or very low (< 15 ng/ml) values of vitD were, but the difference was not significant compared to controls, their study however included only 25 vitiligo patients and 41 controls.<sup>7</sup> In various other studies, investigators have stated the prevalence of lower vitD values in autoimmune diseases, but whether this could be a cause or a consequence of these autoimmune diseases is yet to be proved. One of the studies which compared vitD levels among healthy controls and vitiligo individuals (41), showed significantly lower vitD values in vitiligo

individuals than controls. The doctors postulated on vitD supplementation for the treatment of vitiligo patients as a possibility in the near future.<sup>8</sup>

Different theories explaining the pathogenesis of vitiligo have been suggested but the exact cause for vitiligo still remains obscure. These theories include familial, self destructive, autocytotoxic, antioxidant (oxidative stress mediated), neural and autoimmune theories.

One of the major role in the pathogenesis of vitiligo is found to be played by autoimmunity as evidenced by its coexistence with several autoimmune disorders.<sup>8</sup> In turn, vitD levels have been found reduced in autoimmune disorders consequently leading toward the plausible association of vitD with vitiligo. However, the exact mechanism by which vitamin D effects autoimmunity is still a conundrum, but there is a clear regulation of immune cells by vitD in vitro.

"Sunshine Vitamin" is the synonym for vitD, as it is synthesized by UV (ultraviolet) light in skin and is also a fat soluble vitamin that can be found in our diet. For many years, vitD is used to treat many skin diseases like psoriasis, vitiligo. 1,25-dihydroxy vitminD<sub>3</sub> is the potent form of vitD which as earlier mentioned controls cell proliferation and differentiation, maintaining Ca<sup>++</sup> and bone integrity and also it exhibits immune regulatory activities.

The association of low vitD levels needs to be further assessed as it relates to vitiligo and multiple autoimmunity related diseases. low 25-hydroxyvitamin D levels either confer to superior risk of developing secondary autoimmunity or the autoimmune inflammatory processes consumes excess vitD, resulting in 25-hydroxyvitamin D values falling. However, still screening of 25-hydroxyvitamin D may be a worthwhile tool for deciding whether to test for secondary autoimmune illnesses in patients with vitiligo.

VDR (Vitamin D-receptor) is a nuclear receptor which is seen in keratinocytes, fibroblasts, immune cells of skin, melanocytes. VitD exhibits an important role through various mechanisms on melanocytes and keratinocytes.

VDR also has a role in Ca<sup>++</sup> metabolism. There is a correlation of VDR polymorphism with increased susceptibility to RA, type I DM, multiple sclerosis, and inflammatory bowel disease.<sup>9</sup> VitD3 contribute to repigmentation in vitiligo macules through tyrosinase activity and increased melanogenesis seen in many invitro studies. Also VitD analogue like tacalcitol and calcipotriol also enhances re-pigmentation in vitiligo patients.<sup>10,12</sup> In an another research, immune modulating effects of vitD has been shown to be via inhibition of expression of IL-6, IL-8, TNF-gamma and TNF-alpha and also active form of vitD decreases the apoptotic activity of melanocytes induced by ultraviolet-B. The limitations of our study where mainly due to the relatively small sample size.

### Conclusions

Further studies are required to establish a causal relationship between vitiligo and vitD and likewise exploring the possibilities of use of vitD in treating vitiligo

either alone or in combination with other therapies. Randomized controlled trials with focus on vitD as therapy is the next step forward.

**Conflicts of Interest:** None.

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