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Research Article

# COMPARISON OF SERUM VITAMIN D LEVELS IN PATIENTS WITH VITILIGO AND CONTROLS

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## ABSTRACT

Vitiligo, an autoimmune disorder caused by the destruction of melanocytes in the skin, is characterized by depigmented macules of different shapes. Vitiligo is an acquired depigmentary disorder having social and psychological aspects. Current research data suggest that complex interplay between genetic, autoimmune aberrations and oxidative stress are the key pathways mediating the destruction of melanocytes in vitiligo. To study the clinico-epidemiological profile of vitiligo patients and to detect serum vitamin D levels and determinewhether patients with vitiligo have lower serum vitamin D levels compared to controls. Significantly lower vitamin D levels were found in majority of vitiligo patients,vitamin D levels and the type of vitiligo in patients. However, owing to the widespread levels of vitamin D deficiency in our country, further studies involving a larger sample size are required.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.

**Keywords:-** Vitiligo, Vitamin D, Autoimmune Diseases, Etiopathogenesis.

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## INTRODUCTION

Vitiligo is a common acquired pigmentary skin disorder. Vitamin D is responsible for skin pigmentation, increases tyrosinase activity and melanogenesis, and exhibits immunoregulatory functions. Low levels of vitamin D are associated with many autoimmune diseases, including systemic lupus, diabetes mellitus, rheumatoid arthritis, multiple sclerosis and alopecia areata. Few reports have evaluated serum vitamin D levels in vitiligo patients, and their results are conflicting [1]. Vitamin D is an essential hormone that is synthesized in the skin that plays a role in the protection of the epidermal melanin unit through various mechanisms. It has been observed that Vitamin D levels are low in patients with vitiligo and other autoimmune diseases. There have only been a few studies regarding the relationship between vitamin D levels and vitiligo worldwide, and even fewer from India as a whole, let alone South India.

The disease may affect both genders and all skin types [2] and may also be associated with systemic autoimmune diseases such as lupus erythematosus, scleroderma, autoimmune thyroiditis and alopecia areata [3]. Reduced serum vitamin D levels are found in many autoimmune diseases including systemic lupus erythematosus, diabetes mellitus, rheumatoid arthritis, multiple sclerosis and alopecia areata [1, 4, 5].

Vitamin D is an essential hormone that is synthesized in the skin [6]. The active form of vitamin D, 1,25-dihydroxyvitamin D3, is a hormone that regulates calcium and bone metabolism, controls cell proliferation and differentiation and also exhibits certain immune regulatory functions [1]. Vitamin D may affect both innate and adaptive immune responses through receptors in T and B lymphocytes, macrophages and dendritic cells [7].

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In addition, vitamin D3 increases tyrosinase activity and melanogenesis via a nuclear hormone receptor – the vitamin D receptor (VDR) in melanocytes [1, 8]. Vitamin D and its analogues are used to treat skin disorders, including psoriasis and vitiligo [1]. This study To know the clinico-epidemiological profile of vitiligo patients and to detect serum vitamin D levels and determine whether patients with vitiligo have lower serum vitamin D levels compared to controls.

**Material and Methods:**

After approval of institutional ethics committee an observational cross sectional study was carried out at dermatology outpatients SLIMS, Pondicherry. Total 50 patients clinically diagnosed with vitiligo were enrolled in study and 50 age and sex matched control were included. Participants with liver or kidney disorders, hyperparathyroidism, hypoparathyroidism, those taking vitamin D or calcium or any systemic or topical treatment for vitiligo within the previous month were excluded from the study. Controls were recruited from the partners or relatives of patients. Detailed history, complete clinical examination was carried out and all patients were investigated for complete blood count (CBC), urine analysis, fasting blood sugar (FBS), thyroid stimulating hormone (TSH), serum vitamin D level.

**Statistical Analysis:**

Data of all patients were noted in excel sheet, and analysis of data was done by using SPSS version 11.0. Group comparisons were performed using Student's t-test for continuous variables and a [2] test for categorical variables.

**Table 1: Two-sample t test with equal variances**

| Variable | Observation | Mean | Standard Error | Standard Deviation |
|---|---|---|---|---|
| **Vitamin D case** | 50 | 13.14 | 1.18 | 5.74 |
| **Vitamin D control** | 50 | 14.28 | 1.32 | 6.58 |
| **Combined** | 100 | 13.63 | .88 | 6.17 |
| **Difference** | - | -1.02 | 1.77 | |

Degree Of Freedom = 48
Confidence Interval = 95%
T test = -0.5912
p value = 0.5582
p value >0.05.

**Discussion:**

Vitamin D, which is a fat-soluble vitamin obtained by humans through diet, is of particular interest to dermatologists because it is synthesized in the skin by ultraviolet light. It has been used to treat psoriasis, vitiligo and other skin diseases for many years [9]. The active form of vitamin D,1,25-dihydroxyvitamin D3, not only regulates calcium and bone metabolism, but also controls cell proliferation and differentiation and exerts immunoregulatory activities [1]. In a previous study, it was reported that patients with comorbid autoimmune illnesses are more likely to have very low serum vitamin D levels [13]. Vitiligo is an acquired depigmentary disorder having social and psychological aspects. Current research data suggest that complex interplay between genetic, autoimmune aberrations and oxidative stress are the key pathways mediating the destruction of melanocytes in vitiligo. Vitamin D has a nuclear receptor called vitamin D receptor (VDR). Vitamin D receptors are present in the cells involved in calcium and bone metabolism, and also in keratinocytes, melanocytes, fibroblasts and immune system cells of the skin [1]. Polymorphisms in VDR are correlated with increased susceptibility to multiple sclerosis,inflammatory bowel disease, rheumatoid arthritis and type 1 diabetes mellitus [14].

Vitamin D exerts a significant effect on melanocytes and keratinocytes via various mechanisms. *In vitro* studies have shown that vitamin D3 is associated with an increase in tyrosinase activity and melanogenesis [7], which may contribute to repigmentation in vitiligo macules. Vitamin D analogues, including calcipotriol and tacalcitol, are known to enhance repigmentation in vitiligo patients [15–17]. Another study reported that vitamin D exerts immunomodulatory effects by inhibiting the expression of interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-α, and TNF-γ [18]. The vast majority of participants, irrespective of whether they had vitiligo or not, were found to have either insufficient or deficient levels of vitamin D. This is similar to results obtained by Sehrawat et al, which found that none of the study participants had sufficient levels of vitamin D, in a study with 30 cases and similar age and sex matched controls[15].The role of ethnicity is not considered in estimation of vitamin D levels. In this context it is also important to note that vitamin D levels based on ethnicity has to be standardized. The pathogenesis of vitiligo remains largely unknown.There are different theories explaining the pathogenesis of vitiligo, with all genetic, autoimmune, autocytotoxic and neurogenic causes postulated. The autoimmune theory is the best-supported one, because vitiligo may be associated with other

autoimmune diseases includingpernicious anemia, hyperthyroidism, Hashimoto's thyroiditis, alopecia areata and adrenocortical failure.Furthermore, histological studies have demonstrated a high frequency of cytotoxic T lymphocytes specific to melanocytic antigens in vitiligo lesions, suggesting a direct, melanocyte-specific T cell attack [9, 11, 12].

Vitamin D, which is a fat-soluble vitamin obtained by humans through diet, is of particular interest to dermatologists because it is synthesized in the skin by ultraviolet light. It has been used to treat psoriasis, vitiligo and other skin diseases for many years [9]. The active form of vitamin D, 1,25-dihydroxyvitamin D3, not only regulates calcium and bone metabolism, but also controls cell proliferation and differentiation and exerts immunoregulatory activities . In a previous study, it was reported that patients with comorbid autoimmune illnesses are more likely to have very low serum vitamin D levels [13]. Vitamin D has a nuclear receptor called vitamin D receptor (VDR). Vitamin D receptors are present in the cells involved in calcium and bone metabolism, and also in keratinocytes, melanocytes, fibroblasts and immune system cells of the skin. Polymorphisms in VDR are correlated with increased susceptibility to multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis and type 1 diabetes mellitus [14]. The population prevalence is estimated to be 0.14-2% in different countries based primarily on clinical records of hospitals and dermatology clinics [2]. The observation that vitiligo was more prevalent in the immediate relatives of patients. The risk of a patient's sibling developing the disease is 6% and for an identical twin it is 23% [3].Vitiligo can develop at any age, in most of the studies from India age of onset of vitiligo was mainly in second and third decade; but in our study, 60 % of patients had vitiligo in first and second decade of life;this was comparable to study done by Agarwal et. al. [2]. Both sexes are equally affected although the greater number of reports among females is probably due to the greater social consequences to women and girls affected by this condition. Out of total case group 60 % were female and 40 % were male; which was comparable to other studies [4]. Clinically, vitiligo is classified depending upon the site and extent of involvement into following types: generalized which is the most common, segmental, focal, acro-facial and mucosal type [2]. In our study, 44 % of patients were of generalized vitiligo followed focal (36 %), and other vitiligo; which was comparable to other studies [2]. Few studies have investigated the association between vitiligo and reduced vitamin D levels, but these studies yield conflicting results. Ustun et al.found that vitamin D levels were insufficient (<30 ng/mL) or very low (<15 ng/mL) in most of the patients with vitiligo vulgaris, but not statistically significantly different as a group when compared to the controls [10]. These investigators stated that a large number of studies had reported low levels of circulating vitamin D in autoimmune diseases, but it remains unclear whether this is a cause or result of autoimmune diseases. Another study by Sahel et.found that deficient serum 25(OH) D levels were present in vitiligo patients with and without systemic autoimmune diseases. Accordingly, screening for vitamin D deficiency seems of value in vitiligo patients for the possibility of vitamin D supplementation [11]. Another study concluded that significant relationship between low 25-hydroxyvitamin D levels and vitiligo, but does not prove causation;further studies will be needed to establish whether vitamin D supplementation in this population improves the outcome of vitiligo[12]. Study done by Ebru K et.al.concluded that further study is required to know the causal relationship between vitamin D deficiency and vitiligo[13].

Most of the patients had a perifollicular pattern of repigmentation indicating that melanin is produced by the melanocytes in hair follicles. Vitamin D may act to induce immature melanocytes in hair follicles to produce melanin by stimulating their differentiation and their expression. This high prevalence of vitamin D deficiency may make detection of difference in vitiligo patients more difficult, and a very large number of patients and controls may be needed to show such differences should they exist and complex and multifactorial pathogenesis of vitiligois is another important consideration.

**Conclusion:**

Significantly lower vitamin D levels were found in majority of vitiligo patients,vitamin D levels and the type of vitiligo in patients. However, owing to the widespread levels of vitamin D deficiency in our country, further studies involving a larger sample size are required.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.

**REFERENCES**

1. AlGhamdi K, Kumar A, Moussa N. The role of vitamin D in melanogenesis with an emphasis on vitiligo. Indian J Dermatol Venereol Leprol 2013; 79: 750-8.
2. Nordlund JJ. The epidemiology and genetics of vitiligo. Clin Dermatol 1997; 15: 875-78.
3. Lee H, Lee MH, Lee DY, et al. Prevalence of vitiligo and associated comorbidities in Korea. Yonsei Med J 2015; 56: 719-25.
4. Kamen DL, Aranow C. The link between vitamin D deficiency and systemic lupus erythematosus. Curr Rheumatol Rep 2008; 10: 273-80.
5. Aksu Cerman A, Sarikaya Solak S, Kivanc Altunay I. Vitamin D deficiency in alopecia areata. Br J Dermatol 2014; 170:1299-304.
6. Lips P. Vitamin D physiology. Prog Biophys Mol Biol 2006; 92: 4-8.
7. Adorini L, Penna G. Control of autoimmune diseases by the vitamin D endocrine system. Nat Clin Pract Rheumatol 2008;4: 404-12.
8. Oikawa A, Nakayasu M. Stimulation of melanogenesis in cultured melanoma cells by calciferols. FEBS Lett 1974; 42: 32-5.
9. Ersoy-Evans S. Commentary: vitamin D and autoimmunity: is there an association? J Am Acad Dermatol 2010; 62: 942-4.
10. Birlea SA, Costin GE, Norri DA. New insights on therapy with vitamin D analogs targeting the intracellular pathways that control repigmentation in human vitiligo. Med Res Rev 2009; 29: 514-46.
11. Parsad D, Saini R, Verma N. Combination of PUVAsol and topical calcipotriol in vitiligo. Dermatology 1998; 197: 167-70.
12. Oh SH, Kim T, Jee H, et al. Combination treatment of non-segmental vitiligo with a 308-nm xenon chloride excimer laser and topical high-concentration tacalcitol: a prospective,single-blinded, paired, comparative study. J Am Acad Dermatol 2011; 65: 428-30.
13. Koizumi H, Kaplan A, Shimizu T, Ohkawara A. 1,25-dihydroxyvitamin D3 and a new analogue, 22-oxacalcitriol, modulate proliferation and interleukin-8 secretion of normal human keratinocytes. J Dermatol Sci 1997; 15: 207-13.
14. Sehrawat M, Arora TC, Chauhan A, Kar HK,Poonia A, Jairath V. Correlation of Vitamin D Levels with Pigmentation in Vitiligo Patients Treated with NBUVB Therapy. ISRN Dermatol. 2014; 2014:1-6.
15. Ustun I, Seraslan G, Gokce C, et al. Investigation of vitamin D levels in patients with vitiligo vulgaris. Acta Dermatovenerol Croat 2014; 22: 110-3.
16. Czajkowski R, Męcińska-Jundziłł K. Current aspects of vitiligo genetics. Postep Dermatol Alergol 2014; 31: 247-55.
17. Laddha NC, Dwivedi M, Mansuri MS, et al. Role of oxidative stress and autoimmunity in onset and progression of vitiligo. Exp Dermatol 2014; 23: 352-3.
18. 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; 62:937-41.
19. Ersoy-Evans S. Commentary: vitamin D and autoimmunity: is there an association? J Am Acad Dermatol 2010; 62: 942-4.