PARIPEX - INDIAN JOURNAL OF RESEARCH | Volume - 9 | Issue - 11 | November - 2020 | PRINT ISSN No. 2250 - 1991 | DOI : 10.36106/paripex

ORIGINAL RESEARCH PAPER



Dermatology

VITAMIN D LEVELS IN PATIENTS OF VITILIGO IN INDIAN POPULATION

KEY WORDS: vitiligo, vitamin D, autoimmune diseases, etiopathogenesis.

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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.

INTRODUCTION:

ABSTRACT

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]. 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 determinewhether 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

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dermatology outpatients Sri Balaji Medical college and Hospital, Chennai. Total 25 patients clinically diagnosed with vitiligo were enrolled in study and 25 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 vitaminD 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.

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, 1,25dihydroxyvitamin 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

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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)- , and TNF- [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 bestsupported 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, 1,25dihydroxyvitamin 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 25hydroxyvitamin 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.

Table 1:Two-sample t test with equal variances

Variable	Observati	Mean	Standard	Standard
	on		Error	Deviation
Vitamin D	25	13.14	1.18	5.74
case				
Vitamin D	25	14.28	1.32	6.58
control				
Combined	50	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

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