

## Assessment of Vitamin D Plasma Levels in Patients with Vitiligo Vulgaris

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**Abstract-** Vitiligo Vulgaris is a pigment disorder as the lack of skin pigmentation which its most prevalent cause is autoimmune. Vitamin D has various effects on the natural and acquired immune of the body because of its effectiveness on the T cells and B cells, macrophages and dendritic cells. The object of this study was assessment of the Vitamin D in patients with vitiligo vulgaris in dermatologic clinics in Qazvin in 2012. The 100 patients with Vitiligo were studied through a cross-sectional study. The required data were collected by the questionnaire (age, gender, job, family background, consumption of the dairies and vitamin D supplements), examination (type of skin) and para clinical test (measurement of the serum 25-hydroxyvitamin D level). The 42 (42%) and 58 (58%) people of the population under study were respectively male and female. The mean age of the population under study was 28.7±1.17. The mean serum of 25-hydroxyvitamin D level was 42±24.14 which had a significance difference with a normal level ( $p<0.04$ ). The mean serum 25-hydroxyvitamin D level among patients with Vitiligo had a significance difference with a normal level.

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**Keywords:** Vitamin D; Vitiligo Vulgaris; Iran; Plasma level; Patients

### Introduction

Vitiligo is an acquired pigmentation disorder that is being shown when melanocytes die in the epidermis of mucosal membranes and other tissues of the body and may raise from autoimmune causes (1). Although most cases of Vitiligo are sporadic, the familial ones are not prevalent and about 20% of the patients had family background (2,3). Generally, suffering from such an illness in the brother and sister of patients is 6.1% which is about 18 times of the normal population (2). Epidemiologic studies have shown that Vitiligo is a genetic, multi-factorial non-mendelian disease with a polygenic pattern (2,4). The cause of disease is unknown, but there are different theories including autoimmune, genetic, poisonous metabolites or oxidative stress, neural causes and the lack of melanocyte growth factors (5). The most prevalent cause is autoimmune. Existence of the familial groups

of generalized vitiligo with the other autoimmune diseases shows an autoimmune tendency and raise doubts about a genetic autoimmune disease. Although some of the patients have special anti-melanocyte antibodies or melanocyte proteins, but it is not clear that the antibodies are either the cause or result of the melanocytes. There are also some evidences for cellular immune reactions against melanocytes (6,7). Another reason for this theory is the accompaniment of other autoimmune diseases in patients with vitiligo and their relatives (8). The prevalence of the disease ranges from 0.5% - 1% (9). Extensive studies in China, India and Denmark have estimated its prevalence respectively 0.093%, 0.005% and 0.28% (10-12). The most value of prevalence throughout the world has been reported in the Gujarat province of India that is about 8.8% (13). The involvement value is the same in males and females (14,15) but females are more following the treatments (16,17).

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The maximum involvement in males and females is respectively in their forties and tenth. The disease is almost being diagnosed (64.4%) in the spring and summer (18,19).

Vitiligo may begin in any age, but it would begin before 20 years old in 50% of the patients. The disease develops gradually but sometimes develops rapidly in a few months and then stops (20). The hypopigmentation or depigmentation which are more obvious on areas of the visible skin, around the nose, mouth and eyes may result in social and psychological consequences of this disease especially in dark skinned people and sometimes cause suicide (21,22).

Normally, this disease is diagnosed by separate monotonous white patches and macules with convex brim that is surrounded by healthy skin. Vitiligo diagnosis is usually clinical and by using a wood lamp. When the contacted areas are placed under the wood lamp, the fluorescent turns to golden yellow. The standard treatment of vitiligo is the application of corticosteroid cream and Psoralen and ultraviolet A light. Both treatments cause the skin pigmentation in a considerable portion of patients (23).

Vitamin D is a steroidal hormone which has a key role in the metabolism of minerals such as calcium and phosphor and the solidification of bone tissue. In the past, the role of vitamin D in biological activities like maintaining the mineral homeostasis and also regulation of bone recirculation were focused (24), but recently by identifying the vitamin D receptors in different tissues such as T cells, macrophages, thymus tissue and also in pancreas beta cells has made it more important in insulin osmosis regulation and also body immunity (25,26).

It has been shown in laboratory studies that vitamin D may reduce the generation of some cytokines including interleukins 2, 6, 12 and TNF  $\beta$ , TNF  $\alpha$  and interferon gamma (27,28).

A lack of vitamin D may cause the disorder in the immune system operation including macrophages operation disorder as the activity of chemotaxis, Phagocytosis and increasing of the inflammatory cytokines production (29, 30). As the most prevalent etiology of vitiligo is autoimmune and, on the other hand, vitamin D has been recognized as an important factor in the natural and acquired immune system of the body and also due to the topical effectiveness of the vitamin D on the pigmentation of vitiligo losses, we studied patients with vitiligo coming to clinics in the city of Qazvin and the serum 25-hydroxyvitamin D level.

## Materials and Methods

This analytical cross-sectional descriptive study was performed since March to June 2012 in the dermatology clinics of Qazvin. Regarding that the serum level of vitamin D is affected by the sunshine value, our research was performed during spring, and all patients of dermatology clinic participated in the study and about 100 patients were studied. The Inclusion criterion to be participated in the study was a clinical diagnosis with vitiligo by the dermatologist. After convincing the patients to be studied, the required data was collected through a questionnaire, checklist and tests. The questionnaire included demographic information and medical history of patients, age, gender, job, and family background, consumption of the dairies and vitamin D supplements and autoimmune diseases. The serum 25-hydroxyvitamin D level was measured by the test. The dermatologist determined the skin type and its involvement with vitiligo.

The tests were performed using the IDS kits with reference No. Ac-57F1/Ac-57F2 in a specified laboratory through EIA (Enzyme Immuno Assay) methodology. Then, the patient's serum vitamin D level were registered; if the patients were not visiting the clinic again, the tests were followed up through the related laboratory.

The level of vitamin D in the body; according to the used laboratory kit, the level less than 25nmol/L and the level between 25-47 was described respectively as a severe lack of vitamin D and insufficient level of vitamin D. The normal 25-hydroxyvitamin D level for adults has been defined as 47.7 – 144. Therefore, the serum level of 47nmol/L was considered as cut-off point. Data collection of the patient was unnamed and a consent form was completed from each patient.

Collected data was entered into SPSS software; the mean and standard deviation were used to describe the quantity values, percent was used to describe the quality values, and the necessary data analyses were performed using ANOVA tests, student's t-test, one sample t-test, chi-squared and Fisher's exact test with  $P < 0.05$ .

## Results

The mean age of the population under study and the disease period were respectively  $28.7 \pm 1.17$  and  $5 \pm 5.8$  (Table 1). Participants in the research comprised 42% males and 58% females; from which 23% had outdoor

jobs, and 77% had indoor jobs

The youngest and oldest patients were respectively 8 and 63 years old. The minimum and maximum quantities of milk, yogurt, cheese, and ice cream consumption were non-consumption and two glasses, three glasses, 100g and two daily respectively. The minimum and maximum percent of skin involvement were respectively less than 5% and 50%, and also, the minimum and maximum level of vitamin D was respectively 5nmol/L and 144nmol/L.

The 12% of the participants had thyroid disease, and 1% had thyroid and diabetic diseases simultaneously and 87% did not have any autoimmune disease (Figure 1).

By studying the participants regarding their family background of autoimmune diseases, it was specified that 24% with vitiligo, 10% with diabetes, 6% with thyroid diseases, 4% with diabetes and thyroid diseases, 7% with vitiligo and diabetes, 1% with vitiligo and thyroid diseases and 1% with diabetes, thyroid diseases and rheumatoid arthritis had family background, and 47% had no family background in autoimmune diseases.

Studying the participants based on the Fitzpatrick skin type; 2% were type-1 table2. The mean serum 25-hydroxyvitamin D level in the population, under study was  $42 \pm 24.14$  nmol/L, (Table 2).

**Table 1. mean age, disease period, skin involvement and consumption of the dairies in participants of the study(n=100)**

	Mean
Age	28.7 $\pm$ 1.17
Disease period	5 $\pm$ 5.8
Milk consumption (glass)	0.55 $\pm$ 0.56
Daily consumption of yogurt	0.99 $\pm$ 0.58
Daily consumption of cheese	24.8 $\pm$ 2.2
Daily consumption of ice cream	0.39 $\pm$ 0.5
Skin involvement (%)	13.2 $\pm$ 9
Serum vitamin D level	24 $\pm$ 42

There was a significance difference between the vitamin D serum levels of vitiligo patients due to their much exposure to sunlight and vitiligo patients due to non-exposure to sunlight ( $P < 0.03$ ).

**Table 2. The comparison of serum 25-hydroxyvitamin D level in variables under study (gender, age, job, disease background, disease family background and skin type)**

	Variable	Percent	Mean serum level 25OHD	P
<b>Gender</b>	M	42	44/74 $\pm$ 20	0.12
	F	58	40 $\pm$ 26/6	
	20 >	19	48/7 $\pm$ 35/7	
<b>Age (years)</b>	20 – 39.9	70	38/6 $\pm$ 19/8	0.139
	40 – 59.9	8	55/8 $\pm$ 23/47	
	>60	3	41/6 $\pm$ 16/1	
	Indoors	23	42.3 $\pm$ 26.84	
<b>Job</b>	Outdoors	77	40.9 $\pm$ 11.48	0.035
	Thyroid	12	40/25 $\pm$ 14/6	0.96
<b>Autoimmune disease background</b>	Diabetes and Thyroid	1	42	
	No one	87	42/27 $\pm$ 25/3	
	Vitiligo	24	47.7 $\pm$ 24.2	
	Diabetes	10	39.2 $\pm$ 21.4	
	Thyroid diseases	6	26.3 $\pm$ 3.9	
	Diabetes & thyroid diseases	4	41 $\pm$ 16.7	
<b>Autoimmune disease family background</b>	Vitiligo & Diabetes	7	41.2 $\pm$ 18.4	0.59
	Vitiligo & thyroid diseases	1	16	
	Diabetes, thyroid diseases and rheumatoid arthritis	1	58	
	No one	47	42.13 $\pm$ 27	
<b>Fitzpatrick skin type</b>	Type-1	2	60	0.061
	Type-2	4	26/7 $\pm$ 7/14	
	Type-3	76	39/5 $\pm$ 20/6	
	Type-3	18	55/6 $\pm$ 34/1	

The mean level of vitamin D serum in patients with vitiligo was  $42 \pm 24.14$  which showed a significance

difference with the normal level of 47.7-144nmol/L.

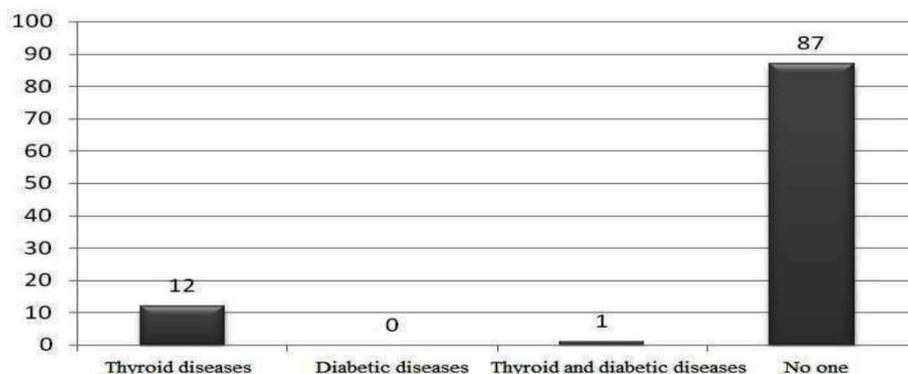


Figure 1. Frequency of patients based on their autoimmune disease background

## Discussion

A lack of vitamin D is prevalent and according to the studies in 2008, lack of vitamin D has been reported as a global pandemic (36).

The mean level of serum 25-hydroxyvitamin D among patients with vitiligo in this study was  $42 \pm 24.14 \text{ nmol/L}$  which had a significance difference with a normal level; ( $P=0.042$ ). There was not a significance difference between males and females participating in the study regarding their serum 25-hydroxyvitamin D level. Generally, the mean level of serum 25-hydroxyvitamin D of different age groups did not show a statistically significance difference among the participating patients with vitiligo. Of course, one of the reasons of low level vitamin D serum level is insufficient exposure to the sunlight and also insufficient supply of foods containing vitamin D (35). As shown in the present study, the daily consumption of foods containing vitamin D is less than the unit amount. According to a multicenter study in the Endocrinology Institute of Tehran University in 2008, the levels 12, 25, 35 and 45 were respectively diagnostic points of normal, low deficit, medium deficit and high deficit in Iran population based on which more than 75% of females and 72% of males were in lack of vitamin D (36).

In the present research, about 2/3 of patients were in their 2nd and 3rd decade of life that could show the importance these age groups consider for treatment and also beautifulness. There was not a significance difference among various skin groups with vitiligo in our study regarding the serum 25-hydroxyvitamin D levels. Of course, 76% and 18% of patients in our study were respectively type-3 and type-4 regarding their skin groups. Silverberg *et al.*, (2009) have showed in a research that the serum level of vitamin D is reduced by

increase of the Fitzpatrick skin type (34). In that research, Silverberg *et al.*, have studied the serum 25-hydroxyvitamin D level in patients with vitiligo vulgaris; it has been reported in the research that vitamin D level in patients with vitiligo and another immune disorder is low, and patients with autoimmune diseases have a low level of vitamin D, and the vitamin D level may help determine whether it is necessary to do another test for diagnosis of other autoimmune diseases or not. They have also showed that increase of age is related to the reduction of vitamin D level, and this may cause the secondary autoimmune disease (34). Among patients with vitiligo participating in our study, there was a significance difference between the serum vitamin D levels of patients that are in exposure of sunlight because of their job and patients, not in exposure of sunlight ( $P=0.035$ ); which may propose the importance of sunlight exposure in the increase of serum vitamin D level. Among the patients with vitiligo participating in the present study, 12% have had thyroid diseases. In a study by Lakovoli *et al.*, (2005), it was declared that about 24% of the children with vitiligo have also had thyroid disorders (31). Also, it was shown in another study on 15126 patients with vitiligo by Fratti *et al.*, (1999) that 18.5% of patients have had thyroid diseases (37). It has been reported in another research by Artatas *et al.*, that thyroid microsomal antibody in patients with vitiligo and their families were high, and also vitiligo was more prevalent in patients with autoimmune thyroid disorders (33).

Generally, the vitiligo involvement in patient's sister and brother is about 6.1% that is about 18 times of the common population. The vitiligo involvement rate among immediate relatives of white, Indian – Pakistani and Spanish patients has been estimated respectively 7.1%, 6.1% and 4.8% (2).

Due to the low level of vitamin D in autoimmune

patients which have been considered in previous studies and the low level of vitamin D in patients with vitiligo has been studied in the present research, This study offers that serum vitamin D level in patients with autoimmune disease should be assessed, and if there is a lack, the patients should be treated. Moreover, similar studies with more samples and accompanied by a control group is necessary for a better judgment regarding that the present study is the only one in Iran.

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