



Serum Vitamin D Levels in Vitiligo Patients Attending A Tertiary Care Centre; A Cross Sectional Study

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Abstract

Background: Vitiligo is a frequently encountered pigmentation disorder that results in the presence of multiple depigmented macules over the body. A Vitamin D level has been found to be deficient in patients having vitiligo in some studies. Aim To study serum vitamin D levels in patients having vitiligo attending a tertiary care centre To compare serum vitamin D levels of patients having vitiligo with serum vitamin D levels of healthy subjects.

Methods: 40 consecutive patients with vitiligo who fulfilled the inclusion criteria were included in the study.. Blood samples were collected from both cases and healthy subjects by venipuncture and the sera separated. Serum vitamin D level was estimated by using chemiluminescence technology

Results: No statistically significant correlation between serum vitamin D levels and age, sex, occupation, duration of the disease, Koebner phenomenon and types of vitiligo (P value> 0.05). In this study the mean value of serum vitamin D in cases and comparison group were 33.06 ± 10.34 ng/ml and 36.57 ± 10.21 ng/ml respectively. In this study 50% of patients had lower than the normal vitamin D levels. The serum vitamin D levels were below normal in patients with vitiligo versus that in the comparison group and this was statistically significant.

Conclusions: Due to the high prevalence of vitamin D deficiency further researches involving larger sample sizes are required, to evaluate whether a low level of serum vitamin D is a causative factor in vitiligo, and to ascertain the need of vitamin D supplements for both the prevention and treatment of vitiligo.

Keywords: Vitiligo, vitamin D, Autoimmune disease, Koebner phenomenon, cosmetics.

Introduction

Vitiligo is a pigmentary autoimmune condition induced by the destruction of functional melanocytes in the epidermis and infundibulum of hair, which is characterized by well demarcated depigmented macules.¹ This affects up to 2% of the world's population and all genders of all races equally.^{2,3} It is a multifactorial, polygenic disorder with complex pathogenesis attributed to autoimmunity and oxidative stress.⁴ The disorder results in significant cosmetic disfigurement. Patients with vitiligo are considered social outcasts and are emotionally affected in some cultures.⁵ Vitamin D is a fat soluble vitamin obtained by human endogenously when the skin is exposed to ultraviolet light and exogenously by dietary consumption.⁶ The active form of Vitamin D: 1, 25-Dihydroxyvitamin D3 is a hormone that regulates the proliferation and differentiation of cells by controlling calcium and bone metabolism. Vitamin D can influence both innate and adaptive immune responses via receptors in T and B lymphocytes, macrophages and dendritic cells.⁷ In addition, vitamin D3 increases the activity of tyrosinase and melanogenesis through the vitamin D Receptor in melanocyte.⁸ By modulating T cell activation and coordinating melanogenic cytokines, vitamin D3 safeguards the epidermal melanin unit.⁹ Cytokines such as IL-6, IL-8, IFN- alpha, TNF-alpha play important roles in pathogenesis of vitiligo. Vitamin D3 exerts immunomodulatory effects by inhibiting these cytokines.¹⁰ Vitamin D3 analogues such as topical Calcipotriene have been used to treat skin conditions, including psoriasis and vitiligo.¹¹ Normal serum vitamin D level is 30-70 ng/ml and low vitamin

D levels has been observed in vitiligo and other autoimmune disorders.¹² The link between vitiligo and decreased vitamin D levels has been studied in a few papers, but these studies provide contradictory results.

Vitamin D is an essential hormone synthesized in the skin and is considered to play a role in normal skin pigmentation. Although the role of vitamin D deficiency has been established in many autoimmune diseases, the association between serum vitamin D levels and vitiligo still needs to be investigated more thoroughly. Vitiligo is a pigmentary autoimmune condition induced by the destruction of functional melanocytes in the epidermis and infundibulum of hair, which is characterized by well demarcated depigmented macules. This disorder results in significant cosmetic disfigurement.

This study has been done to see whether low levels of serum vitamin D can have a probable causative role in vitiligo, which in turn will help to consider whether vitamin D supplements will be useful in both prevention and treatment of vitiligo. Thus aim of the study was to see whether low levels of serum vitamin D can have a probable causative role in vitiligo, which in turn will help to consider whether vitamin D supplements will be useful in both prevention and treatment of vitiligo.

Materials and method

This is a hospital based cross-sectional study with a sample size of 40 from department of Dermatology, Srinivas Medical College, Mukka, Surathkal. This study was done for 1year from November 2022- November 2023(after obtaining ethical clearance).

Study population:

Inclusion criteria

Clinically diagnosed cases of vitiligo attending Dermatology OP constituted the cases. Age and sex matched healthy volunteers constituted the control group. Informed consent was obtained from the participants above 18 years of age. Confidentiality was ensured.

Exclusion criteria

1. Patient with liver / kidney disease.
2. Hyperparathyroidism/ hyperparathyroidism
3. Metabolic bone disorders (eg: osteoporosis)
4. Those taking vitamin D / calcium tablets, any systemic or topical treatment for vitiligo within 1 month.
5. Patient on Phototherapy
6. Photodermatitis patients on sunscreen usage.
7. Paediatric patients

Study Variable

Sociodemographic Variables: Age, Gender.

Variables related to investigation results: Serum Vitamin D

Variables related to comorbidities and medical history

Variables regarding diet, addictions like: smoking, alcoholism.

Data collection

Informed consent was obtained from all persons included in this study and were interviewed for detailed history. Blood samples were taken in the morning under strict aseptic precautions after a minimum fasting period of 8 hours. Serum vitamin D level was estimated by using chemiluminescence technology. The vitamin D levels were classified as Normal (>30 ng/ml), insufficient (20-30 ng/ml) and deficient (<20 ng/ml).(Figure1,2,3,4,5,)

Statistical analysis

All statistical data collected were entered into excel sheet and analyzed by IBM SPSS version 25. The descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. All quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of > 0.05 was considered as normal distribution.

The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. Odds ratio along with 95% CI is presented. Chi square test was used to test statistical significance. For normally distributed quantitative parameters the mean values were compared between study groups using independent sample t-test (2 groups). For normally distributed quantitative parameters the mean values were compared between study groups using ANOVA (>2 groups). P value < 0.05 was considered statistically significant.

Ethical considerations

Institutional Ethics Committee clearance was obtained. Informed consent was obtained from the participants above 18 years of age. Confidentiality was ensured and maintained throughout the study

Results

Among 2 cases with vitamin D deficiency, one belonged to the age group of 18-20 years and other belonged to 31-40 years. Among patients with vitamin D insufficiency, maximum was within the age group of 31-40 years (22.22%) and 51-60 years (22.22%). The mean Serum

Vitamin D level for age group between 31-40 was 25.45 ± 4.25 ng/ml (lowest) and for age group between 61-70 was 41.1 ± 13.43 ng/ml (highest). There was no statistically significant difference in mean Serum Vitamin D level across different age groups in patients with vitiligo (P value 0.123)

Among 2 patients found with vitamin D deficiency, one was a male and other a female. Among patients with vitamin D insufficiency, 4 were males and 14 were females. Ten each of males and females had normal vitamin D levels. Out of 15 males, 33.3% had lower than the normal serum levels of vitamin D and out of 25 females 60% had lower than the normal serum levels of vitamin D. But, there was no statistically significant difference in Serum Vitamin D levels between gender in patients with vitiligo. (P value 0.102).

Among two patients with vitamin D deficiency, one was student and other was skilled laborer. Among patients with vitamin D insufficiency, 44.4% were homemakers and 22.2% were students. There was no statistically significant difference in serum vitamin D level across occupation in patients with vitiligo. (P value 0.835)

Among the cases with disease duration of < 1 year none had vitamin D deficiency, 4 had vitamin D insufficiency. In cases with disease duration of 1-5 years, 2 suffered from vitamin D deficiency, 10 had vitamin D insufficiency. In the group of cases with > 5 years duration of disease, none had vitamin D deficiency, 4 had vitamin D insufficiency. There was no statistically significant difference in serum vitamin D level across duration of disease in patients with vitiligo. (P value 0.881)

Among 2 patients with vitamin D deficiency, one had segmental type of vitiligo and the other had generalized

vitiligo. In patients with vitamin D insufficiency, most of them had acrofacial type of vitiligo (61%) followed by generalized vitiligo (27.7%). There was no statistically significant difference in serum vitamin D level between types of vitiligo in patients. (P value 0.935). (Table 1)

Discussion

The age group of patients involved in this study was between 18-70 years. It is similar to the study conducted by Praksh D et al.¹⁷ (18-76 years) and the mean age was 41.45 years which was also similar to the study by Prakash D et al. (43.78 years). The mean age in this study was more compared to other similar studies conducted by Karagun E (30.96 years) and Takci Z et al (34.5 years).^{18,19}

Male to female ratio of patients involved in this study was 1:1.66. It is lower when compared to the research done by Karagun E (1.27:1) and Takci Z et al (1.2:1). This study showed slight female preponderance, which was comparable to study done by Alshiyab et al (1:1.38).²⁰

Most of the patients (77.5%) included in this study were affected by vitiligo for less than 5 years duration. This is comparable with the studies conducted by Khurram et al²¹ and Takci et al¹⁸, where majority of patients had vitiligo for less than 5 years. The familial incidence of vitiligo in this study was 5%, which is lower when compared to the study conducted by Singla et al (16%) and Silverberg et al (51%).^{22,23} This low familial incidence indicates that genetic variables can play a role in etiology.

The majority of the cases of vitiligo in this study had acrofacial vitiligo (55%), followed by generalized vitiligo (27.5%), segmental vitiligo (10%) and mucosal vitiligo (7.5%). In the studies conducted by Silverberg

et al and Alshiyab et al, most common type was generalized vitiligo.^{20,23} Compared to other studies, this study showed acrofacial vitiligo as the major subtype.

In the studies conducted by Ustun et al and Singla et al, there was no significant change in vitamin D levels with age of vitiligo patients.²⁴ In the study done by Khurram et al, low serum vitamin D levels were found in younger age.⁸⁶ In this study there was no statistically significant difference observed in the mean vitamin D levels across age groups of patients with vitiligo (P value: 0.123), which was consistent with studies done by Ustun et al and Singla et al.^{73,83}

Among the two vitiligo patients found to have vitamin D deficiency, one was a male and other a female. Among patients with vitamin D insufficiency, 4 were males and 14 were females. The studies done by Xu et al and Singla et al showed that female patients with vitiligo were at higher risk of vitamin D deficiency. In the study done by Khurram et al, vitamin D deficiency was more common in male patients.⁸⁶ In this study also, there was no statistically significant difference in the vitamin D levels between gender (P value: 0.102), which was consistent with the studies done by Ramalingam et al²⁵ and Karagun E. In this study, females showed greater preponderance to low vitamin D level. Lower vitamin D levels in females could be due to the lesser sun exposure, lesser outdoor activities and higher use of sunscreen.

Among the two vitiligo patients found to have vitamin D deficiency, one was student and other was skilled laborer. In this study there was no statistically significant difference in serum vitamin D level across occupation in case group (P value 0.835). Study done by Beheshti et al revealed a significant difference between serum vitamin D levels in the patients with

outdoor work as compared to patients with indoor work.²⁶

Among 40 cases of vitiligo, 2 suffered from vitamin D deficiency and they had a disease duration of 1-5 year. In this study there was no statistically significant difference between vitamin D levels and duration of vitiligo (P value 0.881), which was consistent with studies done by Alshiyab et al and Singla et al.^{20,22} In the study done by Khurram et al, there was significant association between low vitamin D levels and long duration of vitiligo.²¹

Among the patients with vitiligo who showed Koebner phenomenon, there were 1 each in Vitamin D deficient, insufficient and normal level groups. There was no statistically significant difference between mean vitamin D levels and presence of Koebner phenomenon (P value = 1.000).

Among 2 patients with vitiligo having vitamin D deficiency, one had segmental type of vitiligo and the other had generalized vitiligo. The studies done by Prakash D et al, Takci et al and Alshiyab et al showed no significant difference between mean vitamin D levels and types of vitiligo.^{16,17} In this study also, there was no statistically significant difference between vitamin D levels and types of vitiligo (P value 0.935).

Among the vitiligo case group, 45% had insufficient vitamin D levels and 5% had vitamin D deficiency which together contributed 50% of the patients. Among the comparison group only 2.5% had vitamin D deficiency, 22.5% had insufficiency and thus 25% were below normal levels of vitamin D.

There were 20 patients with vitiligo who had below normal vitamin D levels while only 10 of the comparison group had lower than the normal vitamin D levels. There was a statistically significant difference

noted in the serum vitamin D levels between patients with vitiligo and comparison group (P value 0.021). The mean serum vitamin D level in cases and comparison group were 33.06 ± 10.34 ng/ml and 36.57 ± 10.21 ng/ml respectively.

In the study conducted by Singla S et al ⁷³, the mean value of serum vitamin D in vitiligo cases and controls were 24.07 ± 6.79 and 38.17 ± 9.54 respectively (P value < 0.001). So, the patients with vitiligo had lower mean vitamin D level than comparison group and there was a statistically significant difference noted in vitamin D levels between study groups in the Singla S study.²²

In the study done by Prakash D et al ¹⁷, the mean vitamin D level among vitiligo cases was 19.31 ± 3.62 while in control group the mean vitamin D level was 20.93 ± 5.63 (P value 0.108). There was no statistically significant difference in vitamin D levels between study groups in the Prakash D study.

The Malaysian study conducted by Ramalingam et al ²⁵, found the mean vitamin D level in vitiligo cases and controls were 25.32 ± 9.92 and 24.59 ± 11.71 respectively (P value 0.652). There was no statistically significant difference in vitamin D levels between study groups in the Ramalingam study.

The Turkish study done by Takci et al ¹⁷, showed that the mean vitamin D level in vitiligo cases and controls were 16.35 ± 7.41 and 23.98 ± 13.5 respectively (P value 0.002). Statistically significant difference was observed in vitamin D levels between the study groups in Takci et al study. In the study done by Karagun et al, the mean vitamin D level in vitiligo cases and controls were 12.01 ± 8.84 and 12.91 ± 6.08 respectively (P value 0.570) and the difference was not statistically

significant. The limitation of this study was smaller sample size of study group.

Conclusion

There was a statistically significant difference noted between the serum vitamin D levels of the patients having vitiligo and those in the comparison group (P value 0.021). However, due to the high prevalence of vitamin D deficiency in India, further researches involving larger sample sizes are required, to evaluate whether a low level of serum vitamin D is a causative factor in vitiligo, and to ascertain the need of vitamin D supplements for both the prevention and treatment of vitiligo.

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Legend Table and Figures

Table 1: Comparison of Types of vitiligo across vitamin D level in patients (N=40)

Types of Vitiligo	Vitamin D Level		Chi square	P value
	Below Normal(Deficient + Insufficient) (N=20)	Normal(N=20)		
Segmental	2 (10%)	(10%)	0.424	0.935
Mucosal	1 (5%)	(10%)		
Acrofacial	11 (55%)	(55%)		
Generalized	6 (30%)	(25%)		



Figure 1: Segmental vitiligo in hand



Figure 4: Mucosal vitiligo



Figure 2: Acrofacial vitiligo



Figure 5: Generalized vitiligo



Figure 3: Segmental vitiligo