

Assessment of clinical, psychological and vitamin D levels on patients with stable vitiligo before and after narrowband - UVB Phototherapy

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Abstract

Background: Vitiligo is an autoimmune disease characterized by the destruction of normal melanocytes. They are clinically presented as hypopigmented patches. It is not merely a cosmetic disease but has an overwhelming psychological effect on the quality of life.

Vitamin D plays a significant role in the pathogenesis and treatment of vitiligo.

Aims

The study aimed to assess and compare vitamin D levels at 0 weeks, 6 weeks, and 12 weeks of therapy. Evaluate the vitiligo impact scale 22 and vitiligo area scoring index at 0 and 12 weeks.

Method: This is a hospital-based study Observational Prospective Study conducted in Dermatology OPD of A.J Institute of Medical Science, Mangalore with a sample size of 45 from February 2023 to August 2023. After proper history taking and clinical evaluation, patients diagnosed with stable vitiligo were subjected to narrowband UV B phototherapy. Phototherapy was administered thrice weekly for all the patients. Patients blood was drawn for vitamin D analysis at 0 weeks, 6 weeks, and 12 weeks. Vitiligo Area Scoring Index (VASI) and Vitiligo Impact Scale (VIS) were assessed at 0 and 12 weeks.

Results: This prospective study comprised 45 patients with 27 females and 18 males. At the enrolment of the study, the majority of the patients had insufficient vitamin D and 20% had deficient levels. At the end of 12 weeks, none were deficient. The mean VASI score reduced from 4.4 (first visit) to 3.3 (last visit) after the administration of narrowband UV – B therapy which was statistically significant. VIS-22 was given to 45 patients at an interval of 12 weeks and the scores at baseline (mean - 11.6) and at 12 weeks (mean - 11) were statistically significant ($p = 0.047$).

Limitation: The sample size is small.

Conclusion: Vitiligo is an autoimmune disorder, caused by the destruction of functional melanocytes in the epidermis. Vitamin D is synthesized in the skin by UVB wavelengths that come from sunlight. Vitamin D and its analogs have been used to treat vitiligo successfully. Its efficiency is increased when used in combination with UV-B. VIS 22 is a patient-reported outcome measurement designed to provide insights into how vitiligo affects various aspects of an individual's life beyond just the physical symptoms.

Keywords: Vitiligo, Vitamin D, Phototherapy, VASI, VIS – 22, Narrowband UVB.

Introduction

Vitiligo is an autoimmune disease affecting the normal melanocytes and melanin, resulting in hypopigmented patches. The lesion is characterized by a nonscaly amelanotic, chalky-white macule or patches with clear margins. Vitiligo is not merely a cosmetic disease, as its consequences can be psychologically overwhelming, often with a considerable effect on the quality of life. [1]

Vitiligo is the most common depigmenting skin disorder, with a likely prevalence of 0.5–2% of the population worldwide. [3] Vitiligo affects people of all skin types with no predilection. [4]

In 2011, an international consensus divided vitiligo into two major forms: nonsegmental vitiligo (NSV) and segmental vitiligo (SV). [5] The term vitiligo would be attributed to all forms of NSV (including generalized, mucosal, acrofacial, universal, mixed and rare variants). One of the most important decisions of the consensus was separating SV from other types of vitiligo most importantly because of its prognostic implications. The diagnosis of vitiligo is generally clinical, based upon the finding of acquired, amelanotic, nonscaly, chalky-white macules with distinct margins in a typical distribution: periorificial, lips and tips of distal extremities, penis, segmental and areas of friction. [8]

Confirmatory laboratory tests are usually not warranted in the diagnosis of vitiligo. A skin biopsy or other tests are not mandatory except to eliminate other disorders. The absence of melanocytes in a lesion can be analysed noninvasively by in vivo confocal microscopy or by a skin biopsy. The histology of lesion reveals complete loss of melanin pigment in the epidermis and absence of melanocytes. [8] The diagnosis of vitiligo may be

simplified by the use of a Wood's lamp, a hand-held ultraviolet (UV) irradiation device that emits UVA. It aids in identifying focal melanocyte loss and detects areas of depigmentation that may not be discernible to the naked eye, particularly in fair skinned individuals. Under the Wood's light, the lesions emanate a bright blueish white fluorescence and is sharply demarcated. [9] Dermoscopy may also be used to separate vitiligo from other depigmenting disorders. Vitiligo normally shows residual perifollicular pigmentation and telangiectasia, which are absent in other hypopigmentation disorders. In particular, it can be helpful in assessing disease activity in vitiligo and the stage of evolution: progressive lesions display perifollicular pigmentation, whereas stable or remitting lesions show perifollicular depigmentation. [10]

Vitiligo is a multifactorial disorder characterized by the loss of functional melanocytes. Numerous mechanisms have been suggested for melanocyte destruction in vitiligo. These include autoimmune responses, oxidative stress, genetic susceptibility, generation of inflammatory mediators and melanocyte detachment mechanisms. Both innate and adaptive mechanisms of the immune system are implicated. None of these proposed theories are in themselves capable of explaining the different phenotypes of vitiligo, and the overall contribution of each of these processes is still under question. However, there is now consensus on the autoimmune nature of vitiligo. Several different mechanisms may be involved in the progressive loss of melanocytes, and they include either immune attack or cell degeneration and detachment. The "convergence theory" or "integrated theory" hypothesises that multiple mechanisms may work in union to cause the destruction of melanocytes, eventually leading to the same result. [11]

Of late, increasing attention is being paid to the significance of vitamin D in the pathogenesis of vitiligo and its treatment. Vitamin D is an important hormone synthesized in the skin, and its deficiency has been associated with several ailments including immune, metabolic, and pigmentary disorders. Most of its active form is synthesized through activation of the pre-vitamin D₃ formed in the skin after sunlight exposure, particularly to UVB (290–320 nm). Dietary sources account only for a minor part of this vitamin. [12]

It was shown that vitamin D promotes melanogenesis and increases the tyrosinase content of cultured human melanocytes. Additionally, it enhances the number of L-3,4-dihydroxyphenylalanine (DOPA) positive melanocytes after 1,25(OH)₂D₃ treatment in the primary neural crest cell (NCC) culture. In a study by Watabe et al., 1, 25(OH)₂D₃ was found to induce endothelin B receptor (EDNRB) expression in immature melanocytes such as NCC-melb4 cells, but not in mature melanocytes such as NCC-melan5 cells. A melanocyte stem cell-like subpopulation is thought to be present in the bulge region of hair follicles, and it is believed that vitamin D may induce immature melanocytes in hair follicles to produce melanin by stimulating their differentiation and their expression of EDNRB. The relationship of the vitamin D receptor (VDR) in vitiligo has been studied, and the level of VDR ApaI locus was found to be increased in vitiligo patients. [13] According to a study by Sauer et al., 1α, 25-dihydroxyvitamin D₃ protects human melanocytes from apoptosis by forming sphingosine-1-phosphate. The role of vitamin D in protecting human melanocytes against oxidative damage has been identified in other studies. [14]

Vitamin D analogs have been effective in the treatment of vitiligo in two ways:

1. By controlling the activation, proliferation, and migration of melanocytes, and augmenting the tyrosinase content of melanocytes.

2. By regulating T-cell activation which hampers the autoimmune damage to melanocytes.

UVB exerts its action through the generation of cytokines that stimulate the proliferation of melanocytes, synthesis of melanin, and migration of melanocytes. It is also involved in the initial stages of vitamin D synthesis by increasing the conversion of 7-dehydrocholesterol to pre-vitamin D3 in the skin. Since vitamin D3 may stimulate the differentiation of immature melanocytes in the bulge of hair follicles and induce melanin production in them, at least part of repigmentation in vitiligo lesions may be justified by vitamin D3 synthesis by UVB [15]

The treatment modalities aim at halting the disease progression and stabilization of the lesions, and the repigmentation of the affected area. The various treatment options are narrowband UVB, Psoralen plus phototherapy, Corticosteroids, topical immunosuppressant's, surgical therapies, micro pigmentation, laser, micro phototherapy, depigmenting agents and camouflaging agents. Topical corticosteroids and phototherapy form the mainstay of therapy. Recalcitrant lesions may require surgical grafting.

Aims and Objectives

1. Assess and compare vitamin D levels at 0 weeks, 6 weeks, and 12 weeks of therapy.
2. Evaluate the vitiligo impact scale 22 and vitiligo area scoring index at 0 and 12 weeks.

Materials and methods

This is a hospital-based Observational Prospective Study conducted in Dermatology OPD from February to August 2023 of A.J Institute of Medical Science, Mangalore with a sample size of 45.

Based on the study conducted by Sehrawat M et al, to detect a mean improvement of 260.59 ± 181.45 in vitamin D levels post phototherapy assuming a 95% confidence interval, 80% power, and a precision of ± 75 , the sample size is estimated for the study is $44.8 \sim 45$.

Inclusion Criteria

Patients with clinical features of stable vitiligo in the age group of 18 years to 45 years presenting in the Department of Dermatology and Venereal Disease, of A.J Institute of Medical Science, Mangalore.

Exclusion Criteria

1. Pregnant and lactating women
2. Patients who had taken treatment for vitiligo in the last 8 weeks
3. Had coexistent diabetes mellitus
4. Thyroid disorder
5. Skin malignancy, or any other malignancy
6. Photosensitivity
7. Had a history of previous intolerance or failure of phototherapy
8. The patient who was taking any known photosensitizer drug

Patients diagnosed with stable vitiligo after proper history taking and clinical evaluation, were subjected to narrowband UV B phototherapy. Phototherapy was administered thrice weekly for all the patients. Patients' blood was drawn for vitamin D analysis at 0 weeks, 6 weeks, and 12 weeks. Vitiligo Area Scoring Index (VASI) and Vitiligo Impact Scale -22 (VIS-22) were assessed at 0 and 12 weeks.

Results

The study comprised of 27 females and 18 males. 45 patients had Fitzpatrick skin type IV and 30 had type V. Mean age of the patients was 31.33 ± 7.73 years. The

youngest patient was 19 years and the eldest was 42 years at the time of inclusion in the study. Figure 1

Figure 2 illustrates the changes in serum vitamin D levels among participants over a 12-week period. At the start of the study (Week 0), the vast majority of participants (66.66%) had deficient levels of vitamin D. This significant deficiency suggests a potential correlation or area of concern that may need addressing. By Week 6, there is no change in the percentage of participants with deficient vitamin D levels, but a slight increase in insufficiency is observed, along with a corresponding decrease in sufficiency.

By Week 12, there is a notable improvement, with the proportion of participants with sufficient vitamin D levels increasing to 26.66%, and those with deficient levels decreasing to 73.33%. This indicates some improvement in vitamin D status among participants, possibly due to an intervention, seasonal changes resulting in increased sunlight exposure, dietary alterations, or supplementation. However, the majority still remain deficient, highlighting a persistent issue that may require additional strategies for improvement. The absence of any participants in the insufficient category at Week 12 may suggest that those individuals have moved into the sufficient category, reflecting a positive trend.

The mean VASI at the first visit was 4.39 which reduced to 3.3 in the 12th week and was statistically significant (p-value 0.03) after the administration of narrowband UV- B therapy.

VIS-22 was given to 45 patients at the first visit and last session. The VIS-22, a modified scale, comprises 22 questions encompassing various domains, including attitude (questions 1, 4, 17, 19), anxiety (2, 11), social interactions (3, 12, 13), self-confidence (5, 18), depression (6, 9, 10, 14), treatment (7, 15, 16), family

(8), marriage (20), occupation (21), and school or college (22). Respondents rate each question on a scale from 0 to 3 (0: not at all, 1: a little, 2: a lot, 3: very much). The total score ranges from 0 to 66, with higher scores indicating a greater impact on life [Figure 1]. Patients report finding the scale easy to comprehend and complete.

The scores at baseline (mean -11.6) and at 12 weeks (mean - 11) were statistically significant (p = 0.047).

Table 2

Figure 5 represents the Vitiligo Impact Scale (VIS-22) scores of participants at two time points: week 0 and week 12. The impact levels are categorized as 'No Impact', 'Mild Impact', 'Moderate Impact', 'Large Impact', and 'Very Large Impact'.

At week 0, the majority of participants report 'No Impact' and 'Mild Impact' (each with 6 instances), followed by 'Moderate Impact' (2 instances), and 'Very Large Impact' (1 instance). There are no reports of 'Large Impact'. By week 12, there is a shift, with 'No Impact' rising to 8 instances, suggesting an improvement in the condition's impact on participants' lives. Meanwhile, 'Mild Impact' and 'Moderate Impact' both decrease to 5 and 1 instance, respectively, and there are no reports of 'Large Impact' or 'Very Large Impact'. The observed trends suggest a positive shift in the impact of vitiligo on participants' lives over the 12 weeks, with a notable increase in the number of participants reporting 'No Impact' and reductions in all other categories. This could be indicative of effective treatment or adaptation strategies improving the quality of life for individuals with vitiligo.

Table 1 presents the Vitiligo Impact Scale (VIS-22) results at baseline (0 weeks) and after 12 weeks. It includes data on the number of participants (N), the

mean and standard deviation of the Vitiligo Area Scoring Index (VASI) score and VIS score, the median values, interquartile range (IQR), and the significance level from the Wilcoxon signed-rank test. The table shows a decrease in the mean VASI score from 4.39 to 3.30 and a decrease in the mean VIS score from 11.60 to 11.00 over the 12-week period, with both reductions being statistically significant.

Table 2 illustrates the distribution of the impact of vitiligo on participants at 0 weeks and 12 weeks, categorized by 'No impact,' 'Mild impact,' 'Moderate impact,' 'Large impact,' and 'Very large impact.' It shows both the count and percentage of participants in each category. At 0 weeks, 40% of participants reported 'No impact' and 'Mild impact,' while 13.3% reported a 'Moderate impact,' and 6.7% reported a 'Very large impact.' After 12 weeks, there was an increase in the percentage of participants reporting 'No impact' to 53.3%, a decrease in those reporting 'Mild impact' to 33.3%, and a decrease in 'Moderate impact' to 6.7%. There were no reports of 'Large impact' at either time point, and the 'Very large impact' category remained at 6.7%. This indicates a general shift towards less impact over the 12-week period.

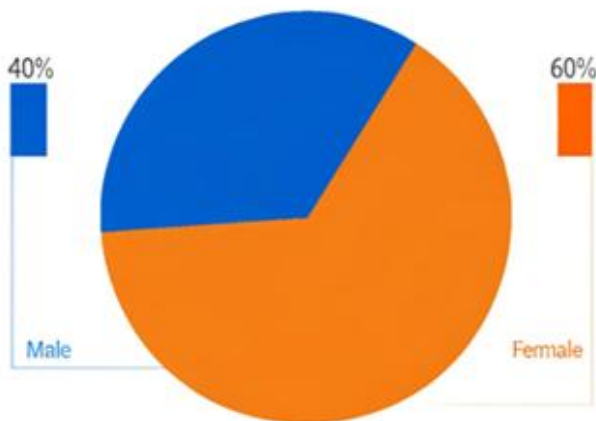


Figure 1: Gender distribution

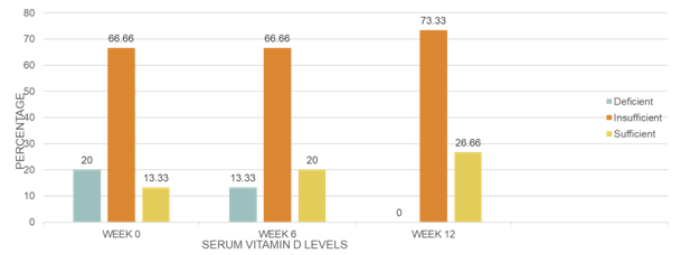


Figure 2: Serum vitamin D levels at week 0, 6 and 12

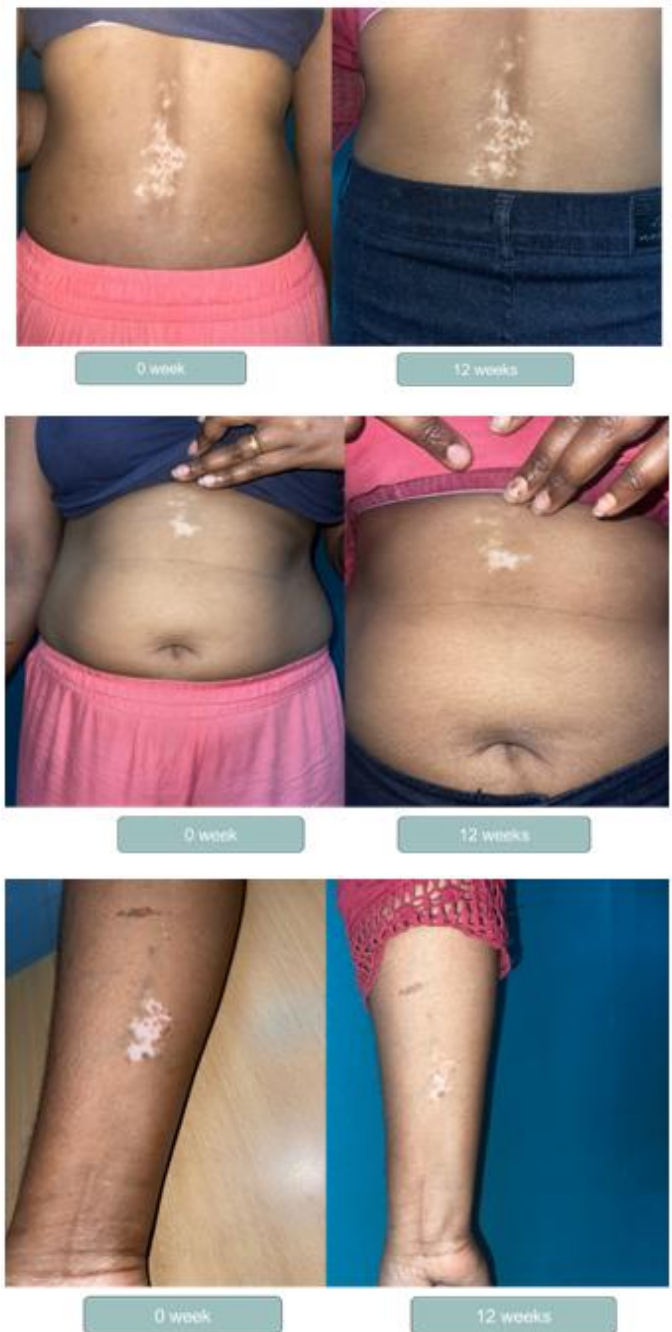


Figure 3: VASI at 0 and 12 weeks

Vitiligo Impact Scale-22 (VIS-22)

This questionnaire is meant to measure the effect of vitiligo on your life. Please read every question carefully and answer them according to the best of your understanding.

0 - Not at all 1 - A little 2 - A lot 3 - Very much

	0	1	2	3
1 Do you think this disease is incurable				
2 Do you change your doctor				
3 Do suggestions and advice from others about the disease bother you				
4 Do other people feel that this disease spreads by touch				
5 Do you have problems in wearing your choice of clothes				
6 Do you feel helpless				
7 Do you face difficulties in adhering to the treatment				
8 Do your parents keep asking you to seek treatment				
9 Do you feel life is not worth living with this disease				
10 Do you feel depressed				
11 Do you keep thinking about this disease				
12 Have you stopped/reduced going to parties/get-togethers				
13 Do your friends/relatives avoid you				
14 Do you think about bringing your life to an end				
15 Do you observe any kind of dietary restriction				
16 Does the amount of money you have spent on the treatment bother you				
17 Do you believe that this is the worst disease anyone can have				
18 Do you get embarrassed when meeting people				
19 How worried will you be if you develop new lesions				
If you are married, please answer the following question				
20 Do your in-laws worry about your white patches				
If you are unmarried, please answer the following question				
20 Are you facing problems in getting married				
If you are working, please answer the following questions				
21 Do your colleagues treat you differently because of the disease				
If you are studying, please answer the following questions				
22 Do your classmates treat you differently because of the disease				

Table 1: VIS 22 questionnaire

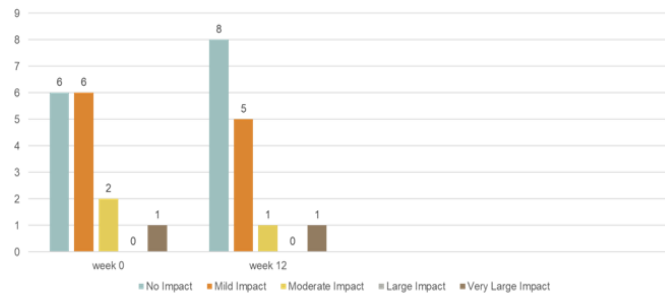


Figure 4: VIS – 22 (Vitiligo Impact Scale - 22) at week 0 and 12

Parameter		N	Mean	Std. Deviation	Median	IQR		Wilcoxon signed-rank test p
						Lower	Upper	
VASI score	0 weeks	15	4.39	3.64	3.40	1.65	5.25	0.031, sig
	12 weeks	15	3.30	3.07	2.00	0.90	4.65	
VIS score	0 weeks	15	11.60	13.55	6.00	4.00	14.00	0.041, Sig
	12 weeks	15	11.00	12.77	5.00	4.00	14.00	

Table 2: VASI and VIS -22 at baseline (0 weeks) and 12 weeks

	0 week		12 weeks	
	Count	Percentage	Count	Percentage
No impact	6	40.0	8	53.3
Mild impact	6	40.0	5	33.3
Moderate impact	2	13.3	1	6.7
Large impact	0	0.0	0	0.0
Very large impact	1	6.7	1	6.7

Table 3: VIS 22

Discussion

Vitiligo currently affects approximately 0.1–2% of the global population. The etiopathogenesis of vitiligo involves several factors, including calcium imbalance [16], vitamin-D receptor-Apa-1 polymorphism, and low levels of circulating 25-OH vitamin D . Notably, patients undergoing NBUVB treatment have demonstrated increased levels of 25(OH) vitamin D . Molecular studies indicate that vitamin D enhances melanocyte tyrosinase content [17] and stimulates the production of melanin by immature melanocytes in the bulge region of hair follicles, suggesting a cellular-level modulation of melanogenesis by vitamin D. This study aims to investigate whether circulating levels of 25 (OH) vitamins D change with successive NBUVB sessions and whether these changes correlate with clinical repigmentation.

The study focused on Indian subjects with skin phototypes IV and V, revealing that majority of the subjects had below the baseline levels of vitamin D. This finding aligns with observations in the Indian subcontinent, where a significant proportion of healthy individuals (60%–70%) exhibited low circulating levels of 25 (OH) vitamins D. These findings may support the Loomis theory, suggesting that melanin pigmentation plays a crucial role in limiting cutaneous vitamin D formation. Additionally, the absence of widespread food fortification with vitamin D3 in India could be a

contributing factor to the low serum levels of 25(OH) vitamin D in the population.

Limitation

1. Small sample size
2. Since it was a follow up based study, many loss to follow up cases hindered the study.
3. The expense associated with serum vitamin d testing imposes a financial burden on the patient

Conclusion

Vitiligo is an autoimmune disorder, caused by the destruction of functional melanocytes in the epidermis. Few studies concluded vitiligo patients, as well as patients with other autoimmune disorders, have low levels of Vitamin D. Vitamin D is synthesized in the skin in the presence of UVB wavelengths that come from sunlight.[12] Vitamin D and its analogs have been used to treat vitiligo successfully. Its efficiency is increased when used in combination with UV-B. Molecular studies have shown that vitamin D increases the tyrosinase content of melanocytes and induces immature melanocytes in the bulge region of hair follicles to produce melanin.

The results of my study showed that levels of 25 hydroxy vitamin D increased significantly with an increase in the cumulative dose of NB-UVB. Also, VASI scores showed improvement with an increase in the cumulative dose of NB-UVB. VIS 22 is a patient-reported outcome measurement designed to provide insights into how vitiligo affects various aspects of an individual's life beyond just the physical symptoms.

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