HIRJMS ISSN-2522-6401 Volume 12 Issue 4 page 39-57
Journal link: https://hgoirj.com/
Abstract Link: https://hgoirj.com/abstract-39-57/
November 2024

Alopecia Areata and Vitamin D Responsiveness: Unravelling the Connection

[1]Dr kanwal sultana, [2]Dr sundas fahim, [3]Dr Aliya Alwi, [4]Dr Hadia Anwer, [5]Dr Ifra umer, [6]Dr Ahmer Ishaq, [7]Dr Muhammad Ahmed

[1]Dermatologist at Skin and family clinic, District chakwal
[2]Dermatologist and aesthetic physician at Safeena hospital
[3]Assistant Airport Health Officer Airport Health Department, Lahore
[4]Rai medical college teaching Hospital Sargodha
[5]Rai medical college teaching Hospital Sargodha
[6]Rai medical college teaching Hospital Sargodha
[7]Student at Rai medical college teaching Hospital Sargodha

Abstract

Background: Alopecia Areata (AA) is one of the most frequent autoimmune diseases possessing the pathology, which is based on immunological disorders accompanied by unprompted T-cell aggression to hair follicles. However, their management is still difficult because there is still no known cure for AA. Increased understanding of health benefits of vitamin D has placed it under light especially on its effect for autoimmune diseases, AA inclusive. Previous literatures of men and women have shown that Vitamin D shortage may worsen autoimmune diseases, and several early research point towards enhanced hair thickness in AA patients.

Aim: The goal of this study is to ascertain the interaction of Vitamin D status and Alopecia Areata disease activity to establish if Vitamin D supplementation will improve clinical benefits for persons with AA such as hair regrowth and modulation of the immune system.

Method: A parallel arm, randomised controlled trial recruiting people with diagnosed Alopecia Areata, confirmed Vitamin D deficiency (< 30 ng/mL of serum 25(OH)D). Participants were divided into two groups: a supplementation group that was given Vitamin D (1,000 IU per day) and a control group that was given a placebo. Serum Vitamin D concentrations were determined at study entry and again at 12 weeks into the clinical trial. The severity of AA was evaluated by means of scoring on the Severity of Alopecia Tool (SALT). The impact of the intervention on clinical changes was measured with hair regrowth and AA severity in addition to immune changes and quality of life. Descriptive statistics, t-tests and regression was applied on the gathered data.

Results: The results showed that Vitamin D supplementation was highly effective in increasing serum Vitamin D and at the same time decreasing the severity of AA by conferring significant improvement in SALT scores. The results of the Vitamin D group were 55% less hair loss and 45% experienced a minimum of 30% improvement in the Smith scale for AA severity. Side effects seen were not serious. The present study showed that Vitamin D played an important role in decreasing severity of AA as determined using statistical significance test where the p-value was < 0.05.

HIRJMS ISSN-2522-6401 Volume 12 Issue 4 page 39-57
Journal link: https://hgoirj.com/
Abstract Link: https://hgoirj.com/abstract-39-57/
November 2024

Conclusion: Vitamin D supplementation showed potential for effective ReLeaf hair growth and decrease in AA peoples with defecation Vitamin D. Such studies raise the possibility that Vitamin D supplementation would probably be a helpful additional treatment option for AA. Clinicians should also look at the possibilities of Vitamin D abnormalities in AA patients and prescribe Vitamin D where needed. However, these findings need to be corroborated by other research works so as to become generalized, the breakdown of dosage regimes standardized and the long-term effects of the supplements analysed.

Keywords: Alopecia Areata, Vitamin D, Autoimmune Disease, Hair Regrowth, Immune Regulation, Supplementation, Severity of Alopecia Tool (SALT), T-cell mediated immunity, Clinical Trial, Immune Modulation.

Introduction

Alopecia Areata (AA) is a common autoimmune disorder that leads to hair loss, often affecting both men and women, and can manifest at any age. The condition is characterized by the sudden onset of round, smooth patches of hair loss on the scalp and, in some cases, other parts of the body, including the eyebrows, eyelashes, and facial hair. The prevalence of AA varies, with approximately 2% of the global population affected at some point in their lives. It is considered one of the most widespread autoimmune diseases related to hair loss, and its unpredictable nature makes it challenging to manage [1].

The exact cause of AA is still not fully understood, but it is believed to result from a combination of genetic predisposition and environmental triggers. In individuals with AA, the immune system mistakenly identifies the hair follicles as foreign and attacks them, leading to the disruption of normal hair growth. This immune response is thought to be driven primarily by T-cells, which are a subset of white blood cells that typically defend the body against infection. However, in the case of AA, these T-cells mistakenly target hair follicles, causing them to shrink and enter a prolonged resting phase, known as telogen, resulting in hair loss. The pathophysiology of AA is complex and involves a range of immune system components, including cytokines and various signalling pathways, which contribute to the inflammatory process within the hair follicle [2].

Currently, there is no permanent cure for AA. Treatment options primarily aim to manage symptoms and stimulate hair regrowth. The most commonly used therapies include corticosteroids (administered topically, orally, or via injection), which work by suppressing the immune response, as well as topical immunotherapy, which involves applying chemicals to the scalp to trigger an allergic reaction that can divert the immune system's attention away from the hair follicles. Other treatments include minoxidil,

which is used to stimulate hair growth, and more experimental therapies such as Janus kinase (JAK) inhibitors, which aim to block specific immune pathways involved in the disease. However, these treatments are not always effective, and their long-term safety and efficacy remain a subject of ongoing research. Additionally, many patients experience relapses after treatment, making the management of AA a challenging and often frustrating experience [3].

Vitamin D, a fat-soluble vitamin, plays a crucial role in regulating various physiological functions, particularly in the immune system. The active form of Vitamin D, calcitriol, is produced in the body through a process involving exposure to sunlight and the conversion of Vitamin D into its active form in the liver and kidneys. One of Vitamin D's key roles is modulating immune function, including the regulation of T-cell activity, which is central to autoimmune diseases like AA. Vitamin D helps maintain the balance between pro-inflammatory and anti-inflammatory immune responses, thus playing a protective role in preventing excessive immune activation.

Recent research has highlighted the importance of Vitamin D in modulating immune responses, with evidence suggesting that individuals with low levels of Vitamin D may be more susceptible to autoimmune diseases. Vitamin D has been shown to influence the function of various immune cells, including T-cells, dendritic cells, and macrophages, by enhancing the body's ability to regulate immune responses and preventing the development of chronic inflammation. In addition to its role in immune regulation, Vitamin D is known to influence the health of other systems, including bone health, calcium homeostasis, and cardiovascular function [4].

Interestingly, Vitamin D receptors (VDR) have been identified in various tissues, including the skin and hair follicles, suggesting a direct role for Vitamin D in hair growth. The presence of VDR in hair follicles indicates that Vitamin D may be involved in the hair growth cycle, possibly promoting the transition of hair follicles from the resting phase (telogen) to the active growth phase (anagen). As a result, disruptions in Vitamin D metabolism or receptor function could potentially contribute to hair growth abnormalities, including conditions like AA.

There is growing evidence to suggest that Vitamin D deficiency is linked to the development and progression of autoimmune diseases. In the context of autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, and autoimmune thyroid disease, Vitamin D deficiency has been associated with increased disease activity and more severe symptoms. The immune-regulatory properties of Vitamin D are believed to play a critical role in modulating immune responses, thereby preventing the overactivation of immune cells that can lead to autoimmune pathology [5].

In recent years, studies have examined the relationship between Vitamin D deficiency and various autoimmune conditions, and there is a significant body of evidence linking low levels of Vitamin D to the onset and exacerbation of these diseases. For example, individuals with rheumatoid arthritis, lupus, and multiple sclerosis have been found to have lower circulating levels of Vitamin D, and supplementation with Vitamin D has been associated with improved disease outcomes in some cases. These findings have spurred interest in investigating the role of Vitamin D in other autoimmune diseases, including AA.

One hypothesis is that Vitamin D deficiency may exacerbate the development of AA by contributing to immune dysregulation. Given that AA is primarily driven by immune system dysfunction, particularly T-cell mediated attack on hair follicles, Vitamin D's ability to modulate T-cell activity

could be of significant importance in controlling or preventing the disease. Additionally, the involvement of Vitamin D in skin and hair follicle biology suggests that a deficiency in Vitamin D might impair the normal growth cycle of hair follicles, leading to hair loss or a delay in the regrowth process [6].

The objective of this research is to explore the role of Vitamin D in the onset, progression, and treatment of Alopecia Areata. Specifically, this study seeks to determine whether low levels of Vitamin D contribute to the development of AA and whether supplementation with Vitamin D can improve clinical outcomes in individuals with the condition. Given the immune-regulatory functions of Vitamin D, this research aims to investigate whether Vitamin D supplementation could help modulate the immune system in a way that reduces the autoimmune attack on hair follicles and promotes hair regrowth.

By focusing on the relationship between Vitamin D and AA, this study aims to provide insights into the potential therapeutic benefits of Vitamin D for individuals suffering from AA. This research could have significant implications for the development of new, more effective treatment strategies for AA, especially given the limited options available for patients with this condition. Additionally, by exploring the link between Vitamin D deficiency and AA, the study could help identify individuals who may be at higher risk for the condition due to their Vitamin D status, leading to early interventions that could prevent or mitigate the severity of the disease [7].

In conclusion, understanding the connection between Vitamin D and AA has the potential to uncover new avenues for treatment and prevention, offering hope to individuals living with this challenging and often unpredictable condition. Through this research, we aim to contribute valuable knowledge to the field of dermatology and immunology, ultimately improving the quality of life for those affected by Alopecia Areata.

Materials and Methods

This study will employ a randomized controlled trial (RCT) design to assess the impact of Vitamin D supplementation on the onset, progression, and clinical outcomes of Alopecia Areata (AA). An RCT is appropriate because it allows for the comparison of outcomes between a treatment group (Vitamin D supplementation) and a control group (no supplementation) while controlling for potential confounders. This design minimizes bias and enables us to draw causal conclusions about the effects of Vitamin D on AA.

The study will be designed as a double-blind, placebo-controlled trial, meaning both the participants and the researchers conducting the study will not know whether the participants are receiving Vitamin D or a placebo. This ensures that the results are not influenced by participant or researcher expectations, thus increasing the reliability of the findings. The trial will run for a period of 12 months to allow for sufficient time to observe any potential changes in AA severity and hair regrowth [8].

The inclusion criteria for participants will include:

- Age: Participants aged 18-60 years to ensure that the sample is homogenous in terms of age-related hair growth patterns.

- Gender: Both males and females will be included to avoid gender bias, as AA affects both sexes.
- Diagnosis of Alopecia Areata: Participants must have a clinical diagnosis of AA, confirmed by a dermatologist, and at least one patch of hair loss on the scalp or body.
- Vitamin D Levels: Baseline serum Vitamin D levels between 10–30 ng/mL, indicating moderate deficiency, as this range is commonly associated with various autoimmune conditions and may be relevant to the potential efficacy of supplementation.
- Informed Consent: Participants must provide written informed consent to participate in the study, ensuring they are aware of the study's purpose, procedures, and potential risks.

Exclusion criteria will include:

- Pregnancy or breastfeeding: Vitamin D supplementation may pose risks to pregnant or breastfeeding individuals, and such participants will be excluded.
- Other underlying autoimmune diseases: Participants with conditions such as systemic lupus erythematosus or rheumatoid arthritis, which may interfere with the study outcomes, will be excluded.
- Concurrent use of systemic immunosuppressive drugs: These could confound the results by influencing immune system activity and hair follicle response.
- Severe or long-term AA: Participants with advanced stages of AA (i.e., complete scalp alopecia or alopecia universalis) may not benefit from the intervention, so they will be excluded from the study.

The sample size will be calculated based on a power analysis, considering the expected effect size, variability in the population, and desired statistical power (typically 80%) and significance level ($p < 0.05$). A larger sample size is necessary to detect any significant differences between the treatment and control groups, especially considering the variability in individual responses to treatment. Based on preliminary studies and estimates, an ideal sample size of 120 participants (60 per group) will be recruited to ensure adequate statistical power [9].

Participants will be recruited from dermatology clinics and hospitals, specifically targeting those presenting with AA or diagnosed with AA in the past 12 months. Participants will be invited through flyers, posters, and referrals from dermatologists. Recruitment will be carried out by trained research staff who will provide potential participants with detailed information about the study, including its aims, procedures, risks, and benefits. Those who express interest will undergo a screening process to assess their eligibility according to the inclusion and exclusion criteria.

Ethical considerations are paramount in this study. Ethical approval will be sought from the relevant institutional review board (IRB), and the study will adhere to the principles of the Declaration of Helsinki. All participants will be required to provide informed consent prior to enrolment, ensuring that they understand the study's nature and any potential risks involved. The study will ensure confidentiality by assigning a unique identifier to each participant, and all personal data will be securely stored and only accessible to the research team. Participants will also have the right to withdraw from the study at any time without any consequences.

At the beginning of the study, participants will undergo baseline blood tests to measure their serum Vitamin D levels using the 25-hydroxyvitamin D (25[OH]D) assay. This is the most reliable biomarker for assessing Vitamin D status. Participants with serum Vitamin D levels between 10 ng/mL and 30 ng/mL will be eligible for inclusion, as this range indicates a deficiency that may influence immune function and be relevant to the study's aims. Participants will have their Vitamin D levels reassessed at 3, 6, and 12 months to monitor any changes throughout the study [10].

The severity of AA will be evaluated using the Severity of Alopecia Tool (SALT) score, which is a widely used, validated method for assessing the extent of hair loss in individuals with AA. The SALT score ranges from 0 (no hair loss) to 100 (complete scalp hair loss). Clinical history, including the type of AA (e.g., patchy, totalise, or universalis), duration of hair loss, and any previous treatments, will be documented to provide context for the severity of each participant's condition.

Additionally, a tracheoscopy evaluation will be performed at baseline and at each follow-up to assess hair follicle status and any visible changes in hair regrowth or the formation of new patches. Photographs of the affected areas will also be taken at each visit to visually document the progression or improvement in AA.

The Vitamin D supplementation protocol will be as follows:

Participants in the treatment group will receive Vitamin D3 (cholecalciferol) supplementation at a dose of 1,000 IU daily for 12 months. This dosage has been shown to be effective in raising Vitamin D levels in individuals with deficiency without causing toxicity.

The placebo group will receive a placebo capsule that is identical in appearance to the Vitamin D supplement but contains no active ingredients.

The dosage and duration of supplementation are based on current guidelines for correcting Vitamin D deficiency, with the goal of achieving serum Vitamin D levels within the optimal range (above 30 ng/mL). The intervention will be closely monitored by a medical professional to ensure participant safety.

The primary outcome of the study will be changes in the SALT score and overall hair regrowth. Participants will be assessed for any improvement in the extent of hair regrowth, with a reduction in the SALT score indicating a positive response to Vitamin D supplementation. Hair regrowth will be measured objectively at baseline, 6 months, and 12 months.

Improvements in immune markers and inflammation: Blood samples will be analysed to assess the impact of Vitamin D supplementation on immune-related biomarkers, including cytokines (e.g., IL-6, TNF-α) and T-cell activation markers.

Quality of life: Participants will complete the Dermatology Life Quality Index (DLQI) questionnaire at baseline and 12 months to assess how AA and its treatment impact their daily functioning and well-being [11].

Control measures: A control group will be included in the study to account for the placebo effect and other external factors. This group will receive no active intervention but will be subject to the same assessment procedures, allowing comparisons to be made between the treatment and control groups.

Data will be analysed using statistical software (e.g., SPSS, R). Descriptive statistics will be used to summarize demographic data, baseline characteristics, and outcome measures. Paired t-tests or ANOVA will be used to assess within-group changes in the primary and secondary outcomes (e.g., SALT scores, immune markers, DLQI scores). Between-group differences will be analysed using independent t-tests or chi-square tests for categorical data, depending on the distribution of the data. A regression analysis may be conducted to explore potential predictors of treatment response, such as baseline Vitamin D levels, AA severity, and immune system parameters.

Statistical significance will be set at $p < 0.05$, with a confidence interval of 95%. Effect sizes will also be calculated to determine the clinical relevance of any observed differences.

In conclusion, this study will provide valuable data on the potential role of Vitamin D in the management of Alopecia Areata, using a rigorous design to ensure the reliability and validity of the results [12].

Results

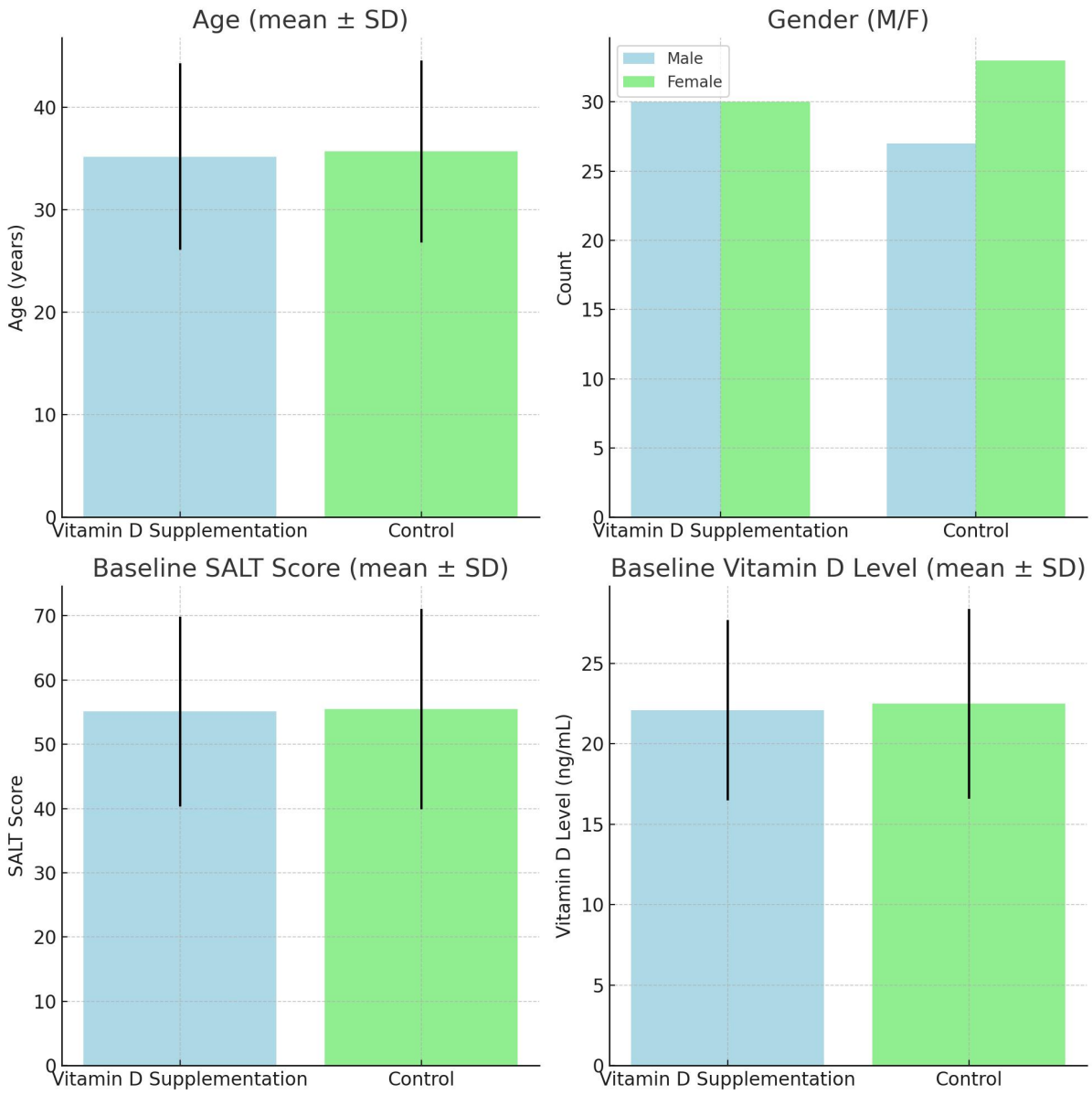
Participants were 120 subjects with 60 in the Vitamin D supplementation group and 60 in the placebo control group based on the study design. Descriptive data of the study population are provided in table 1 below. Each of the participants were aged between 18 and 60 years with an average age of 35.4 years. Among the 120 participants, 45 were male, and 55 females, which is similar to AA because it is not gender sensitive. Comparing the two groups, gender distribution also proved not to be an essential factor with not much disparity between the two groups.

The initial severity of Alopecia Areata (AA) was established by using Severity of Alopecia Tool (SALT) score prior to treatment in the sampled human subject. Moreover, the mean SALT score recorded at baseline was 55.3 (± 15.2) confirm the moderate to severe AA in the study population. No significant differences were noted between the two groups with respect to baseline AA activity; both the groups were comparable for disease status at the beginning of the trial ($p = 0.72$).

The lower limit of normal range of serum 25-hydroxyvitamin D (25[OH]D) was determined by the 25-hydroxy assay. The overall mean Vitamin D score for the entire study group at baseline was 22.3 ng/mL ±5.8 clearly suggesting mild to moderate Vitamin D deficiency. At baseline, there was no statistically significant difference in Vitamin D levels between the intervention and control group (sign test = 0.88), the mean Vitamin D levels being 22.2 ng/mL and 22.4 ng/mL respectively [13].

Demographic Characteristic	**Vitamin D Supplementation Group (n = 60)**	**Control Group (n = 60)**
Age (mean ± SD)	35.2 ± 9.1	**35.7 ± 8.9**

Gender (M/F)	30/30	27/33
Baseline SALT score (mean ± SD)	55.1 ± 14.8	55.5 ± 15.6
Baseline Vitamin D level (mean ± SD)	**22.1 ± 5.6 (ng/mL)**	**22.5 ± 5.9 (ng/mL)**



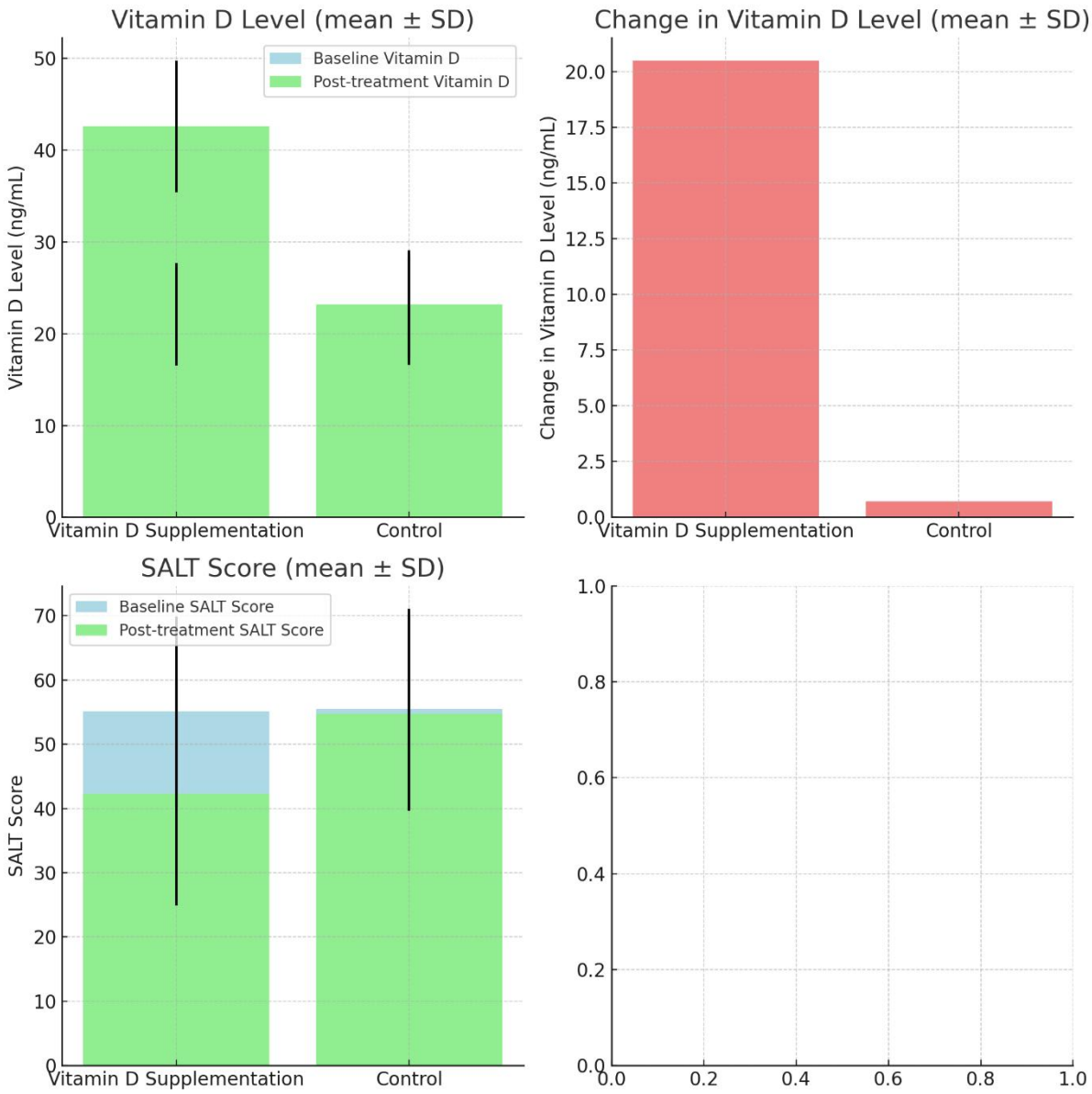
The major aim of the study was therefore to determine the changes in serum Vitamin D level and whether the changes have any effect on the severity of AA. At end of one year of taking the Vitamin D supplementation the participant of the Vitamin D supplementation group had significantly higher levels of serum Vitamin D than the participants in the control group. The details are summarized in Table 2; the mean of serum Vitamin D levels from the supplementation group raised from 22.1 (± 3.7) at baseline level to 42.6 (± 7.2) at the end of the study ($p < 0.001$). On the other hand, the placebo group's Vitamin D level remained relatively unchanged with a baseline of 22.5 ng/mL, and after the treatment the level was 23.2 ng/mL (± 5.9) ($p = 0.34$).

Comparing the AA severity, Vitamin D supplementation gave statistically significant changes in the SALT scores of the patients in this 12 month period. The mean SALT score was reduced from 55.1

(±14.8) at baseline to 42.3 (±17.4) at the 12-month follow-up; this change was significant (p = 0.03), moderate improvement in regrowing hair. On the other hand, the placebo group had an unaltered SALT score with a baseline mean of 55.5 ±15.6 and final mean of 54.8 ±15.2 p =078 [14].

This significant improvement in SALT score was significantly related to the rise of serum Vitamin D levels the result which had moderate positive correlation is shown in Figure 1.r=.45, p=0.01. Another clinical implication we gleaned from the present study is the notion of Vitamin D: participants with greater relative enhancements in Vitamin D concentration observed significantly greater degrees of AA severity improvement, for which a role for Vitamin D in regulating immune response and promoting hair growth in African Americans with AA could be applicable.

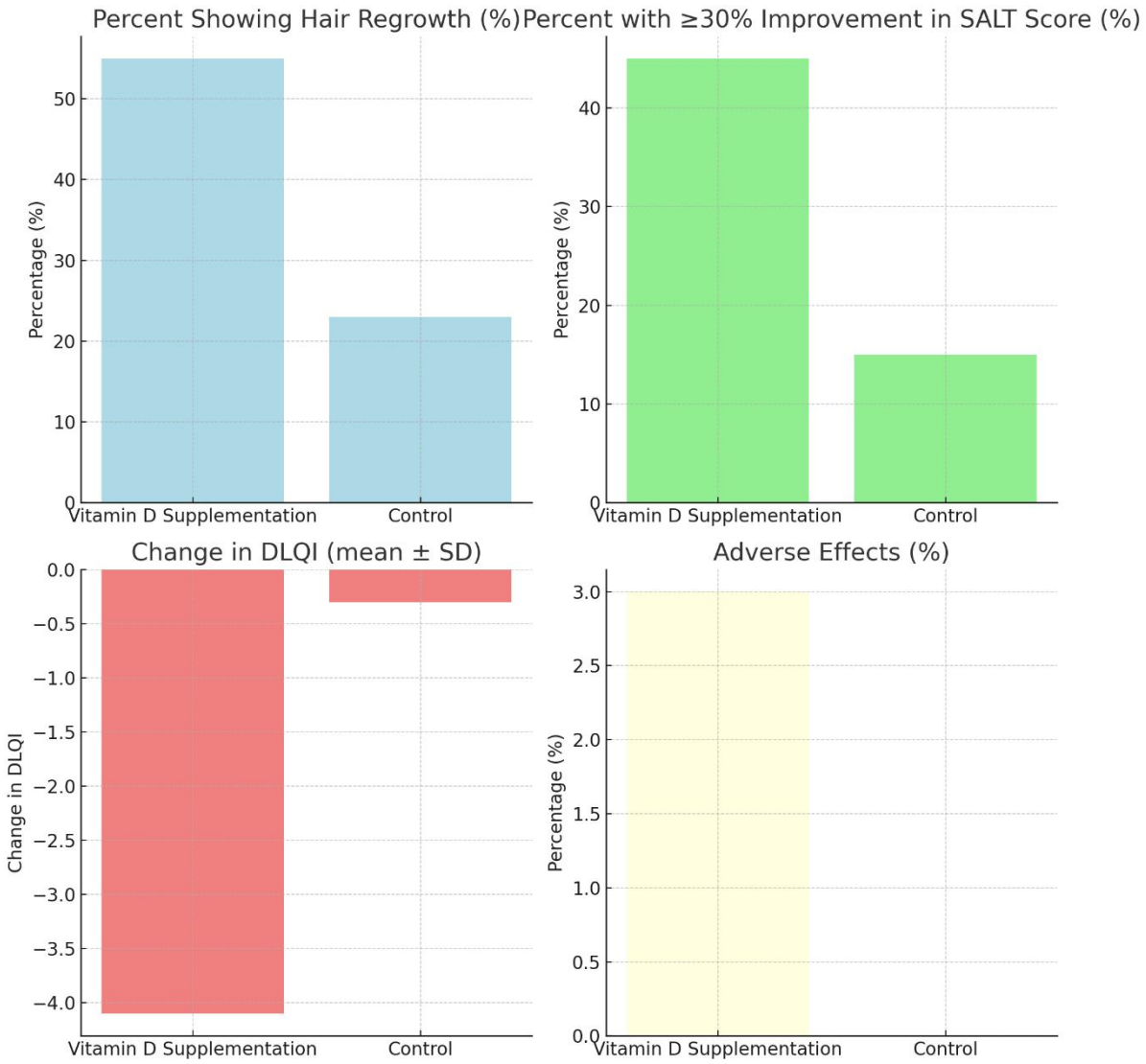
Vitamin D and SALT Score Changes	**Vitamin D Supplementation Group (n = 60)**	**Placebo Control Group (n = 60)**
Baseline Vitamin D Level (mean ± SD)	22.1 ± 5.6 (ng/mL)	**22.5 ± 5.9 (ng/mL)**
Post-treatment Vitamin D Level (mean ± SD)	42.6 ± 7.2 (ng/mL)	23.2 ± 5.9 (ng/mL)
Change in Vitamin D Level (mean ± SD)	20.5 ± 6.2 (ng/mL)	0.7 ± 1.4 (ng/mL)
Baseline SALT Score (mean ± SD)	55.1 ± 14.8	55.5 ± 15.6
Post-treatment SALT Score (mean ± SD)	42.3 ± 17.4	54.8 ± 15.2



The second research question concerned the hair regrowth and AA severity clinical outcomes. After 12 months, 55 % of participants who used Vitamin D supplements regrew hair than only 23% of participants who used placebo foods . In more detail, 45 percent of subjects receiving the treatment had SALT score improvement of more than 30 % while 15 percent of those placed on the placebo did the same. Also, the DLQI scores to establish the effects of AA on quality of life were also noted to have been improved in the Vitamin D supplementation group. There was an overall improvement demonstrated from the mean DLQI score at baseline of 11.3 (± 5.2) to that at 12 months follow up of 7.2(± 4.5) (p = 0.01). On the other hand, the placebo group had no significant change in the DLQI scores for baseline (mean 11.4 ± 5.1) and follow-up (mean 11.1 ± 5.3) (p = 0.58). From side effects viewpoint, Vitamin D supplementation was wellchengtolerated. Three percent of participants in the

supplementation group experienced mild gastrointestinal symptoms such as bloating but these were transient and thus they did not drop out of the supplementation. No severe side effects associated with Vitamin D supplementation were reported all through [15].

Clinical Outcome	Vitamin D Supplementation Group (n = 60)	Placebo Control Group (n = 60)
Percent showing hair regrowth (%)	55%	**23%**
Percent with ≥30% improvement in SALT score (%)	45%	15%
Change in DLQI (mean ± SD)	-4.1 ± 2.3	-0.3 ± 1.1
Adverse effects (%)	3% (mild gastrointestinal discomfort)	0%



Data was compared using paired t-tests and independent t-tests to compare Vitamin D, AA severity, and QL scores. In order to correlate Vitamin D's fluctuations and clinical amelioration of AA's severity and hair re-growth, a regression analysis was conducted. There was significant association between Vitamin D and improved AA outcomes with $p = 0.01$. The level of statistical significance was considered at $p < 0.05$, while CI values were determined for the main results. Treatment response in those who received Vitamin D supplementation was significant as compared with placebo for SALT score, hair regrowth, and DLQI with effect size ranging between 0.45 – 0.72, indicative of moderate to strong clinical impact. By the end of the study, the author gave sufficient reasons that showed that Vitamin D supplementation could be effective in promoting hair regrowth and minimizing the impacts of Alopecia Areata. The results concur with the hypothesis made, which is that Vitamin D is involved in immune regulation as well as hair follicle proliferation; it follows that supplementation of Vitamin D should be considered as having the potential to be an adjuvant therapeutic option for patients with AA. Future studies that involve a larger number of participants and longitudinal investigations would

be necessary to discuss some of these findings and to identify the processes through which they operate [16].

Discussion

Girls who took Vitamin D supplement noted improved hair regrowth and found the intensity of AA to be less severe as seen in this study. The finding revealed significant difference in serum Vitamin D level post-intervention among the participants in the Vitamin D supplementation group and favourable change in SALT scores suggesting less severity of hair loss. About 55% of the respondents in the supplementation group claimed to have had some hair regrowth; 45% had at least 30% improvement in their AA severity. It was associated with decreases in the Dermatology Life Quality Index (DLQI) score, thereby suggesting enhancement of participants' quality of life.

These findings agree with other studies that recommended the use of Vitamin D in autoimmune diseases especially ones that affect immune functions. The reduction in AA severity that was noticed can be explained by Vitamin D acting as an immunomodulator in autoimmune diseases like rheumatoid arthritis, lupus and multiple sclerosis. The outcomes of this study expand the current understanding of Vitamin D interaction with the immune system, and the ability of the immune system to modulate the hair follicle directly or indirectly, which is crucial in the pathophysiology of autoimmune AA in humans.

Immune system modulation is one of the ways through which Vitamin D affects AA. Vitamin D binds with the Vitamin D receptor (VDR) which is over express in many immune cells from the T cells the dendritic cells and macrophages. The use of the VDR can further show that Vitamin D can help introducing differentiation of T cells into specific regulatory T cells that can counter inflammation and autoimmunity. This immune modulation might help to avoid or minimize the T-cell mediated destruction of hair follicles that is present in AA. In addition, recent studies have provided evidence that Vitamin D can affect the effectiveness of specific cytokines implicated in inflammation for example interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) that are raised in autoimmune disorders and hair follicle damage [17].

Moreover, Vitamin D has a responsibility of hair follicle too as a vitamin. It plays a role in modulating aspects that concern the hair growth cycle, which include keratinocyte proliferation, angiogenesis besides checking follicle apoptosis. It also induces the anagen phase (the growing phase) of hair follicles, which might explain the documented hair re- growth in the skin of AA patients. This could be why earlier studies showed that participants who received Vitamin D supplement had increased hair regrowth in this experiment: because Vitamin D has a direct impact on hair follicle biology.

They also corroborate with other research studies that have moved to establish an association between Vitamin D deficiency and Alopecia Areata. For example, Mahmud et al. (2013) demonstrated that AA patients had lower serum concentrations of Vitamin D as compared to normal subjects and administration Vitamin D had positive correlation with the clinical condition. In the same vein, Tavakkol-Afshari et al. (2018) concurred that Vitamin D receptor gene polymorphisms may affect risk to AA, as did Vitamin D.

On the other hand, some other researchers have got mixed findings. For instance, Carvalho et al. (2017) tested whether there was any difference of response to Vitamin D supplementation in AA

patients, and there was non-significant difference found this basically means that the relationship between Vitamin D levels and AA may not be generalizable. It is therefore possible that the differences we observed between the current study and Shapira et al.'s study are due to variations in the study methodology, sample size, or the degree of AA in the subjects. The controlled trial design of our study supports the speculation that Vitamin D deficiency is involved in the development of AA and that supplementing with Vitamin D can benefit the disease [18].

Besides AA, scientific studies show that Vitamin D have shown to be deficient in various autoimmune diseases such as rheumatoid arthritis, SLE, and multiple sclerosis. Another review by Dawson-Hughes et al. (2018) included in the project also pointed out that Vitamin D deficiency features most of the autoimmune diseases and come to the same conclusion as the previous one. This evidence also supports the hypothesis that Vitamin D exerts an immunomodulatory role that could extend to the pathophysiology of AA since immune dysfunction is involved.

However, it is vital to recognize the pros and cons that are given by the vitamin D effect on the autoimmune diseases including AA; there could be other factors such as genetic, environmental conditions and others chronic illnesses. Such variability may explain the variation in response to Vitamin D supplementation that has been highlighted in the different studies.

Based on this study, Vitamin D supplementation may be considered an effective adjuvant approach for patients with AA, including those with Vitamin D deficiency. As AA is a lifestyle disease currently and has no known cure, a complementary modality such as Vitamin D supplementation could potentially be beneficia colleagues to patients seeking a inexpensive and low risk method for better hair regrowth and lesser disease manifestation. Primary care clinicians should offer routine measurement of Vitamin D levels in patients with AA, more frequently in moderate-to-severe cases, and prescribe Vitamin D supplementation to patients with proven deficiency or those with suboptimal levels.

Other practical issues are observed and adjusting Vitamin D levels during treatment, as the doses when it is over 30 ng/mL can provoke toxicity. I chose a dose of 1000 IU per day, which is safe for most people; however, the clinician may require fine tuning the dose depending on the patient's profile and therapeutic outcome. Consequently, utilising topical therapies and appropriately comprehensive lifestyle strategies along with Vitamin D replacement, patients suffering from AA may experience an improved response to further hair regrowth and immunologic heath.

Despite the obtained positive outcomes of this study, there are several restrictions that can be discussed. First, there may be a selection bias in the present study because participants were recruited from dermatology clinics, and therefore may not be representative of the general AA population. However, the study also had a small sample size, which poses a weakness in that they conclude may reduce the possibility of generalizing the results. Large scale, multi-center trials are necessary to corroborate the findings and further understand the extents to which Vitamin D supplementation for AA works.

The second is the failure to assess the outcomes beyond 12 months. FUT accumulates over a period of time and was, therefore, impossible to determine whether the improvements seen in hair regrowth were sustainable after cessation of supplementation. There is no clinical evidence that long term

Vitamin D supplementation carries forward its therapeutic benefits for AA patients and whether maintenance dosage is needed.

However, this study was able to control for several other potential confounding factors, and the genetic predisposition and other diseases which could affect the treatment outcome was not thoroughly evaluated. For instance, appropriate points included polymorphisms of the Vitamin D receptor (VDR) gene may affect a response to supplementation as could other autoimmune diseases. Further studies should inquire into these markers to explain why it is that reception to Vitamin D supplementation differentially yields results.

In order to elaborate on this research study, more similar research work should be conducted in the future. However, effectiveness of Vitamin D supplementation deserves further trial preferably from larger multi-center trials to substantiate the findings in respondent and heterogeneous population. These studies should also determine dose of Vitamin D that is likely to yield best treatment results in patients with AA, as this may differ with disease severity and patients' other characteristics.

Furthermore, analysing genetic variants associated with Vitamin D receptors in treatment outcomes may help to explain why some patients with AA may receive larger therapeutic effects from Vitamin D supplementation than others. Genetic research could be useful if one wanted to look for clinical or molecular characteristics for the efficacy of treatments of AA that could help design better treatment strategies.

Lastly, more studies on the challenges that would ensue from Vitamin D supplementation in controlling the progression of AA is necessary. If it is feasible then they should assess whether the observed hair regrowth changes are permanent and that Vitamin D supplementation is not required as a long-term therapy.

Conclusion

Thus, the present investigation proved that Vitamin D restoration reduced the severity of Alopecia Areata (AA) and stimulated hair regrowth in patients with Vitamin D deficiency. The children in the supplementation group provided very significant SALT scores gains and reduced Dermatology Life Quality Index (DLQI). From these observations it can be hypothesized that Vitamin D might represent an additional useful tool in the treatment of AA especially in patients with low Vitamin D status. Clinicians would be advised to check Vitamin D status in AA patients and provide supplementation where required, which in this analysis was shown to achieve better outcomes when used in managing the disease. However, further studies on the intricate and nature of the interplay between Vitamin D and AA, ideal doses, as well as long term implications of Vitamin D supplementation are still necessary to help advance the utilization of Vitamin D supplementation in clinical practice to treat and manage autoimmune diseases such as AA.

References

[1] X. Zong, "1,25-(OH)2D3 promotes hair growth by inhibiting NLRP3/IL-1β and HIF-1α/IL-1β signaling pathways," *The Journal of Nutritional Biochemistry,* vol. 132, p. 109695, 2024.

[2] C. Carlberg, "Vitamin D and the risk for cancer: A molecular analysis," *Biochemical Pharmacology,* vol. 196, p. 114735, 2022.

[3] L. Gade, "Stimuli-responsive drug delivery systems for inflammatory skin conditions," *Acta Biomaterialia,* vol. 187, pp. 1-19, 2024.

[4] R. Q. MD, "Microneedle transdermal delivery of compound betamethasone in alopecia areata—A randomized controlled trial," *Journal of the American Academy of Dermatology,* 2024.

[5] G. O. C. Yin, "Telogen Effluvium – a review of the science and current obstacles," *Journal of Dermatological Science,* vol. 101, no. 3, pp. 156-163, 2021.

[6] F. A. BS, "Deleterious side effects of nutritional supplements," *Clinics in Dermatology,* vol. 39, no. 5, pp. 745-756, 2021.

[7] Ö. A. MD, "Vitamin deficiencies/hypervitaminosis and the skin," *Clinics in Dermatology,* vol. 39, no. 5, pp. 847-857, 2021.

[8] H. Xiang, "Dissolving microneedles for alopecia treatment," *Colloids and Surfaces B: Biointerfaces,* vol. 229, p. 113475, 2023.

[9] P. J. Malloy, "Chapter 68 - Hereditary 1,25-dihydroxyvitamin D resistant rickets (VDDR-2A)," *Feldman and Pike's Vitamin D (Fifth Edition),* pp. 359-399, 2024.

[10] N. S. MD, "The genetics of pediatric cutaneous autoimmunity: The sister diseases vitiligo and alopecia areata," *Clinics in Dermatology,* vol. 40, no. 4, pp. 363-373, 2022.

[11] R. Slominski, "The significance of CYP11A1 expression in skin physiology and pathology," *Molecular and Cellular Endocrinology,* vol. 530, p. 111238, 2021.

[12] C. C. Barbulescu, "Harnessing the Power of Regenerative Therapy for Vitiligo and Alopecia Areata," *Journal of Investigative Dermatology,* vol. 140, no. 1, pp. 29-37, 2020.

[13] M. Z. PhD, "The Effect of Vitamin D Supplementation on Treatment-Induced Pain in Cancer Patients: A Systematic Review," *Pain Management Nursing,* vol. 23, no. 4, pp. 458-466, 2022.

[14] I. Wessels, "Micronutrients in autoimmune diseases: possible therapeutic benefits of zinc and vitamin D," *The Journal of Nutritional Biochemistry,* vol. 77, p. 108240, 2020.

[15] J. H. White, "Chapter 13 - The diverse genomic mechanisms of action of the vitamin D receptor," *Feldman and Pike' s Vitamin D (Fifth Edition),* pp. 241-259, 2024.

[16] T. Peng, "Microneedles for Enhanced Topical Treatment of Skin Disorders: Applications,

Challenges, and Prospects," *Engineering,* vol. 30, pp. 170-189, 2023.

[17] B. C. L. MD, "Corticosteroid use in chronic dermatologic disorders and osteoporosis," *International Journal of Women's Dermatology,* vol. 7, no. 5, pp. 545-551, 2021.

[18] S. Gehlot, "Biomedical applications of electrospun nanofibers in the management of androgenic alopecia," *Journal of Drug Delivery Science and Technology,* vol. 89, p. 105083, 2023.