



## Update on the role of vitamin D in the Pathogenesis of Female pattern hair loss

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### Abstract:

**Background:** Female Pattern Hair Loss (FPHL), also known as female androgenetic alopecia (AGA), is the leading cause of hair loss in adult women, with a significant impact on patients' quality of life. It develops from progressive follicle thinning, which leads to a decrease in hair density, resulting in non-scarring widespread alopecia with distinct clinical, dermoscopic, and histological patterns. The lack of knowledge about the etiology of the hair-thinning process and the factors regulating follicular development limits the promise of novel therapeutics. Topical minoxidil, used to treat androgenetic alopecia since the 1990s, is the most highly evidenced medication and remains the first choice. However, some patients do not show improvement with it, so it is crucial to seek alternative lines of treatment. It is commonly recognized that maintaining the regular hair cycle requires keratinocytes to express vitamin D receptors. The writers of this article examine vitamin D's potential contribution to hair development in a critical manner.

**Objectives:** This paper will provide a brief overview of vitamin D biology within the hair follicle, its role in the etiology of hair loss, and the justification for supplementing in FPHL.

**Conclusion:** A number of signaling pathways that control the proliferation and differentiation of hair follicles depend critically on vitamin D. Many studies reveal a link between serum vitamin D levels and FPHL, as well as other types of alopecia. Nonetheless, there aren't enough compelling studies to back up the utility of vitamin D analogues in treating these conditions and reversing hair loss. As a result, further research is required before vitamin D is consistently proposed as a therapy option for these illnesses.

**Keywords:** Female pattern hair loss, Vitamin D, Topical vit D analogue, Alopecia

**Abbreviations:** (FPHL) female pattern hair loss, (VDR) vit D receptor, (AGA) androgenetic alopecia.

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## Introduction

Female pattern hair loss (FPHL) is the most common cause of hair loss in females and significantly lowers the social and psychological well-being of its patients. It is thought to be multifactorial, while the precise pathogenic mechanism is unknown. Only topical minoxidil 5% solution and systemic finasteride are FDA-approved treatments for AGA. Our search for alternative therapies is often driven by side effects and incomplete responses. The expression of VDR in the hair root sheath has led numerous studies to conclude that vitamin D plays a crucial role in the differentiation of hair follicles. Several studies have discovered low levels of serum 25 (OH) D in patients with non-scarring alopecia. This suggests that vitamin D may have a role in the development of hair loss.

## Review methodology

We conducted a thorough analysis of the connection between FPHL and vitamin D. Our discussion centered on the current understanding of the etiopathogenesis of FPHL and the possible function of vitamin D supplementation. The search phrases "FPHL," "Vit D," "Topical Vit D analogue," "VDR," "alopecia," and "Androgenetic alopecia" were combined with one or more of the other terms.

## Female pattern hair loss

Female pattern hair loss (FPHL) is characterized by progressive non-scarring alopecia caused by hair follicle thinning in the frontal, parietal, and central scalp. FPHL is the commonest cause of hair loss in adult females; the frequency increases with age, and the disorder responds inconsistently to treatment.<sup>(1)</sup> FPHL's pathophysiology involves both androgen-dependent and androgen-independent mechanisms. FPHL is more frequent in women over 70 years old, accounting for 55% of all cases. Advanced cases have been infrequently noticed throughout puberty. FPHL typically has a first peak incidence during the reproductive years and a second peak following menopause.<sup>(2)</sup>

## Pathophysiology of FPHL

FPHL is influenced by genetics, hormones, and the environment. Approximately 50% of FPHL patients have a family history of female hair loss, indicating a hereditary component, particularly in cases of early clinical presentation (<30 years).

The reality that female pattern hair loss (FPHL) occurs with varying degrees of severity and onset at different ages suggests a multigenetic pattern of androgenetic alopecia (AGA).<sup>(3)</sup> The role of androgens in the development of FPHL remains unknown as FPHL can occur in females with normal androgen levels.<sup>(4)</sup>

## Vitamin D and its role in hair

The VDRs are present in the outer sheath of the hair follicle and hair follicle bulb. These receptors help to differentiate hair follicles in gestation and start the first hair cycle after delivery. The identification of VDR's role in hair follicles began with the analysis of patients with vitamin D-dependent rickets who had a VDR defect.<sup>(5)</sup>

These children are delivered with normal hair follicle morphogenesis but lose their hair between the ages of one and three months due to an anagen initiation defect.

The first hair cycle occurs at the end of embryological development and is unaffected by the growth factors required to maintain the hair follicles. As a result, deficiencies in components needed for maintaining the hair cycle, like VDR, are not visible until first hair sheds.<sup>(6)</sup>

A possible relationship between serum vitamin D and FPHL has been hypothesized, as its concentration is lower in FPHL patients compared to controls.<sup>(12, 13)</sup> There is an association between vitamin D levels and alopecia in persons with congenital VDR deficiency and a previous study has indicated that VDR is a vital stage of hair follicle formation.<sup>(14)</sup>

VDR activity is required for keratinocyte stem cells to survive in the bulge region of hair follicles, and insufficient vitamin D levels result in improper stem cell renewal and hair follicle cycle disruption.<sup>(7)</sup>

## Diagnosis of FPHL

FPHL is often characterized clinically by gradually increasing hair thinning, mainly over the vertex and upper parietal scalp, which may or may not be accompanied by increased shedding. Unlike in men, the frontal hairline is usually retained, and the thinning is less pronounced. However, in some women, hair thinning is more severe, affecting the parietal and occipital areas of the scalp, resulting in a diffuse alopecia pattern.<sup>(8)</sup>

Commonly, FPHL can have three different patterns at presentation:

- 1-This pattern is distinguished by diffuse thinning of the crown region while retaining the frontal hairline. It can be described on two scales: the 3-point Ludwig scale and the 5-point Sinclair scale.
- 2-The Olsen scale describes the thinning and broadening of the center scalp, including a break of the frontal hairline, similar to the Christmas tree pattern. on addition to the scattered thinning, there is an emphasis on the central line, which opens up into a triangle at the front hairline.
- 3-Hamilton-Norwood scale measures thinning during bi-temporal recessions.

### Diagnostic criteria of FPHL

FPHL is diagnosed both clinically and by dermoscopy. In 2009, major and minor trichoscopic criteria for FPHL were established by Rakowska et al. <sup>(11)</sup> Major criteria for the frontal area include more than 4 yellow spots in 4 fields, lower average hair thickness relative to the occiput, and more than 10% of tiny hairs (<0.03mm). Minor factors include <sup>(1)</sup> a higher frontal-to-occipital ratio of single-hair pilosebaceous units, <sup>(2)</sup> vellus hairs, and <sup>(3)</sup> perifollicular discoloration.

FPHL is diagnosed when two major criteria are present, or when one major and two minor criteria exist.

### Treatment of FPHL

Despite its widespread incidence, AGA can be difficult to treat because of its chronic nature and the interaction of hereditary and environmental variables.

Currently, the US Food and Drug Administration (FDA) has approved only two medicines for AGA: topical minoxidil and oral finasteride. However, various non-FDA-approved medications have proven to be beneficial in the treatment of patterned alopecia.

### Vitamin D in FPHL

As previously stated, an error in Vit D or VDR function causes improper stem cell regeneration and hair cycle loss. Zhao et al. found a strong relationship among deficient vitamin D and alopecia areata, female and male AGA. <sup>(9)</sup> Moreover, previous studies discovered severe vitamin D deficiency in patients with FPHL. <sup>(6,7)</sup>

Furthermore, vitamin D levels showed an inverse relationship with the severity of hair loss. As regards levels of tissue VDR, Fawzi et al. found considerably reduced levels of serum and tissue VDR in patients with patterned alopecia. <sup>(10)</sup> According to a past study, Vit D deficiency is connected with a more severe and early start of AGA. <sup>(11)</sup>

Several studies investigated the use of oral and topical Vit D as a possible treatment for various kinds of hair loss. A study on mice animals found that treatment with vitamin D3 mimics stimulated hair follicle growth. <sup>(12)</sup> As a result, we looked at research that tested topical vitamin D3 mimics on human participants. Narang et al. discovered that alopecia areata patients treated with topical Vit D responded better. <sup>(9)</sup>

### Oral Vit D

As previously stated, in the Egyptian study <sup>(13)</sup>, serum vitamin D3 levels were considerably lower in FPHL than control group. Thus, blood Vit D levels are increasingly being considered when approaching patients with FPHL. <sup>(14)</sup> A recent study found considerable improvement in FPHL both clinically (Ludwig grade) and dermoscopically when oral vitamin D (5000 IU daily dose for 6 months) was combined with topical minoxidil rather than either treatment alone. <sup>(15)</sup>

### Topical Vit D analogue:

In dermatology, many vitamin D derivatives (metabolites) such as calcipotriol, calcitriol, tacalcitol, and maxacalcitol are employed. <sup>(16)</sup> Many writers have examined the usefulness and safety of vitamin D and its compounds.

as a potential treatment for AA. Some writers claim that taking oral vitamin D supplements improves telogen effluvium (TE) and androgenetic alopecia (AGA). <sup>(9)</sup>

**Dose and uses of topical calcipotriol:** Adult dose: calcipotriol ointment 50 µg /g twice daily not exceeding 100gm/week. <sup>(13)</sup>

### Conclusion

Vitamin D has a critical function in various signaling pathways that control hair follicle development and differentiation. Several studies have identified a link between deficient serum Vit D levels and various types of alopecia, including FPHL. More research is needed on the vitamin D

supplementation regimen and the use of topical vitamin D analogs in the treatment of FPHL.

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