Vitamin D3 deficiency and androgenetic alopecia: Is there a connection?

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Abstract

Background: Multiple studies have evaluated the role of Vitmain D deficiency in the pathogenesis of hair loss in disorders such as Alopecia Areata, Telogen effluvium, male and female pattern hair loss. Studies conducted to evaluate the role of Vitamin D deficiency in androgenetic alopecia have shown contrasting results and none have established a clear causal relationship.

Methods: We conducted a case control study over a time period of four months in a public sector, tertiary care hospital. 50 cases, both male and female, of androgenetic alopecia and 50 controls, matched for age, skin phototype, sun exposure, and socioeconomic status were recruited for the study. In all the participants, we measured Serum 25-hydroxy vitamin D3 levels using radioimmunoassay technique. The results were compared between the two groups and analyzed.

Results: A total of 50 cases and 50 controls were enrolled for the study. The mean age of cases and controls was 31.12 ± 9.82 years and 30 ± 10.19 years respectively. In cases there were 38(56.7%) male and 12(17.9%) females while in controls there were 36(53.7%) male and 14(20.9%) female. The vitamin D levels were significantly decreased in cases i.e. 40(59.7%) as compared to controls i.e. 18(26.9%). Our results showed a positive correlation between serum 25-hydroxy vitamin D3 deficiency and androgenetic alopecia. This correlation was statistically significant (p-value < 0.001). The odds ratio was calculated to be 7.111 (2.885, 17.526), indicating that Vitamin D deficient participants had a 7 times higher risk of having androgenetic alopecia than the recruits with normal vitamin D levels.

Conclusion: Our study supports a correlation between Androgenic Alopecia and Vitamin D deficiency. Further larger scale studies are required to validate this finding and the question of whether vitamin D supplementation prevents the onset or delays the progression of androgenetic alopecia in susceptible individuals still remains.

Keywords: Vitamin D, Androgenetic Alopecia.

Introduction

Androgenetic alopecia is a non-scarring, hereditary form of hair loss that is androgen dependent and occurs in both men and women. It results in the gradual conversion of terminal hair follicles to miniaturized hair follicles, under the effect of a variety of etiopathological factors [1]. Hormonal changes, hair cycle abnormalities, genetics, aging, and altered end organ sensitivity have been proposed to be some of these factors. Androgenetic alopecia is divided into male and female pattern hair loss, both being the most common causes of hair loss in men and women respectively. While male androgenetic alopecia is characterized by reduced hair density in the bitemporal regions and recession of the frontal hair line, female pattern hair loss typically starts with diffuse thinning of hair in the mid-frontal region of the scalp followed by frontal accentuation [2]. Androgenetic alopecia can be graded with the use of Norwood Hamilton Scale. It typically begins in the third and fourth decades of life. However, it is being seen with increasing frequency in the younger population and leads to significant psychological distress and self-esteem issues in this group [3].

Vitamin D has an irreplaceable role in maintaining in human health. It is a fat-soluble vitamin that can be acquired exogenously *via* food sources, or manufactured in the skin by the conversion of ergosterol to Vitamin D2, and 7-dehydrocholesterol to previtamin D3 following UV irradiation of the epidermal keratinocytes [4]. This is followed by both α- and β- hydroxylation, which results in the formation of the active form, 1,25-dihydroxyvitamin D3, the final product in the synthesis pathway. The storage form of Vitamin D in the body is actually considered to be 25-hydroxy vitamin D3 which is a pro-hormone. It is the most abundant

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Table 1: *Comparison of age, gender and vitamin D levels in both study groups.*

		Case	Control	p-value
Age	Mean ± S.D	31.12 ± 9.82	30 ± 10.19	0.57
	Minimum	19	17	
	Maximum	55	56	
Gender	Male	38(56.7%)	36(53.7%)	0.208
	Female	12(17.9%)	14(20.9%)	
Vitamin D level	Deficient	40(59.7%)	18(26.9%)	<0.001
	Normal	10(14.9%)	32(47.8%)	

and stable form of Vitamin D. It has a half-life of around 3 weeks. The best way to assess the Vitamin D status is thus measuring the serum levels of 25-OH-Vitamin D3 [5].

Vitamin D has recently been implicated in the pathogenesis of multiple autoimmune, neuronal, reproductive, cardiac and infectious diseases. This recent attention has also brought to light the role of Vitamin D receptors in normal hair cycling, especially for the initiation of the anagen phase [6]. Reduced expression of Vitmain D receptors in hair follicles and keratinocytes has been found to result in decreased epidermal differentiation and hair growth. It has been suggested that a normal level of Vitamin D is essential to delay aging and prevent hair loss, and measuring the serum levels of Vitamin D has become a part of the approach towards patients presenting with hair loss [7].

Considering the role of Vitamin D in maintaining hair health and growth, multiple studies have been done evaluating the serum levels of vitamin D in hair disorders. The role of Vitamin D has been hypothesized in diseases such as alopecia areata, telogen effluvium, and male and female pattern hair loss. Studies on vitamin D levels in androgenetic alopecia have shown contrasting results and none have established a clear causal relationship. There is a paucity of relevant research having been conducted in the South Asian population. In this study, we hypothesize a correlation between reduced Vitamin D levels and androgenetic alopecia. Identifying a relationship with altered Vitamin D levels may allow us to explore new treatment options for patients with this chronic and often refractory disorder, bringing relief and social confidence to a large part of the population.

Methodology

This case control study was conducted on 50 patients of androgenetic alopecia, between the ages of 16 to 60 years, of Fitzpatrick skin type III, IV, and V, and 50 controls, matched for age, skin phototype, sun exposure and socioeconomic status. Patients and controls both were selected from the outpatient department of Mayo Hospital Lahore after written informed consent regarding the study. These patients were selected over a four-month period (April to July).

The exclusion criteria comprised of patients suffering from other causes of alopecia, both cicatricle and non-cicatricial, patients with clinical or lab evidence of hyperandrogenemia, patients suffering from malnutrition or malabsorption disorders and patients with chronic liver or kidney disease. A careful clinical history was taken from all the patients. The diagnosis of Androgenetic alopecia was established upon clinical examination, with the use of Norwood-Hamilton and Ludwig scales, to note the pattern of hair loss, a positive hair pull test and a Dermoscopy examination. Dermoscopy findings of increased villous to terminal hair ratio and hair shaft diameter of various sized were seen as evidence of androgenetic alopecia.

All the participants of the study were tested for dehydroepiandrosterone sulphate and free testosterone levels to eliminate hyperandrogenism. Serum levels of 25-hydroxy vitamin D3 were measured *via* radioimmunoassay technique and a value less than 20ng/ml was considered to be deficient.

Results

Data was entered in SPSS (Statistical Package for Social Sciences) version 25. Mean ± S.D were used for quantitative data like age. Frequencies and percentages were used for categorical data. Independent sample test was applied to compare mean age in both groups. Chi-square test was applied to compare gender and serum vitamin D levels in both groups taking p-value ≤ 0.05 as significant. Odds ratio was also applied to know the risk of androgenetic alopecia in presence of low vitamin D level (Table 1).

The mean age of case and controls was 31.12 ± 9.82 years and 30 ± 10.19 years respectively. In cases there were 38(56.7%) male and 12(17.9%) females while in controls there were 36(53.7%) male and 14(20.9%) female. The vitamin D levels were significantly decreased in cases i.e. 40(59.7%) as compared to controls i.e. 18(26.9%), p-value < 0.001. The odds ratio =7.111 (2.885, 17.526), shows that there was a 7.111 times higher chance of androgenetic alopecia in those who had a low level of 25-hydroxy vitamin D3.

Discussion

Vitamin D affects the growth of hair in the human body *via* several proposed mechanisms. The role of Vitamin D receptor in the regulation of the hair cycle was hypothesized for the first time on the basis of Alopecia Universalise being one of the symptoms of Type IIA Vitamin D dependent rickets (VDDR IIA). Neonates with VDDR IIA have normal hair at the time of birth, but they begin to lose hair after 1 to 3 months, when the embryonic hair is shed off and the first post-natal hair cycle begins. It is evident that that the normal functioning of Vitamin D Receptor (VDR) is essential for the timely initiation and maintenance of the hair cycle [8]. Another study suggests that the VDR gene and the hairless gene are actually part of the same genetic signalling pathway,

and work in collaboration to regulate the hair cycle. This is derived from the pathogenesis of Generalized Atrichia resulting from the mutations in the hairless gene, which is clinically and histologically similar to VDR IIA [9]. Studies also show that Vitamin D3 stimulates the terminal differentiation of hair follicles in the human body [10]. This is particularly important because androgenetic alopecia is characterized by a miniaturization of the hair follicles, resulting in an increased ratio of villous to terminal hair. The results of our study support the idea that hair loss associated with androgenetic alopecia is associated with reduced levels of serum 25-hydroxy vitamin D3. This is based upon a statistically significant difference between the Vitamin D levels of cases and controls, the cases falling in the category of Vitamin D deficient. Hence, low Vitamin D levels may be one of the contributing factors of Androgenetic Alopecia.

These findings are coherent with the results of another study conducted at Fayoum University Hospital [11] where a mean vitamin D level of 37.1ng/ml was documented in cases, in comparison to a mean of 44.2ng/ml in controls. The Vitamin D levels of cases were significantly lower than the controls, with a p-value of 0.02. Similar findings were also reported by 2017 [12] and 2014 [13]. Their results showed significantly lower levels of Vitamin D in cases of as compared to matched controls. However, both these studies were conducted on female patients only, targeting the Female Pattern Hair Loss variant of androgenetic alopecia. Moreover, these studies comprised of patients from a younger age group, 20-40 years in the study included both male and female patients between the ages of 16 and 60, providing a wider age range. This is of importance because the serum levels of Vitamin D are known to decline with advancing age.

Vitmain D levels in the body can be affected by individual variables such as age, skin phototype, and exposure to the sun. Since our cases and controls were matched for age, skin type and sun exposure, these confounding factors had minimal effect on the results of our study and their interpretation. Environmental and seasonal factors such as weather conditions, season, geographical location, outdoor exposure and air pollution can also affect the serum levels of Vitamin D3. We tried to minimize the role of these factors in our study by choosing patients from one district of the country over the course of 4 months in the summer season only. Our sample size was relatively small, but it was broadly representative of the population of the target district.

In our study, Serum Vitamin D levels were decreased in 59.7% of the cases, as compared to only 26.9% of cases. This is statistically significant, with a p-value of < 0.001. Furthermore, Odds ratio of 7.111 suggests that people who were vitamin D deficient had a 7 times greater risk of developing androgenetic alopecia. Based on this, we suggest that Vitamin D deficiency is indeed one of the factors associated with androgenetic alopecia. Future studies on the contribution of vitamin D receptors in the regulation of hair cycle and hair growth are warranted. Moreover, Serum Vitamin D levels should be checked early after the diagnosis of androgenetic alopecia, providing the opportunity to replace Vitamin D in the patients presenting with a measurable deficiency. Studies should also be conducted on Vitamin D supplementation as a possible therapeutic measure for androgenetic alopecia and its possible effect on halting the disease process.

Conclusion

Our study supports a correlation between Androgenetic Alopecia and Vitamin D deficiency. Further larger scale studies are required to validate this finding and the question of whether vitamin D supplementation prevents the onset or delays the progression of androgenetic alopecia in susceptible individuals still remains.

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