The importance of vitamin-D in androgenic alopecia and telogen effluvium

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Abstract

Aim: Androgenic alopecia (AA) is defined as progressive miniaturization of hair follicle prevailing among both male and female. Telogen effluvium (TE) is the most common hair loss form accompanying systemic diseases. It is aimed to determine the role of vitamin D, the significance of which has been increasing in recent years, in hair loss problem within the scope of this study.

Methods: The patients who applied to Dermatology clinic with the complaint of hair loss and diagnosed androgenic alopecia and telogen effluvium by clinic examination between the years 2015-2016 were included in this study. The age, gender and 25'OHVitamin-D level of the patients were recorded retrospectively.

Results: One-hundred eighty seven (N=187) participants (140 female / 47 male) were included in this study. Fifty-eight (N=58) patients (28 female / 30 male) with androgenic alopecia diagnosis formed the first group; 71 patients (65 female / 6 male) with telogen effluvium were formed the second group and 58 healthy volunteers (47 female / 11 male) were included in the control group. When Vitamin-D level of first group (AA) was compared with that of the second group (TE) and the control group, there was a statistically significant difference observed (p=0.01/p=0.01 respectively). However, there was no statistically significant difference between the vitamin-D level of second group (TE) and that of the healthy control group (p=0.61).

Conclusion: The level of 25'(OH) vit D was found high in androgenic alopecia group than telogen effluvium and controls. Revealing the relationship between vitamin-D level and hair loss might give us the opportunity to come up with new treatment options considering refractory patients.

Keywords: vitamin D, telogen effluvium, androgenic alopecia
Introduction

Androgenic alopecia (AA) is defined as progressive miniaturization of non-scarring alopecia hair follicle prevailing among both male and female. Level of androgen, age and genetic factors have been stated as the primary causes concerning pathogenesis of the disease [1]. However, the loss of hair has seemed prevalent among genetically prone individuals even with normal androgenic hormone level [2]. The occurrence and development of AA depends on the interaction of endocrine factors and genetic predisposition [3]. Its pathogenesis is androgen dependent, and genetic predisposition is the major requirement for the phenotype [4]. Although AA is a very prevalent condition, approved therapeutic options are limited. Finasteride and minoxidil for male AA and minoxidil for female are prevailing among both male and female. Level of androgene, ferritin and zinc levels recorded from hospital data. Patients with AA, the second group was formed with the ones with TE and the last group included the ones with no distinct diagnosis (healthy control group). The age, gender and 25(OH) vitamin-D level of the patients were recorded retrospectively. Complete blood count, thyroid function test, Vit B 12, folic acid, ferritin and zinc levels recorded from hospital data. Patients detected any abnormalities from these tests were excluded from the study.

Material and methods

The patients who applied to Dermatology clinic with the complaint of hair loss and diagnosed AA/ TE by clinic examination between the years April 2015 - April 2016 were included into this study. With a prior written consent form taken from the participants, they were divided into three main categories according to diagnosis: the first group consisted of the ones with AA, the second group was formed with the ones with TE and the last group included the ones with no distinct diagnosis (healthy control group). The age, gender and 25(OH) vitamin-D level of the patients were recorded retrospectively. Complete blood count, thyroid function test, Vit B 12, folic acid, ferritin and zinc levels recorded from hospital data. Patients detected any abnormalities from these tests were excluded from the study.

Statistical analysis of the study was performed with SPSS 17 (SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Normal distribution analysis of the data acquired was evaluated with Kolmogorov-Smirnov test method. Descriptive tests were used for the defining data. Independent student T-test was used for the comparison of groups with normal distribution, and Mann Whitney U test was applied for the comparison of groups with non-central distribution. P<0.05 was regarded as statistically significant.

Results

One-hundred eighty seven (N=187) participants (140 female / 47 male) were included in this study. Fifty-eight (N=58) patients (28 female / 30 male) with AA diagnosis formed the first group; 71 patients (65 female / 6 male) with TE formed the second group and 58 healthy volunteers (47 female / 11 male) were included in the control group. For the AA group, the mean age was 30.3±8.8 years with a mean 25(OH) Vitamin-D level of 16.02±8.3 ng/dl; for the TE group, the mean age was 26.6±8.4 years with a mean 25(OH) vit D level of 11.6±5.2 ng/dl; the mean age of the control group was 28.5±10.1 years with a mean 25(OH) vitamin-D level of 11.6±5.2 ng/dl. Although AA is a very prevalent condition, approved therapeutic options are limited.

Abbreviations: AA: Androgenic alopecia; TE: Telogen effluvium; F: female; M: male;

Table 1 Distribution of 25(OH) Vitamin-D, age, gender according to the groups

| Group   | Age (Median) | 25(OH)Vit D (Mean±SD) | Gender (N/%) |
|---------|--------------|----------------------|--------------|
| AA (N=58) | 30 | 16.02±8.3 (T) | F 30 / S 17 |
| TE (N=71) | 26 | 11.6±5.2 | F 65 / 9.15 |
| Control (N=58) | 28 | 12.2±8.3 | M 11/9 |

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When vitamin-D level of the first group (AA) was compared with that of the second group (TE) and the control group, there was a statistically significant difference observed ($p=0.01/p=0.01$ respectively) (Table 2). However, there was no statistically significant difference between the vitamin-D level of second group (TE) and control group ($p=0.61$).

**Table 2** Comparisons of vit D levels according to the groups

|                      | Group 1-2 | Group 1-3 | Group 2-3 |
|----------------------|-----------|-----------|-----------|
| Age                  | P=0.15    | P=0.294   | P=0.247   |
| Gender               | P=0.050   | P=0.080   | P=0.080   |
| 25'(OH) Vit D        | P=0.01*   | P=0.01*   | P=0.61    |

Abbreviations: group 1: androgenic alopecia; group 2: telogen effluvium; group 3: control *$p<0.05$, statistically significant.

**Discussion**

Hair loss is one of the major reasons among all the patients applying to Dermatology clinic. It has a considerable influence on social interactions among people as most people indicate that hair loss can have adverse effects on their self-confidence and self-esteem. People with hair loss are rather inclined to feel older than they actually are, and they are quite often abstained from daily interactions both socially and physically. Therefore, it can be concluded that alopecia has more diverse effects than assumed for individuals who suffer from this disease as it causes stress along with a dissatisfaction with the body image. As a result of a foreshaid desperate situations, millions of dollars are being spent for its treatment every year [11, 12].

Level of androgen, age and genetic factors have been stated as the primary causes concerning pathogenesis of the disease [13]. Telogen effluvium is the most common hair loss form accompanying systemic diseases. On all over the scalp, hair becomes diffusely sparse [8]. There are several factors which might play important role in TE, such as iron deficiency, thyroid gland dysfunctions, systemic diseases, some varieties of medication, hypoproteinemia and low zinc level [14, 15]. Despite the fact that there is no efficient treatment for AA and TE, cause-oriented treatments should be administered after doing necessary tests.

Vitamin-D has a key role in the regulation of calcium homeostasis and bones metabolism. Over the last two decades, immune-regulatory effects of Vitamin-D has arisen ever-increasing curiosity with respect to the emergence of some diseases characterized by inflammation, malignancy, autoimmune disorders and chronic infections due to its deficiency [16].

Vitamin-D also plays a vital role in many dermatologic cases. It is used in the treatment of psoriasis for its anti-proliferative effect, in healing vitiligo for its melanocytes synthesis stimulating effect and as a remedy for scleroderma and generalize morphea due to its effect of decreasing the collagen synthesis and inhibiting active T-cells functions [17-19]. Wegienka et al have identified significant relevance between the 25-OH vitamin-D levels in prenatal cord blood and some eczema types [20]. They have also discussed that vitamin-D supplement might become a current issue as it can be used for preventive treatment in progress of allergic diseases. In another study conducted, it was contemplated that vitamin-D has important role within the progress, severity and process of some allergic diseases such as asthma, eczema and food allergies. It has also been suggested that extensive vitamin-D deficiency in all over the world can account for the increase of allergic diseases to a certain extent within the last 50-60 years [21].

Vitamin-D has a notable role in the keratinocyte differentiation and forming healthy hair cycle. The intense presence of vitamin-D receptor, the lack of which can affect hair growth, has been identified in hair follicles [22]. It has been claimed by Mady LJ et al. in their experimental animal model that calbindin-D9k knockout pump, maternal vitamin-D deficiency or low calcium diet cause alopecia with no temporary scar [23]. Accordingly, in another experimental animal study conducted by Xie Z et al., it has been found that there is a relation between insufficient activity of vitamin-D receptors and reduced epidermal differentiation as well as the growth of hair follicles [24]. In yet another study, the findings have posed that the mice whose vitamin-D receptor was mutated alopecia monitoring the role of vitamin-D receptor was stronger than that of the hormone itself, while alopecia was not a frequent symptom in the case of mice fed on vitamin-D poor diet [25].

In a study conducted on by Mahamid M et al., low vitamin-D level was detected in alopecia areata patients [26]. In another study conducted by Fawzi et al., it was found that vitamin-D receptor levels in serum and tissue were relatively low in patients with AA and alopecia areata in pathogenesis of which vitamin-D receptors are of vital importance [27]. Apart from the literature according to our study the level of Vit D was statistically higher than the control group and TE group. Yet another study conducted by H Rasheed et al. on 80 female patients suffering from hair loss with TE diagnosis has revealed a strong correlation between low serum vitamin-D and ferritin level and hair loss occurred [28]. With the realization of this relationship, the importance of vitamin-D and iron supplements in the treatment of hair loss problem will be better appreciated. We did not detect any statistically difference of Vit D levels between TE and control group. There may be other factors (age, gender, etc.) affecting the level of Vit D in TE group.

The correlation between vitamin-D level and alopecia has been more widely established in alopecia areata within the literature. There have been only limited number of studies related to AA and TE. In this study statistically significant vitamin-D level has been found in AA group when compared to that of the healthy control group. On the other hand, there was no statistically significant difference between the vitamin-D level of TE group and that of the healthy control group. Of 58 healthy volunteers within the control group 47 were female and 11 were male. Owing to cultural values and clothing habits in our society, the vitamin-D level of female was found to be lower. Uneven sampling distribution of male and female in our study can be regarded as one of the vulnerabilities. We consider this uneven sampling distribution might have affected the findings and results of this study.

**Limitation of the study**

Not considering other bone turnover biomarkers (calcium, parathormone, alkaline phosphatase, telopeptide) and menopausal status of females are the limitations of the study. Another limitation of our study is that we live in a geography where women are covered and little exposed to the sun. This may have affected the outcome of vitamin D in female patients.

**Conclusion**

We have found high vit D levels in AA group than TE and controls. The studies conducted on a larger patient population
with vitamin-D level will most likely to be guiding the further research in a better way. Revealing the relationship between vitamin-D level and hair loss might give us the opportunity to come up with new treatment options considering refractory patients.

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References
1. Herskovitz I, Tosti A. Female Pattern Hair Loss. *Int J Endocrinol Metab.* 2013; 11:9860.https://doi.org/10.5812/ijem.9860
2. Dawber RPR, Ebling FJG, Wojnarowska FT. Disorders of hair. Textbook of dermatology. Ed. Champion RH, Burton JL, Ebling FJG. 5. Ed.ition. Oxford, Blackwell ScientificPubl, 1992; 2533-638.
3. Lolli F, Pallotti F, Rossi A, Fortuna MC, Caro G, Lenzi A, Sansone A, Lombardo F. Androgenetic alopecia: a review. *Endocrine.* 2017; 57(1):9-17. https://doi.org/10.1007/s12020-017-1280-y
4. Hillmer AM, Hanneken S, Ritzmann S, Becker T, Freudenberg J, Brockschmidt FF, et al. Genetic variation in the human androgen receptor gene is the major determinant of common early-onset androgenetic alopecia. *Am J Hum Genet.* 2005; 77(1):140-8. https://doi.org/10.1086/341425
5. Kelly Y, Blanco A, Tosti A. Androgenetic Alopecia: An Update of Treatment Options. Drugs. 2016; 76(14):1349-64. https://doi.org/10.1007/s12020-016-0629-5
6. Saitoh M, Uzuka M, Sakamoto M. Human haircycle. *J Invest Dermatol.* 1970; 54:65-81. https://doi.org/10.1111/1523-1747.ep12551679
7. Malkud S. Telogen Effluvium: A Review. *J Clin Diag Res.* 2015; 9(9):WE01-3. https://doi.org/10.7860/ICDR/2015/15219.6492
8. Grover C, Khurana A. Telogen effluvium. *Indian J Dermatol Venereol Leprol.* 2013; 79(5):591-603. https://doi.org/10.4103/0378-6323.116731
9. Rebora A. Intermittent Chronic Telogen Effluvium. *Skin Appendage Disord.* 2017; 3(1):36-38. https://doi.org/10.1159/000455882
10. Gerkowicz A, Chyl-Surdacka K, Krasowska D, Chodorowska G. The Role of Vitamin D in Non-Scarring Alopecia. *J Cosmet Dermatol.* 2017; 18(12):E2653. https://doi.org/10.3390/jcmd18122653
11. Cash TF: The psychosocial consequences of androgenic alopecia: a review of the research literature. *Br J Dermatol.* 1999; 141:398-405. https://doi.org/10.1046/j.1365-2133.1999.03030.x
12. Kutlubay Z, Bağlama S, Engin B, Serdaroglu S. Erkeklerde androgenetik alopesi. *Türkderm.* 2014; 48:36-9.
13. Hamilton JB: Male hormone stimulation is prerequisite and an incitant in common baldness. *Am J Anat.* 1942; 71:451-80. https://doi.org/10.1002/aja.1000710306
14. Headington JT. Telogen effluvium. New concepts and review. *Arch Derm.* 1993; 129(3):356-363. https://doi.org/10.1001/archderm.1993.0168040096017
15. Whiting DA. Chronic telogen effluvium: increased scalp hair shedding in middle-aged female. *J Acad Dermatol.* 1996; 35(6):899-906. https://doi.org/10.1016/S1090-9622(96)90113-9
16. Myszka M, Klinger M. The immuno modulatory role of Vitamin D. *Postepy Hig Med Dosw (Online).* 2014;68:865-78 https://doi.org/10.3390/jcmd6822693.1110168
17. Morimoto S, Kumahara Y. A patient with psoriasis cured by 1 alpha-hydroxy VitD3. *Med J Osaka Univ* 1985; 35:51-4
18. Parsad D, Saini R, Nagpal R. Calcipotriol in vitiligo: a preliminary study. *Indian J Dermatol Venereol Leprol.* 2013; 9(9):WE01-3. https://doi.org/10.3390/ijms9090125
19. Mady LJ, Ajibade DV, Hsiao C, Teichert A, Fong C, Wang Y, et al. The Transient Role for Calcium and Vitamin D during the Developmental Hair Follicle Cycle. *J Invest Dermatol.* 2016; 16: S0022-202X(16)03876-4. https://doi.org/10.1016/j.jid.2016.02.813
20. Xie Z, Komuves L, Yu QC, Elalieh H, Ng DC, Leary C, et al. Lack of the vitamin D receptor is associated with reduced epidermal differentiation and hair follicle growth. *J Invest Dermatol.* 2002;118(1):11-6. https://doi.org/10.1046/j.1525-1737.2002.01644.x
21. Beer S, Tieder M, Kohelet D, et al: Vitamin D resistant rickets with alopecia: A form of end organ resistance to 1,25 dihydroxy vitamin D. *Clin Endocrinol.* 1981; 14:395-402. https://doi.org/10.1111/j.1365-2265.1981.tb00624.x
22. Sakai Y, Kishimoto J, Demay MB: Metabolic and cellular analysis of alopecia in vitamin D receptor knock out mice. *J Invest Dermatol.* 1999; 16:317-20. https://doi.org/10.1046/j.1525-1470.1999.00083.x
23. Cunningham BB, Landells ID, Langman C, Sailer DE, Paller AS. Topical calcipotriene for morphea/linearscleroderma. *Pediatr Dermatol.* 2015; 16:317-20. https://doi.org/10.1016/j.jidi.2015.02.813
24. Whitaker WA, Tieder M, Kohelet D, et al: Vitamin D resistant rickets with alopecia: A form of end organ resistance to 1,25 dihydroxy vitamin D. *Clin Endocrinol.* 1981; 14:395-402. https://doi.org/10.1111/j.1365-2265.1981.tb00624.x
25. Mahamid M, Abu-Elhija O, Samamra M, Mahamid A, Nseir W. Association between vitamin D levels and alopecia areata. *Isr Med Assoc J.* 2014; 16(6):367-70.
26. Fawzi MM, Mahmoud SB, Ahmed SF, Shaker OG. Assessmalet of vitamin D receptors in alopecia areata and androgenic alopecia. *J Cosmet Dermatol.* 2016; doi:10.1111/jocd.12224
27. H. Rasheed a D. Mahgoub a R. Hegazy a M. El-Komy a M.A. Hamid a E. et al. Serum Ferritinand Vitamin D in Female Hair Loss: Do They Play a Role? *Skin Pharmacol Physiol.* 2013; 26:101-107.https://doi.org/10.1159/000346698