

Serum ferritin and vitamin D levels should be evaluated in patients with diffuse hair loss prior to treatment

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Adv Dermatol Allergol 2020; XXXVII (3): 407–411

DOI: <https://doi.org/10.5114/ada.2020.96251>

Abstract

Introduction: Various factors like physiological and emotional stress, drugs and nutritional deficiencies can result in hair loss. Results of laboratory tests examining the underlying aetiology of hair loss vary in patients.

Aim: We aimed to compare the serum levels of ferritin, folate, vitamin B₁₂, zinc, thyroid stimulating hormone and vitamin D in patients complaining of diffuse hair loss and in healthy individuals.

Material and methods: Fifty-four patients with hair loss (47 females, 7 males) and 55 healthy individuals within the control group (47 females, 8 males) were included in this study. Serum levels of ferritin, folate, vitamin B₁₂, zinc, thyroid stimulating hormone and 25-hydroxyvitamin D were evaluated in all participants retrospectively.

Results: Serum concentrations of folate, vitamin B₁₂, zinc and thyroid stimulating hormone were similar in the two groups. However, the mean serum ferritin and 25-hydroxyvitamin D levels were significantly lower in patients with hair loss than in healthy individuals. The mean serum ferritin levels of the patients and healthy individuals were 14.72 ±10.70 ng/ml and 25.30 ±14.41 ng/ml, respectively. The mean serum 25-hydroxyvitamin D levels of the patients and healthy individuals were 14.03 ±8.09 ng/ml and 17.01 ±8.59 ng/ml, respectively. Eleven (20.4%) patients had low serum ferritin levels, while 43 (79.6%) patients had low vitamin D levels.

Conclusions: The results obtained from this study reveal that serum ferritin and 25-hydroxyvitamin D levels are generally low in patients complaining of hair loss. Therefore, serum ferritin and vitamin D levels should be evaluated and supplemented prior to treatment in all patients complaining of diffuse hair loss.

Key words: alopecia, hair loss, iron, vitamin D.

Introduction

Hair loss is a common complaint which can affect all ages and genders. Women usually visit dermatologists as a result of cosmetic concerns. Therefore, hair loss seems to be more common in women than in men [1]. The hair growth cycle consists of three distinct stages. These are anagen (growth phase), catagen (regression phase), and telogen (resting phase) [1, 2]. Various growth factors and receptors including insulin like growth factor 1, fibroblast growth factor 7, and hormones including oestrogens, androgens, thyroid hormones, glucocorticoids, retinoids, prolactin, and growth hormone play a role in regulating hair-follicle development and cycling [3]. Daily loss of 50–150 scalp hairs in the telogen phase is regarded as normal. However, an increasing percentage of telogen follicles results in excessive hair shedding [3]. Hair loss in the anagen stage is considered as abnormal

since active hair-follicle growth is interrupted as in patients receiving chemotherapy [1, 3]. Genetic predisposition, physiological stress, emotional stress, drugs, various medical conditions, and dietary deficiencies can lead to diffuse hair loss [1, 4]. However, necessity of examining the nutritional status, and effect of supplements in the treatment of hair loss still remains controversial [4]. Evaluation of iron deficiency and thyroid hormone disorders is usually recommended in all patients with diffuse hair loss. However, the exact role of zinc deficiency in the aetiology of diffuse hair loss has not been proved [5]. Recently, it has been suggested that vitamin D deficiency could lead to diffuse hair loss [1].

Aim

The aim of this study is to compare the serum levels of ferritin, folate, vitamin B₁₂, zinc, thyroid stimulating

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Received: 16.06.2018, **accepted:** 9.11.2018.

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hormone and vitamin D in patients with diffuse hair loss and in healthy individuals, to evaluate their role in the etiopathogenesis of hair loss.

Material and methods

This study included 54 patients who complain of diffuse hair loss and 55 healthy individuals within the control group who were admitted to the dermatology outpatient clinic between March 2016 and March 2017. Medical records of the participants were reviewed retrospectively.

The exclusion criteria were pregnancy, menopause, metabolic and endocrine disorders, hormone-replacement therapy, chemotherapy, immunosuppressive therapy, vitamin and mineral supplements, scarring alopecia, eating disorders and diet restrictions. Moreover, patients with female pattern hair loss usually have a positive family history, miniaturized hair, bitemporal recession, diffuse thinning over the mid-frontal scalp, wide midline part and preserved frontal hairline [6]. Therefore, patients with female pattern hair loss were also excluded from the study.

Laboratory tests of each participant including serum levels of ferritin, folate, vitamin B₁₂, zinc, thyroid stimulating hormone (TSH) and 25-hydroxyvitamin D (25(OH)D) were evaluated.

Dermatological examinations of the scalp of the patients were normal, without any obvious abnormality. All the patients within this study had Fitzpatrick skin types III and IV.

The hair pull test was used to evaluate the severity of hair shedding [7]. Approximately 40 to 60 hairs were grasped between the thumb and forefinger, and grouped hairs were pulled gently until the end. Six or more hairs extracted from the scalp were regarded as positive [7].

Statistical analysis

Data were represented as mean \pm standard deviation or median for quantitative variables; counts and per-

centage for categorical variables. Differences between 2 groups were tested with a *t*-test or Mann Whitney *U* test for continuous variables and χ^2 or Fisher exact tests as appropriate for categorical variables. The data were analysed using SPSS version 17.0 (SPSS Inc., Chicago, Illinois).

Results

Fifty-four patients with hair loss (47 females, 7 males) and 55 healthy individuals within the control group (47 females, 8 males) were included in the study ($p = 0.81$). The mean age of the patients and control group was 24 \pm 6 years and 23 \pm 6 years, respectively ($p = 0.59$). The mean disease duration was 4 \pm 2 months.

One (1.9%) patient had leukonychia punctata and 2 (3.7%) patients had onychoschizia on the fingernails. The past medical history was significant for seborrheic dermatitis in 2 (3.7%) patients and hypertension in 1 (1.9%) patient. The patient with hypertension was treated with oral valsartan 80 mg/day over a year. Nine (16.7%) patients stated irregular use of 2% topical minoxidil and hair loss shampoo previously. However, clinical improvement was not achieved in any patient. None of the patients had subjective symptoms like pruritus or pain. Eight (14.8%) patients reported psychological stress as a triggering factor for the onset of hair shedding. The hair pull test was positive in 17 (31.5%) patients.

The hair pull test helps to assess active hair loss. However, the hair pull test has low diagnostic sensitivity and specificity. It is both difficult to standardize the hair pull test and to perform it in patients with short hair [7]. Therefore, the hair pull test was positive in only 17 patients.

Laboratory tests of the participants revealed as stated below (Tables 1 and 2).

The mean serum ferritin level was 14.72 \pm 10.70 ng/ml in patients and 25.30 \pm 14.41 ng/ml in healthy individuals ($p < 0.001$) (normal range is 10 to 204 ng/ml). The serum ferritin level was decreased in 11 (20.4%) patients while 43 (79.6%) patients had normal serum ferritin levels. However, 5 (9.1%) healthy individuals had a decreased serum ferritin level, while 50 (90.9%) healthy individuals had normal serum ferritin levels ($p = 0.09$).

The mean serum vitamin B₁₂ level was 291 \pm 233 pg/ml in patients, and 330 \pm 247 pg/ml in healthy individuals ($p = 0.18$) (normal range is 190 to 880 pg/ml). The serum vitamin B₁₂ level was decreased in 7 (13%) patients while 47 (87%) patients had a normal serum vitamin B₁₂ level. However, 4 (7.3%) healthy individuals had a decreased serum vitamin B₁₂ level, while 51 (92.7%) healthy individuals had normal serum vitamin B₁₂ levels ($p = 0.33$).

The mean serum folate level was 5.97 \pm 1.92% ng/ml in patients and 6.07 \pm 2.29 ng/ml in healthy individuals ($p = 0.87$) (normal range is 3.1 to 20 ng/ml). The serum folate level was decreased in only 1 (1.9%) patient. How-

Table 1. Laboratory test results of the participants

Parameter	Patients Mean \pm SD	Control group Mean \pm SD	P-value
Vitamin B ₁₂ [pg/ml]	291 \pm 233	330 \pm 247	0.18
Folate [ng/ml]	5.97 \pm 1.92	6.07 \pm 2.29	0.87
TSH [μ IU/ml]	1.32 \pm 0.96	1.56 \pm 1.18	0.10
Zinc [μ g/dl]	84.90 \pm 21.80	88.50 \pm 23.10	0.41
Ferritin [ng/ml]	14.72 \pm 10.70	25.30 \pm 14.41	< 0.001
25(OH)D [ng/ml]	14.03 \pm 8.09	17.01 \pm 8.59	0.01

SD – standard deviation, TSH – thyroid stimulating hormone, 25(OH)D – 25-hydroxyvitamin D. Serum vitamin B₁₂, folate, TSH and zinc levels were similar in patients and healthy individuals. However, serum ferritin and 25(OH)D levels were significantly lower in patients when compared with the control group.

Table 2. Distribution of patients according to laboratory test results

Parameter	Patients n (%)		Control group n (%)			P-value
	Low	Normal	Low	Normal	High	
Vitamin B ₁₂	7 (13)	47 (87)	4 (7.3)	51 (92.7)		0.33
Folate	1 (1.9)	53 (98.1)	0 (0)	55 (100)		0.31
TSH	1 (1.9)	53 (98.1)	1 (1.8)	53 (96.4)	1 (1.8)	0.56
Zinc	5 (9.3)	49 (90.7)	2 (3.6)	53 (96.4)		0.23
Ferritin	11 (20.4)	43 (79.6)	5 (9.1)	50 (90.9)		0.09
25(OH)D	43 (79.6)	11 (20.4)	39 (70.9)	16 (29.1)		0.29

TSH – thyroid stimulating hormone, 25(OH)D – 25-hydroxyvitamin D. The number of participants with low/normal levels of vitamin B₁₂, folate, TSH, zinc, ferritin and 25(OH)D were statistically similar in both groups.

ever, 53 (98.1%) patients and all healthy individuals in the control group had normal serum folate levels ($p = 0.31$).

The mean serum TSH level was 1.32 ± 0.96 μ U/ml in patients and 1.56 ± 1.18 μ U/ml in healthy individuals ($p = 0.10$) (normal range is 0.4 to 4.2 μ U/ml). The serum TSH level was decreased in 1 (1.9%) patient, it was within normal limits in 53 (98.1%) patients. The serum TSH level was decreased in 1 (1.8%) healthy individual and it was increased in 1 (1.8%) healthy individual. 53 (96.4%) healthy individuals within the control group had normal serum TSH levels ($p = 0.56$).

The mean serum zinc level was 84.90 ± 21.80 μ g/dl in patients and 88.50 ± 23.10 in healthy individuals ($p = 0.41$) (normal range is 60 to 150 μ g/dl). The serum zinc level was decreased in 5 (9.3%) patients and it was within normal limits in 49 (90.7%) patients. The serum zinc level was decreased in 2 (3.6%) healthy individuals and it was normal in 53 (96.4%) healthy individuals within the control group ($p = 0.23$).

The mean serum 25(OH)D level was 14.03 ± 8.09 ng/ml in patients and 17.01 ± 8.59 ng/ml in healthy individuals ($p = 0.016$) (normal range is 20 to 70 ng/ml). The serum 25(OH)D level was decreased in 43 (79.6%) patients, and it was within normal limits in 11 (20.4%) patients. The serum 25(OH)D level was decreased in 39 (70.9%) healthy individuals, and it was normal in 16 (29.1%) healthy individuals within the control group ($p = 0.29$).

Discussion

Iron deficiency is the most common nutritional deficiency worldwide [8]. Both iron deficiency anaemia and iron deficiency without anaemia can be determined in patients with diffuse alopecia. Some of these cases do not respond to iron replacement therapy. However, in some patients oral iron treatment leads to cessation of hair loss and regrowth of the hair. Interruption of iron replacement makes these patients suffer from hair shedding again. Therefore, iron deficiency is regarded as a causative factor in patients with alopecia [9]. Hard investigated 96 female patients complaining of diffuse hair loss

without any underlying skin disease. Eighteen of these patients had iron deficiency without anaemia. They were treated with oral iron supplements. All of the 18 patients stated that hair loss stopped during the follow-up [8, 10]. Rasheed *et al.* compared serum ferritin and vitamin D levels of 80 female patients with chronic telogen effluvium and female pattern hair loss to 40 healthy individuals. Serum ferritin and vitamin D concentrations were significantly lower in patients than in control subjects [6]. Malkud evaluated the aetiological factors of diffuse hair loss in female patients. The study included 180 patients with telogen effluvium, chronic telogen effluvium, female pattern hair loss and anagen effluvium. Psychological stress and iron deficiency anaemia were reported as common underlying causes of telogen effluvium. However, chronic telogen effluvium was idiopathic in many cases [11].

In contrast, Bregy *et al.* evaluated serum ferritin levels of 181 women with female pattern hair loss and diffuse telogen effluvium. Trichogram was also performed in each patient to determine the telogen rate. No correlation was reported between serum levels of ferritin above 10 μ g/l and telogen rates [12]. Sinclair *et al.* investigated 194 women with chronic diffuse telogen hair loss. Twelve (6%) patients had serum ferritin of 20 μ g/l or less. Scalp biopsy of 5 of 12 patients revealed normal histopathological features. Despite iron supplementation, cessation of hair loss was not observed in these patients [13].

The decreased serum ferritin level is a very specific finding of iron deficiency. Serum ferritin is regarded as the most valuable laboratory test for iron deficiency [8]. Within this study, the mean serum ferritin level was significantly lower in patients than in healthy individuals. Furthermore, a low serum ferritin level was observed more frequently in patients than in the control group. Our results indicate that serum ferritin concentrations may play a role in the etiopathogenesis of diffuse hair fall.

Zinc is an essential micronutrient that plays a role in protein and nucleic acid synthesis. It has been suggested that zinc inhibits hair regression and accelerates recovery of the hair follicle [14]. For instance, acrodermatitis

enteropathica, a rare genetic disorder due to malabsorption of zinc clinically presents with hair loss [14, 15]. However, the association between zinc and hair loss is still controversial [14]. Kil *et al.* evaluated the serum levels of zinc and copper in patients with alopecia areata, male pattern hair loss, female pattern hair loss, telogen effluvium and healthy individuals. The serum level of zinc was significantly lower in patients than in healthy individuals. Patients who had serum zinc values lower than 70 µg/dl were more prevalent in the alopecia areata and telogen effluvium group. However, serum copper concentrations were similar between patients and healthy controls. Kil *et al.* suggested a possible role of zinc metabolism disturbances in the aetiology of hair loss [14]. Within this study, a mean serum zinc level was statistically similar in patients and the control group. A low serum zinc concentration was observed only in 5 patients and 2 healthy individuals. Our results have not revealed any correlation between serum zinc levels and hair fall.

Laboratory tests to assess thyroid dysfunction is recommended in patients with diffuse effluvium of unknown aetiology [16]. Deo *et al.* evaluated thyroid function tests in 135 females with telogen effluvium, alopecia areata, female pattern hair loss, frontal fibrosing alopecia and anagen effluvium. The most common alopecia type was telogen effluvium, followed by female pattern hair loss. Fourteen of 135 patients had previously known hypothyroidism or hyperthyroidism. Moreover, 5 patients had newly diagnosed hypothyroidism whereas 4 patients had hyperthyroidism. Therefore, Deo *et al.* suggested thyroid function tests to reveal subclinical thyroid disorders in women with hair loss [17]. Within this study, we observed a low serum TSH level in 1 patient and in 1 participant within the control group. Moreover, 1 participant within the control group had a high serum TSH level. Thyroid function disorders were not observed more frequently in the patient group when compared with the control group.

It has been suggested that vitamin D, vitamin B₁₂ and folate might play a role in the hair growth cycle. Cheung *et al.* evaluated serum levels of 25-hydroxyvitamin D, ferritin, vitamin B₁₂, folate, and zinc in 115 patients with telogen effluvium. Decreased serum ferritin, vitamin D and zinc levels were reported in 45.2%, 33.9% and 9.6% of patients, respectively. Vitamin B₁₂ deficiency was stated only in 2.6% of patients. All the participants had normal serum folate concentrations [18]. Ozuguz *et al.* reported no statistically significant difference in serum levels of vitamin B₁₂ and folic acid between patients with chronic telogen effluvium and healthy individuals [19]. Within this study, the mean serum vitamin B₁₂ and folate levels were statistically similar in patients and healthy individuals. A low serum vitamin B₁₂ concentration was observed in 7 patients and 4 healthy individuals. Vitamin B₁₂ deficiency was observed at similar frequency in both groups. Furthermore, serum folate levels of the participants were

all in normal limits except for 1 patient who had a low serum folate concentration.

Vitamin D is a steroid hormone synthesized in the epidermis via ultraviolet B exposure. It can also be obtained from diet and supplements. The role of vitamin D in the proliferation and differentiation of keratinocytes has been well established. Furthermore, it has been suggested that vitamin D might have an impact in hair growth and the hair cycle. Vitamin D receptors of the epidermal keratinocytes and mesodermal papilla cells increase in the late anagen and catagen phase. The progression of the hair cycle is thought to be associated with vitamin D receptors [20].

It has been suggested that decreased serum 25-hydroxyvitamin D levels might play a role in the etiopathogenesis of non-scarring alopecia. Vitamin D supplementation has been considered as the treatment of choice in patients with alopecia areata, female pattern hair loss, or telogen effluvium [21]. Similarly, topical application of vitamin D is reported to be helpful to prevent chemotherapy-induced alopecia [20].

Banihashemi *et al.* compared serum vitamin D₃ levels of patients with female pattern hair loss to healthy women. Vitamin D₃ levels were significantly lower in the patient group. Banihashemi *et al.* suggested a relationship between decreased serum vitamin D₃ concentrations and incidence of female pattern hair loss. Therefore, Banihashemi *et al.* recommended to evaluate the serum vitamin D₃ level in cases with female pattern hair loss [22]. Rasheed *et al.* reported significantly lower serum 25-hydroxyvitamin D levels in females with chronic telogen effluvium and female pattern hair loss than in healthy controls [6]. Nayak *et al.* evaluated serum vitamin D₃ concentrations in 22 young adults complaining of diffuse hair loss. Vitamin D deficiency was significantly more frequent among patients when compared to healthy controls. The median value of serum vitamin D was significantly lower among cases with diffuse hair fall [1]. Within this study, the mean serum 25(OH)D level was significantly lower in patients than in healthy individuals. However, we determined low serum 25(OH)D levels in 79.6% of the patients and in 70.9% of healthy individuals. Our results showed that the low serum vitamin D level was common in both patient and control group.

Conclusions

Since we have demonstrated significantly low serum levels of ferritin and 25(OH)D in the patient group, we suggest that serum iron and vitamin D status should be evaluated in all patients with diffuse hair loss prior to further treatment. Vitamin B₁₂ and zinc deficiencies were determined in a few patients. Therefore, it does not need to be mandatory to check vitamin B₁₂ and zinc levels routinely in every patient complaining of diffuse hair loss.

Conflict of interest

The authors declare no conflict of interest.

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