Dermatology Practical & Conceptual

Micronutrient Deficiencies and Digital Computerized Phototrichogram Analysis in Telogen Effluvium: a Retrospective Correlation Study in a Tertiary Medical Center

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Key words: telogen effluvium, trichoscan, automated digital photothrichogram, vitamin deficiencies, mineral deficiencies

Citation: Arslan H, Gündüz Ö. Micronutrient Deficiencies And Digital Computerized Phototrichogram Analysis in Telogen Effluvium: A Retrospective Correlation Study in a Tertiary Medical Center. *Dermatol Pract Concept.* 2023;13(3):e2023202. DOI: https://doi.org/10.5826/dpc.1303a202

Accepted: March 11, 2023; **Published:** July 2023

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

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Abbreviations: ADCP: Automated digital computerized phototrichogram, AHR: Anagen hair ratio, HGB: Hemoglobin, TE: Telogen effluvium, Vit-B12: Vitamin B12, Vit-D: Vitamin D

ABSTRACT

Introduction: Telogen effluvium (TE) is a common form of non-scarring alopecia that may manifest as acute or chronic hair shedding. Several studies evaluated a possible relationship between various vitamin and mineral deficiencies and TE, but it is still a controversial topic.

Objectives: This study aimed to investigate the status of vitamin and mineral deficiencies in patients diagnosed with TE and to evaluate their correlation with anagen hair ratios (AHR) calculated with an automated digital phototrichogram (ADCP).

Methods: Electronic records of 973 TE patients were retrospectively analyzed. Demographic, clinical data, parameters such as ferritin, vitamin B12 (Vit-B12), vitamin D (Vit-D), folic acid, zinc and hemoglobin (HGB) serum levels were evaluated. Anagen to telogen hair ratios were also assessed in forty-two patients via ADCP.

Results: The rates of anemia, low ferritin level, and Vit-B12, folate, Vit-D, and zinc deficiencies were 11.9% (N = 109), 44% (N = 332), 1.5% (N = 13), 2.5% (N = 14), 87% (N = 51), and 4.5% (N = 2), respectively. A positive correlation was found between HGB levels and AHR in female patients

(Spearman rank, r = 0.417, P = 0.008). No statistically significant relationship was found between ferritin, Vit-B12, folate, zinc serum levels and AHR. The relationship between Vit-D and AHR could not be assessed due to the insufficient number of patients with Vit-D data.

Conclusions: HGB value is the only marker that is positively correlated with the AHR of patients with TE. Ordering HGB can be used as an initial test for managing TE patients cost-effectively.

Introduction

The hair is an ectoderm-originated skin appendage with high cosmetic and psychological importance. It helps individuals maintain their self-esteem, which encourages healthy social interactions.

Telogen effluvium (TE) is the most common cause of diffuse hair shedding [1]. The actual prevalence of TE is unknown because of its subclinical nature. Both sexes may be affected; however, women tend to seek more medical advice and be over-represented [2].

Objectives

Although vitamin and mineral deficiencies have been associated with TE, this is still a controversial topic. This study aimed to investigate demographic features, define the detectable vitamin and mineral deficiencies in patients with acute and chronic TE, and associate their levels with the anagen hair ratio (AHR) on an automated digital computerized phototrichogram (ADCP).

Methods

The study was approved by the local ethics committee (decision no. 15/31, 01.10.2018). Laboratory results, electronic medical records, and ADCP findings of patients who were diagnosed with TE between March 2015 and March 2018 were retrospectively obtained from the medical electronic and dermoscopy unit databases of our hospital.

The following demographic and clinical features were extracted from the electronic medical records: age, sex, application month, and biochemical test results, including hemoglobin (HGB), ferritin, vitamin B12 (Vit-B12), folate, vitamin D (Vit-D), zinc, and AHR. Raw data were anonymized. Patients were categorized into four groups according to age: <20, 20–29, 30–50, and >50 years. Normal values of variables were determined as follows: HGB, 14–18 g/dL for men and 12–16 g/dL for women; ferritin, >40 µg/mL; Vit-D, >25 ng/mL; Vit-B12, >200 pg/mL; folate, >4 ng/mL; zinc, >70 µg/dL; and AHR, 80%–100%.

Hair examination data on ADCP were collected from our clinic dermoscopy unit. The procedure was as follows: on day 1, the plate with a 1 cm^2 circular incision was placed on the highest point of the patient's right pinna. Subsequently, the hair in the selected area was trimmed to a length of 0.5 mm using a hair trimmer Rowenta® TN9160 (Rowenta Werke GmbH, Erbach) and photographed with 20× magnification via FotoFinderdermoscope® (FotoFinder System GmbH). The patients were instructed not to bathe for three days and then to revisit our clinic. On the second visit, the trimmed area was stained with black dye (Wella®Koleston, Darmstadt). The dye was cleaned with 80% alcohol solution 15 minutes later, and another set of images was taken at 20× magnification again. The most suitable image was selected, and the results were evaluated using automatic computerized phototrichogram software (Tricholog GmbH), which is based on the principle of analyzing hair length on each hair strand, and then differentiating and categorizing growing hairs (≥ 0.35 mm/day) as anagen and non-growing hairs (<0.35 mm/day) as telogen.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp). Descriptive statistics were presented as a number, percentage, mean, standard deviation, median, minimum, and maximum. The Kolmogorov–Smirnov test and graphics were used to investigate whether the numerical data fit the normal distribution. The independent t-test was performed for two groups, whereas the one-way analysis of variance (ANOVA) test was performed for more than two groups with normal distributions. Pearson correlation coefficient was used to analyze the relationship between two numeric variables when the data set showed normal distribution, whereas Spearman correlation was used for non-normally distributed ones. A P value < 0.05 was considered statistically significant.

Results

A total of 973 patients diagnosed with TE who applied between March 2015 and March 2018 were included in this retrospective study. Of these patients, 86.3% (N = 840) were female, and 13.7% (N = 133) were male, with a female/male ratio of 6.31. The mean age was 27.54 ± 9.42 (minimum, 13; maximum, 72) years. Of the patients, 18.1% (N = 176) were < 20 years old; 51.8% (N = 504), 21–29 years old; 27.1% (N = 264), 30–50 years old; and 3% (N = 29), ≥ 51 years (Table 1).

Patients were also distributed according to the months of admission: January, 7.9% (N = 77); February, 7.1% (N = 69); March, 5.5% (N = 54); April, 3.9% (N = 38); May, 6.3% (N = 61); June, 4.3% (N = 42); July, 6.4% (N = 62); August, 8.2% (N = 80); September, 8.7% (N = 85); October, 12.7% (N = 124); November, 18.5% (N = 180); and December, 10.4% (N = 101). November and April had the highest and lowest number of admissions, respectively (Figure 1).

The following biochemical tests were evaluated: 94.1% (N = 916), 77.5% (N = 755), 86.4% (N = 841), 58.5% (N = 570), 5.9% (N = 58), and 4.5% (N = 44) of the patients had available HGB, ferritin, Vit-B12, folate, Vit-D, and zinc data, respectively. The rates of anemia, low ferritin level, and Vit-B12, folate, Vit-D, and zinc deficiencies were 11.9% (N = 109), 44% (N = 332), 1.5% (N = 13), 2.5% (N = 14), 87% (N = 51), and 4.5% (N = 2), respectively.

AHR obtained in the dermoscopy unit was available in 4.3% (N = 42) of the patients. The mean AHR value of the female patients was 68.57 ± 8.88%, and that of male patients was 74.73% ± 5.36%. No significant difference was found between sex and AHR (independent t-test, P = 0.247). Additionally, no significant difference was found between age groups (≤ 20, 21–30, and 31–50) and AHR (ANOVA, P = 0.197). The age group > 50 years was not included in the analysis because there were not enough subjects.

The correlation analysis between biochemical tests and AHR was conducted only for female patients (N = 39) because there were not enough male patients for the correlation analysis (N = 3). For female patients, no significant relationship was found between ferritin, Vit-B12, and folate levels and AHR (Spearman rank, r = –0.112, P = 0.523; r = 0.149, P = 0.386; r = 0.186 and p = 0.346, respectively). No significant relationship was found between zinc levels and AHR (r = –0.423, P = 0.577). The relationship between Vit-D and AHR was not assessed because there were insufficient patients with Vit-D data. A positive correlation was available between the HGB levels and AHR of female patients (r = 0.417, P = 0.008, Table 2 and Figure 2).

Table 1. Sociodemographic characteristics of patients with telogen effluvium.

		N	%
Sex	Male	133	13.7
	Female	840	86.3
Age	≤ 20	176	18.1
	21–29	504	51.8
	30–50	264	27.1
	≥ 51	29	3.0

Conclusions

This study focused on the deficiency rates of HGB, ferritin, Vit-B12, folic acid, Vit-D, and zinc levels in patients diagnosed with TE and correlation between the micronutrient levels and AHR.

Hair follicle cells have a high-turnover rate. Thus, they need organic and inorganic molecules, minerals, and oxygen for their metabolic activities. Congenital or acquired deficiencies of these metabolites due to low intake, insufficient absorption, or pathological losses may result in abnormalities

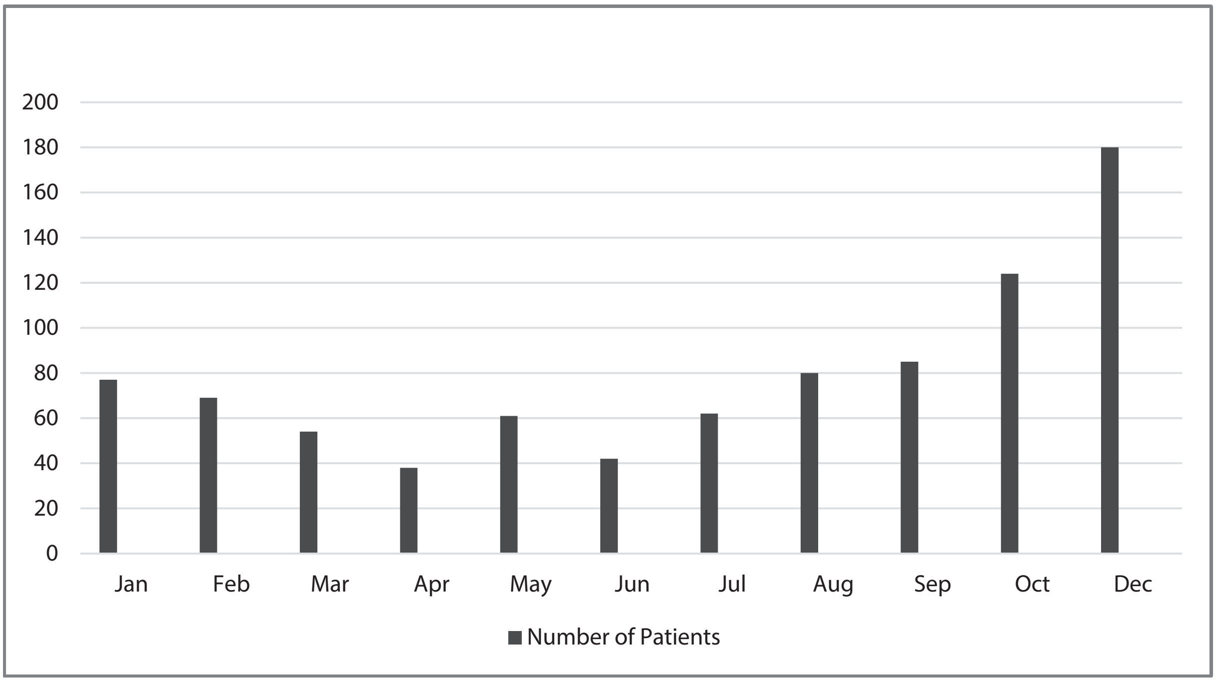

Figure 1. Number of the patients according to the month of admission.

Table 2. Distribution of the anagen hair ratios, zinc, and vitamin levels of the patients.

	N	Mean	Median	SD	Min	Max
AHR, %	42	69.01	70	8.78	50.7	84.2
Ferritin, µg/mL	755	33.56	22	32.75	2	293
Vit-B12, pg/mL	841	325.88	299.60	149.72	61.4	2000
Folate, ng/mL	570	8.21	7.75	3.45	1.73	20
Vit-D, ng/mL	45	15.58	13.97	8.68	3.37	45.10
Zinc, µg/dL	44	92.35	91.40	16.47	64	131.1

AHR = anagen hair ratios; SD = standard deviation.

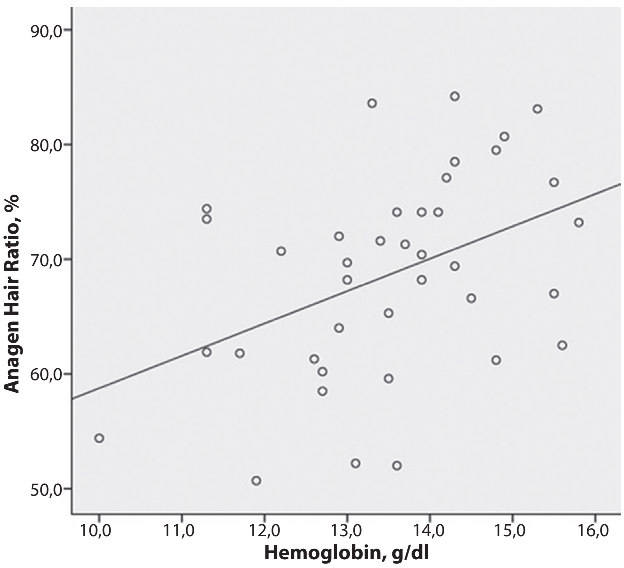

Figure 2. Positive correlation between the hemoglobin level and anagen hair percentage of female patients.

in the structure of the hair, pigmentation changes, and hair loss [3,4].

In this study, 86.3% of the patients with TE who applied to our dermatology department were female. These patients were mostly between 20 and 30 years old (51.8%), followed by patients aged 30–50 (27.1%). The most frequent application month was November with 18.5% (N = 180), followed by 12.7% (N = 124) in October. The incidence of TE changes with seasonal transitions [5]. However, our hospital is located within the university campus, and the population of the district where it is located doubles as other departments of the university start education in October–November. The true incidence and seasonal fluctuations in TE are not well established due to the lack of data regarding particularly subclinical cases. Furthermore, male patients are significantly less likely to consult a physician than their female counterparts. Therefore, large-scale field studies are needed to determine the true incidence of TE.

Iron deficiency is the world's most common nutritional deficiency and is considered one of the most prevalent causes of hair loss [6]. To define iron deficiency, different laboratories use different ferritin levels, ranging from 20 to 70 µg/mL; however, a cutoff below 41 µg/mL yields sensitivity and specificity of 98% [7]. Deloche et alinvestigated the relationship between iron deficiency and hair loss in more than 5000 women aged 35–60 [8]. They were divided into three groups according to their hair loss status, namely, absence of hair loss, moderate, and excessive. Moreover, 59% of the patients with ferritin levels < 40 µg/L were placed in the excessive hair loss group, whereas this rate was 48% in other participants. Their regression analysis revealed that the probability of excessive hair loss increased by 28% with a 30 µg/L decrease in ferritin levels in women; in other words, the severity of hair loss increases as the ferritin level decreases. Moeinvaziri et al reported that ferritin levels were significantly lower in their 30 patients with diffuse telogen hair loss than in their 30 healthy volunteers without hair loss [8]. However, some researchers did not find a direct relationship between iron level and hair loss [9,10]. In their study, Sinclair investigated the relationship between iron deficiency and chronic telogen hair loss, and five of their patients were treated with iron to increase serum ferritin levels >20 µg/L; however, hair loss did not improve during follow-up [10]. Another study investigated serum ferritin levels and telogen hair ratio in 181 female patients, who were divided into three groups according to their ferritin levels: ≤10 µg/L, 10–30 µg/L, and >30 µg/L. The telogen hair ratios of these groups were compared, and no significant statistical correlation was found [11]. In the present study, 755 patients had ferritin data, and 44% of these patients had low ferritin levels. However, no significant correlation was found between AHR and ferritin levels in patients with TE ($r = -0.112$, $P = 0.523$).

Vit-B12 and folate have very important functions on both hematologic and nervous systems. Vit-B12 is a cofactor for methylmalonyl-CoA mutase and homocysteine methyltransferase, a folate-dependent pathway [12]. The critical importance of homocysteine methyltransferase is that the reaction of the conversion of 5-methyltetrahydrofolate to tetrahydrofolate takes place at this stage, and it catalyzes a reaction associated with the synthesis of purine and pyrimidine bases and thus DNA synthesis [12,13]. This makes both

Table 3. **Correlation study between biochemical tests and anagen hair ratio.**

		Ferritin	Vit-B12	Folate	Zinc	Vit-D	HGB
Anagen hair ratio	r[a]	0.149	0.149	0.186	−0.423	0.149	0.417
	P	0.386 [b]	0.386 [b]	0.346 [b]	0.577 [c]	0.386 [b]	0.008 [b]

HGB = hemoglobin.
[a]Correlation coefficient
[b]Spearman rank correlation coefficient test
[c]Pearson correlation coefficient test

Vit-B12 and folate important for the high-turnover rates in hair follicle cells. However, no sufficient evidence confirms the association between Vit-B12 and folate deficiencies and hair loss. In this study, 841 patients had Vit-B12 data, of which 1.5% had Vit-B12 deficiency, whereas 2.5% of 570 patients with folate data had folate deficiencies. No significant correlation was found between AHR and levels of these vitamins (r = 0.149, P = 0.386).

Vit-D modulates the growth and differentiation of hair follicle keratinocytes via nuclear Vit-D receptor (VDR) with the highest activity in the anagen stage [4]. VDR mutations cause Vit-D-dependent rickets type 2, which equates to full body hair loss and present evidence for the relationship between hair loss and Vit-D deficiency [15,16]. In this study, 87.9% of 58 patients with Vit-D data had low Vit-D levels. The correlation analysis between Vit-D levels and AHR could not be performed because there were not enough subjects with Vit-D results and ADCP analysis.

Zinc is an essential trace element involved in protein and nucleic acid synthesis and various metabolic pathways. Transient zinc deficiency in acrodermatitis enteropathica, resulting in hair loss, demonstrated effects on hair. Kil et al reported that zinc levels were significantly lower in patients with alopecia areata, TE, and androgenetic alopecia (three main hair loss diseases) compared with healthy volunteers [17]. In our study, 4.5% of the 44 patients with serum zinc data had zinc deficiency. Correlation analysis with AHR was not significant (r = −0.423, P = 0.577).

In our study, 916 patients had HGB data, of which 12.3% of the female and 9.1% of the male patients were anemic. In addition, a significant positive correlation was found between HGB level and AHR in female patients (r = 0.417 and p = 0.008). This suggests that deficiencies in micronutrients such as Vit-B12, folate, and iron can indirectly alter the severity of TE if they decrease HGB level.

The main limitation of our study was its retrospective nature and that some analyses could not be performed due to missing data, such as Vit-D level and AHR correlation and male patient's correlation analysis. Also, our city is a college town. Its population increases in the winter months. This may affect the monthly admission rates and cause an increase in patient numbers in certain months.

In our study, large-scale TE patients' biochemical tests were evaluated in a tertiary care center. Also, correlation analysis was performed to detect essential ones which was only HGB level. In order to manage TE patients cost-effectively, a complete blood count can be used as an initial test.

References

1. İbiş S, Aksoy Saraç G, Akdağ T. Evaluation of MCV/RDW Ratio and Correlations With Ferritin in Telogen Effluvium Patients. *Dermatol Pract Concept.* 2022;12(3):e2022151. DOI: 10.5826/dpc.1203a151. PMID: 36159144. PMCID: PMC9464528.
2. Mysore V, Parthasaradhi A, Kharkar RD, et al. Expert consensus on the management of Telogen Effluvium in India. *Int J Trichology.* 2019;11(3):107-112. DOI: 10.4103/ijt.ijt_23_19. PMID: 31360038. PMCID: PMC6580807.
3. Cheung EJ, Sink JR, English Iii JC. Vitamin and Mineral Deficiencies in Patients With Telogen Effluvium: A Retrospective Cross-Sectional Study. *J Drugs Dermatol.* 2016;15(10):1235-1237. PMID: 27741341.
4. Yorulmaz A, Hayran Y, Ozdemir AK, et al. Telogen effluvium in daily practice: Patient characteristics, laboratory parameters, and treatment modalities of 3028 patients with telogen effluvium. *J Cosmet Dermatol.* 2022;21(6):2610-2617. DOI: 10.1111/jocd.14413. Epub 2021 Aug 27. PMID: 34449961.
5. Liyanage D, Sinclair R. Telogen Effluvium. *Cosmetics.* 2016;3(2):13. DOI:10.3390/cosmetics3020013.
6. Trost LB, Bergfeld WF, Calogeras E. The diagnosis and treatment of iron deficiency and its potential relationship to hair loss. *J Am Acad Dermatol.* 2006;54(5):824-844. DOI: 10.1016/j.jaad.2005.11.1104. PMID: 16635664.
7. Shrivastava SB. Diffuse hair loss in an adult female: approach to diagnosis and management. *Indian J Dermatol Venereol Leprol.* 2009;75(1):20-72; DOI: 10.4103/0378-6323.45215. PMID: 19172026.
8. Deloche C, Bastien P, Chadoutaud S, et al. Low iron stores: a risk factor for excessive hair loss in non-menopausal women. *Eur J Dermatol.* 2007;17(6):507-512. DOI: 10.1684/ejd.2007.0265. PMID: 17951130.
9. Olsen EA, Reed KB, Cacchio PB, Caudill L. Iron deficiency in female pattern hair loss, chronic telogen effluvium, and control groups. *J Am Acad Dermatol.* 2010;63(6):991-999. DOI: 10.1016/j.jaad.2009.12.006. PMID: 20947203.
10. Sinclair R. There is no clear association between low serum ferritin and chronic diffuse telogen hair loss. *Br J Dermatol.* 2002;147(5):982-984. DOI: 10.1046/j.1365-2133.2002.04997.x. PMID: 12410711.

11. Bregy A, Trueb RM. No association between serum ferritin levels >10 microg/l and hair loss activity in women. *Dermatology.* 2008;217(1):1-6. DOI: 10.1159/000118505. PMID: 18309237.
12. Brescoll J, Daveluy S. A review of vitamin B12 in dermatology. *Am J Clin Dermatol.* 2015;16(1):27-33. DOI: 10.1007/s40257-014-0107-3. PMID: 25559140.
13. Stabler SP. Clinical practice. Vitamin B12 deficiency. *N Engl J Med.* 2013;368(2):149-160. DOI: 10.1056/NEJMcp1113996. PMID: 23301732.
14. Almohanna HM, Ahmed AA, Tsatalis JP, Tosti A. The Role of Vitamins and Minerals in Hair Loss: A Review. *Dermatol Ther (Heidelb).* 2019;9(1):51-70. DOI: 10.1007/s13555-018-0278-6. PMID: 30547302. PMCID: PMC6380979.
15. Vupperla D, Lunge SB, Elaprolu P. Vitamin D-Dependent Rickets Type II with Alopecia: A Rare Case Report. *Indian J Dermatol.* 2018;63(2):176-179. DOI: 10.4103/ijd.IJD_434_17. PMID: 29692463. PMCID: PMC5903051.
16. Santos R, Neves S, Gomes C, Neves F, Correia AJ. Raquitismo vitamina D dependente tipo II [Rickets vitamin-D-dependent type 2]. *Acta Med Port.* 2009;22(6):861-866. PMID: 20350471.
17. Kil MS, Kim CW, Kim SS. Analysis of serum zinc and copper concentrations in hair loss. *Ann Dermatol.* 2013;25(4):405-409. DOI: 10.5021/ad.2013.25.4.405. PMID: 24371385. PMCID: PMC3870206.