INTERNATIONAL JOURNAL OF
MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2018.75047
Int J Med Biochem 2018;1(3):111-4

Research Article

Reduced ferritin, folate, and vitamin B12 levels in female patients diagnosed with telogen effluvium

Ebru Yorulmaz Ertug[1], Ruken Alp Yilmaz[2]

[1]Department of Clinical Biochemistry, Cerkezköy State Hospital, Tekirdag, Turkey
[2]Department of Dermatology, Cerkezköy State Hospital, Tekirdag, Turkey

Abstract

Objectives: Telogen effluvium (TE) is the most common cause of diffuse hair shedding. It is a non-inflammatory process characterized by the widespread loss of hair follicles in the telogen phase. Identification of its etiology requires laboratory tests involving endocrine, nutritional, and autoimmune disorders, and detailed anamnesis. The aim of this study was to examine serum ferritin, folate, and vitamin B12 levels in female patients with TE, and to investigate their possible role in the disease pathogenesis.

Methods: The study included 651 female patients: 455 in the TE group and 196 in the control group. Serum ferritin, folate, and vitamin B12 levels were measured in both the groups.

Results: Patients with TE had significantly lower serum ferritin concentrations compared to those in the control group (17.35±18.54 ng/ml vs. 39.27±29.44 ng/ml) (p=0.001). The folate levels were significantly lower in the TE group compared to those in the control group (7.94±8.98 ng/ml vs. 11.31±4.7 ng/ml) (p=0.001). Vitamin B12 concentrations were also significantly lower in the TE group (232.13±123.35 pg/ml) (p=0.001).

Conclusion: It was concluded that reduced levels of ferritin, vitamin B12, and folate might play a role in development of TE.

Keywords: Ferritin, folate, telogen effluvium, vitamin B12

Hair is an ectodermal structure with cosmetic importance. It has no vital function in humans, but it is significant for social interactions. Although male baldness can be accepted due to its genetic nature, hair loss in a woman causes significant reduction in quality of her life [1].

Telogen Effluvium (TE) is one of the most common causes of diffuse hair shedding. It is characterized by loss of hair in its telogen phase. Every hair follicle follows three cyclical phases: anagen (growth), katagen (regression leading to apoptosis), and telogen (resting). There are approximately 100,000 hairs on the scalp, of which 10–15% are in the telogen phase, and 85%–90% are in the anagen phase. For the scalp, the anagen phase lasts about 2–6 years, katagen phase 4–6 weeks, and telogen phase 3–4 months [2]. Normally, every hair follicle follows an independent cycle. While some hairs grow, others rest or are shed. Thus, the hair density remains unchanged, and the same amount of hair is preserved. This cycle repeats itself 10–30 times during the lifetime of a follicle, and on average, the normal hair cycle results in complete renewal of all hairs once in every 3–5 years. While an average loss of 100 hairs is considered normal in the telogen phase, this amount of loss in the anagen phase is pathological [3].

Hair loss is a common condition. The most common cause of diffuse hair loss is TE. TE is a non-inflammatory process characterized by the widespread loss of hair follicles in the telogen phase [4]. The hair shedding is sudden, fast, and diffuse. TE is examined in two forms: acute and chronic. Acute or classical TE manifests with diffuse hair loss starting 2–3 months after triggers such as high fever, major surgery or childbirth, and it limits itself within 2–3 months. If the triggering factor persists, the condition lasts longer than 6 months, and then it is referred

Address for correspondence: Ebru Yorulmaz Ertug, MD. Department of Clinical Biochemistry, Cerkezköy State Hospital, Tekirdag, Turkey
Phone: +90 282 736 80 00/6484 **E-mail:** ebruertug@yahoo.com **ORCID:** 0000-0002-1297-5556
Submitted Date: May 15, 2018 **Accepted Date:** July 21, 2018 **Available Online Date:** September 20, 2018

as chronic. The main difference between acute and chronic TE is that the duration in the chronic condition is longer than 6 months [5]. The exact incidence is unknown due to lack of data particularly from subclinical cases [6]. The diagnosis of TE is made with detailed anamnesis and exclusion of other diseases causing diffuse loss of the telogen hair follicles. Diagnosis can be confirmed with the hair pull test. In this test, 25–50 hair filaments are lightly pulled, and shedding of more than 4 hair filaments and presence of depigmented, keratinized, and rod-shaped hair follicles are considered pathological [7]. Identification of the etiology requires laboratory tests that can reveal endocrine, nutritional, and autoimmune causes, and detailed patient anamnesis [8].

Iron deficiency is one of the most commonly encountered nutritional deficiencies in the routine clinical practice. The hemoglobin (Hb) and ferritin levels can be measured to screen iron deficiency. Low iron stores are considered a contributing factor for hair loss. Therefore, serum ferritin measurement is recommended as a part of the routine investigation. Although there are some studies that suggest the role of low ferritin levels in TE [9-12], other studies failed to find an association between ferritin levels and TE [13, 14].

The aim of this study was to examine serum ferritin, folate, and vitamin B12 levels in female patients with TE, and to investigate their possible role in the disease pathogenesis.

Materials and Methods

This study was designed as a case-control study. The study included 455 female patients aged between 18 and 45 years (mean age 29.01±8.71 years) who presented to Dermatology outpatient clinic of Cerkezkoy Hospital between January 2016 and October 2017 and were diagnosed with TE. Study exclusion criteria were history of surgical operation, pregnancy, breastfeeding, presence of systemic disease, serious weight loss, being on a low-calorie diet, receiving iron supplementation, presence of menstrual irregularities, and using drugs that could induce hair loss. All patients were examined by the same dermatologist. The diagnosis was made with detailed physical examination, patient history (shedding daily more than 100 hairs), and the hair pull test (more than 4 hairs shed with light pulling), and by excluding other diseases causing hair loss such as androgenetic alopecia, alopecia areata, and trichotillomania.

The control group consisted of 198 female patients who presented to the outpatient clinic for nevus treatment, did not complain of hair loss, presented to the outpatient clinic for nevus treatment, met the same exclusion criteria with the TE group, and were aged between 18 and 45 years (mean age 31.29±8.7 years).

Serum iron, Hb, ferritin, folate, and vitamin B12 concentrations in TE and control groups were compared against the reference intervals. For female patients, the reference intervals were 60–180 µg/dL for iron, 10.8–15.1 g/dL for Hb, 11–306 ng/mL for ferritin, 5.2–20 ng/mL for folate, and 180–914 pg/mL for vitamin B12.

Venous blood samples were obtained after at least 10 h of fasting. Serum separator tubes were allowed to stand for 30 min, and then they were centrifuged at 3000 rpm for 10 min. For complete blood count, blood samples were drawn into EDTA-containing tubes and analyzed immediately.

Iron levels were photometrically measured using Beckman Coulter Inc. reagents on Beckman Coulter AU680 analyzer (Beckman Coulter, USA). According to the manufacturer's instructions, intraassay CV was 1.02%, interassay CV was 2.09%, and linearity range was 10–1000 µg/dL for iron. Ferritin, folate, and vitamin B12 levels were measured with sandwich immunoenzymatic method using Access reagents on Beckman Coulter DXI 800 (Beckman Coulter, USA) analyzer. Intraassay CV, interassay CV, and linearity range were given by the manufacturer as 3.6%, 4.3%, and 0.2–1500 ng/mL for ferritin, respectively; 3.8%, 7.4%, and 0.5–20.0 ng/mL for folate, respectively; and 4.8%, 6.6%, and 50–1500 pg/mL for vitamin B12, respectively. Complete blood count was performed on ABX Pentra 120 (HORIBA, Japan) using histochemical and flow cytometric methods.

The medical ethics committee of Tekirdag Provincial Health Directorate approved the study (number: 93966460-605.01 Date: 08/17).

Statistical Analysis

The data were evaluated for normality with the Shapiro–Wilk test. Comparison of non-normally distributed numerical data between two independent groups was made with the Mann–Whitney U test. The relationships between numerical variables were analyzed with Spearman's rank correlation analysis, and the relationships between categorical variables were analyzed with the Chi-square test. The effect of multiple variables on a categorical dependent variable was tested with binary multivariate logistic regression analysis. The analyses were performed with SPSS for Windows version 24, and the results were reported within 95% confidence interval. Value of $p<0.05$ was accepted as statistically significant.

Results

Table 1 shows demographic and biochemical parameters of totally 651 women, 455 of them in TE and 196 of them in control groups. The ferritin levels in the TE group (17.35±18.54 ng/mL) were significantly lower than those in the control group (39.27±29.44 ng/mL) (p=0.001). The folate levels were significantly lower in the TE group (7.94±8.98 ng/mL) compared to those in the control group (11.31±4.7 ng/mL) (p=0.001). Vitamin B12 levels were significantly lower in the TE group (232.13±123.35 pg/mL) compared to those in the control group (p=0.001). The Hb levels were significantly lower in the TE group (12.76±1.33 g/dL) compared to those in the control group (13.51±1.2 g/dL) (p=0.001). Iron levels were significantly lower in the TE group (65.07±31.86 µg/dL)

Table 1. Comparison of telogen effluvium and the control groups

Parameter	TE group (n=455)	Control group (n=196)	P value
Age (years)	29.01±8.71	31.29±8.7	Not significant
Ferritin (ng/ml)	17.35±18.54	39.27±29.44	0.001*
Folate (ng/ml)	7.94±8.98	11.31±4.7	0.001*
Vitamin B12 (pg/ml)	232.13±123.35	306.41±182.28	0.001*
Hemoglobin (g/dl)	12.76±1.33	13.51±1.2	0.001*
Iron (µg/dl)	65.07±31.86	74.48±31.82	0.001*

*significant at 0.05 level; Mann Whitney U test. TE: Telogen Effluvium

compared to those in the control group (74.48±31.82 µg/dL) (p=0.001).

According to between-groups correlation analysis results, there was no significant correlation between the parameters in the control group. In the TE group, there was very weak correlation between age and folate level (r=0.104, p=0.026), between age and vitamin B12 level (r=0.095 p=0.042), between ferritin and folate levels (r=0.094, p=0.046), between ferritin and vitamin B12 levels (r=0.101 p=0.032); and there was weak correlation between folate and vitamin B12 levels (r=0.221 p=0.001).

We performed binary multivariate logistic regression analysis to identify risk factors for hair loss, and the results indicated that iron, ferritin, folate, and vitamin B12 levels were significant predictors of hair loss (OR=1.96, p=0.002; OR=15.54, p=0.001; OR=6.77, p=0.001; and OR=1.77, p=0.016, respectively).

Discussion

In our study, serum ferritin, folate, and vitamin B12 levels were significantly lower in the TE patients. We also found iron levels to be low in these patients.

Almost all the studies investigating the relationship between iron deficiency and hair loss focused mainly on women. Some studies suggest that iron deficiency can cause hair loss even in the absence of iron deficiency anemia [9-12]. However, opposite view exists [13, 14]. Nevertheless, it is a common practice for dermatologists to administer iron supplementation thinking that low iron stores can cause hair loss.

Our results indicate that iron deficiency is an important risk factor for the TE development (p<0.002, OR:1.96). The Hb levels in the TE group were significantly lower compared to those in the control group (p<0.001). Similarly, the ferritin levels were markedly lower in the TE group (p<0.001). Fatani et al. [7] conducted a study in which they compared 160 patients diagnosed with TE to the control group comprised of 450 individuals with no complaint of hair loss. They found significantly lower ferritin levels among patients with TE. This result is consistent with ours. In the same study, patients with TE with an age range of 16–62 years were stratified for age, and majority of the patients were found to be in 20–29 years age group. They attributed this result to the assumption that individuals at this age group complained more of hair shedding [9].

Similarly, in a study comparing 63 female patients with TE to 50 controls, authors found significantly lower ferritin level in the TE group. [10] They stratified patients according to ferritin level, and they found that low ferritin level was a notable risk factor for TE [10]. Our results support of this finding; we found that reduced ferritin level was an important risk factor for TE (p<0.001, OR:15.03).

Moeinvaziri et al. [9] compared 30 female patients with TE with 30 controls, and found significantly lower ferritin level in the TE group. They determined that ferritin level below 10 ng/mL was a significant risk factor for TE. The authors stated that the difference between the groups regarding ferritin level was not due to age, since average age was close between the two groups [11]. In our study, we also did not find a significant difference between the groups with regard to age.

Rasheed et al. [10] stratified 80 patients with TE and female-pattern hair loss (FPHL) according to the severity of hair loss as severe, moderate, and mild. They compared the ferritin levels with control group comprised of 40 individuals. The lowest ferritin levels were found in the group with severe hair loss. Moreover, ferritin levels of both the TE and FHPL groups were significantly lower when compared to those in the control group. No difference was found between the TE and FPHL groups regarding the ferritin levels [10].

In contrast to the studies mentioned above, Bregy et al. [11] stated that there was no association between ferritin level and hair loss. They stratified 181 female patients diagnosed with TE and FHPL according to trichogram and clinical assessment results, and compared ferritin levels and mean age across groups. Additionally, to investigate the association between ferritin level and telogen ratio, patients were stratified to three groups according to the ferritin levels as <10 µg/L (n=14), 10–30 µg/L (n=55), and >30 µg/L (n=112). While they found significant correlation between age and ferritin levels, no correlation was found between ferritin level and telogen ratio [13].

Sinclair et al. [12] administered at least three months of iron therapy to 12 patients who were diagnosed either with androgenetic alopecia (AGA) or with TE and had serum ferritin level <20 µg/L. At the end of three months, four of the patients still

had serum ferritin level below 20 µg/L, and they continued to receive three more months of iron supplementation. In the end, despite the fact that serum ferritin levels were brought to above 20 µg/L in all patients, there was no improvement in hair shedding or increase in hair density at the end of the treatment. Based on this finding, they proposed that low iron stores did not cause hair loss [14].

Kantor et al. [15] examined 30 cases with TE aged between 18 and 71 years. They reported that serum Hb and ferritin levels were not outside the normal range, with only four cases younger than 40 years old having significantly lower Hb and ferritin levels compared to six control cases [15].

The differences between the studies regarding iron, ferritin, and Hb levels may have multifactorial reasons in our opinion. There may be variations in the results depending on the behavioral habits in the society such as insufficient iron intake and reduced iron absorption because of excess consumption of tea and coffee. Although ferritin is the best indicator of iron deficiency, the results may be unreliable in conditions such as chronic inflammation, infection, neoplasia, or renal failure. Under such circumstances, confirmatory tests may be needed.

Vitamin B12 is a complex cyanocobalamin. There are limited studies on the role of vitamin B12 in hair growth. Özden and colleagues et al. [16] found low vitamin B12 levels in only 2% of 100 individuals with diffuse hair loss [16]. We found significantly lower vitamin B12 level in the TE group compared to that in the control group (232.13±123.35 vs. 306.41±182.28 pg/mL, $p<0.001$). Additionally, we found a very weak correlation between age and vitamin B12 level ($r=0.095$, $p=0.042$), very weak correlation between ferritin and vitamin B12 levels ($r=0.101$ $p=0.032$), and a weak correlation between folate and vitamin B12 levels ($r=0.221$ $p=0.001$).

Folate is abundant in liver and green vegetables, and its deficiency in humans is generally because of poor nutrition. Its role in hair growth is unknown. We found significantly lower levels of folate in the TE group compared to those in the control group (7.94±8.98 ng/mL vs. 306.41±182.28 ng/mL, $p<0.001$). We also found a very weak correlation between age and folate level in the TE group ($r=0.104$, $p=0.026$).

We conclude that low levels of ferritin, vitamin B12, and folate might play a role in the TE development. Studies related to vitamin B12 and folate in the literature are limited in number, and those with different ethnic populations might have different results. Hair loss may be related to emotional stress and anxiety. Identification of the underlying etiology is the key for planning the best treatment. We believe that it would be the best approach in planning the TE treatment to assess these parameters in patients presenting with hair loss and to correct any deficiency when detected.

Ethics Committee Approval: The medical ethics committee of Tekirdag Provincial Health Directorate approved the study (number: 93966460-605.01 Date: 08/17).

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – E.Y.E., R.A.Y.; Design – E.Y.E.; Supervision – R.A.Y.; Fundings - E.Y.E.; Materials – E.Y.E.; Data collection &/or processing – E.Y.E.; Analysis and/or interpretation – E.Y.E.; Critical review – E.Y.E., R.A.Y.

References

1. Dinh QQ, Sinclair R. Female pattern hair loss: current treatment concepts. Clin Interv Aging 2007;3:189–99.
2. Grover C, Khurana A. Telogen effluvium. Indian J Dermatol Venereol Leprol 2013;79:591–603. [CrossRef]
3. Shrivastava SB. Diffuse hair loss in an adult female: approach to diagnosis and management. Indian J Dermatol Venereol Leprol 2009;75:20–7. [CrossRef]
4. Jain VK, Kataria U, Dayal S. Study of diffuse alopecia in females. Indian J Dermatol Venereol Leprol 2000;66:65-8.
5. Liyanage D, Sinclair R. Telogen Effluvium. Cosmetics 2016;3:13.
6. Malkud S. Telogen effluvium: a review. J Clin Diagn Res 2015;9:WE01–3. [CrossRef]
7. Fatani MI, Bin Mahfoz AM, Naqqash S, Hussain WA, Khan AS, Zahrallayali AM, et al. Serum Ferritin Levels in Women with Telogen Effluvium: Do They Play a Role? Journal of Health Science 2015;5:10–3.
8. Karadağ AS, Ertuğrul DT, Tutal E, Akın KO. The role of anemia and vitamin D levels in acute and chronic telogen effluvium. Turk J Med Sci 2011;41:827–33.
9. Moeinvaziri M, Mansoori P, Holakooee K, Safaee Naraghi Z, Abbasi A. Iron status in diffuse telogen hair loss among women. Acta Dermatovenerol Croat 2009;17:279–84.
10. Rasheed, H, Mahgoub D, Hegazy R, El-Komy M, Abdel Hay R, Hamid MA, et al. Serum ferritin and vitamin d in female hair loss: do they play a role? Skin Pharmacol Physiol 2013:26;101–7. [CrossRef]
11. Bregy A, Trueb RM. No association between serum ferritin levels >10 microg/l and hair loss activity in women. Dermatology 2008;217:1–6. [CrossRef]
12. Sinclair R. There is no clear association between low serum ferritin and chronic diffuse telogen hair loss. Br J Dermatol 2002;147:982–4. [CrossRef]
13. Gathers R, McMichael A. Hair disorders in systemic disease. In: Callen JP, Jorizzo JL, editors. Dermatological Manifestations of Internal Disease. 3rd ed. Philadelphia: Saunders; 2003. p. 840–63.
14. Schneider MR, Schmidt-Ullrich R, Paus R. The hair follicle as a dynamic miniorgan. Curr Biol 2009;19:R132–42. [CrossRef]
15 Kantor J, Kessler LJ, Brooks DG, Cotsarelis G. Decreased serum ferritin is associated with alopecia in women. J Invest Dermatol 2003;121:985–8. [CrossRef]
16. Güler Özden M, Öztaş MO, Gülekon A, Gürer MA. Diffuse Hair Loss in Females and Associating Findings [Article in Turkish]. O.M.Ü. Tıp Dergisi 2008;25:50–6.