

Original Research Article

Evaluation of serum ferritin, vitamin B12 and vitamin D levels as biochemical markers of chronic telogen effluvium in women

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ABSTRACT

Background: Diffuse hair loss is a common complaint encountered by dermatologists in clinical practice and can be alarming to the patients. Chronic telogen effluvium (CTE) is characterized by an abrupt onset of diffuse loss of scalp hair persisting for more than six months, predominantly affecting healthy women in their fourth to fifth decade of life. Although CTE is considered to be associated with various nutritional deficiencies, currently the evidence to substantiate this assertion is conflicting.

Methods: A cross-sectional study was conducted on 100 adult non-pregnant women with CTE to document serum ferritin, B12 and vitamin D levels in an attempt to validate their role as biochemical markers using Statistical package for social sciences (SPSS) version 25:0 and Fisher's exact test.

Results: Mean ferritin level was 31.17 ng/dL. 23% patients had serum ferritin levels lower than the normal range (13-150 ng/dL). Vitamin D levels (normal range 5.2-60.4 ng/ml, mean 21.41 ng/ml) were low (deficiency range) in 2%. Vitamin B12 levels (normal range 191-663 pg/ml, mean 239.79) were low in 35.7% patients. Other parameters like duration, family history, past history of treatment did not demonstrate any statistically significant correlation.

Conclusions: Our study detected low levels of serum ferritin and vitamin B12 in approximately one-fourth and a third of females with chronic telogen effluvium respectively with vitamin D deficiency found in only a small proportion. Although a statistically significant correlation could not be established between these nutrients and participant age or other parameters; we concur with most authors who recommend that all females with diffuse hair loss deserve a thorough screening for nutritional deficiencies to facilitate prompt recognition and timely supplementation.

Keywords: Chronic telogen effluvium, Serum ferritin, Vitamin D, Vitamin B12

INTRODUCTION

Hair loss or alopecia of scalp is not a serious life-threatening disorder, but it can cause tremendous psychological distress and adversely affect quality of life. It is a common problem that affects up to 50% of men and women throughout their lives.¹ Unlike men who may accept the loss of hair as a part of aging, women are often less tolerant of the thinning of hair due to societal

perceptions. Many females nowadays present with complaints of diffuse hair loss (DHL) at a relatively younger age with the majority of consultations occurring between the ages of 30 and 59 years.² The causes of acquired diffuse non-cicatricial hair loss are diverse including telogen effluvium (TE), diffuse female pattern hair loss, anagen effluvium, diffuse alopecia areata etc. The actual prevalence rate of TE is not reported since most of the cases are subclinical in nature. Further, as women

get more distressed by hair fall and promptly seek treatment, they tend to be over-represented.³

Telogen effluvium (TE) and diffuse cyclical hair loss in women are two clinical conditions characterized by chronic and fluctuating increases in hair shedding with or without decrease in hair volume. Chronic telogen effluvium is diagnosed by excluding other causes of chronic telogen hair loss. Although deficiency of vitamins and minerals is considered to be associated with telogen effluvium, there is a paucity of studies analyzing these parameters in order to establish a definite correlation. Hence, we undertook this study to determine whether ferritin, vitamin D and vitamin B12 deficiency have a causative association with chronic telogen effluvium.

METHODS

This was a cross-sectional study conducted on 100 females presenting with chronic telogen effluvium (CTE) to the Out-patient department of Skin and Venereal Diseases at a tertiary care hospital during January 2019 to March 2019. Participants were enrolled after Institutional Ethics Committee approval and written informed consent. The diagnosis of CTE was made based on detailed history and responses to a questionnaire (including but not restricted to family history, triggering events, duration and treatment taken) followed by clinical and trichoscopic examination (Figure 1) and hair pull test (to assess type and activity of hair loss). Baseline investigations were performed to rule out underlying medical and autoimmune disorders. Pregnant and lactating females and those reporting obvious exacerbating events (physical/psychological stress, febrile illness, chemical applications and cosmetic hair procedures) were excluded. Blood samples were sent for estimation of serum ferritin, vitamin D and vitamin B12 levels.

Data analysis was performed using Statistical package for social sciences (SPSS) version 25:0. Qualitative data variables were expressed as frequency and percentage. Fisher’s exact test was used to find the association of serum ferritin, vitamin D and vitamin B12 levels with chronic telogen effluvium and correlate it with parameters such as age, family history and history of previous treatment. p-value <0.05 was considered as significant.

RESULTS

Our study included 100 females with chronic telogen effluvium aged between 19 to 50 years (mean 32.63 years). Of these, 78% were below 40 years with majority (38%) in age group 31 to 40 years. (Table 1,2) 27% of the total participants had taken some oral or topical treatment within last 6 months. Overall, 70% offered a maternal history of diffuse hair loss (67.9% aged below 40 years and 77.2% above 40 years) (p value 0.445.(Table 3). Mean ferritin level was 31.17 ng/dL. 23% patients had serum ferritin levels lower than the normal range (13-150 ng/dL).

Table 1: Frequency of subjects in small age groups.

Age (years)	No. of subjects (%)
≤ 20	11
21 - 30	29
31 - 40	38
> 40	22
Total	100

Table 2: Frequency of subjects in broader age groups for easier comparison.

Age (years)	Frequency (%)
≤ 40	78
> 40	22
Total	100

Table 3: The broader age groups with frequency according to presence or absence of family history.

		Age group (years)		Total	P value
		≤ 40	> 40		
Family history	Present	53	17	70	0.455
	Absent	25	5	30	
Total		78	22	100	

Table 4: The broader age groups with frequency according to normal or low serum ferritin levels.

Serum Ferritin levels	Age group		Total	P value
	≤40	>40		
Normal	63	14	77	0.149
Low	15	8	23	
Total	78	22	100	

Table 5: The broader age groups with frequency according to normal or low serum vitamin D levels.

Serum Vitamin D levels	Age group		Total	P value
	≤ 40	> 40		
Normal	76	22	98	0.999
Low	2	0	2	
Total	78	22	100	

23% in age group below 40 years and 36.36% in age group above 40 years had low serum ferritin with p value of 0.149 (table 4). Vitamin D levels (normal range 5.2-60.4 ng/ml, mean 21.41) were low (deficiency range) in 2% of the patients; 2.56% of females younger than 40 years were in the low range (p value 0.999). All participants aged above 40 years had normal values (Table 5). Vitamin B12 levels (normal range 191-663 pg/ml, mean 239.79 pg/ml) were low in 35.7% patients. 35.06% of females below 40 years and 38.10% of those above 40 years had low levels

(p value 0.802) (Table 6). Other parameters like duration, family history, past history of treatment did not demonstrate any statistically significant correlation with serum ferritin, vitamin D and vitamin B12 levels.

Table 6: The broader age groups with frequency according to normal or low serum vitamin B 12 levels.

Serum Vitamin B12 levels	Age group		Total	P value
	≤ 40	> 40		
Normal	50	13	63	0.802
Low	27	8	35	
Total	77	21	98	



Figure 1: Trichoscopic image (chronic telogen effluvium), decreased hair density, increased single follicular hair units and absence of characteristic features of other scalp disorders.

DISCUSSION

First described by Kligman, telogen effluvium (TE) is characterized by an abrupt onset, rapid, diffuse, excessive shedding of normal club hairs, usually seen 2-3 months after a triggering event. Among the various triggering events, the most common ones are severe febrile illness (example: malaria), postpartum (telogen gravidarum), accidental trauma, major surgery, emotional stress, chronic systemic illness, large hemorrhage, and crash diet.⁴⁻⁷ In one-third of cases, no trigger can be identified. Premature termination of anagen into catagen and telogen hair follicle is the main mechanism behind TE.

Acute or classical TE is a self-limiting condition lasting for about 3-6 months; however, if the stimulus/event persists beyond six months, the condition becomes chronic. Chronic TE is diffuse hair loss persisting beyond six months, may be primary/idiopathic, or secondary to some underlying disease and is described under the heading 'chronic diffuse telogen hair loss' in the Textbook of Dermatology by Rook. Among the various causes of chronic diffuse TE, iron deficiency anemia, hypo/hyper thyroidism, malnutrition, acrodermatitis enteropathica, and acquired zinc deficiency have been the most widely accepted.

There are several reasons to suspect a role for micronutrients in non-scarring alopecia which includes telogen effluvium. Micronutrients are major elements in the normal hair follicle cycle, playing a role in cellular turnover, a frequent occurrence in the rapidly dividing matrix cells in the follicle bulb. Management of alopecia is an essential aspect of clinical dermatology given the prevalence of hair loss and its significant impact on patients' quality of life. The role of nutrition and diet in treating hair loss represents a dynamic and growing area of inquiry. Deficiency of such micronutrients may represent a modifiable risk factor associated with the development, prevention, and treatment of alopecia. The human scalp contains approximately 100,000 hair follicles. Of these, 90% are in the anagen phase (when there is no alopecia), requiring essential elements, such as proteins, vitamins, and minerals, to efficiently produce healthy hair.^{8,9} Micronutrients, including vitamins and trace minerals, are therefore crucial components of our diet.¹⁰

Vitamin B12 is necessary for DNA synthesis, neurological function, and red blood cell formation.¹¹ The active forms of B12 are called methyl cobalamin and 5-deoxyadenosylcobalamin. Vitamin B12 is a cofactor for methionine synthase and thereby affects the synthesis of nearly 100 substrates including DNA, RNA, and proteins.¹¹ The recommended dietary allowance of vitamin B12 is 2.4 mcg for adults.^{11,12} Thus, theoretically, vitamin B12 levels can be expected to correlate with telogen effluvium. In our study, participants had values ranging between 25 to 767.3 pg/ml (mean of 239.79 pg/ml) with 36% having low levels. Thus, the proportion of females with low B12 levels was greater than a retrospective study that found only 2.6% of subjects deficient in vitamin B12.¹³ Similarly, Durosoy et al found no statistically significant difference in folate and B12 levels between patients of hair loss (androgenetic alopecia and CTE) and controls.¹⁴

Vitamin D is a hair follicle differentiation promoter without having much effect on its proliferation. Correlation of vitamin D levels has been seen among patients with hereditary vitamin D receptor (VDR) deficiency with alopecia.¹⁵ Previous studies show that VDR is necessary for an essential stage of hair follicle development that appears to be independent of 1,25(OH)2D3.^{16,17} Furthermore, calcitriol was found to be effective in treating chemotherapy-induced alopecia in animal models.¹⁸ In our study, mean value of vitamin D was found to be 21.41 ng/ml (range 3.36 to 55.4 ng/ml) with low levels detected in just 2% females. There are contradictory data from previous studies evaluating vitamin D in CTE. While some studies have demonstrated lower levels than controls, others have shown either no correlation or even the opposite result.¹⁹⁻²³

The most common nutritional deficiency in the world is iron deficiency, which contributes to TE.^{24,25} The serum ferritin (iron-binding protein) level is considered to be a

good indicator of total body iron stores and is relied upon as an indicator in hair loss studies.²⁶ However, serum ferritin levels may be raised in patients with inflammatory, infectious, and neoplastic conditions, and in those with liver disorders.

Iron deficiency is common in women with hair loss.²⁷ Nevertheless, the association of hair loss and low serum ferritin level has been debated for many years. There is an ongoing discussion of whether low serum ferritin levels ought to be designated as a nutritional deficiency triggering hair loss (mainly TE).²⁸ Using serum ferritin levels as a marker for iron storage deficiency, the definition of iron deficiency (but not specifically iron deficiency anemia) in several studies has ranged from a serum ferritin concentration of ≤ 15 to < 70 ng/dL.²⁹⁻³⁴ A cut-off of 30 ng/dL has a sensitivity and specificity in detecting iron deficiency of 92% and 98%, respectively while a cut-off of 41 ng/dL has a sensitivity and specificity of 98%.³⁵ In our study the cut off was 13 ng/dL. In order to reverse severe hair loss due to TE, some authors recommend maintaining serum ferritin at levels of > 40 ng/dL 36 or 70 ng/dL.²⁴ We found mean serum ferritin level to be 31.17 ng/dL which is within normal limits (5.12 - 95.4 ng/ml). There is insufficient evidence on the efficacy of iron replacement on the outcome of TE, although some benefits have been achieved in a few controlled studies.³⁷ Menstrual blood loss and pregnancy are the biggest causes of iron deficiency in otherwise healthy premenopausal Indian women. In our study, most of the females were below 40 years and in the reproductive age which probably explains (besides nutritional deficiency) the low levels of ferritin observed in nearly a quarter of the participants.

Although several studies have examined the association between iron deficiency and hair loss, the exact causative relation is unclear. Iron is a known cofactor in ribonucleotide reductase, a rate-limiting enzyme for DNA synthesis. Hair follicle matrix cells are among the most rapidly dividing cells in the body. They may be very sensitive even to a small reduction in iron availability, resulting in reduced hair growth in the presence of iron deficiency.³⁸ However, currently there is insufficient evidence to recommend a routine screening for iron deficiency and replacement of iron in the absence of iron-deficiency anemia in patients with hair loss. Sinclair et al. reported that iron deficiency is not increased in patients with female pattern hair loss or chronic TE compared to controls. This is also concordant with Olsen and colleagues who performed a controlled study on 381 women to determine if iron deficiency may play a role in FPHL or CTE.³⁹ They noted that iron deficiency is common in females, but not increased in patients with FPHL or CTE as compared with controls. On the other hand, Ozuguz et al found relatively low levels of hemoglobin and ferritin in their study group of CTE.

The evidence from Indian studies is also inconsistent. In a cross-sectional study to evaluate the prevalence of nutritional deficiencies in 100 Indian patients with hair

loss, Gowda et al indicated that a relatively higher proportion of participants with TE (20.37%) had iron deficiency compared to those with FPHL (16.67%) and male pattern hair loss (MPHL) (2.94%) ($p = 0.069$). Furthermore, transferrin saturation and ferritin levels were lower in patients with FPHL (41.67%) and TE (40.74%) than MPHL (11.76%).⁴⁰ Iron deficiency was found to be related to gender rather than to type of hair loss.

In contrast, another Indian study conducted by Deo et al. aimed to detect the prevalence of several forms of hair loss in females and to correlate these data with levels of hemoglobin and serum ferritin. Among 135 subjects, majority (62.2%) had TE, followed by FPHL (23.7%). Neither low hemoglobin (< 12 gm %; 73.4%) nor low serum ferritin (< 12 μ g/L; 6.7%) levels were found to be statistically significant.⁴¹

The strength of our study was the sample size which is at par with most of the previous studies. Moreover, we explored the correlation of serum ferritin, vitamin B12 and D with multiple parameters like age, duration, family history and treatment history. We were unable to find any other studies analyzing these variables to compare our observations. However, our study was limited by lack of controls.

CONCLUSION

The present study detected low levels of serum ferritin and vitamin B12 in approximately one-fourth and a third of females with chronic telogen effluvium respectively, with vitamin D deficiency found in only a small proportion. Majority of the women were younger than 40 years. Thus, although a statistically significant correlation could not be established between these nutrients and chronic telogen effluvium or participant age, we concur with most authors who recommend that all women with diffuse hair loss deserve a thorough screening for nutritional deficiencies to facilitate prompt recognition and timely supplementation. However, more robust evidence is required to validate their role as biochemical markers of this challenging disorder.

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