

Estimation of Serum Ferritin Level in Female Patients with Telogen Effluvium

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Abstract

Background: Telogen Effluvium (TE) is the most common cause of diffuse hair loss in adult females. TE may be a sequel of various metabolic alterations such as pregnancy, malnutrition especially iron deficiency anemia in premenopausal women. Hemoglobin concentration can be used to screen for iron deficiency, whereas serum ferritin concentration can be used to confirm iron deficiency. In this study we tried to put a light spot on the role of serum ferritin level in female patients with TE.

Methods: A case control study was done including 100 female patients less than 40 years (their age ranged from 18 to 40 years) divided into 2 groups. The patient group containing 80 female patients with telogen effluvium the control group containing 20 normal females without hair loss. A full history was done with full clinical examination. Blood samples were collected from all studied groups and examined for: serum ferritin level (by Ferritin ELISA -EIA-1872 test kits), Unbound T₄ (by FT₄ RIA KITS) and Complete blood counts (Haemoglobin level, RBCs, HCT values, MCV, MCH, MCHC).

Results: The results of this study showed normal serum ferritin level in female patients suffering from telogen effluvium as well as normal serum Hg level, HCT value, RBCs count and Blood Indices. Insignificant relation was found between control and study groups using SPSS statistical data analysis.

Conclusion: There was no closely linked relationship between iron metabolism and TE.

Keywords: Ferritin; Iron deficiency anemia; Telogen effluvium

Introduction

The term telogen effluvium, first coined by Kligman in 1961, refers to the loss of club (telogen) hair in disease states of the follicle [1].

Telogen effluvium is the most common cause of diffuse hair loss in adult females. In the normal scalp, 90-95% of the follicles will be in the anagen phase and the remainder (5-10%) will be in the telogen phase (with about 50-100 hairs shed daily). Various metabolic alterations such as pregnancy, malnutrition and other stresses are capable of adjusting the biologic clock within hair follicles, and it is possible for abnormally large numbers of hairs to enter the telogen phase simultaneously. When this happens, the hair loss is termed a TE [2].

Telogen effluvium includes increased shedding of club hairs with diffuse hair loss from all over the scalp. There should be a positive pull test of telogen hairs. In some cases there may be bitemporal thinning of hair. In cases of resolving TE, shorter, re-growing frontal hairs can often be observed [2].

Investigators have addressed the relationship of iron stores to nonscarring scalp hair loss in 13 studies [3]. Some suggest that iron deficiency may be related to AA, AGA, TE and diffuse hair loss, while others do not [4].

In premenopausal women, the most common causes of iron deficiency anemia (IDA) are menstrual blood loss and pregnancy. Hemoglobin concentration can be used to screen for iron deficiency, whereas serum ferritin concentration can be used to confirm iron deficiency [4].

Ferritin is a highly conserved protein complex that plays an

important role in iron storage and is recognized as the main iron-binding protein in non-erythroid cells [1]. Intracellular ferritin is synthesized by the smooth endoplasmic reticulum. Serum ferritin is synthesized by the rough endoplasmic reticulum and glycosylated by the Golgi apparatus before being secreted. Generally, serum ferritin is directly related to intracellular ferritin and thus total body iron stores. Investigators consider serum ferritin to be the most powerful screening tool for iron deficiency. In iron overload, ferritin is increased [5].

Ferritin serves to store iron in a non-toxic form, to deposit it in a safe form, and to transport it to areas where it is required. The function and structure of the expressed ferritin protein varies in different cell types. The presence of iron itself is a major trigger for the production of ferritin, with some exceptions [6]. Ferritin concentrations increase drastically in the presence of an infection or cancer; this is necessary to counter the infective agent's attempt to bind iron from the host's tissue. The inflammatory response may cause ferritin to migrate from the plasma to within cells, in order to deny iron to the infective agent [7]. The objective of our study was to estimate the serum ferritin level in female patients with telogen effluvium.

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Patients and Methods

Subjects

This study (case control study) included 100 females under 40 years their age ranged from (18-40) years, they were selected from the attendants of the outpatient clinic of dermatology at Al-Hussein university hospitals.

Faculty of Medicine, AL-Azhar University, Cairo, Egypt. They were divided into two groups:

- The patient group included 80 female patients with telogen effluvium;
- The control group included 20 normal females without hair loss.

All members of the study were subjected to full history as regard: Age, occupation, history of physical and mental stress, family history of hair loss, previous operations, head trauma, excessive blood transfusion or donation, history of systemic diseases, medications (topical or systemic), diet, childbearing history including (menstruation, pregnancy and lactation), onset, course and duration of hair loss.

History of chronic telogen effluvium

The patients presented with abrupt, excessive, alarming, diffuse, generalized shedding of hair from a normal looking head. Chunks of hair were seen in the bathroom, pillow, brush, and comb. A hand full of hair was displayed by the patient to corroborate the complaint of excessive shedding.

Full clinical examination

Body built, scalp abnormalities, infections or scarring, manifestation of anemia, manifestation of hyperandrogenism (acne or hirsutism), lymph nodes examination, thyroid examination, liver and spleen examination and nail abnormalities.

Local examination

Inspection: Hair length, color, luster, density, diffuse or localized hair loss, scales, nets of pediculosis, signs of scalp inflammation, visible follicular openings (to exclude cicatricial alopecia);

Palpation: Hair texture, hair tips (broken, tapered or miniaturized), hair root and attachment (loose or firm);

Gentle pulling test: Approximately, 60 hairs were grasped between thumb, index and middle fingers and gently pulled. A negative test (≤ 6 hairs obtained) indicates normal shedding, whereas a positive test (>6 hairs obtained) indicates active hair shedding.

Exclusion criteria

Any patients with thyroid abnormality, haemochromatosis and androgenetic alopecia were excluded

Methods

Blood samples were collected from all studied groups and examined for: 1-Serum ferritin level (by Ferritin

ELISA-EIA-1872) test kits with normal range (12-150 ng/ml) by the following steps:

- Serum prepared from a whole blood specimen without any additives with avoidance of grossly haemolytic, lipemic or turbid samples [8];

- Specimens capped and stored for up to 48 hours at 2-8°C. Samples inverted several times prior to testing;
- Specimens mixed with kits for ferritin for 30 seconds then incubated at room temperature for 45 minutes;
- Manual pipetting of all samples was done and reading the optical density at 450 nm [9];

2- Unbound T₄ (by FT₄ RIA KITS) with normal range (0.89-1.79 ng/dl);

3- Complete blood counts (Haemoglobin level, RBCs, HCT values, MCV, MCH, MCHC).

Statistical analysis

Data was done using statistical package for social science (SPSS) statistical programs and described in terms of range, mean, median, standard deviation, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative data between the control and subject groups was done using tests for independent samples. Analytical tests used included Pearson correlation (r), where all the parameters were tested for correlation. Significance and P value (P stands for probability) was used, were P value <0.05 was considered to be statistically significant.

Results

The obtained results were analyzed regarding the serum ferritin, hemoglobin, RBCs and RBCs indices. It shows insignificant difference between patient and control groups as regard age, hemoglobin level, RBCs count, HCT value, MCV, MCH, MCHC, serum ferritin level (P value=0.231, 0.123, 0.949, 0.078, 0.06, 0.557, 0.058, 0.394) respectively (Table 1). Also there was insignificant correlation between age, hemoglobin, HCT, RBCs MCV, MCH, and MCHC and serum ferritin level with p value=0.080, 0.540, 0.682, 0.237, 0.860, 0.244, 0.127 respectively) (Table 2).

Discussion

Telogen effluvium is the most common cause of diffuse hair loss in adult females. In the normal scalp, 90-95% of the follicles will be in the anagen phase and the remainder (5-10%) will be in the telogen phase (with about 50-100 hairs shed daily). Various metabolic alterations such as pregnancy, malnutrition and other stresses are capable of adjusting the biologic clock within hair follicles, and it is possible for abnormally large numbers of hairs to enter the telogen phase simultaneously. When this happens, the hair loss is termed a TE [10].

In this study we tried to put a light spot on the role of serum ferritin level in female patients with telogen effluvium. The results of this study showed normal serum ferritin level in patients suffering from telogen

| | | Patient group No: 80 Mean \pm SD | Control group No: 20 Mean \pm SD | t test | P value |
|------------|--------------------|--|--|--------|---------|
| Age | years | 24.950 \pm 6.042 | 23.200 \pm 4.720 | -1.205 | 0.231 |
| Hemoglobin | g/dl | 11.698 \pm 1.396 | 11.150 \pm 1.450 | -1.557 | 0.123 |
| RBC | $\times 10^9/cm^2$ | 4.356 \pm 0.534 | 4.365 \pm 0.5277 | 0.064 | 0.949 |
| HCT | vol. % | 36.053 \pm 2.787 | 37.360 \pm 3.492 | 1.781 | 0.078 |
| MCV | fl | 82.473 \pm 5.128 | 84.967 \pm 3.834 | 1.942 | 0.06 |
| MCH | pg | 27.303 \pm 2.731 | 27.680 \pm 1.703 | 0.589 | 0.557 |
| MCHC | % | 33.490 \pm 1.824 | 32.630 \pm 1.673 | -1.915 | 0.058 |
| Age | years | 34.338 \pm 29.250 | 57.639 \pm 37.800 | 0.856 | 0.394 |

Table 1: Comparison between patient and control groups.

| | | Serum ferritin ng/ml | |
|------------|---------------------------|----------------------|---------|
| | | R | P-value |
| Age | years | 0.280 | 0.080 |
| Hemoglobin | g/dl | 0.100 | 0.540 |
| RBC | $\times 10^9/\text{cm}^2$ | -0.047 | 0.682 |
| HCT | vol. % | -0.134 | 0.237 |
| MCV | fl | -0.020 | 0.860 |
| MCH | pg | 0.132 | 0.244 |
| MCHC | % | 0.172 | 0.127 |

Table 2: Correlation between ferritin level and other parameters.

effluvium as well as normal serum Hb level, HCT value, RBCs count and Blood Indices. Investigators have addressed the relationship of iron stores to non scarring scalp hair loss in 13 studies. These include studies of subjects with AA, TE, and AGA. Five were cross-sectional studies; 4 were case control studies; 3 were prospective cohort studies; and one was a double-blind placebo-controlled study. These studies included between 12 and 5110 subjects. Only 3 of these studies evaluated the direct effect of iron supplementation, and interventions included oral iron supplementation alone, oral iron and L-lysine supplementation or oral iron supplementation with spironolactone therapy and their relation to TE [11].

The following studies were similarly did not find the relationship between scalp hair loss and low iron stores. Aydingoz et al. [12] did not find statistically significant difference in serum ferritin levels among 43 women with diffuse alopecia and female pattern alopecia compared with 46 healthy control subjects. Sinclair [13] found that in a study of 194 women presenting with diffuse telogen hair loss, 12 were found to be iron deficient (defined as serum ferritin $<20 \mu\text{g/l}$). Of these 12 patients, 7 had AGA whereas the other 5 showed normal histology. All the women were treated with oral iron supplementation, and those with AGA were also treated with spironolactone. Subjective improvement was seen only in those individuals with AGA receiving both treatments. Kantor et al. [14] compared serum ferritin levels of female patients with TE (n=30), AGA (n=52), AA (n=17), and AA totalis/universalis (n=7) with a healthy control group of 11 patients. Mean serum ferritin levels were lower in subjects with AGA (37.3 $\mu\text{g/l}$) and AA (24.9 $\mu\text{g/l}$) compared with healthy control subjects (59.5 $\mu\text{g/l}$), but not lower when compared with those with TE (50.1 $\mu\text{g/l}$) or AA totalis/universalis (52.3 $\mu\text{g/l}$). Overall, the investigators concluded that ferritin levels were reduced in women with AGA and AA as compared with healthy control patients and there were no statistically differences between TE and control groups.

Corresponding to our study Bregy and Trueb [15] performed a cross-sectional study of 181 healthy women with diffuse TE, female pattern hair loss, or both. Diagnosis of TE was made by trichogram analysis (a telogen rate $>15\%$ in individual hairs removed from all areas of the scalp). Diagnosis of female pattern hair loss was made by clinical observation or was based on an abnormal trichogram (a telogen rate $>15\%$ in individual hairs removed from the frontal and centroparietal scalp regions). These women were then further subdivided into 3 groups based on serum ferritin levels: less than or equal to $10 \mu\text{g/l}$ (n=14), between 10 and $30 \mu\text{g/l}$ (n=55), and greater than $30 \mu\text{g/l}$ (n=112). There was no statistically significant difference in the telogen rate between the two groups. The group with serum ferritin less than or equal to $10 \mu\text{g/l}$ was too small to draw statistical significance [15].

On the contrary to our study few studies supported an association between diffuse hair loss and iron deficiency. In 1963, Hard performed one of the earliest studies addressing the relationship between diffuse

scalp hair loss and iron deficiency as measured by serum iron alone. He observed 100% regrowth in 18 non-anemic women with iron deficiency and diffuses hair loss treated with oral iron therapy. Furthermore, he reported that hair loss recurred upon discontinuation of iron therapy. A case-control study by Rushton et al. [16] showed that almost three quarters of 50 premenopausal women with diffuse scalp alopecia had serum ferritin levels less than $40 \mu\text{g/l}$. Patients with cicatricial alopecia, AA, male pattern hair loss, and thyroid dysfunction were excluded. The control population was composed of 10 women without hair loss or evidence of gynecologic irregularity, among other criteria. The lowest serum ferritin measured in this control group was $40 \mu\text{g/l}$.

In 2002, Rushton et al. [17] reported a cross-sectional study of women diagnosed with chronic TE as defined by increased hair shedding and decreased hair volume. Of the 200 women studied, 65% had ferritin levels less than $40 \mu\text{g/l}$ and 95% had serum ferritin levels less than $70 \mu\text{g/l}$. Taking a different approach Rushton [18] performed a prospective cohort study of 22 women with chronic TE. Patients were prescribed 72 mg of oral iron along with a 1.5 g supplement of the essential amino acid L-lysine. After 6 months of treatment, the mean serum ferritin level of all subjects had increased from 33 to 89 $\mu\text{g/l}$, and the percentage of hairs in telogen was significantly reduced, from 19.5% to 11.3%. Using the same treatment as described above, Rushton [18] then performed a double-blind placebo- controlled study of iron and L-lysine therapy for treatment of chronic TE. Seven patients were treated with 72 mg of oral iron and 1.5 g of L-lysine daily for 6 months and 5 patients received placebo. The study group demonstrated a significant increase in serum ferritin levels from 41.3 to 68.9 $\mu\text{g/l}$ whereas serum ferritin levels in the control group were unchanged during the 6month period. The study group also showed a 30% decrease in hair shedding compared with 9% in the control group.

A study by Deloche et al. [19] of 5110 women assessed the amount of hair loss with relation to ferritin and hemoglobin levels. Perceived hair loss was rated as none, moderate, or excessive, as classified by descriptive questions on hair loss and a hierarchical cluster analysis. In premenopausal women, low serum ferritin levels were significantly associated with the perception of hair loss by premenopausal women. In all, 10.2% of the women with serum ferritin less than $15 \mu\text{g/l}$ and 12.3% of women with serum ferritin between 15 and $40 \mu\text{g/l}$ believed they had excessive hair loss, compared with only 6.8% of women with serum ferritin greater than $70 \mu\text{g/l}$. In premenopausal women, anemia (defined as hemoglobin $<120 \text{g/l}$) was seen in 19.6% of premenopausal women with serum ferritin less than $15 \mu\text{g/l}$, 3.4% of those with serum ferritin 15 to $40 \mu\text{g/l}$, but only 1% of those with serum ferritin greater than $70 \mu\text{g/l}$. A similar trend in perception of hair loss and ferritin levels was seen in postmenopausal women but did not reach statistical significance.

The studies that were in disagreement with our study may be most probably due to the presence of differences in the number of the patients, gender of the patients as well as differences in methodological studies that were done by their authors. From the previously mentioned studies that didn't prove the possibility if the abnormalities in iron metabolism are closely linked with hair loss, additional laboratory and population-based research are needed. An appropriately powered randomized placebo controlled trial would be helpful in leading us toward a better understanding of the role of iron in hair loss.

Conclusion

The results of this study showed normal serum ferritin level in female patients suffering from telogen effluvium. So we can suggest the

absence of closely linked relationship between iron metabolism and hair loss.

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