

## Association of serum ferritin with chronic diffuse alopecia in female patient

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### Abstract

**Background:** Diffuse alopecia is a psycho-social stressor on human life. As iron is involved in crucial physiological processes within the hair follicle, iron deficiency is suspected to disrupt hair growth. Chronic telogen effluvium (CTE) and female pattern hair loss (FPHL) are the most common causes of chronic diffuse alopecia in females. In both conditions, low iron store have been considered as a possible contributing factor.

**Materials and Methods:** This was a hospital-based case control study, conducted in the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU) to evaluate the association of serum ferritin with chronic diffuse alopecia in female patient.

**Results:** The mean age of the females with chronic diffuse hair loss was  $26.83 \pm 7.78$  year and 92.9% females had serum ferritin level  $< 30$  ng/ml. The mean serum ferritin level in females with chronic diffuse hair loss, CTE and FPHL were  $16.3 \pm 11.61$  ng/ml,  $12.35 \pm 7.15$  ng/ml and  $20.25 \pm 16.07$  ng/ml respectively, which were lower than control  $54.37 \pm 26.07$  ng/ml. A highly significant ( $p < 0.001$ ) difference found in the mean serum ferritin level between the groups. In females with CTE, 42.5% had serum ferritin level  $< 12$  ng/ml (iron deficient) and 37.5% had 12-20 ng/ml (iron depletion). In females with FPHL, 23.3% and 30% patients had serum ferritin level  $< 12$  ng/ml and 12-20 ng/ml respectively.

**Conclusion:** This study found the level of serum ferritin were significantly low in females with chronic diffuse hair loss both in chronic telogen effluvium (CTE) and female pattern hair loss (FPHL), indicating there is a definite association of decreased iron store and diffuse hair loss.

**Keywords:** Diffuse Hair Loss; Chronic Telogen Effluvium (CTE); Female Pattern Hair Loss (FPHL); Chronic Diffuse Alopecia; Serum Ferritin Level.

### 1. Introduction

Alopecia, the "absence or loss of hair," is worrisome for all individual, irrespective of age or gender. Females with diffuse alopecia have a higher prevalence of psychiatric problems.<sup>1</sup> Diffuse alopecia typically occurs without inflammation or scarring, affects the entire scalp, characterized by ingress of a large number of hairs prematurely into telogen phase resulting in diffuse hair shedding.<sup>2</sup> Chronic telogen effluvium (CTE) followed by female pattern hair loss (FPHL) are the major causes of chronic diffuse alopecia.<sup>3</sup> Telogen effluvium is diffuse, non-scarring hair loss, resulting from synchronous transition of hair follicles from the growing stage (anagen) to the resting stage (telogen) of the hair cycle. Acute telogen effluvium is a self-limiting condition, persists for 3-6 months; when the stimulus persists beyond 6 months, the condition becomes chronic.<sup>3</sup> Chronic telogen effluvium (CTE) is more insidious in onset, represents a diagnosis of exclusion or secondary representation of a variety of systemic disorders like iron deficiency, thyroid disease, other metabolic diseases.<sup>4</sup> Female pattern hair loss (FPHL) is another main cause of chronic diffuse hair loss in

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women, characterized by non-scarring, progressive miniaturization of hair follicles with shortening of the anagen phase, with characteristic pattern in genetically susceptible women. FPHL is polygenic and multifactorial. Besides hereditary, factors like testosterone, stress, hypertension, diabetes mellitus, minimal physical activity, hypothyroidism, hyperprolactinemia, obesity, and lower serum ferritin are implicated as risk factors for FPHL.<sup>5</sup>

Iron is an integral factor in the growth of hair follicle, iron shortage may impair hair growth. Hair follicle matrix cells are one of the most rapidly proliferating cells in the body, demanding higher level of ferritin. They are extremely sensitive even to a minor drop in iron availability.<sup>6</sup> As iron is an essential cofactor for ribonuclease reductase which involves DNA synthesis, depletion of iron could impede proper functioning of this enzyme, resulting in inhibition of proliferation of hair matrix cells.<sup>7</sup> Iron also upregulates certain genes like CDC2, NDRG1, ALAD, RRM2 in the bulge region of hair follicle, which promote hair re-growth, affected by iron deficiency.<sup>8</sup> Iron supplementation has been suggested prior to and parallel to care.<sup>9</sup> Haemoglobin levels are not representative of true iron status in females with diffuse hair loss.<sup>10,11</sup> For detection of iron deficiency, serum ferritin level can be used as an early marker. Serum ferritin level is the first to drop, if individuals suffer any iron shortage, so a low serum ferritin is very specific for iron deficiency.<sup>12</sup> Diverse results have been observed regarding the relation between chronic diffuse alopecia and serum ferritin level. Some studies showed that mean serum ferritin level found lower in females with chronic diffuse hair loss.<sup>13,14</sup> Few studies reported no remarkable difference in the prevalence of iron deficiency in females with or without hair loss.<sup>15,16</sup> This study was intended to ascertain the association of iron deficiency with chronic diffuse alopecia in females.

## 2. Materials and methods

This was a hospital-based, case control study conducted in the Department of Dermatology and Venerology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Prior approval was taken from institutional review board. Total 140 females aged between 18-45 years were enrolled according to inclusion and exclusion criteria. Among them, 70 females had diffuse hair loss more than 6 months including both CTE and FPHL, were selected from outpatient department of Dermatology, BSMMU, as case and 70 age matched healthy females who had no complain of hair loss were included as control. Diagnosis of CTE was based on clinically, positive hair pull test and absence of widening of central parting. Diagnosis of FPHL was done clinically, on negative hair pull test and reduction of hair density over the crown and widening of central parting with preservation of anterior frontal hair line. By taking careful history, forming a questionnaire, clinical examination, hair pull test, emphasis was given on right selection of patients. All the eligible participants were participated in the study after given written informed consent. With aseptic measures 5 ml blood sample were collected for estimation of serum ferritin level from all participants. Measurement of serum ferritin were done by chemiluminescence immunoassay, by Liaison XL analyzer, in the Department of Biochemistry, BSMMU. For Haemoglobin, samples were analyzed by Hematology Autoanalyzer (Sysmex XN-2000) in the Department of Laboratory Medicine, BSMMU. The tests other than serum ferritin level were done to exclude the metabolic and systemic causes of chronic diffuse hair loss.

Data were statistically described in terms of mean  $\pm$  standard deviation ( $\pm$  SD) or frequencies (number of cases) and percentages. Student t-tests were used to compare quantitative variables and Chi-Square tests were used for comparing categorical variables. ANOVA test and post-Hoc analysis by Bonferroni method were done to compare subgroups of cases. A level of  $p < 0.05$  was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for Social Science; SPSS Inc., Chicago, Ill., USA) version 26 for Microsoft Window.

## 3. Results

**Table 1** Distribution of study subjects by age (N=140)

| Age (years)   | Case (n=70) No. (%) | Control (n=70) No. (%) | p value* |
|---------------|---------------------|------------------------|----------|
| <20           | 17(24.3%)           | 13(18.6%)              |          |
| 20-29         | 28(40.0%)           | 33(47.1%)              |          |
| 30-39         | 19(27.1%)           | 23(32.9%)              |          |
| >40           | 6(8.6%)             | 1(1.4%)                |          |
| Mean $\pm$ SD | 26.83 $\pm$ 7.78    | 26.34 $\pm$ 6.12       |          |
| Range         | 18-45               | 18-40                  |          |

\* unpaired student's t-test; Case: Females with chronic diffuse alopecia; Control: Age matched healthy females with no history of hair loss

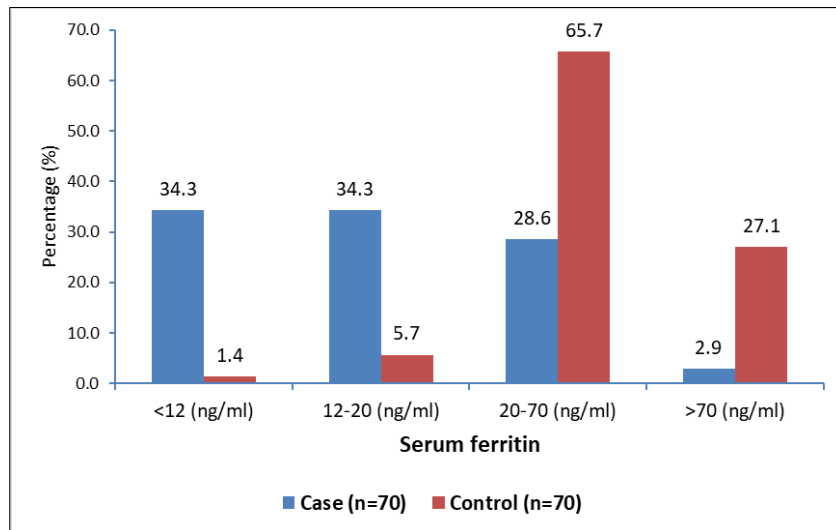
Table 1: Shows that majority of females belonged to age group of 20-29 years. Mean age of case group was (26.83 ± 7.78) SD years and control group (26.34 ± 6.12) SD years. There was no significant difference between the two groups regarding their mean age (p=0.682).

**Table 2** Distribution of the study subjects by laboratory finding (N=140)

| Variables              | Case (n=70) No. (%) | Control (n=70) No. (%) | p value* |
|------------------------|---------------------|------------------------|----------|
| Haemoglobin (g/dl)     |                     |                        |          |
| <12 (g/dl)             | 53(75.7%)           | 28(40.0%)              | <0.001   |
| >12(g/dl)              | 17(24.3%)           | 42(60.0%)              |          |
| Mean±SD                | 10.92±1.45          | 12.15±1.37             |          |
| Range                  | (6.40-13.80)        | (7.12-15.10)           |          |
| Serum ferritin (ng/ml) |                     |                        |          |
| < 30 (ng/ml)           | 65(92.9%)           | 14(20.0%)              | <0.001   |
| > 30 (ng/ml)           | 5(7.1%)             | 56(80.0%)              |          |
| Mean±SD                | 16.3±11.61          | 54.37±26.07            |          |
| Range                  | (3.12-72.20)        | (10.42-109.7)          |          |

\* Chi-square test

Table 2 shows that 75.7% females with chronic diffuse hair loss had low Hb(<12g/dl) with mean Hb 10.92±1.45 g/dl. 92.9% females with chronic diffuse hair loss had low serum ferritin level (<30 ng/ml) with mean serum ferritin level was 16.3±11.61 ng/ml. A highly significant difference has been found in Hb level and serum ferritin level (<30 ng/ml) between the groups (p<0.001).



**Figure 1** Bar diagram showing distribution of serum ferritin level (ng/ml) among the groups.

In this study patients were categorized based on their serum ferritin levels into 4 groups: Serum ferritin level <12ng/ml (iron deficiency) 12-20 ng/ml (iron depletion) 20-70 ng/ml (lower than require for normal hair cycle) >70 ng/ml (normal ferritin level)

**Table 3** Comparison of serum ferritin between study groups (N=140)

| Serum ferritin                  | Case (n=70)        |                     | Control (n=70)<br>No. (%) | p value  |
|---------------------------------|--------------------|---------------------|---------------------------|----------|
|                                 | CTE (n=40) No. (%) | FPHL (n=30) No. (%) |                           |          |
| <12 (ng/ml)                     | 17(42.5%)          | 7(23.3%)            | 1(1.4%)                   |          |
| 12-20 (ng/ml)                   | 15(37.5%)          | 9(30.0%)            | 4(5.7%)                   |          |
| 20-70 (ng/ml)                   | 8(20.0%)           | 12(40.0%)           | 46(65.7%)                 |          |
| >70 (ng/ml)                     | 0(0.0%)            | 2(6.7%)             | 19(27.1%)                 |          |
| Mean±SD                         | 12.35±7.15         | 20.25±16.07         | 54.37±26.07               | <0.001*  |
| Range (min-max)                 | (3.12-27.17)       | (5.44-72.20)        | (10.42-109.7)             |          |
| Post Hoc test (Bonferroni test) |                    |                     |                           |          |
| CTE vs Control                  |                    |                     |                           | <0.001** |
| FPHL vs Control                 |                    |                     |                           | <0.001** |

\*ANOVA test to compare among groups ; \*\* Post Hoc (Bonferroni) test between the groups.

Table 3 shows 42.5% females with CTE had serum ferritin < 12 ng/ml (iron deficient) and 37.5% had 12-20 ng/ml (iron depletion). 23.3% females with FPHL had serum ferritin level <12 ng/ml, 30% had 12-20 ng/ml. Only 1.4% healthy female had serum ferritin level <12ng/ml. A highly significant ( $p<0.001$ ) difference in the mean serum ferritin level between the groups in post hoc test.

#### 4. Discussion

In present study, incidence of hair loss was highest in the 20-29 years age group of females. Other studies reported highest incidence of hair loss was in age group 21-30 years.<sup>14,17</sup> This is probably because this age group of females are more concerned about their hair loss. In current study, majority females with CTE and FPHL had low Hb (<12g/dl) level. Hb level significantly lower in CTE group, suggesting anemia especially iron deficiency anemia could be a major factor for CTE. A Nepali study reported mean Hb level in CTE was 10.01±1.33 g/dl.<sup>18</sup>

In present study 92.9% females with diffuse hair loss showed lower serum ferritin level (SFL) (<30 ng/ml) with mean SFL 16.3±11.61 ng/ml. Tamer et al. found mean SFL of females with chronic diffuse hair loss was 14.72±10.70 ng/ml.<sup>19</sup> Poonia et al. also found 70% patients with nonscarring chronic diffuse hair loss had SFL <30 ng/ml.<sup>17</sup> In this study, among females with diffuse hair loss, 75.7 % had iron deficiency anemia, but 92.9% women had low SFL. It is remarkable that low iron store in the body will lead to hair shedding before the development of microcytic anemia. So, in the evaluation of diffuse hair loss, it should not be dependent on Hb value alone. An Iraqi study also concluded it.<sup>11</sup>

As, only iron deficiency causes low serum ferritin concentration, serum ferritin is the most powerful screening tool for iron deficiency. A cut-off of 30 ng/ml has a 92% sensitivity and 98% specificity in detecting iron deficiency.<sup>7</sup> A detail breakdown of iron deficiency state: when SFL<12ng/ml (iron deficiency state), SFL 12-20 ng/ml (iron depletion state), SFL 20-70 ng/ml (lower than required for normal hair cycle), SFL >70 ng/ml (normal ferritin level).<sup>20</sup>

In this study, females with CTE and FPHL had significantly lower SFL than females who had no hair loss, with mean SFL 12.35±7.15 ng/ml and 20.25±16.07 ng/ml respectively. Karim et al. found significantly lower SFL in females with CTE in Bangladesh<sup>21</sup>, indicating strong association between iron deficiency and CTE. A Nepali study found mean SFL in FPHL was 18.39±9.14 ng/ml.<sup>18</sup> A Bangladeshi study also found significantly lower mean SFL in FPHL with a mean SFL 12.50 ±3.37 ng/ml.<sup>22</sup> In this study, females with chronic diffuse hair loss, 34.3% subjects were in iron deficiency state (SFL<12ng/ml), 34.3% were in iron depletion state (SFL 12-20 ng/ml) and only 2.9% had normal ferritin level (SFL >70 ng/ml). An Indian study found 65% of the subjects were in iron deficient state and 20% of the subjects were in iron depleted state.<sup>20</sup> In current study, 42.5% females with CTE and 23.3% females with FPHL were in iron deficient state and 37.5% females with CTE and 30% females with FPHL were in iron depleted state. A Nepali study also found 14.29 % females with CTE and 23.08% females with FPHL were in iron deficient state and 14.29% females with CTE and 30.77 % females with FPHL were in iron depleted state.<sup>10</sup> Few studies could not find a significant association with chronic diffuse hair loss with low iron store.<sup>6,8,12,16</sup> The lower SFL observed in the present study, might be related to inclusion of

reproductive age group of females, duration of hair loss >6 months, non-inclusion of postmenopausal women, and selection of otherwise healthy women with diffuse alopecia eliminated confounding variables.

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## 5. Conclusion

The result of this study showed that serum ferritin level was significantly lower in females with chronic diffuse hair loss, both in CTE and FPHL, when compared to control. It can be concluded that there is a definite association of lower serum ferritin level with chronic diffuse hair loss in women of reproductive age group. Measurement of serum ferritin level should be routinely investigated in all females with chronic diffuse hair loss and supplementing with them when they are deficient, is beneficial in the treatment of alopecia before starting other anti-hair loss modalities.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

All authors of the manuscript have no conflict of interests to declare.

### *Statement of ethical approval*

This study was approved by Institutional Review Board (IRB), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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