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Research Article

CORRELATION OF SERUM FERRITIN LEVEL AMONG WOMEN WITH ALOPECIA

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ABSTRACT

Background: Hair loss, or alopecia, is a very common presenting symptom, and more than one third of women have clinically significant hair loss during their lifetime. The effect of hair loss on patients' emotions is often greatly underestimated by physicians. Many metabolic derangements can be manifested with alopecia, and hair loss may be the first clinical sign of systemic disease. The literature suggests that iron deficiency (ID) may play a role in hair loss in women.

Aim: To find out the correlation between serum ferritin and hair loss in women population.

Materials and Methods: The hospital based cross-sectional study was carried out in 74 women presenting with hair loss in Dermatology out patient department of Manipal Teaching Hospital, Pokhara, Nepal. Subjects on iron supplementation, thyroid disorder or having any immunological disease were not included. Blood samples were collected and serum ferritin was estimated. Other parameters such as TIBC, Serum iron and hemoglobin was also investigated. ANOVA, Kruskal Wallis test as well as ANOVA with post hoc test was applied in the study.

Result: The mean serum ferritin was low in cases with TE and FPHL but the result was not statistically significant in both cases ie mean serum ferritin 40.92 +/- 20.49 in TE cases and 33.19 +/- 18.58 in FPHL cases. In AA mean serum ferritin was 49.9 with SD of 36.3. The mean TIBC and serum iron were in normal cases of AA, TE and FPHL. Statistically significant no of cases in FPHL had serum ferritin level less than 41 µg/L and statistically significant no of cases with serum ferritin less than 41 µg/L also had Hb less than 12 gm/dl.

Conclusion: Participants of this study had low serum ferritin levels at different definitions of ID. Iron deficiency is the most common nutritional deficiency disorder of the world. Serum ferritin correlate with the amount of total body iron store. So, iron deficiency does play a role in alopecia in women.

Keywords: Iron-deficiency, anemia, ferritins, alopecia, dietary supplements.

INTRODUCTION

Hair is found in mammals, during the course of evolution its primary role were to serve as insulation. In human's hair has no vital functions yet its psychological functions are extremely important. Scalp baldness is reluctantly tolerable to some extent in genetically predisposed men, but in women loss of Hair from the scalp is distressing.[1]

Hair loss is a common problem that affects up to 50 percent of men and women throughout their lives.[2] Hair loss, or alopecia, is a very common presenting symptom, more than one third of women have clinically significant hair loss during their lifetime. The scalp contains, on average, 100,000 hairs. More than 90% of these hairs are actively growing, and they are referred to as anagen hairs.[3] Anagen phase is followed by a 2 week phase of catagen, where programmed apoptosis occurs. After catagen hair goes into resting phase of 3 months known as telogen. Normally, the scalp loses approximately 100 telogen hairs per day.[3]

After bone marrow, hair is the second fastest growing tissue of the body. As a result, many metabolic derangements can be manifested with alopecia, and hair loss may be the first clinical sign of systemic disease.[1] Iron deficiency is the most common deficiency disorder in the world.[4]

Anaemia is most prevalent in Central and West Africa and South Asia. Anaemia is estimated to affect 29% of non-pregnant women and 38% of pregnant women worldwide.[5] Iron deficiency is one of the major causes of anaemia and can also exist in the absence of anaemia.[6] Measurement of serum or plasma ferritin is a commonly utilized assay for evaluation of iron stores and it correlates well with the amount of iron stores.[7] Conflicting observations exists between alopecia and iron deficiency in women, so we evaluated whether common types of alopecia in women are associated with decreased tissue iron stores, as measured by serum ferritin.

MATERIALS AND METHODS

This was a hospital-based cross-sectional study conducted during the period of January 2018 to June 2019. Prior approval of institutional ethical committee was undertaken. Total number of 74 patients with hair loss were obtained with the help of history and clinical examination done by two dermatologists. Written informed consent was obtained from all the patients before their participation in the study. Examination of the scalp was performed to determine thinning, temporal recession, pattern of hair loss, severity of the condition and hair pull test was done in every patient. FPHL was graded according to the Ludwig scale findings as mild (Ludwig I), moderate (Ludwig II) or severe (Ludwig III). The diagnosis of TE was made if the patients had increased shedding by history or physical examination. The diagnosis of alopecia areata was made by clinical examination and history of patchy hair loss. Exclusion criteria consisted of patients with abnormal thyroid status, who failed to give consent, who were on iron therapy and patients with trichotillomania and tractional alopecia.

Labratory investigations:

From the selected patients Hb and iron profile (serum ferritin, TIBC, serum iron) was send. Serum

ferritin was tested by Electrochemiluminescence immunoassay (ECLIA) by the help of ECiQ. In this study the cutoff value of ferritin was kept at 41 µg/L. Hb of less than 12 gm/dl was considered as less.
Serum iron was tested by method of dry chemistry, by the VITROS 350.TIBC was calculated by ECiQ kit.

Statistical Analysis:

Data was entered and analyzed in Statistical Package for the Social Sciences (SPSS) version 16. Descriptive statistics was interpreted in terms of percentage, mean and standard deviation.

Analytical statistics was done using Chi square test to test the significance of association between Serum ferritin and hair loss. Non parametric test Kruskal Wallis test was used as data was not normal across type of hair loss categories. Only TIBC showed normal distribution curve, so ANOVA for TIBC was used.

RESULT

A total of 74 female with hair loss were examined during the study period. Out of 74 patients 24 (32.4%) had Alopecia areata, 25 (33.8%) has Telogen effluvium, 25 (33.8%) had FPHL. The minimum age of patient enrolled was 17 years and maximum was 67 years with mean of 39.4 and SD of 11.2. Frequency of duration of hair loss was less than 6 months in 34 (45.9%) patients while 40 (54.1%) had hair loss for more than 6 months. 24 (32.4%) had abrupt onset of hair loss without trigger, 25 (33.8%) had abrupt onset of hair loss with some underlying triggering factor while 25 (33.8) had gradual onset of hair loss. Severity of hair loss in FPHL according to Ludwig's classification with mild, moderate, severe FPHL were 3 (12%), 12 (48%), 10 (40%) respectively. Result of hair pull test was negative in 50 patients (67.6%), positive in 24 (32.4%) patients. 17 (23%) patient had family history of hair loss while 57 (77%) did not had family history of hair loss. 10 (13.5%) patients had previous history of major illness and stress while 64 (86.5%) did not had previous history of major illness or stress. In patient with AA mean Hb was 11.6, mean serum ferritin was 49.9, mean serum iron was 46.3, mean TIBC was 374. Patient with telogen effluvium had mean Hb 11.5, mean serum ferritin was 40.9, mean serum iron was 50.5 and mean TIBC was 368.8. While patient with FPHL had mean Hb 11.4, mean serum ferritin was 33.2, mean serum iron was 49.6 and mean TIBC was 379.2.

The frequency of patients with serum ferritin level than 41 µg/L were 10 (25%) in AA, 11 (27.5%) in TE while in FPHL it was statistically significant (p value 0.007) with frequency of 19 (47.5%). This study showed that 32 females with serum ferritin less than 41 µg/L also had Hb less than 12 gm/dl.

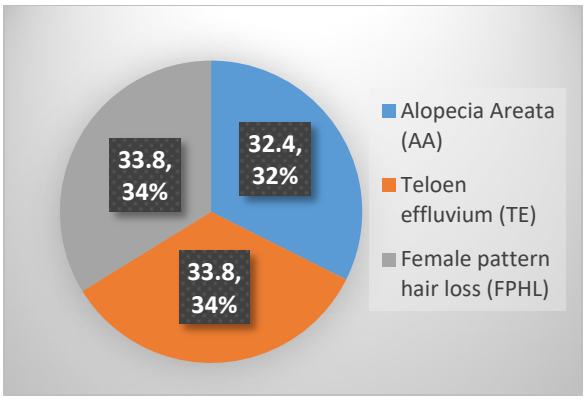

Figure 1: Shows total number of patients with different types of hair loss expressed in percentage in which out of total 74 number patients 33.8% had alopecia areata, 33.8% had TE, 32.4% had FPHL.

	Alopecia Areata (AA)			Telogen effluvium (TE)			Female pattern hair loss (FPHL)			chi square	p
	Median	Q1	Q3	Median	Q1	Q3	Median	Q1	Q3		
Age	34.5	28	45	35	28.5	45	45	41	50	12.214	0.002
Age at onset	35	28	45	35	28.5	45	42	36.5	49	6.784	0.034
Hemoglobin	11.2	10.6	12.4	11.8	10.5	12.7	11.5	10.5	12	0.533	0.766
Serum Ferritin	**44.5**	**34**	**56.3**	**45.8**	**23.4**	**56.9**	**28.5**	**21.8**	**38**	**5.642**	**0.060**
Serum Iron	45	29.3	54.5	40	35.5	57.5	50	31	66	1.594	0.451
TIBC Total Iron Binding Capicity	373.5	298.5	475.3	388	289	456	376	266	491		

Table 1: Shows median, Q1, Q3 of age, age of onset, Hb, serum ferritin, serum iron and TIBC in different types of hair loss.

Serum Ferritin	Alopecia Areata (AA)	%	Others	%	Total	chi square	p
>=41	14	41.2	20	58.8	34		
< 41	10	**25.0**	30	75.0	40		
Total	24	32.4	50	67.6	74	2.195	0.138

Table 2: Frequency of patients with AA with serum ferritin level less than 41 µg/L

Serum Ferritin	Female pattern hair loss (FPHL)	%	Others	%	Total	chi square	p*
>=41	6	17.6	28	82.4	34		
< 41	**19**	**47.5**	21	52.5	40		
Total	25	33.8	49	66.2	74	7.322	**0.007**

Table 3: Frequency of patients with TE with serum ferritin level less than 41 µg/L

Serum Ferritin	Telogen effluvium (TE)	%	Others	%	Total	chi square	p
>=41	14	41.2	20	58.8	34		
< 41	**11**	**27.5**	29	72.5	40		0.215
Total	25	33.8	49	66.2	74	1.537	

Table 4: Frequency of patients with FPHL with serum ferritin level less than 41 µg/L

Hb	Serum ferritin				Total	P
	<=41	%	>41	%		
< 12	32	71.1	13	28.9	45	0.005
>= 12	11	37.9	18	62.1	29	
Total	43		31		74	

Table 5: Cross tabulation between serum ferritin less than or equal to 41 µg/L and Hb in gm/dl

DISCUSSION

The present study was designed to see if there was any association between low serum ferritin values and 3 most common cause of non-scarring alopecia (AA, AGA, TE) with typical clinical presentation.

Out of total no of 74 patients, the present study had equal no of women with TE (n=25) and FPHL (n=25) ie 33.8% each followed by AA 32.4% (n=24). This differs from the study of Pradhan M et al out of 60 female patients of alopecia, 23 were suffering from alopecia areata, 18 from androgenetic alopecia and 19 had telogen effluvium.[8] Chisti M. et al studied total of 100 patients were studied in which most no. of cases had AA (n=46), followed by TE (n=29) and 25 no of cases had FPHL.[7] In a study of Kantor J et al 52 no patients had FPHL, 30 had TE and 17 had AA.[9] Malkud S concluded that TE was the commonest type of diffuse hair loss.[10] Norwood OT. studied 1,008 Caucasoid women revealed an overall prevalence was 19%.[11] A study conducted by Paik JH et al. with 4601 Korean women with FPHL in 2001 found an overall prevalence of 5.6%.[12] Su L. et al in their study showed the prevalence of FPHL to be 11.8% for all ages.[13]

In a study conducted by Moeinvaziri M. et al the mean age of women presenting with TE was 28.8±8.3 suggesting that any differences in ferritin levels between subjects with or without telogen hair loss were not due to age difference.[14] Jayashankar S. et al showed mean age of patient with telogen hair loss was 29 years.[15] Study by Ibrahem M. et al in patients with TE mean age was 24.95±6.042.[16] In a study done by Shashikant M. the range of age in patients with TE was 12-54 years with mean of 25.9±7.99, incidence was highest in age group 21-30 years. In the same study age varied from 20-55 years in patients with FPHL.[10] In another study done by Kantor J et al mean age of women with AGA, TE and AA was 29.6, 25.3, 26.2 respectively.[9]

Hemoglobin: In our study the mean Hb in AA was 11.6 gm/dl with SD 1.3, in TE mean Hb was 15.6 with SD 2 and in FPHL mean Hb was 11.4 with SD 1.3. In our study the mean value was 12.9 with SD 11.7 (p=0.766)

The study Chisti MA et al found the mean Hb value 12.30 with SD 1.40 g/dl which was not statistically significant.[7] Kantor J et al showed mean Hb were not significantly lower than in normal women which were 13.3, 13.4, 13 gm/dl in patients with FPHL, TE and AA respectively.[9] Study by Pradhan M et al mean value of Hb significantly lower in AA and FPHL.[8] Gangaiah N et al concluded that serum ferritin mainly less than 40µg/L and Hb 12 g/dl are significantly linked to the presence of hair loss in non-menopausal women.[17] In a study Hb less than 12gm/dl was observed in 60.2% of TE and 30% in FPHL.[10]

In another study the mean hemoglobin levels in patients with AGA, TE and AA were not significantly lower than normal ie 13.3, 13.4, 13, respectively.[9]

Serum Iron: In present study the mean serum iron was 46.3 mg/dl with SD 26.4 in AA, the median, Q1 and Q3 was 45, 29.3 and 54.5 mg/dl respectively. TE patient had mean serum iron 50.5 mg/dl with 26, while median, Q1 and Q3 40, 35.5,57.5 mg/dl respectively. The mean Hb in FPHL 33.2 mg/dl with SD of 18.6. The median, Q1 and Q3 in FPHL was 50, 31 and 66 mg/dl.

TIBC (Total Iron Binding Capacity): In AA the mean 374 mg/dl with SD 117.4 while median, Q1 and Q3 is 373.5,298.5 and 475.3 mg/dl. In TE the mean TIBC was 368.8 mg/dl with SD of 104.8. The median, Q1 and Q3 was 388, 289 and 456 mg/dl. The mean TIBC in FPHL was 379.2 with SD 133.8, while median, Q1 and Q3 was 376, 266, 491 mg/dl.

Serum ferritin:

Present study showed that mean serum ferritin among all 74 patients was 41.2 µg/L with SD of 26.7. In our study mean serum ferritin of patients with AA was normal ie 49.9 µg/L with SD of 36.3, cases of TE had decreased mean serum ferritin of 40.9 µg/L with SD of 20.5 and cased of FPHL also had decreased mean serum ferritin of 33.2 with SD of 18.6.

Frequency of patients having AA with serum ferritin less than 41 µg/L was 25% which was not statistically significant, frequency of patients of TE with serum ferritin less than 41 µg/L was 27.5% though was not statistically significant. Number of patients with FPHL was statistically significant 47.5%.

Our study showed that in AA 1(4.2%) patient had serum ferritin ≤12 µg/L indicating iron deficiency, 3(12.5%) had iron depletion ie iron depletion in the range of 13-20 µg/L, 17 (70.8%) that is lower than

required for normal hair cycle (ie 21 -70 µg/L), 3 had normal ie more than 70 µg/L of serum ferritin.

Out of 25 patients of TE 16% ie 4 had ID (serum ferritin≤ 12 µg/L), 4% had iron depletion ie in between 13-20 µg/L and 76% (19 patients) had serum ferritin level in between 21- 70 µg/L, 1(4%) had normal serum ferritin level.

FPHL showed 8%(2 patients), 12% (3 patients) and 72%(18 patients) had serum ferritin ≤12 µg/L, 13-20 µg/L and 21-70 µg/L respectively. Whereas 2% ie 2 patients had normal serum ferritin.

Studies which included AA, FPHL and TE:

Our study is in concordance with the study of Kantor J et al in patients with FPHL in which mean ferritin levels (37.3 µg/L) which was significantly lower than levels in women without hair loss.[9] The same study also had significantly lower mean serum ferritin in AA (24.9 µg/L) which is in contrast to our study. Ferritin levels in patients with TE was not statistically significantly lower than in normal which also differs from our study.[9]

In the study conducted by Pradhan M et al. The mean serum ferritin in cases (19.68 ± 8.70 ng/ ml) was found to be significantly lower than controls (23.14 ± 6.99 ng/ml) [p=0.018] On further analysis of subgroups of alopecia, the mean serum ferritin in androgenetic alopecia (18.39 ± 9.14 ng/ml) was significantly lower than that in controls which was in concordance with our study. Although the mean serum ferritin of patients with TE (22.79 ± 7.85 ng/dl) was lower than that of controls, but there was not statistically significant difference as well as their study showed decreased serum ferritin in AA (18.12 ± 8.70 ng/ml) which doesn't support our study.[8]

In study carried by Chisti M et al. AA and FPHL was significantly associated with lower values of serum ferritin whereas there was no significant association of serum ferritin and TE.[7]

Studies including TE and FPHL:

In study by Gangaiah N et al. among 40 cases with non-scarring hair loss ie, FPHL and TE 60.7%(n=17) presented with iron depleted stores (serum ferritin level less than 40 µg/L with mean Hb 8.9 g/dl) and was significantly linked to hair loss in non-menopausal women.[17]

In study conducted by Malkund S 14 out of 17 patients with FPHL had serum ferritin level less than 70 µg/L with mean of 36.11 µg/L though the study was not statistically significant. Same study showed statistically insignificant relation between TE and serum ferritin (69 out of 74 patient had serum ferritin less than 70 µg/L).[10]

Oslen E et al concluded that there was no statistically significant increase in the incidence of ID in premenopausal or postmenopausal women with FPHL and TE compared to control subjects however taking serum ferritin ≤40 µg/L. ID occurred in 58.8%, 63.8% premenopausal women with FPHL (n=170) and CTE (n= 115) respectively while only 26.1% and 36.8% of post-menopausal women respectively.[18]

Raichur S et al showed statistically significant low mean serum ferritin level in all participants with chronic diffuse hair loss, 60% of patients with FPHL had serum ferritin ≤41 µg/L and 85.71% with TE had serum ferritin ≤41 µg/L.[19]

Rushton DH et al Depleted iron stores (serum ferritin ≤41 µg/L) was low in 65% of women with TE(n=200).[20]

Rasheed H et al in their study of serum ferritin in female hair loss showed that serum ferritin levels in the TE (14.7 ± 22.1 µg/l) and FPHL (23.9 ± 38.5 µg/l) candidates were significantly lower than in controls. Serum ferritin cut-off values for TE and FPHL were 27.5 and 29.4 µg/l respectively.[21]

Studies which included TE only:

Present study showed similar results as Jayashanker CA et al where serum ferritin levels were found to be low in 76% of patients with TE (less than 40 µg/L). Out of 76% patients 10 patients had significantly low serum ferritin levels (less than 40 µg/L), in spite of having normal hemoglobin levels.[15]

Similarly Obaidat et al in their study of iron deficiency in telogen effluvium had significantly low level of serum ferritin in 50 patients (out of 72 with TE) using a cut-off point of 20 ng/ml.[22]

In a study of Moeinvaziri et at decreased serum ferritin level was found significantly low in 10 (33.3%) out of 30 patients with TE. Although in this study lower limit was taken as less than 10 ng/ml.[14]

Ibrahem M et al however concluded that there was no closely linked relationship between iron metabolism and TE as serum ferritin as well as Hg were normal in female patient with TE.[16]

Studies which included FPHL only:

Siah T et al in retrospective study of FPHL had mean serum ferritin 76.94 µg/L in 150 patients only 29% had ferritin level less than 30 µg/L.[23] Park S et al. in 113 FPHL patients showed significantly low serum ferritin with mean of 49.27 µg/L and it was significantly lower in premenopausal FPHL patients.[24]

Zang X et al. in their clinic-laboratory study in 60 patients of FPHL overall mean serum ferritin level was 58.8±57.3 µg/l and serum ferritin level lower than required for normal hair cycle (20 µg/l <serum ferritin <70 µg/l) was seen in 25% (15/60) of patients with FPHL.[25]

Studies which included AA only:

Jin W et al in their meta-analysis concluded that there was no significant difference between the AA patients and controls in level of serum ferritin which is in concordance with our study.[26]

Similar results were shown by Wani A et al in which no significant difference was found in mean serum ferritin in AA patients and control group.[27]

Sinclair R in his study contradicted that above observation and showed that there is no clear association between low serum ferritin levels and alopecia (low limit of serum ferritin was taken as 20ng/ml whereas other studies has taken as 40-70ng/ml).[28]

CONCLUSION

Among the ongoing debates, the definition of iron deficiency in hair loss remains an important question.

Of the studies that have examined the relationship between iron deficiency and hair loss, almost all

have addressed women exclusively and have focused on non-cicatricial hair loss. Some suggest that iron deficiency may be related to AA, AGA, TE, whereas others do not. Currently, there is insufficient evidence to recommend universal screening for iron deficiency in patients with hair loss. In addition, there is insufficient evidence to recommend giving iron supplementation therapy to patients with alopecia and iron deficiency in the absence of IDA.

Determining the cause of hair loss in women can be difficult and should be guided by the patient's history, including the pattern of hair loss, other medical conditions, the use of hair treatments, and the family history of hair loss, as well as by the physical examination.

This study shows that decrease in ferritin levels might be considered as a potential risk factor for excessive hair loss in women of Nepalese origin.

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