

Estimation of Serum Ferritin Levels in Patients with Various Forms of Alopecia: A Case-Control Study.

Pokhrel K.¹, Parajuli S.², Shah M.³, Sushma Subedi⁴

¹Lecturer, Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, Nepal.

²Associate Professor, Department of Dermatology, Maharajgunj Medical Campus, Institute of Medicine, Nepal

³Consultant, Anandban Community Hospital, Nepal.

⁴Lecturer, Department of Microbiology, Nepalgunj Medical College and Teaching Hospital, Nepal.

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ABSTRACT

Background: Hair is considered as one of the most essential feature of human appearance. It is an ectodermal structure with no vital function, yet its cosmetic and emotional significance is enormous, as is evident from the distress of losing hair. It is a widespread hitch affecting up to 50 percent of males and females during their lives. The most commonly accepted causes of hair loss include nutritional deficiencies, particularly that of iron. Hair loss could also be a sign of underlying systemic illness like anemia, hypothyroidism, hyperthyroidism, chronic infectious diseases, etc. Serum ferritin is directly related to intracellular ferritin and thus to total body iron stores. Iron deficiency results in low serum ferritin concentrations. The association of low serum ferritin level with hair loss has been a controversial topic over the years. Hence, the present study was conducted to measure the serum ferritin level in various types of alopecia and comparison with controls. **Objectives:** To measure the serum ferritin level in various types of non-cicatricial alopecia and comparison with controls. **Methods:** This study was conducted on 100 non-cicatricial alopecia patients reporting to the Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, Nepalgunj, Nepal for the period of one year from May 2014 to June 2015. All study participants were enrolled after a detailed medical history and clinical examination by the same experienced dermatologist to rule out conditions that can cause hair loss. In addition to clinical examination, the baseline investigations including, haemoglobin level, ESR and serum ferritin levels were also carried out. Serum ferritin was measured by standard enzyme-linked immunosorbent assay (ELISA) method. The lower reference limit of serum ferritin taken in this study was 40 ng/ml. The statistical analysis was done using student 't' test for the difference of means and chi-square test for ratios. The p-value of <0.05 was taken to be significant. **Results:** Out of 100 cases, 80% were that of alopecia areata, followed by 12% of telogen effluvium and 8% of androgenetic alopecia. Amongst 100 patients of alopecia, alopecia areata was observed in 21-25 years of age group (25%); telogen effluvium was found between 15-20 year age group (41.7%) and androgenetic alopecia was seen most commonly in the 26-30 year age group (50%). Alopecia areata and telogen effluvium were found more in female patients (82.5% and 91.7%, respectively) where as androgenetic alopecia was observed mainly in males (62.5). An extremely significant difference ($p < 0.001$) in the mean serum ferritin levels was seen in the cases (68 ± 41.89 ng/ml) and controls (26.37 ± 16.01 ng/ml). The mean ferritin levels of patients with alopecia areata (59.46 ± 53.37 ng/ml) and androgenetic alopecia (114.88 ± 58.15 ng/ml) were significantly higher than that in the controls ($p < 0.0001$), whereas the mean ferritin level of patients with telogen effluvium (29.67 ± 14.14 ng/ml) was not significantly different from that of controls ($p = 0.49$). **Conclusion:** Estimation of total serum ferritin levels may be important in cases of unexplained hair fall. Appropriate counselling and treatment can then be particularly directed at the etiology of hair loss, thus improving the patient outcome.

Keywords: Alopecia, alopecia areata, androgenetic alopecia, serum ferritin, telogen effluvium.

INTRODUCTION

Hair is considered as one of the most essential feature of human appearance.^[1] It is an ectodermal structure with no vital function, yet its cosmetic and emotional significance is enormous, as is evident from the distress of losing hair.^[2]

The hair cycle in human beings consists of 3 phases: anagen, catagen, telogen. Loss of the dead hair from the follicle occurs either late in telogen or early in anagen phase. Hair loss is a widespread hitch affecting up to 50 percent of males and females

during their lives. It may be widespread; however, the scalp is most commonly affected.^[3]

Name & Address of Corresponding Author

Dr. Pokhrel K.
Lecturer,
Dept of Dermatology,
Nepalgunj Medical College and Teaching Hospital,
Nepal.
E mail: dr@kumarpokhrel.com.np

Hair loss can be classified into many types' namely diffuse alopecia areata, alopecia totalis or universalis, telogen effluvium, anagen effluvium,

androgenetic alopecia, tinea capitis, traction alopecia patchy and trichotillomania.^[4] The term androgenetic alopecia was initially used to describe this condition in both males and females. Now this term has been replaced by female pattern hair loss or telogen effluvium.^[5]

The most commonly accepted causes of hair loss include nutritional deficiencies particularly that of iron.^[6] Hair loss could also be a sign of underlying systemic illness like anemia, hypothyroidism, hyperthyroidism, chronic infectious diseases, etc.^[7] Serum ferritin is directly related to intracellular ferritin and thus to total body iron stores. Iron deficiency results in low serum ferritin concentrations. The association of low serum ferritin level with hair loss has been a controversial topic over the years.^[7] Against this backdrop, the present study was conducted to measure the serum ferritin level in various types of non-cicatricial alopecia and comparison with controls.

MATERIALS AND METHODS

This study employed a hospital-based cross-sectional study and was conducted in the Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, Nepalgunj, Nepal for the period of one year from May 2014 to June 2015. The study was approved by the institutional review board and a written consent was taken from all the subjects before their inclusion in the study.

One hundred patients of non-cicatricial alopecia (NCA) aged between 15 and 50 years presenting to our outpatient department were enrolled as the study group. It included clinically typical cases of commonest types of NCA [alopecia areata (AA), telogen effluvium (TE) and androgenetic alopecia (AGA)]. Equal number of age- and sex-matched controls was taken. The control group was selected from among patients who were treated at the study hospital for a condition other than NCA. The exclusion criteria considered was subjects with acute fever, thyroid dysfunction, postpartum hair loss, inflammatory lesions on the scalp, raised ESR and hemorrhagic disease, or those on certain medications. All study participants were enrolled after a detailed medical history and clinical examination by the same experienced dermatologist to rule out conditions that can cause hair loss.

Laboratory investigations

In addition to clinical examination, the baseline investigations including, haemoglobin level, ESR and serum ferritin levels were also carried out in the patients. Serum ferritin was measured by standard enzyme-linked immunosorbent assay (ELISA) method. The lower reference limit of serum ferritin taken in this study was 40 ng/ml.

Statistical analysis

Data was analyzed using SPSS 14.0 software programme and analyzed the demography, type of NCA and appropriate comparisons were made. Values were reported as mean±standard deviation. The statistical analysis of the data was done using student 't' test for the difference of means and chi-square test for ratios. These tests were referenced for p-values and p-value of <0.05 was taken to be significant.

RESULTS

Out of 100 cases, 80% were that of AA, followed by 12% of TE and 8% of AGA [Figure 1]. The age range of cases and controls in our study was 15-50 years [14.29±9.26 years (cases) and 14.29±10.06 years (controls)] and were divided into different age groups. Amongst 100 patients of NCA, AA was observed most frequently in 21-25 years of age group (25%) while TE was found mostly in the 15-20 year age group (41.7%). Androgenetic alopecia was seen most commonly in the 26-30 year age group (50%). Age wise distribution of the subjects is depicted in [Table 2].

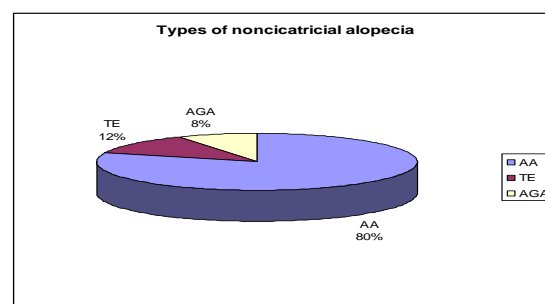


Figure 1: Types of non-cicatricial alopecia.

Table 1: Age distribution for cases and controls.

Age group (in years)	AA n (%)	TE n (%)	AGA n (%)	Total n (%)	Control n (%)
15-20	17 (21.3)	05 (41.7)	--	22	24
21-25	20 (25)	03 (25)	03 (37.5)	26	29
26-30	18 (22.5)	01 (8.3)	04 (50)	23	20
31-35	09 (11.3)	01 (8.3)	01 (12.5)	11	11
36-40	07 (8.8)	02 (16.7)	--	09	08
41-45	02 (2.5)	--	--	02	03
46-50	07 (8.8)	--	--	07	05
Subtotal	80	12	08	100	100

Mean ± SD	11.43±6.85	1.71±1.80	1.14±1.68	14.29±9.26	14.29±10.06
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Overall females (64%) outnumbered males (36%) in the present study. Alopecia areata was found significantly more commonly in female patients (82.5%) as well as TE (91.7%). On the contrary AGA was observed mainly in males (62.5%).

Gender distribution of the subjects is depicted in [Table 2].

There was no significant difference in haemoglobin (12.09±1.14 g/dl c.f. 12.34±0.79 g/dl; $p=0.07$) and ESR (9.48±3.67 mm c.f. 8.86±2.97 mm; $p=0.19$) as well. [Table 3].

Table 2: Gender distribution for cases and controls.

Study group	Male n (%)	Female n (%)	Total n (%)	χ^2	p-value
AA	30(37.5)	50(82.5)	80	0.78	0.38
TE	01(8.3)	11 (91.7)	12	5.67	0.02 ^{SS}
AGA	05(62.5)	03(37.5)	08	1.02	0.31
Subtotal	36(36.0)	64(64.0)	100	1.33	0.25
Controls	44 (44.0)	56 (56.0)	100	--	--

^{SS}Statistically significant

Table 3: Comparison of various red cell indices between cases and controls.

	Cases	Controls	T value	p-value
Hb (gm/dl)	12.09±1.14	12.34±0.79	1.8025	0.07
ESR (mm)	9.48±3.67	8.86±2.97	1.3132	0.19

Hb=haemoglobin

On gender-wise comparison among cases and control there was no statistically significant difference ($p=0.33$) for serum ferritin level ≤ 40 ng/ml. But for serum ferritin level >40 ng/ml, the findings were statistically significant ($p=0.01$) as shown in [Table 4].

An extremely significant difference ($p<0.001$) in the mean serum ferritin levels was seen in the cases (68±41.89 ng/ml) and controls (26.37±16.01 ng/ml).

Further analysis of data revealed that the mean ferritin levels of patients with AA (59.46±53.37 ng/ml) and AGA(114.88±58.15 ng/ml) were significantly higher than that in the controls ($p<0.0001$), whereas the mean ferritin level of patients with TE (29.67±14.14 ng/ml) was not significantly different from that of controls ($p=0.49$) as shown in [Table 5].

Table 4: Gender-wise comparison of serum ferritin levels among cases and controls.

Serum ferritin level (ng/ml)	Study group		Controls		χ^2	p-value
	Male n (%)	Female n (%)	Male n (%)	Female n (%)		
≤ 40	21 (41.2)	30 (58.8)	18	38	0.94	0.33
>40	15 (30.6)	34 (69.4)	26	18	7.63	0.01 ^{SS}
Total	36 (36.0)	64 (64.0)	44	56	1.33	0.25

^{SS}Statistically significant

Table 5: Comparison of mean serum ferritin levels in different NCA and controls.

Study group	Number	Mean±S.D. (ng/ml)	t' value	p-value
AA	80	59.46±53.37	5.88	<0.0001 ^{SS}
TE	12	29.67±14.14	0.68	0.49
AGA	08	114.88±58.15	11.19	<0.0001 ^{SS}
Total cases	100	68±41.89	9.28	<0.0001 ^{SS}
Controls	100	26.37±16.01	--	--

^{SS}Statistically significant

We further analyzed the data using the serum ferritin value of ≤ 40 ng/ml as the lower limit of normal and it was found that lower number of patients had ferritin levels of ≤ 40 ng/ml (51% c.f. 56% of controls. It was also seen that no significant number

of patients with AA ($p=0.64$), TE($p=0.69$), AGA ($p=0.31$) had serum ferritin levels of ≤ 40 ng/ml when compared with those of controls as depicted in [Table 6].

Table 6: Comparison of cases and controls in relation to serum ferritin levels.

Study group	≤ 40 ng/ml n (%)	>40 ng/ml n (%)	χ^2	p-value
AA	42	38	0.22	0.64
TE	06	06	0.16	0.69
AGA	03	05	1.02	0.31
Total cases	51	49	0.50	0.48

Controls	56	44	--	--
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DISCUSSION

The present case-control study was designed to see if there is any association between low serum ferritin values and various types of NCA. Alopecia is a widespread hitch affecting up to 50 percent of males and females during their lives.^[3] The most commonly accepted causes of hair loss include nutritional deficiencies particularly that of iron.^[6] Hair loss could also be a sign of underlying systemic illness like anemia, hypothyroidism, hyperthyroidism, chronic infectious diseases, etc.^[7] Other factors that may be associated with the etiopathogenesis include; the genetic constitution, nonspecific and organ-specific autoimmune reactions and emotional stress.^[8]

In our study, out of 100, 80% cases were that of AA, 12% of TE and 8% of AGA. Our findings were in concordance with the study conducted by Muzamil et al^[3] where AA was found in majority of the cases (49% cases), followed by TE (29% cases) and AGA (25% cases).

In the present study, the patients with AA were between 15 to 50 years of age. The study conducted by Thomas et al^[8] found that the patients with AA in their study ranged between 20 to 40 years. Telogen effluvium was prevalent between 15 to 20 years, however in the study conducted by Fatani et al^[9] it was found between 21 to 40 years. Androgenetic alopecia was found between 26 to 30 years; Quan et al^[10] found its prevalence between 31 and 35 years.

Alopecia areata and TE were prevalent amongst females in our study. These findings were in concordance with those conducted by Rasheed et al^[11] and Moeinvaziri et al^[12] respectively. Androgenetic alopecia in our study was prevalent in males like the study conducted by Kaliyadan et al.^[13]

An extremely significant difference ($p < 0.001$) in the mean serum ferritin levels was seen between the cases (68 ± 41.89 ng/ml) and controls (26.37 ± 16.01 ng/ml). These findings were similar to the findings given by Rasheed et al^[11] in his study where the serum ferritin levels ranged from 2.2 to 131.3 $\mu\text{g/l}$ with a mean of 14.7 ± 22.1 $\mu\text{g/l}$, being significantly lower than that detected for the controls (range 3.2–73.8 $\mu\text{g/l}$ and mean \pm SD 43.5 \pm 20.4 $\mu\text{g/l}$, $p < 0.001$).

There was a statistically significant difference in the serum ferritin levels in patients with AA and AGA in comparison to controls. Similar findings were noted by Muzamil et al^[2] where patients with AA and AGA had significantly lower values of serum ferritin than the controls ($p = 0.011$ and 0.015 , respectively). The levels of serum ferritin in TE were statistically insignificant in comparison to the control group. These findings were in concordance to the study conducted by Fatani et al^[14] wherein

the mean serum ferritin level was 34.30 ng/ml among TE patients compared with 75.57 ng/ml among controls.

Kantor et al^[15] proposed that low body iron stores are not imperative in triggering alopecia in patients with strong genetic predisposition. Individuals with a mild genetic predisposition or with the presence of other triggering factors, low iron stores may lower their brink to the point of developing alopecia.

So far, in literature none of the studies has been performed on males. This study is one of its kinds as it involves the estimation of levels in both the gender. Hair loss can have an emotional impact on patients, leading to anxiety and frustration. Therefore, diagnosis of the aetiology is essential for the prompt management of the condition. Further studies with huge sample sizes are required to scrutinize the role of iron deficiency.

CONCLUSION

Diffuse hair loss is a widespread clinical condition affecting upto 50% of population. Alopecia areata was the most common type of alopecia found in our study. Estimation of total serum ferritin levels may be important in cases of unexplained hair fall. Appropriate counselling and treatment can then be particularly directed at the etiology of hair loss, thus improving the patient outcome.

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