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Association of Low Serum Ferritin Levels in Patients Having Alopecia Areata: A Case Control Study

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ABSTRACT

Introduction: Alopecia areata is a medical condition characterized by non-scarring hair loss occurring in patches. Etiopatho-genesis of the disease involves genetic, immunological and various other factors. Reduced ferritin stores lead to impaired DNA synthesis disrupting hair follicle production hence playing a role in the patho-physiology of alopecia areata.

Aims & Objectives: To establish the association of low serum ferritin levels and alopecia areata.

Place and Duration of Study: The study was conducted for duration of six months from February to August 2022 at Dermatology Department Shalamar Hospital, Lahore.

Material & Method: A total of 104 participants were recruited for this study, into a group of 52 patients having alopecia areata and 52 age and gender matched healthy controls. All these participants were advised to get their serum ferritin levels done from the same laboratory to control bias. Values of serum ferritin levels were recorded in ng/ml on a predesigned proforma. The data was analyzed using SPSS version 23.0. Frequencies and percentages were calculated for qualitative variables, $p \leq 0.05$ was considered statistically significant.

Results: Mean age was 30.63±4.15 years in case group and 29.94±3.65 years in control group. Within each group (n=52), 16 were males whereas 36 were females (p=1.000). Serum ferritin levels were 18.82±4.47ng/ml in case group and 20.92±4.31ng/ml in control group (p=0.017). Frequency of low serum ferritin level was 63%(29) in case group and 37 %(17) in control group (p=0.029) with significant Odds Ratio of 2.596.

Conclusion: We concluded that there is significant association of alopecia areata and low serum ferritin levels and early detection and restoration of iron stores may potentially enhance the management of alopecia areata.

Keywords: Alopecia Areata, Serum ferritin levels, Iron deficiency

INTRODUCTION

Alopecia Areata is an autoimmune disorder characterized by temporary non-scarring hair loss, usually appearing in round patches[1]. The overall incidence of alopecia areata is estimated to be around 20.2 cases per 100,000 person-years[1]. In the general population, the lifetime risk of experiencing alopecia areata is approximately 2%[2]. There is 55% concordance rate among identical twins and genome-wide association studies have predominantly linked the HLA-DRB1 region to alopecia areata[1]. Although the prevalence of alopecia areata appears to rise linearly with age[3], in more than 80% of the patients the disease appears before 40 years of age[4]. The more severe variant typically manifests in early onset alopecia areata (between 5 and 10 years of age)[2]. No discernible sex preference is shown by the data[2]. Histological analysis reveals a distinctive pattern known as the "bee-swarm pattern," which shows dense lymphocytic infiltration surrounding the bulb of actively growing hair follicles[1]. Within the follicular epithelium are found CD8+T cells while CD4+T cells are present around the hair follicles[5]. The development of alopecia areata is believed to involve oxidative stress and imbalance between the increased production of free radicals and antioxidant defense mechanisms observed[6].

Levels of iron, cytokines, hormones and oxidative stress regulate the expression of ferritin. Ferritin also has different immunological activities such as suppression of antibody production by lymphocytes. Iron serves as a cofactor for the enzyme ribonucleotide reductase, which plays a crucial role in the rate-limiting step of DNA synthesis. Thus, a depletion of iron stores can disrupt the proper functioning of this enzyme and hinder cell

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proliferation. Furthermore, the inhibition of other iron-dependent enzymes, such as stearyl CoA desaturase found in human hair follicles, may also contribute to hair loss[7].

New insights have been introduced into the etiopathogenesis of Alopecia Areata, including genetics, immunology, oxidative stress, microbiome, allergy, microbiota, epigenetics, and other factors[8]. Various studies have been done to find an association of alopecia areata and decreased ferritin levels but they have yielded conflicting results. Devraj Y.et al. discovered that the severity of alopecia areata is affected by the levels of serum ferritin[6]. Gangaiah N, et al. revealed that iron plays a role in the physiological processes of the hair cycle, and disruptions in normal hair growth are suspected in cases of iron deficiency (ID)[9]. Meah N, et al. conducted a study to produce an international consensus statement on the utility of iron in treatments for Alopecia Areata[10].

Currently very limited data regarding this condition is available in our country. Therefore, the aim of our study was to evaluate the association of serum ferritin levels with alopecia areata in our local population and see the regional variations of this disease so that early detection and replacement of iron stores may help in the better management of this cosmetically disabling condition.

MATERIAL AND METHODS

It was a case control study conducted at Outpatient Department of Dermatology, Shalamar Hospital, Lahore from Feb 2022 to August 2022. Approval was obtained from Institutional Ethical Committee (IRBNo: 0509). Sample size of 104 was calculated with 5% level of significance and 80% power of test, using expected frequency of low serum ferritin levels by 65.2% in patients with Alopecia Areata as compared to 38% in patients without Alopecia areata[11]. Patients were enrolled in two groups through non-probability consecutive sampling, (52 in a group having alopecia areata and 52 in a group having age and gender matched healthy controls. Informed consent was taken. Inclusion criteria included patients of 15-50 years of age presenting with patches of non-scarring hair loss in the scalp or beard area and age and gender matched healthy controls. Exclusion criteria included patients taking supplements for last 3 months or known cases of anemia, those having any other form of alopecia, malabsorption syndromes, chronic skin and systemic diseases or malignancies, and those having major surgeries or blood transfusions in the last 3 months. Pregnant and lactating females were also excluded from the study. Patients underwent a thorough evaluation, which included a comprehensive assessment of their medical history and a detailed clinical examination. Basic demographic information such as age, gender, body mass index (BMI) and duration of alopecia areata were documented. Serum ferritin levels of all patients were estimated in the same laboratory to avoid bias. Data was collected for serum ferritin levels in ng/ml. Patients were considered to have low serum ferritin levels if their values were < 20ng/ml[8,21].

Data Analysis:

The data was analyzed using SPSS version 23.0. Frequencies and percentages were calculated for qualitative variables. Quantitative variables were presented as mean ± standard deviation (SD). The odds ratio (OR) was computed to assess the association between low serum ferritin levels and alopecia areata, with an OR greater than 01 indicating significance. Stratification was performed to evaluate the impact of different variables on serum ferritin levels. Post-stratification analysis using the chi-square test was applied to both groups, and a significance level of $p \leq 0.05$ was considered statistically significant.

RESULTS

In each group (n=52) there were 16 males (31%) and 36 females (69%). In the case group, 12 (23%) were married and 40 (77%) were unmarried whereas in control group 10 (19%) were married and 42 (81%) were unmarried. The mean age was calculated as 30.63 ± 4.15 years in case group and 29.94 ± 3.65 years in control group. The mean BMI was 25.00 ± 2.66 kg/m2 in case group and 26.05 ± 2.67kg/m2 in control group. The mean duration of alopecia areata was 9.36 ± 4.31 (Table-1). Mean Serum ferritin levels were 18.82 ± 4.47 ng/ml in case group and 20.92 ± 4.31 ng/ml in control group (p=0.017). Frequency of low serum ferritin level was 63.0% (29) in the case group and 37.0% (17) in the control group (p=0.029) with a significant Odds Ratio of 2.596 (Table-2). Stratification of serum ferritin levels with various variables showed hypo-ferritinemia was statistically significant in case group in unmarried people (p=0.04) and in age group of 15-30 years (p=0.046). However no statistically significant association was seen with respect of gender, BMI and duration of disease. (Table-3)

Sr #	Demographics	Cases	Controls
1	**Gender**		
	Males	16(31%)	16(31%)
	Females	36(69%)	36(69%)
	Total	52(100%)	52(100%)
2	**Marital Status**		
	Married	12(54.5%)	10(45.5%)
	Unmarried	40(48.8%)	42(51.2 %)
	Total	52(100%)	52(100%)
3	**Age Group**		
	15-30 years	31(47.0%)	35(53.0%)
	31-50 years	21(55.3%)	17(44.7 %)
	Total	52(100%)	52(100%)
4	**BMI** (Mean)	25.00±2.66	26.05±2.67

Table-1: Demographics of Cases and Controls

Low serum ferritin levels	Groups		Total	p-value
	Case group	Control group		
Yes	29(63.0%)	17(37.0%)	46(100.0%)	0.029
No	23(39.7%)	35(60.3 %)	58(100.0%)	
Total	52(50.0%)	52(50.0%)	104(100.0%)	

Table-2: Association of Low Serum Ferritin levels and Alopecia Areata

Odds ratio = 2.596

95% confidence interval = 1.170-5.760

Variable	Age group	Low serum ferritin levels	Groups		Total	p-value
			Case group	Control group		
Age Group years	15-30	Yes	18 (62.1%)	11 (37.9%)	29 (100.0%)	0.046 OR= 3.021
		No	13 (35.1%)	24 (64.9%)	37 (100.0%)	
	31-50	Yes	11 (64.7%)	6 (35.3%)	17 (100.0%)	0.342 OR= 2.017
		No	10 (47.6%)	11 (52.4%)	21 (100.0%)	
Marital Status	Married	Yes	7 (63.6%)	4 (36.4%)	11 (100.0%)	0.670 OR= 2.100
		No	5 (45.5%)	6 (54.5%)	11 (100.0%)	
	Un-Married	Yes	22 (62.9%)	13 (37.1%)	35 (100.0%)	0.044 OR= 2.726
		No	18 (38.3%)	29 (61.7%)	47 (100.0%)	
BMI Kg/m^2	17-25	Yes	15 (75.0%)	5 (25.0%)	20 (100.0%)	0.069 OR= 3.545
		No	11 (45.8%)	13 (54.2%)	24 100.0%)	
	>25k	Yes	14 (53.8%)	12 (46.2%)	26 (100.0%)	0.193 OR= 2.139
		No	12 (35.3%)	22 (64.7%)	34 (100.0%)	

Table-3: Stratification of both groups for low serum ferritin levels with respect to variables using chi-square test (odds ratio) (n=104)

DISCUSSION

Alopecia areata is a common problem, and observational data has produced contradictory outcomes regarding the possible association between alopecia areata and iron deficiency.

Extensive research is currently being conducted to determine the precise reason for alopecia areata. Immunological processes and genetic factors play a substantial role in the development of alopecia areata, and it is also believed that environmental factors add up to the initiation of this condition. Researchers are currently investigating the potential correlation between alopecia areata and iron deficiency, and multiple studies are underway to explore this connection[12]. In a study conducted by Olsen et al., a cutoff level of 15 ng/ml was established, and the outcomes indicated no significant disparity in the occurrence of iron deficiency between individuals with non-scarring hair loss[13]. However our current study revealed a positive association between low serum ferritin levels and alopecia areata. Most of the studies done have taken 20 ng/ml as the cut off value of low serum ferritin levels.

Within the case group, 63.0% (n=29) displayed low serum ferritin levels, while the control group had 37.0% (n=17) with low levels. This disparity was determined to be statistically significant, with a p-value of 0.029 and an odds ratio of 2.596. A significant difference (p=0.017) in the mean serum ferritin levels was seen in the cases and controls. In a study by Abdal jawad et al. similar results were reported concerning the link between low serum ferritin levels and alopecia areata[14]. Study conducted by Chishti et al. also demonstrated decreased serum ferritin levels among patients with non cicatricial alopecia[11]. A study done previously by Omer U et al. demonstrated the role of various micronutrients including iron deficiency in alopecia which showed a correlation between iron deficiency and hair loss[15]. A study conducted in Jammu Kashmir by Aejaz et al. aimed to investigate the iron levels in patients diagnosed with alopecia areata. However, the results didn't find any link between the two conditions[16].

In our study, the case group had a mean age of 30.63±4.15 years, while the control group had a mean age of 29.94±3.65 years. In the study conducted by Esfandiarpour I et al. the patients had an average age of 23.52 ± 14.42 years, while the controls had a mean age of 22.86 ± 13.03 years[12]. This may be attributed to the fact that in our population, patients tend to seek medical attention at a later stage, after trying various home remedies without success. A large meta-analysis done which included studies from countries all over the world also demonstrated a strong relationship between iron deficiency and non-scarring hair loss in women[17]. In our study we did not find any noteworthy difference in the serum ferritin levels between the males and females**.** In Saudi Arabia, Chishti et al. establish that women with alopecia areata had a higher occurrence of iron deficiency as compared to the general population[11]. However, the study by Esfandiarpour I et al. did not observe iron deficiency anemia in any of the male participants with alopecia areata[12]. Our findings were contrary to the findings of previous studies. Our region, being a developing country, faces the presence of numerous nutritional deficiencies.

In our study, the duration of ailment in the alopecia areata group was observed to be 9.36 ± 4.31 months. A separate study conducted by Goksin S. reported average disease duration of 18.1 months, with a significantly larger sample size as compared to our study[18]. The findings from our study provide additional evidence to support the hypothesis linking low serum ferritin levels with alopecia areata. Specifically, our observations suggest that the occurrence of alopecia areata is more likely to be triggered when serum ferritin levels drop below a certain threshold. Considering that low serum ferritin levels are primarily attributed to iron deficiency[19], it is reasonable to speculate that patients experiencing alopecia areata could potentially derive benefits from oral iron supplementation. Muhammad Fawad Aslam conducted a study aimed at investigating the connection between serum ferritin levels and non-scarring alopecia among females[20]. The analysis revealed that the individuals in the case group exhibited lower levels of hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and transferrin saturation compared to those in the control group. These differences suggest that the patients were experiencing a deficiency of iron. Additionally, the case group displayed a decrease in mean ferritin levels when compared to the control group. The results of our study offer further support for the theory that there is a link between low serum ferritin levels and alopecia areata. In our research, we defined low serum ferritin levels as those below 20 ng/mL, which is consistent with the lower limit of normal serum ferritin levels established in a study conducted by Muhammad Fawad et al[20]. His study also reported that the average serum ferritin level in the group with alopecia areata was 19.71 ± 18.56 mg/mL, and 65.2% of individuals in the case group had low serum ferritin[20]. These findings closely mirror the results obtained in our own study.

CONCLUSION

In our current study, we investigated the relationship between low serum ferritin levels and alopecia areata. The statistical analysis showed a significant association between low serum ferritin levels and alopecia areata, with a p-value of 0.029 and an odds ratio of 2.596. Hence iron deficiency may have a role in the pathogenesis of this condition. Early detection and correction may result in better outcome in its management.

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