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**Dermatology**

# Assessment of Serum Ferritin Levels in Patients with Alopecia Areata in Jordan

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| **Abstract** | | **Original Research Article** |
|---|---|---|

**Background:** Multiple studies have been conducted to look for a relationship between iron body storage and the development of conditions associated with hair loss such as alopecia areata (AA). However, their findings have not been consistent. Therefore, the main objective of this study is to evaluate serum ferritin levels amongst patients with alopecia areata in Jordan. **Methods:** This study looked into ferritin levels among alopecia areata patients and compared them with the controls. Diagnosis of alopecia areata was done clinically and the selected patients were investigated for serum ferritin and hemoglobin. **Results:** Amongst our study sample, which included 183 patients; 97 patients were in the alopecia areata group and 86 were in the control group. Out of the Alopecia Areata group, 62(63.9%) were males and 35(36.1%) were females with a mean age of 29.9 years. As for the control group, 45(52.3%) were males and 41(47.7%) were females with a mean age of 32.05 years. We drew the inference that the serum ferritin was significantly higher in the alopecia areata group. **Conclusion:** We concluded that the numerical value for serum ferritin was significantly higher in the alopecia areata group but was still within normal range.
**Keywords:** Alopecia, areata, Hair loss, ferritin, Iron, autoimmune disease.

# INTRODUCTION

Alopecia Areata is an autoimmune, recurring, unpredictable condition that is characterized by T lymphocyte hyperactivity against hair follicles during anaphase, which usually presents with well-circumscribed round patches of non-scarring hair loss [1]. The etiology of this disease is not clear, and many hypotheses have been proposed to explain it, mostly revealing the cause to be due to an exposure to an environmental trigger in genetically susceptible individuals [2].

This disease is common, with a 2% lifetime risk worldwide [3]. It can affect patients of any age and both genders, although some studies may suggest a slightly increased prevalence in females [4]. Alopecia areata is known to be associated with much physical and psychological comorbidity, such as increased incidence of other autoimmune diseases, iron deficiency anemia, vitamin D deficiency, depression, and anxiety, which makes this disease a heavy burden for patients [5].

Although it might remit without intervention, many treatment options are currently available for this condition; some of those treatments include topical corticosteroids and immunotherapy [6].

Ferritin, the main iron storage protein in the body, which plays an important role in iron homeostasis and many other functions and roles in malignancies, inflammation, infection, modulation of the immune response, and autoimmune diseases [7, 8], has also been linked to the growth of hair follicles. However, present literature has failed to provide conclusions on the association between ferritin levels and the development and progression of alopecia areata.

# METHODOLOGY

This is a multi-centric case-control study conducted at Jordanian Royal Medical Services out-patient dermatology clinics in Jordan, for a period of two years from January 2020 to January 2022. The hospitals included were King Hussein Medical Center, Prince Rashid bin Al-hasan Military Hospital in Irbid,

Prince Hashem bin Al-hussein Military Hospital in Zarqa, and king Talal bin Al-Hussein Military Hospital in Mafraq. This study was approved by the ethical board committee at Royal Medical Services, and a written informed consent was obtained from all patients. A total of 200 patients were recruited to participate in this study; 100 alopecia areata cases and 100 controls. The following parameters were obtained: age, gender, associated disease and treatment. Complete clinical examination was performed by specialists to detect the pattern of alopecia areata, extent and size of the patches, as well as involved sites and nail changes. The exclusion criteria included; autoimmune disorders, anemia, any chronic disease, pregnancy, iron supplementation, drug use and other diseases that could affect serum ferritin level. The control group included patients without any forms of hair loss that had presented to our outpatient dermatology clinics for other cutaneous disorders and the same exclusion criteria were applied. For all subjects, the following labs were obtained: serum ferritin level, hemoglobin (Hb) and hematocrit (Hct). Serum ferritin level was measured with the radioimmunoassay method and hemoglobin with hemocue hemoglobin analyser. Patients with Hb levels lower than the normal level for age were considered anemic. The serum ferritin levels were compared with those of the controls. The statistical analysis was carried out using IBM SPSS 23 edition.

The following analyses were made; Arithmetic mean, standard deviation, standard error, and Student's "t" Test. One-sided p-values were obtained with the traditional cut-off point of p<.05.

## RESULTS

A total of 183 patients were included in this study; 97 patients in the alopecia areata group and 86 in the control group as summarized in (figure 1). Out of the Alopecia Areata group, 62(63.9%) were males and 35(36.1%) were females with a mean age of 29.9 years. As for the control group, 45(52.3%) were males and 41(47.7%) were females with a mean age of 32.05 years as summarized in table (1). The duration of hair loss ranged from 5 days to 125 months. The onset of disease was sudden in 60 (61.9%), slowly progressive in 26(26.8%), and rapidly progressive in 11(11.3%) patients. 45(46.4%) of the patients had recurrent lesions, and nail involvement was reported in 9 (9.3%) patients. The scalp was the most affected site, followed by the face as summarized in table 2. Serum ferritin levels were within normal range in both groups despite the statistical difference between the two mean values (44.1 vs 35.2, p .037). However, hemoglobin levels did not show any significant difference between the two groups.

**Table 1: Demographic Charictaristics**

| | AA group | control | P value |
|---|---|---|---|
| gender | | | .133 |
| Male | 62(63.9%) | 45(52.3%) | |
| female | 35(36.1%) | 41(47.7%) | |
| Age mean (SD) | 29.9(9.6) | 32.05(13.6) | .222 |
| Serum ferritin Mean (SD) | 44.1(29.09) | 35.2(28.23044) | .037 |
| Hemoglobin (Hb) | 13.5 | 13.4 | .994 |

**Table 2: The Involvement Sites of Alopecia Areata**

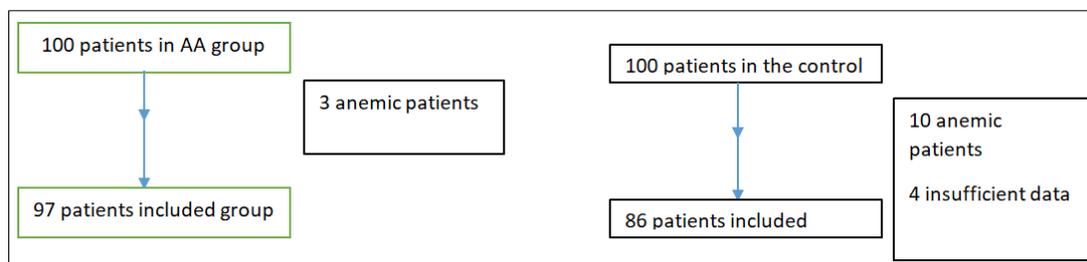| Scalp | 48(49.5%) |
|---|---|
| Face | 21(21.6%) |
| Scalp and face | 28(28.9%) |



**Figure 1: flow charts for patients included and execcluded from the study**

## DISCUSSION

Alopecia areata is the second most common type of non-scarring hair loss in humans. It is regarded as an autoimmune disease with a variable course; typically, relapsing or remitting, but can be persistent. AA hair loss usually presents in small annular or patchy lesions (patchy AA), commonly on the scalp, that could progress to loss of all scalp hair (alopecia totalis), and even loss of all body hair (alopecia universalis). Many hypotheses on the causes of AA have been proposed, for example; thallium acetate poisoning, infection, trophoneurotic hypothesis, thyroid, and hormonal

fluctuations. Leukocyte-mediated inflammation of the hair follicles, along with several immune-related and several key pathogenetic factors have been linked to AA development since the late 1950s [9-11].

Ferritin is the unique and conserved method that animals use to control the use of iron. It is believed to be controlled by dual, genetic DNA and mRNA sequences in response to iron or oxidant signals and links ferritin to proteins of iron, Oxygen, and antioxidant metabolism [12-14]. Elevated ferritin level is associated with inflammation, infection, and many autoimmune diseases such as Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE), and Multiple sclerosis (MS) [7]. However, there is conflicting data from observational studies regarding alopecia and iron level, especially in females. Pradhan *et al.,* [15], Kantor *et al.,* [16], and Rushton *et al.,* [17]; reported significantly lower serum ferritin in females with AA and androgenic alopecia than in controls, but these levels were still within normal range. In our study, Serum ferritin was found to be higher in the patients' group compared to controls; 44.1 vs 35.2, p = .037. This variation may be related to the difference in the proportion of males and females between cases and controls. Esfandiarpour *et al.,* [18], also found a higher mean of serum ferritin level in AA patients but the findings were not statistically significant. When we analyze females only, there is no statistically significant difference between patients and controls 26.7 vs 26.9, p =.955. Furthermore, males had a higher statistically significant level of ferritin in AA patients than in the control group, 53.9 vs 42.7 p-value =.057. Similar findings were reached by Wani *et al.,* [19], Boffa *et al.,* [20], Esfandiarpour *et al.,* [18], Mussalo *et al.,* [21], and White *et al.,* [22]. They concluded that females with AA had a high risk for the development of iron deficiency in comparison with the general population and suggested that serum ferritin and iron studies should be included in the work-up of the disease. In the White *et al.,* study, none of the men had IDA. These conflicting findings may be a result of the small sample size in each study. Therefore, larger studies are needed to find a true association between the level of ferritin and iron, and AA.

**Study Limitations**

The study limitations include no matching between cases and controls, as well as ferritin levels being measured at a single time point regardless of the onset of AA. To draw accurate conclusions, we recommend measuring serum ferritin at different time points during the course of the disease.

# CONCLUSION

Our findings suggest that there is no clinical association between low ferritin levels and AA. This conclusion goes well in concordance with the nature of AA as an autoimmune disease.

**Author Contribution**

This work was carried out in collaboration between all authors. Authors AlSaleem, Obeidat, Daise and Almashagbeh designed the study. Authors Alsaleem and Alhadidi managed data collection. Authors Obeidat and Daise managed the statistical analysis. Authors Obeidat, AL-Nusair, Warawreh and Daise managed the literature searches, and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

**CONFLICT OF INTEREST STATEMENT**

No conflict of interest to declare.

**DATA SHARING STATEMENT**

Not applicable.

**INFORMED CONSENT STATEMENT**

Not applicable.

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