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ORIGINAL ARTICLE

Serum Ferritin Levels amongst Individuals with Androgenetic Alopecia in Ile-Ife, Nigeria

Taux de Ferritine Sérique chez les Personnes Atteintes d'Alopécie Androgénétique à Ile-Ife, au Nigeria

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ABSTRACT

BACKGROUND: Androgenetic alopecia (AGA) is the most common form of alopecia, affecting 50% of the adult population world-wide. The exact mechanisms of this common hair disorder are yet to be fully elucidated. It is believed to be related to high circulating androgen levels in the blood and it is genetically determined. Deficiencies of micronutrients such as iron in the development of AGA have been a subject of debate.

OBJECTIVE: This study sought to determine the association between serum ferritin levels and androgenetic alopecia among patients attending the Dermatology clinic at a tertiary health facility in South-Western Nigeria.

METHODS: This was a hospital based cross sectional study with a total of 114 participants, which consisted of 57 subjects with AGA and 57 age and sex-matched healthy adults without AGA who met the inclusion criteria. The diagnosis of AGA was made clinically and with the aid of a Dermatoscope (Wi-Fi Digital Microscope RoHS YPC_X03 V2018, HD Colour CMOS sensor with 50X-1000X magnification and HD resolution 1920x1080P).

RESULTS: The mean age of the study participants was 41.68 ± 12.86 years with age ranging from 24 to 80 years. The mean serum ferritin levels among the subjects and control group were 188.65 ± 97.92ng/ml and 194.49 ± 76.67ng/ml respectively but this difference was not statistically significant (p = 0.724). However, subjects with premature AGA had a significantly lower serum ferritin level compared to those with adult-onset AGA (p = 0.020).

CONCLUSION: Iron deficiency is known to cause quantitative defect in haemoglobin production, limiting the amount of oxygen transported for hair growth and this, in addition to genetic factors, may explain why individuals with premature AGA have a significantly low serum ferritin levels. **WAJM 2022; 39(10): 1026–1031.**

Keywords: Androgenetic alopecia, Pattern hair loss, Micronutrients, Iron, Ferritin, Nigeria.

RÉSUMÉ

CONTEXTE: L'alopécie androgénétique (AGA) est la forme la plus courante d'alopécie, affectant 50% de la population adulte dans le monde. Les mécanismes exacts de ce trouble capillaire commun n'ont pas encore été entièrement élucidés. On pense qu'il est lié à des taux élevés d'androgènes circulants dans le sang et qu'il est génétiquement déterminé. Les carences en micronutriments tels que le fer dans le développement de l'AGA ont fait l'objet de débats.

OBJECTIF: Cette étude a cherché à déterminer l'association entre les niveaux de ferritine sérique et l'alopécie androgénétique chez les patients fréquentant la clinique de dermatologie d'un établissement de santé tertiaire du sud-ouest du Nigeria.

MÉTHODES: Il s'agissait d'une étude transversale en milieu hospitalier avec un total de 114 participants, dont 57 sujets atteints d'AGA et 57 adultes en bonne santé, appariés selon l'âge et le sexe, sans AGA, qui répondaient aux critères d'inclusion. Le diagnostic de l'AGA a été établi cliniquement et à l'aide d'un dermatoscope (microscope numérique Wi-Fi RoHS YPC_X03 V2018, capteur CMOS couleur HD avec un grossissement de 50X-1000X et une résolution HD 1920x1080P).

RÉSULTATS: L'âge moyen des participants à l'étude était de 41,68 ± 12,86 ans avec un âge allant de 24 à 80 ans. Les taux moyens de ferritine sérique chez les sujets et le groupe témoin étaient respectivement de 188,65 ± 97,92ng/ml et 194,49 ± 76,67ng/ml mais cette différence n'était pas statistiquement significative (p = 0,724). Cependant, les sujets atteints d'AGA prématurée avaient un taux de ferritine sérique significativement plus bas que ceux atteints d'AGA à l'âge adulte (p = 0,020).

CONCLUSION: La carence en fer est connue pour provoquer un défaut quantitatif dans la production d'hémoglobine, limitant la quantité d'oxygène transportée pour la croissance des cheveux et ceci, en plus des facteurs génétiques, peut expliquer pourquoi les individus atteints d'AGA prématuré ont un taux de ferritine sérique significativement bas. **WAJM 2022; 39(10): 1026–1031.**

Mots clés: Alopécie androgénétique, chute de cheveux, micronutriments, fer, ferritine, Nigeria.

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Abbreviations: AGA, Androgenetic alopecia

INTRODUCTION

Androgenetic alopecia is a common hair disorder with a global prevalence of 50% among adult men and perhaps as many women worldwide.[1,2] Locally, AGA has a prevalence of 29.95% among the adult population in the South-Western Nigeria and a prevalence of 65% among the male adults in Northern Nigeria.[3,4] It is a genetically determined, hormone dependent form of alopecia and many studies have investigated a causal relationship between AGA and genetics[5-13] Two genetic risk loci for androgenetic alopecia have been identified: the X-chromosomal AR/EDA2R locus and the PAX1/FOXA2 locus on chromosome 20.[14] A German genome-wide association study compared more than 1,100 severely affected cases of androgenetic alopecia and controls (581 cases of severe AGA and 617 controls) and the study revealed that *HDAC9* is the third androgenetic alopecia susceptibility gene, apart from the two genetic loci (X-chromosomal AR/EDA2R locus and the PAX1/FOXA2) mentioned earlier.[14,15] The findings by this German study was further subjected to fine-mapping and a similar result was obtained in an Australian study.[15] Additionally, dihydrotestosterone (DHT), chronic micro inflammation and the induction of oxidative stress have been implicated in the development of androgenetic alopecia.[16] These factors cause gradual conversion of terminal hairs into vellus hairs in a highly reproducible pattern which eventually results into baldness.[16] The exact role of iron in hair growth is poorly understood. However, thinning of hair and hair loss have been found in iron deficiency states.[17] An explanation given for hair loss in iron deficiency is the quantitative defect in haemoglobin production, limiting the amount of oxygen transported for growth and repair of body cells, including those that stimulate hair growth.[18] A number of studies[19–24] have implicated iron deficiency in the development of AGA. However, few other studies[25–27] did not find any relationship between iron status and AGA. Androgenetic alopecia is considered premature if it develops before 30 years of age and reaches at least Hamilton-Norwood class III.[28]

Considering the significant burden of AGA locally and globally, universally accessible and affordable treatment options are necessary, especially in resource poor settings like Nigeria, where expensive treatment options such as hair transplant with hormonal therapy may be unaffordable and/or unavailable. Studies on serum ferritin and AGA have been conducted among the Caucasians and Asians with varying outcomes.[19,23,25,27] Many researchers in Nigeria have looked into the prevalence and patterns of hair disorders and alopecia generally among different populations and age groups.[3,4,29] However, there is paucity of data on serum ferritin and AGA in this environment. This study therefore sought to determine the serum ferritin levels among subjects with AGA as well as the association between serum ferritin and AGA.

SUBJECTS, MATERIALS AND METHODS

This was a hospital based cross-sectional study conducted on fifty-seven (57) adults with androgenetic alopecia at the Dermatology clinic of Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile Ife, Nigeria. The control group comprised fifty-seven (57) apparently healthy age- and sex-matched adults without AGA. Individuals with other forms of alopecia other than androgenetic type and those who have had iron therapy, blood transfusion or donation in the preceding six months; as well as those with medical conditions that affect body iron status (e.g., haemoglobinopathy, bleeding disorders, pregnancy and lactation, recent gastrointestinal surgery, sepsis, chronic diseases such as chronic kidney disease etc.) were excluded from the study. Ethical clearance was obtained from the Ethics and Research committee of the institution. Non-probability sampling technique was used in the selection of subjects, in which consenting patients meeting the inclusion criteria were consecutively recruited from the Dermatology outpatient clinic. Following the recruitment of subjects with AGA, healthy volunteers for the control group were then recruited using selective or purposeful sampling technique. The controls were selected based on their age and gender in order to match the cases. A proforma was used to obtain information such as the socio-demographic data and history related to AGA, including duration of baldness, family history of baldness etc. Clinical examination was done and features of hyperandrogenism such as seborrhoea, acne, excessive body hairs and hirsutism were specifically looked out for and documented. Androgenetic alopecia was graded using the Hamilton-Norwood classification for male pattern hair loss (Type I, II, IIa, III, IIIa, IV, IVa, V, Va, VI, VII) and the Ludwig classification (Type I, II, III) for female pattern hair loss. Trichoscopy was carried out using a Wireless Digital Microscope (RoHS YPC_X03 V2018, HD Colour CMOS sensor with 50X-1000X magnification and HD resolution 1920x1080P) on all the study participants to reinforce the diagnosis of AGA, using a combination of parameters such as hair shaft heterogeneity, focal atrichia, increased interfollicular distance, perifollicular pigmentation, multi-hair follicular unit etc., and exclude possible differential diagnoses of non-scarring vertex alopecia such as seborrheic dermatitis of the scalp. Blood samples were taken and analysed for serum ferritin, liver function test, peripheral blood film, genotype, retroviral screening, random blood glucose, electrolytes, urea and creatinine to exclude medical conditions that can influence iron status. Serum ferritin levels $\geq$70ng/ml was considered normal, ferritin levels from 30 to 69ng/ml were considered low and ferritin levels below 30ng/ml were considered very low. The data obtained was analyzed with IBM Statistical Package for Social Sciences (IBM SPSS Statistics) version 25 software with level of statistical significance set at 0.05.

RESULTS

The study comprised a total of 114 participants divided into two groups. The first group consisted of 57 adults with AGA, referred to as subjects, and the second group, regarded as control, consisted of 57 age and sex-matched adults without AGA. The age of the study participants ranged from 24 to 80 years,

with a mean age of 41.68 ± 12.86 years for both groups. The majority of the study participants (35.1%; N= 20) were in their fourth decade of life. All the three female subjects had Ludwig class II (moderate) AGA (Figure 1) but the 54 male subjects had AGA ranging from class III to VII using the Hamilton-Norwood system (Figures 2 to 4). The AGA class III had the highest frequency, accounting for 24 (44.4%) of the subjects followed by AGA class IV (29.6%; N= 16). There was only one case of AGA class VII (1.9%). Male pattern hair loss (MPHL) was sub-divided into mild (Hamilton-Norwood class I to III), moderate (Hamilton-Norwood class IV and V) and severe (Hamilton-Norwood class VI and VII).

As shown in Table 1 below, the lowest serum ferritin levels among subjects with AGA was 10.53ng/ml and the maximum was 379.74ng/ml, while their mean ± SD serum ferritin was 188.65 ± 97.92ng/ml. On the other hand, the control group had mean ± SD serum ferritin of 194.49 ± 76.67ng/ml (Table 2), with minimum and maximum values of 89.11ng/ml and 380.14ng/ml, respectively (Table 1). All the 57 participants in the control group had normal serum ferritin levels (serum ferritin ≥70ng/ml), while 53 (93%) of the subjects had their serum ferritin levels within the normal range. Serum ferritin levels were reduced in 4 participants (7%): low in two (3.5%) of the subjects (both male) and very low in another two (one male and one female), as shown in Table 1.

There was no statistically significant difference in the serum ferritin levels of the subjects and the control group (p = 0.724), as shown in Table 2. The serum ferritin levels among the study participants were further analyzed according to gender and mean age but no significant difference was found. Similarly, there was no significant difference in the serum ferritin levels among the subjects based on AGA duration, family history of AGA, features of hyperandrogenism (such as seborrhoea, acne, and excessive body hairs and hirsutism) and the severity of MPHL. However, premature AGA (AGA onset before 30 years of age) was significantly associated with lower ferritin level compared to the adult-onset AGA (AGA onset at 30 years and above), t = –2.387, p = 0.020 as shown in Table 2. Low serum ferritin weakly predicted AGA (Odd's Ratio = 1.002) but the odds of having AGA was 9.994 with a positive family history of AGA. The male gender was 1.4 times more likely to develop AGA than the female gender and age increased AGA's risk by 1.5 folds (Table 3).

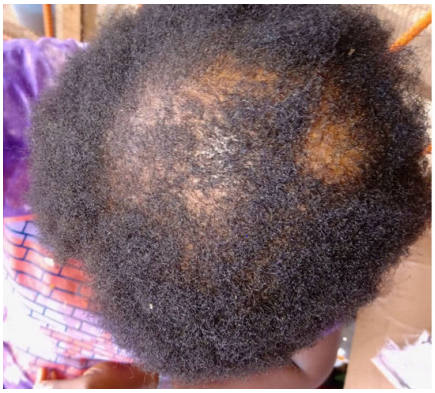

Figure 1: Ludwig Class II FPHL

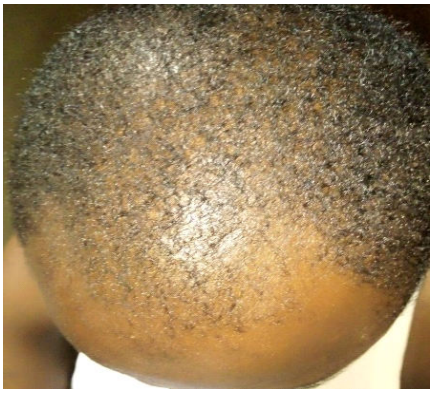

Fig. 2: Hamilton-Norwood Class III MPHL

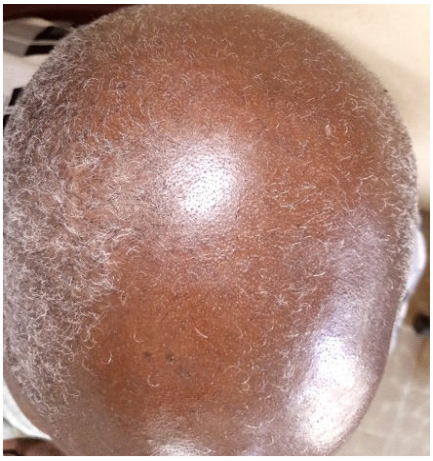

Fig. 3: Hamilton-Norwood Class VI MPHL

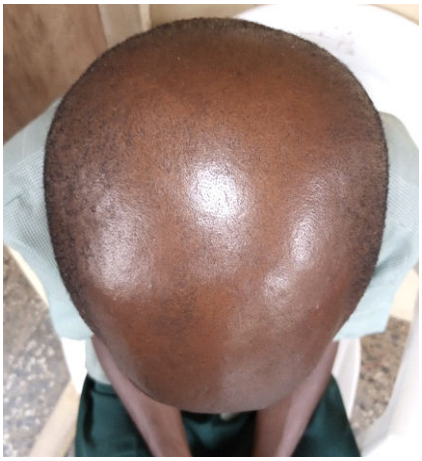

Fig. 4: Hamilton-Norwood Class VII MPHL

FPHL, Female Pattern Hair Loss; MPHL, Male Pattern Hair Loss

Table 1: Serum Ferritin Levels among the Study Participants

	Subjects		Controls	
Serum Ferritin (ng/ml)	Male N=54(%)	Female N=3(%)	Male N=54(%)	Female N=3(%)
Minimum	10.53	16.36	89.11	102.35
Maximum	379.74	373.61	342.69	380.14
Mean ± SD	189.94 ± 93.79	106.38(16.4–373.6)*	193.91 ± 72.98	132.14(102.4–380.1)*
Normal (≥70)	51(94.4)	2(66.7)	54(100)	3(100)
Low (30–69)	2(3.7)	0(0)	0(0)	0(0)
Very low (<30)	1(1.9)	1(33.3)	0(0)	0(0)

*SD, Standard Deviation; N, Number; *, median (IQR).*

DISCUSSION

The mean age obtained for the male participants (41.33±11.91 years) was similar to the finding by Park, *et al*[20] and Han, *et al*[30] both in Korea. However, the mean age of the female patients in this study was slightly higher than the mean ages reported in many other studies for female pattern hair loss (FPHL).[20–22,25] This

Table 2: Association between Serum Ferritin and AGA

Variables	Mean Serum Ferritin ± SD (ng/ml)		Statistics	
	Subjects	Controls	Student's t-test	p-value
All the patients (N=57)	188.65±97.92	194.49±76.67	–0.354	0.724
Male (N=54)	189.94±93.79	193.91±72.98	–0.246	0.806
Female (N=3)	106.38(16.36–373.61)*	132.14(102.35–380.14)*	–0.655**	0.513
Mean age (years)				
Below 42	124.45±76.99	177.19±74.64	–1.555	0.137
42 and above	194.95±89.90	171.09±73.16	0.363	0.920
AGA duration (years)				
Below 11 (N=39)	182.89±93.32			
11 and above (N=18)	201.14±108.99		–0.651	0.518
Premature AGA versus Adult-Onset AGA				
Before 30 years (Premature)	169.27±88.07			
Adult-onset (≥30 years)	234.26±107.27		–2.387	0.020
Family history of AGA				
Yes (N=44)	195.16±101.76			
No (N=13)	166.60±83.43		–0.923	0.360
Features of Hyperandrogenism				
Yes (N=24)	192.73±87.52			
No (N=33)	185.68±106.08		–0.266	0.791
Severity of MPHL				
Mild (N=26)	176.54±83.93			
Moderate (N=24)	192.29±97.45		1.513***	0.230
Severe (N=4)	262.92±123.25			

*SD, Standard Deviation; N, Number; vs, versus; MPHL, Male pattern hair loss; *, Median (IQR); **, Mann-Whitney U test; ***, One-way analysis of variance (ANOVA).*

Table 3: Logistic Regression Analysis of Predictive Factors of AGA

Variable	Exp (B)	95% C.I for Exp (B)	p-value
Family history of AGA	9.994	4.038 – 24.734	0.001*
Features of hyperandrogenism	3.652	1.322 – 10.090	0.012*
Age	1.521	0.949 – 1.027	0.534
Gender	1.426	0.200 – 10.190	0.723
Serum ferritin	1.002	0.997 – 1.008	0.413

*AGA, Androgenetic Alopecia; *, Statistically significant.*

difference may be as a result of genetic factors and low number of female patients in this study, while the other studies were carried out on female patients only. The lower mean age obtained in this study may have been due to the fact that young and middle-aged patients are more likely to visit a Dermatologist, out of concern for their looks and may be able to afford treatment, when compared to the older age group who are sometimes less bothered, or are dependent on families and relations for finances and support. This can also explain the low number of elderly participants in the study. Additionally, AGA usually starts during young adulthood and some patients will likely present within few months or years of onset.[31]

The male gender constituted the bulk of the subjects while the female gender accounted for 5.3% of the study population. This is in contrast to the report by Park, *et al*[20] where females accounted for more than half of the patients in their study on pattern hair loss. However, majority of patients (67.4%) with androgenetic alopecia in the study by Yoo, *et al* in Korea were males.[32] Most of the other studies on alopecia are however gender based and a number of others focused on more than one type of alopecia.[22,19,21,33,34] The low number of females in this study is majorly due to the fact that many females seen at the Dermatologic clinic with hair loss during this study had other forms of alopecia, especially traction alopecia, either alone or in combination with FPHL and were excluded from the study. Also, it has been documented that AGA affects men more than women possibly due to higher androgen levels in men.[14]

Most other studies focused on FPHL and the mean serum ferritin level obtained in this study among the female patients with AGA is 3 to7 times higher than the findings among women with AGA in other parts of the world. Rasheed, *et al*[22] in Egypt and Bregy, *et al*[25] in Switzerland[25] reported lower mean serum ferritin levels for FPHL just like Kantor, *et al,*[19] Olsen, *et al*[23] and Rushton, *et al*[24] in the United States of America (USA). Among the Asian population with FPHL, Park, *et al*[20] in Korea reported mean serum ferritin level of 49.27±55.8ng/ml and Raichur, *et al*[21] in India reported a lower value of 36.64ng/ml. The high but normal serum ferritin values found in this study among patients with AGA may be due to racial and nutritional differences. For instance, Pan, *et al*[35] in the United States of America corroborated the existing reports of consistently higher serum ferritin levels among Blacks, despite their lower haemoglobin (Hb) concentrations, compared with Whites. They attributed this difference in serum ferritin levels between the Black and the Whites race to factors such as the overall nutrition and health, iron status, and the hepatic well-being.

This study found a significantly lower serum ferritin level among the subjects with premature AGA compared to those with adult-onset AGA (p = 0.020). While studies have established several hormonal abnormalities in individuals with premature AGA (increased luteinizing hormone,

dehydroepiandrosterone and total testosterone with reduced follicle stimulating hormone and sex hormone binding globulin),[28,36,37] there is paucity of data on the role of iron in the development of premature AGA and this deserves a close attention. Iron, along with other nutrients like vitamin D, selenium and zinc, play an important role in the normal hair follicular cycle[38,39] and its deficiency can, possibly, trigger hair loss in a genetically susceptible individual. Sanke, *et al* studied serum vitamin D in premature AGA and found significantly reduced vitamin D levels in the subjects, with a correlation between vitamin D deficiency and severity of male pattern hair loss (MPHL).[40]

Overall, there was no statistically significant difference in the serum ferritin levels between the subjects and the controls (T-Test= –0.354, P = 0.724). This outcome is similar to the finding by Bregy, *et al*[25] who, in their study titled 'No Association between Serum Ferritin Levels >10 g/l and Hair Loss Activity in Women' in Switzerland, found no correlation between serum ferritin and FPHL, diffuse telogen effluvium (TE) or both FPHL and TE (P > 0.05). Sinclair, *et al*[26] in Australia found low iron store in only 6% of patients with AGA and there was no cessation or reversal of hair loss in any of the patients with AGA following correction of iron deficiency over a period of 3 to 6 months. This finding of no association between serum ferritin and AGA was also reported by Aydingoz, *et al*[27] in Turkey in their study on tissue iron status and female alopecia (P= 0.610).

CONCLUSION

Androgenetic alopecia is a common hair disorder in the South-Western part of Nigeria. There was no significant difference in the overall serum ferritin levels among subjects with AGA compared to the age and sex-matched healthy adults without AGA. However, subjects with premature AGA have significantly lower serum ferritin levels compared to those with adult-onset AGA.

Conflict of Interest

None.

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