Assessment of Serum Vit D and Serum Ferritin in Female Pattern Androgenic Alopecia

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Abstract

Introduction: Androgenic Alopecia (AGA) is a non-scarring alopecia that affects both men and women. It is characterized by a progressive miniaturization of hair follicles with a characteristic pattern distribution in genetically predisposed men and women.

Aim of the study: To assess the level of serum ferritin and vit D3 in female pattern of androgenic alopecia.

Patients and method: A prospective case control study carried out at Department of Dermatology in Baladgeneral hospital, Iraq at the period from the first of January 2019 to the end of Dec 2019.

Results: serum vit D3 for patients was (22.8 ± 11.5) in case group and (34.4±5.7) in control group, while for S. ferritin was (35.7±5.0) in control group and (44.8±7.3) in control group. Vit D3 deficiency (<20 mg/dl) were found in 68% of patients while 30% with vit D3 insufficiency.

In three grades of severity, it was found that vit D3 level in grade I was (24.2±6.9), in grade II (20.7±7.2), and in III (18.9±9.2). While for ferritin was (37.4±10.8) in grade I, (30.7±9.4) in grade II, and (25.9±12.1) in grade III.

No significant differences were found between the three grades groups regarding serum vitamine D3, while significant difference present among S. ferritin. The sensitivity of the vit D3 test to predict the disease were (90.9%), the specificity was excellent (95.1%), while for ferritin the sensitivity was (88.3%), the specificity was (89.0%).

Conclusion: Serum Vit D3 and Ferritin concentrations were significantly decrease in female with androgenic alopecia.

Keyword: *Androgenic Alopecia, Vit D, Ferritin, Female pattern, Non scarring alopecia.*

Introduction

Definition: Androgenic Alopecia (AGA) is a non-scarring alopecia that affects both men and women. It is characterized by a progressive miniaturization of hair follicles with a characteristic pattern distribution in genetically predisposed men and women. Is the most frequent type of hair loss in both sexes.[(1)]

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Epidemiology: The onset of AGA is usually gradual and the condition slowly develops over the years. The frequency and severity of this type of hair loss increases with age [(4)]. It usually appears in the third and fourth decades and affects 30% to 50% of men by the age of 50 and around 80% of Caucasian men aged over 70 years.[(2)]

The prevalence of AGA is different between populations; among Asian, native American, and many men of African heritage is lower than that among Caucasians with a decreased frequency of frontal hair loss and less extensive hair loss.[(3)]

Although AGA is more frequent in adults, it can also appear in adolescents, though its prevalence among this younger population is not well-established.[4] On an average, adolescent AGA onset starts after puberty between 13.5 and 15 years of age.[5] Although it is not expected to see AGA in pre-pubertal patients without androgen levels. Tosti, et al, reported 20 pre-pubertal children with AGA with a very early onset age between 6 and 10 years. According to the authors, all patients had a strong genetic predisposition to the disease with a strong family history and the Dihydrotestosterone-Sulfatase (DHEA-S) levels were consistent with post-adrenarche, but none of them was affected by premature puberty, as demonstrated by physical and laboratory assessments. [6] In adolescents with a genetic predisposition, the first signs of AGA usually appear with rising androgens at puberty.[7]

Classification of AGA:

There are several classifications that help to determine the degree of androgenic alopecia for male and female patients. This allows staging the degree of alopecia at the time of diagnosis and control the evolution and response to the treatment. For male pattern hair loss, the classification widely used is: [1]

- **Hamilton-Norwood Classification**: the most widely classification used for MPHL.[8] There are seven stages of evolution, involving the fronto-temporal area and evolution of hair loss to the vertex. There is absence of frontal hairline, however, in some cases; men develop diffuse thinning of the crown with retention of frontal hairline that resembles a female pattern observed in Ludwig Classification.

For female pattern hair loss, the most common classifications are:

- **Ludwig's Classification**: divided into three progressive stages based on hair density: I - minimal alopecia; II - Moderated alopecia and III - severe alopecia.[9]

- **Ebling's Classification**: includes a five-stage classification system for FAGA. The first two stages are the same as the Ludwisystem. Type III includes the diffuse hair loss and the initial loss of hair from the fronto-temporal hair line; Type IV besides the diffuse loss there's evidence of fronto-temporal recession; type V, appears like the male pattern of baldness (MPHL) with a there is complete loss of hair on the top of the scalp.[10]

- **Olsen's Classification:** classification proposed by Olsen with 3 degrees of severity. The main characteristic of this classification is the "christmas tree" distribution, with a frontal accentuation in a triangular [11].

- **Savin Scale:** a recent classification scale of 8 levels similar to Hamilton–Norwood's classification with frontal and lateral views of the hair loss patterns, that uses a computer analysis based in "the density of hair by unit of area" [12].

Female AGA:

Clinical Features

FAGA may have three different patterns [13]:

1. diffuse thinning of the crown region with preservation of the frontal hairline: two scales are used to describe this pattern: the commonly 3-point Ludwig scale (Figure 1) and the 5-point Sinclair scale (Figure 2);

Figure 1: Ludwig pattern of hair loss in women. Three-point scale. Diffuse thinning of the crown region with preservation of the frontal hairline. Drawing by Thierry Huart based on Ludwig et al.

Figure 2: Sinclair scale: 5-point scale for grading of FPHL with diffuse thinning of the crown region with preservation of the frontal hairline. Drawing by Thierry Huart based on the Sinclair Scale, Sinclair et al.

2. thinning and widening of the central part of the scalp with breach of frontal hairline, described by Olsen scale: Christmas tree pattern (Figure 3);

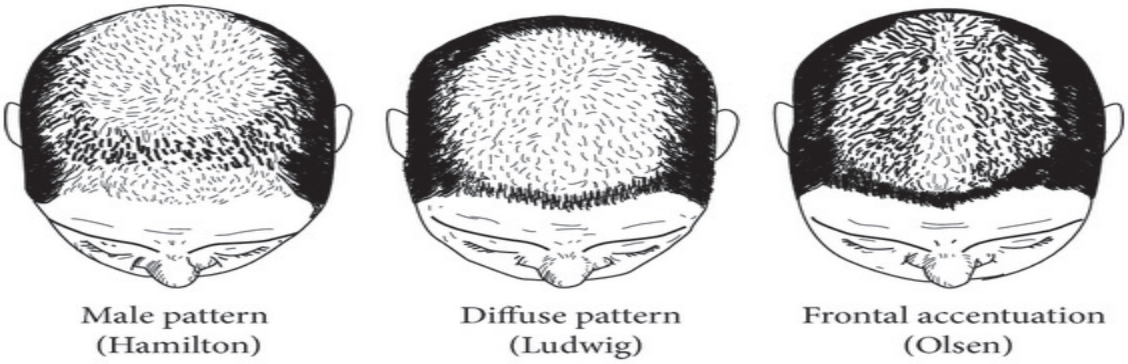

Figure 3: Olsen scale: Christmas tree pattern in female pattern hair loss. Thinning associated with bitemporal recession. Drawing by Thierry Huart based on Olsen scale,

3. Thinning associated with bitemporal recession; Hamilton-Norwood scale.[13]

All these common patterns spare the occipital area, a phenomenon explained probably by hormonal influences explained above. This behavior's difference between the frontal/parietal follicles and the occipital follicles is found in other hair disorders like alopecia areata, a condition where occipital follicles affected by the ophiasis pattern are typically more resistant to regrowth.[14] These differences may result from the embryological derivation of the dermis in the two regions. It is known from avian embryology that the dermis of the frontal/parietal scalp is of neural crest origin, whereas the dermis of the occipital scalp is of mesodermal origin.[15]

Vitamin D

Vitamin D is a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects.[16] In humans, the most important compounds in this group are vitamin D3 (also known as cholecalciferol) and vitamin D2 (ergocalciferol).[17]

Role of Vitamin D in Female Pattern Androgenic Alopecia

Female pattern Androgenic Alopecia (FPAGA) is one of the most common types of alopecia in women. Clinically, it is characterized by diffuse hair shedding with maintained frontal hairline.[18] Recent literature data include genetic, hormonal, and environmental factors in the pathogenesis of FAGA.[2] The possible link between serum 25-hydroxyvitamin D and FAGA has been suggested since its decreased concentration was demonstrated in patients with FAGA compared to control group [19, 20].

Moneib et al. reported a significantly lower serum 25(OH)D levels in patients with FAGA than in controls. The majority of patients with FAGA (96.6%) showed a vitamin D deficiency or insufficiency. Sufficient levels were observed only in 3.3% of patients. There was no significant difference between different serum 25(OH) D levels and mean disease duration or patients' age; however, a significant difference between the severity of hair loss and mean serum 25(OH)D concentration was observed. The authors suggested that the higher serum 25(OH)D concentration in patients with most severe hair loss in comparison with less severe alopecia may result from increased exposure to ultraviolet light due to more decreased scalp hair density.[20]

Contrary to this, in another study, patients with mild and moderate FAGA had significantly higher mean serum levels of 25(OH) D compared to those suffering from the severe form.[21] It cannot be excluded that conflicting results observed in both studies were determined by different patterns of sun exposure and evaluation of serum 25(OH) D level in different parts of the year. It has also been pointed out that women with positive family history of FAGA and vitamin D deficiency or insufficiency are more prone to develop FAGA in comparison with women with sufficient serum 25(OH)D levels. Contrary to this, Banihashemi et al. did not find any significant correlation between serum 25(OH)D concentration and positive family history of FAGA.[19-21]

Serum ferritin

Ferritin is present in most tissues as a cytosolic protein, although a mitochondrial form has recently been described and nuclear localization and functions have been proposed. Ferritin plays an important role in the storage of intracellular iron. Ferritin is a 24-subunit protein that is composed of two types of subunits, termed H and L. H refers to the original isolation of isoforms of ferritin from human heart, which are rich in the H subunit, or to its electrophoretic migration as the heavier of the two subunits. L refers to ferritin isolated from human liver, which is rich in a lighter subunit. [22]

Role of serum ferritin in female AGA:

Iron is the most abundant trace element in humans. It mediates chemical reactions that are critical for life, forming part of the enzymes implicated in DNA synthesis and cell respiration. An earlier study demonstrated that the mean ferritin level in patients with AGA was significantly lower than that in normal individuals without hair loss.[23]

It is often believed that the trace element content of hair reflects the total body trace element status and the extent of environmental or occupational exposure. Furthermore, serum levels of trace elements may vary depending on many factors such as dietary intake and even with daily rhythm, while hair is a stable specimen from which stable and long-lasting results can be obtained.[23]

The number of androgen-sensitive receptors at the female frontal area were approximately 40%, which is lower than that in male and 5α-reductase I and II enzymes activities in this area had 2 and 3.5 times less activity than those in man. Even more, the aromatase enzyme activity at the frontal area in women was 6 times more active than that in men.[25]

The investigators found that the mean ferritin level in patients with androgenic alopecia was statistically significantly lower than in normal subjects without hair loss. Dermatologists commonly assess the serum iron status in women with AGA because of the assumption that iron deficiency can cause alopecia.[26] Also, Iron deficiency anemia has been reported in as many as 72% of women presenting with diffuse telogen hair loss and the patients treated with oral iron had regrowth of their hair associated with normalization of their iron stores.[27]

Aim of the Study

To estimate the level of serum ferritin and vit D3 in female pattern of androgenic alopecia in comparison to healthy individual.

Patients and method:

Study design and setting:

A prospective case control study carried out at Department of Dermatology in in Balad general hospital, Iraq Iraq at the period from the first of January 2019 to the end of Dec 2019.

Patients:

A total number of (100) woman within the age between 14-35 years were enrolled in the current study. The respondents divided into two groups:

1. Case group which included 50 patients clinically diagnosed with Androgenic Alopecia

2. Control group which included 50 healthy subjects

The participants in the first group selected based on clinical algorithm for diagnosis of FAGA

Statistical Analysis

Data entered by the researcher by use of computerized statistical software; Statistical Package of the Social Sciences (SPSS) version 23. Descriptive statistics are presented in the form (mean ± standard deviation). To compare between more than two means we used One-way ANOVA. In all statistical analyzes, the significance level (p-value) was set at ≤ 0.05 and the result was presented in tables and / or graphs.

Results

vit D3 for patients was (22.8 ± 11.5) in case group versus (34.4±5.7) in control group, while for S. ferritin was (35.7±5.0) for patients' group than (44.8 ±7.3) for control group. There is a significant decrease in vit D and ferritin level in case (AGA) group than that in control (healthy) group (P<0.001) (table 1).

Table 1: Relation between S. vit D3 and ferritin and the studied groups

	Case group	Control group	P value
Serum vit D3	22.8 ± 11.5	34.4±5.7	< 0.001 Hs
S. Ferritin (ng/mL)	35.7±5.0	44.8 ±7.3	< 0.001 Hs

Hs= highly significant

To determine whether vit D3 and ferritin levels in serum were significantly correlated with severity of female androgenic alopecia, patient group was divided into three grades (I, II and III) according to Ludwig's classification. The results showed that grade I reported in 19 patients (38.0%), grade II reported in 22 patients (44.0%) and grade III reported in 9 patients, about (18.0%). No statistically relation were found between the three gradesof S.vitD3, while significant difference present among S. ferritin, all these were shown in table 2.

Table 2: Association between vit D3 and ferritin with severity of the disease

Parameter	Grade I (Mean±SD) (n=19)	Grade II (Mean±SD) (n=22)	Grade III (Mean±SD) (n=9)	P value
Serum vit D3 ng/ml	24.2±6.9	20.7±7.2	18.9±9.2	0.1 Ns
Serum ferritin ng/mL	37.4±10.8	30.7±9.4	25.9±12.1	0.01 S

Ns= not significant, S= significant

serum vit D3 in diagnosing AGA it's revealed that the sensitivity of the test to predict the disease were (90.9%), the specificity were excellent (95.1%), (94.8%) negative predictive value (NPV), (90%) for positive predictive value (PPV) and accuracy of the test was (93.0%) (Table 3).

Table 3: Validity test of S. vitD3

Cutoff value of S.vitD3	Sensitivity	Specificity	NPV	PPV	Accuracy
27.5	90.9%	95.1%	94.8%	90.0%	93.0%

In diagnosing AGA when the cutoff value (38.9) it's revealed that the sensitivity of the test to predict the AGA was (88.3%), the specificity was (89.0%), (84.0%) negative predictive value, (86.0%) for positive predictive value (PPV) and accuracy of the test was (85.0%) (Table 4).

Table 4: Validity test of S. ferritin in patients with AGA

Cutoff value of S. ferritin	Sensitivity	Specificity	PPV	NPV	Accuracy
38.9 ng/mL	95.3	89.0	86.0	54.0	70.0

Discussion

The current study revealed that there is no significant difference were found regarding age distribution between the studied groups (case and control), which is in agreement with that reported by Moneib H et al, and Rasheed H et al.[20]

In the present study we found that (34%) of the patients have family history of alopecia which is less than that mentioned by Sarda O et al., when family history of female androgenic alopecia was found in (38%) [99].

The current study was carried to shed light and focus on the role of vit D3 and ferritin in women with AGA, we found that the level of s. ferritin and vit D3 were significantly reduced than that in control group (<0.001). Same finding by an Egyptian study carried by Rasheed H et al [21], that revealed that s. ferritin and vitamin D levels was significantly reduced in female with AGA in relation to control group (P<0.001). [28, 29]

Moreover regarding to vit D the current study is in agreement with Iranian study carried by Tabrizi R et al, when they found that there is a significant decrease in Vitamin D3 mean level of FPHL patients group than that in healthy group.[30]

Moreover Our findings agree with Moneib et al, study that was conducted to evaluate serum 25-(OH) D levels in 42 TE female patients, 38 patients with FAGA, and 40 age- matched healthy female controls. They found that mean serum vitamin D levels in women with FPHL were significantly lower than that in controls group, suggesting that the reduced hair density seen FPHL patients may possibly be associated with low serum levels of vitamin D.[20]

There were many suggested mechanisms by which vitamin D might have a possible influence on hair follicle cycling and growth. It suggests that an ideal concentration of vitamin D is essential to deferment aging occurrences, including loss of hair.[31,32]

Also the present study revealed that deficiency, rather than Insufficiency, was more common among patients group (34 patients, 68.0%%), whereas insufficient levels were found in (11 controls, 22%), implying the possible role of vitamin D deficiency as one of the important prerequisites to develop hair loss. This is similar to that found in Monib et al study.[21]

Iron deficiency has been demonstrated to be more common in patients with hair loss conditions such as FAGA, TE, and alopecia areata.[33,34]

Mean serum ferritin level (35.7±5.0 µg/L) in the patient group and it was in agreement with that found, but higher by Rasheed H et al, (23.9 µg/L).[21]The mean levels of serum ferritin was meaningfully greater in mild cases of alopecia than in severe form (P=0.01) which is same that reported by Rasheed H et al [21],

While in apposite to that Bolland M et al., [31] study carried in 2008 in New Zealand, on patients with male alopecia, found that no relationship between the degree and strictness of with level of vit D3 level and pattern of alopecia

But it is not agree with Moneib H et al., [21] study when they surprisingly found that mean level was the highest in degree III compared with degrees I and II. The reason for this increase in 25-(OH)D levels in their patients was not known, but they suggest that it might be related to an increased exposure to ultraviolet light due to more decreased scalp hair density.

In the Vegesna et al., study the therapeutic effect of Vitamin D3 and its equivalents in hair growth motivating studied in animal (mice) with congenital type alopecia due to congenital lack of Vitamin D receptor (VDR).[35]

The severity of hair loss was Ludwig I in the majority of our patients (66.7%), which was similar to the study that concluded in Sarda O et al., when it represented in (66%) [36]. Moreover, it is in agreement with Zhang *et al*. and Aktan *et al*., when found that Ludwig I pattern was the most common in FAGA patients.[37,38]

As for Vit D. in the current study, it was revealed that the validity of the test was: sensitivity (90.1%), specificity was (95.9%). While in Rasheed et al, [21] study the sensitivity of the test was (100.0%) and specificity was (75%) this may be due to difference in cutoff value used between the studies.

For serum ferritin, it was found that the sensitivity of the test was (88.3%), the specificity (89.0%), (84.0%) negative predictive value, (86.0%) for positive predictive value (PPV) and accuracy of the test was (85.0%)

Conclusion

Serum Vit D3 and Ferritin concentrations were significantly decrease in female with androgenic alopecia.

No conflicts of Interest

Self-funding source

Ethical Clearance: From the Ministry of health and Environment/ scientific committee

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