

Research Paper

Role of Vitamin D in Female Pattern Hair Loss Among Iraqi Women: A Case- Control Study

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Abstract

Background: Low serum level of Vitamin D may have a potential role in the pathogenesis of female pattern hair loss (FPHL).

Aims: To evaluate serum vitamin D level in Iraqi women with female pattern hair loss and compare it with normal healthy control.

Settings and Design: A case-control study was carried out on 190 women: 95 patients with FPHL aged ≥ 15 years and 95 healthy age-matched control.

Methods and Material: The diagnosis and severity of FPHL were based on clinical examination and using Ludwig classification. All participants were investigated for vitamin D level and alkaline phosphatase. Data were collected and statistically analyzed.

Results: The mean \pm SD level for vitamin D was significantly lower in the FPHL group than control (13.8 ± 2.6 ng/mL vs 37.6 ± 4.7 ng/mL, $p < 0.001$). Eighty-two patients (86.1%) of the FPHL group and 35 (36.9%) of the control group had a low vitamin D level ($p < 0.001$). Alkaline phosphatase level was significantly elevated in 77 of FPHL compared to the control group (81% versus 19%, $p < 0.001$). Low vitamin D level was significantly correlated with the duration of hair loss, alkaline phosphatase elevation, and symptom of bone pain.

Conclusions: Women with low serum vitamin D levels have a high potential for the development of FPHL suggesting that vitamin D may have a possible role in the etiopathogenesis of this pattern of hair loss.

Keywords: Vitamin D, Female, hair

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Key Messages: The majority of women with female pattern hair loss have low serum vitamin D levels and this may have their significant etiological role. Measurement of vitamin D should be taken into account when evaluating women with diffuse hair loss.

Introduction

Female pattern hair loss [FPHL] is one of the most common complaints among female patients referred to dermatology clinics. It is the most common cause of alopecia involving 6-12 % of women aged 20-30 years and over 55% of women aged over 70 years. FPHL is clinically characterized by diffuse non-scarring hair loss without obvious hair thinning in frontal, central, and partial lobes of the scalp. The frontal hairlines are characteristically maintained.¹ The pathophysiology of FPHL is not well understood yet, and it is likely to be a multifactorial genetic trait. Androgen-independent mechanisms may

contribute to this phenotype.²⁻⁴ The possible link between serum vitamin D and FPHL has been suggested since its decreased concentration was demonstrated in patients with FPHL compared to the control group.⁵⁻⁸ Vitamin D is a hair follicle differentiation promoter without having much effect on its proliferation. Correlation of Vitamin D levels has been seen among patients with hereditary Vitamin D receptor (VDR) deficiency and alopecia. Previous studies reported that VDR is important for an essential stage of development of hair follicles.⁹ The function of VDR is critical for keratinocyte stem cells remaining in the bulge region of hair follicles and impaired Vitamin D function will lead to defective stem cell renewal and loss of hair follicle cycle.¹⁰ It has been suggested that an optimum concentration of vitamin D is essential to delay aging and hair loss, and a possible link has been proposed between the lack of vitamin D in serum and hair loss¹¹ and thereby measuring serum level of vitamin D is a factor recently considered in approaching patients with hair loss complaint.¹²

The study aims to investigate the serum level of vitamin D in women with FPHL and to compare the result with the age-matched control group.

Patients and Methods

A case-control study was carried out on 150 females (95 with FPHL aged ≥ 15 years, and 95 age-matched controls). Patients who chose to take part in this study were selected from the Dermatology Outpatient Clinic of Basrah Teaching Hospital, Basrah City, South of Iraq and evaluated in the period from April 2018 to July 2019. As for the control group, it was chosen from the patients' companions, some students of the College of Medicine, in addition to other volunteers. A careful history was obtained from all participants with a special

emphasis on menstrual history, family history of FPHL, a symptom of bone pain, history of any disease, and drug intake that could alter the serum vitamin D level. Exclusion criteria include any participant suffering from other causes of hair loss (e.g. telogen hair loss, female androgenetic alopecia), diseases of the scalp, evidence of hyperandrogenemia, manifested clinically (e.g. hirsutism, menstrual irregularities) or by laboratory investigations (raised total and or free serum testosterone and or raised dehydroepiandrosterone- sulfate DHEA-S), women who take any drugs that could alter serum vitamin D levels (e.g. systemic corticosteroids, contraceptives, antiepileptic drugs, weight loss drugs, and cholesterol-lowering agents), and patients suffering from systemic diseases. The diagnosis of FPHL was based on clinical findings (the pattern of hair loss: reduction in hair density over the crown and widening of the central part) and negative hair pull test. The severity of hair loss was recorded using Ludwig classification by a questionnaire developed for this purpose (Grade I or mild, Grade II or moderate, and Grade III or severe).¹³ The following investigations were done for both eligible patients and control groups:

The serum level of vitamin D was measured in the laboratory by ELISA using a Vitamin D kit (Biosource, USA). The quantitative values of vitamin D level were interpreted as follows: < 20 ng/mL: deficient, 21–29 ng/mL: insufficient, > 30 ng/mL: sufficient and >150 ng/mL: intoxication.¹⁴ Serum levels of Alkaline phosphatase (ALP) were also measured using the colorimetric method by Biolyzer 300 using a diagnostic kit manufactured by Analytican Biotechnologies, Germany.

Statistical analysis was performed using frequencies and percentages to describe categorical data and means \pm standard

deviations for continuous data. To calculate differences between data, Chi-square tests were used for categorical data and Student's t-test was used for continuous data. One-Way ANOVA test and Receiver operating characteristics (ROC) curve test were applied to assess the validity of the relationship between vitamin D values and FPHL and to determine the cut-off level of Vitamin D. The area under the curve (AUC) was performed to compare the of vitamin D level with hair loss with the help of Z-test. AUC ranged from 0 to 1, the higher AUC more than 0.5 indicate the better predicting ability of a test, and AUC close to one is the best valid and accurate test. In the ROC curve, the true positive rate (sensitivity) is plotted to the false positive

rate (100-Specificity) for different cut-off points of vitamin D level. Each point in the ROC curve represents a sensitivity/specificity pair corresponding to a particular decision threshold.¹⁴ In all tests, the significance level was considered < 0.05. The Statistical Package for the Social Sciences 22 (SPSS Inc., Chicago, IL) was used for data analysis.

Results

A total of 190 women were enrolled, 95 were patients (FPHL group) and 95 were normal (control group). The demographic characteristics of all participants are shown in (Table-1).

Table 1. Demographic and general characteristics of the study participants (N 190)

Variable	Cases group: No. (%)=95 (50)	Control group: No. (%)=95 (50)	P VALUE
Mean age ± (SD) (years)	28.7 (8.6)	27.7(4.5)	
Symptom Bone pain	75(84.3%)	14(15.7%)	P < 0.001
Duration of hair loss	<1 year = 35 (36.8)		
	≥1 year = 60 (63.2)		
Severity of alopecia (Ledwig' classification)	Grade I: 69(73%) Grade II: 20(21%) Grade III: 6(6%)		

The symptom of bone pain was significantly more noticed in the FPHL group than in the control group (p < 0.001). The mean serum level of vitamin D in the FPHL group was 13.84 ± 5.2 ng/ml (ranged from 6.5 to 34.5 ng/ml), while that of the control group was 37.64 ± 4.6 ng/mL (ranged from 9.3 to 76 ng/ml) and it was significantly lower in FPHL group than in

normal control (p < 0.001). The mean alkaline phosphatase (ALP) level was 233 ± 6.9 IU/L in the FPHL group and 109 ± 3 IU/L in the control group and the difference was statistically significant (p < 0.001). Also, 77(81%) of the FPHL group had an elevated level of ALP (ranged from 155 - 253 IU/L) compared to 11 (11.6%) of normal control (p < 0.001) (Table-2).

Table 2. Serum level of vitamin D and alkaline phosphatase (ALP) in both Female Pattern Hair loss (FPHL) and control groups (p value < 0.05 was significant)

Variable		Fphl Group No=95(%)	Control Group No=95(%)	P Value
vitamin D (ng/mL)	Mean ± SD	13.84 ± 5.2	37.64 ± 4.6	< 0.001
	Sufficient	13 (13.7%)	60 (63.2%)	
	Insufficient	24 (25.2%)	15 (15.8%)	
	Deficient	58 (61.1%)	20 (21.1%)	
ALP (IU/L)	Mean ± SD	233±6.9	109 ± 3	< 0.001
	Normal	18(19%)	84 (88.4%)	< 0.001
	Elevated	77(81%)	11(11.6%)	
	Vit D deficient	53(68.8%)		
	Vit D insufficient	14(18.2%)		
Vit D sufficient	10(12.9%)			

Depending on the Ludwig classification for FPHL, the mean level of vitamin D with various grades of FPHL are shown in (Figure-1) and it was significantly lower in patients with grade III alopecia than in both grade II and grade I. (7.66

± 1.6ng/ml versus 17.7 ± 3.2ng/ml and 16.16 ± 2.8ng/ml respectively, p < 0.001).

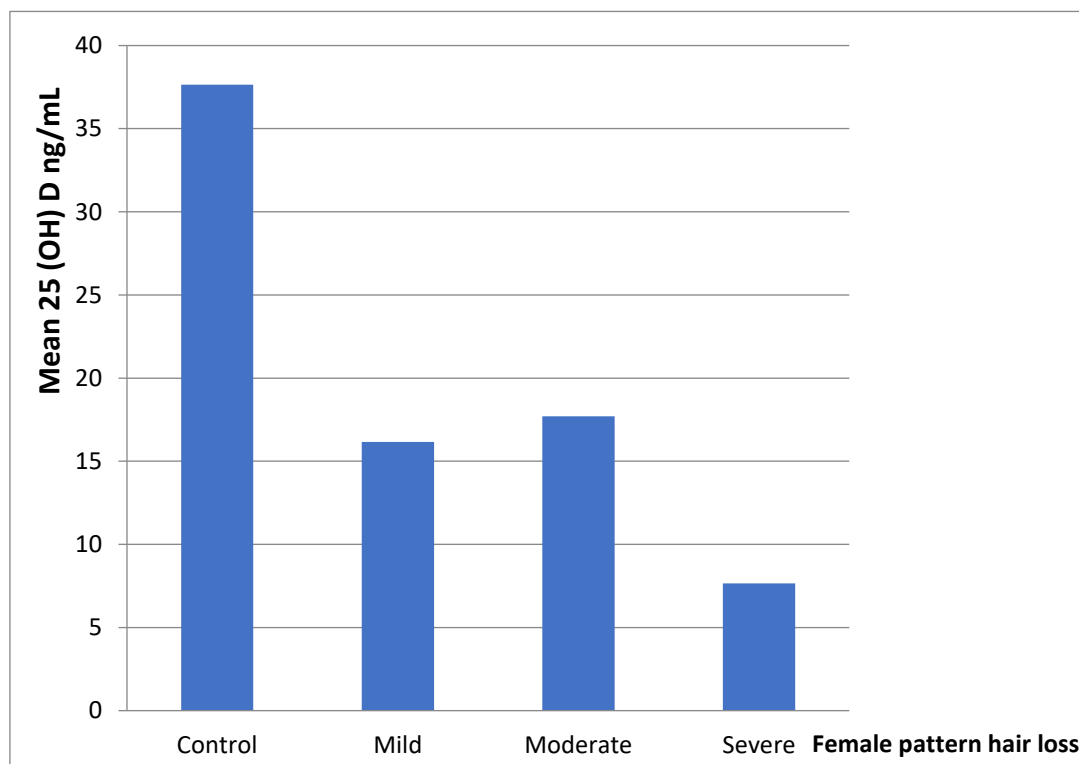


Fig 1. One-way Anova for the correlation between mean level of vitamin D in control group and Ludwig classification of FPHL group.

As shown in (Table-3), the serum level of vitamin D was significantly lower in those

patients with hair loss duration more than one year than in those patients with a duration of less

than one year and the difference was statistically significant (p-value < 0.001). On the other hand, serum ALP level was inversely higher in patients with hair loss longer than one year than less than one year (91.5 % versus 8.5%, p < 0.001). Concerning patients with bone pain, 19 (25.3%) patients with FPHL had hair loss of less

than one year, and 56(74.7%) patients had hair loss more than one year, while in asymptomatic patients; 16(80%) had hair loss less than one-year duration and 4(20%) patients had more than one year, the difference was statistically significant (P <0.001, table-3).

Table 3. Serum level of vitamin D, alkaline phosphatase (ALP) *and symptom of bone pain in relation to the duration of hair loss within FPHL group.

Parameters		Duration of hair loss		P value
		< 1year, No. (%)	> 1year, No. (%)	
vitamin D level	Sufficient	11 (84.6)	2 (15.4)	< 0.001
	Insufficient	9 (37.5)	15 (62.5)	
	Deficient	15 (25.9)	43 (74.1)	
ALP level	Normal	22 (45.8)	26 (54.2)	0.028
	Elevated	4 (8.5)	43 (91.5)	
Symptom of bone pain	Symptomatic	19 (25.3)	56 (74.7)	< 0.001
	Asymptomatic	16 (80)	4 (20)	

*Serum level of vitamin D was measured by ELISA and Alkaline phosphatase (ALP) by colorimetric method.

The correlation between vitamin D level and FPHL showed a significant Receiver Operating Characteristic (ROC) curve (area under the curve AUC 0.8, P<0.0001, 95% CI: 0.80-0.94). Serum vitamin D level equal and below 28.75 ng/mL had 90% sensitivity and 91% specificity

for FPHL (94.4% of FPHL group and 16.7% of the control group). This level also had positive and negative predictive values of 94.4% and 83.3% respectively for FPHL (Figure 2 A and B).

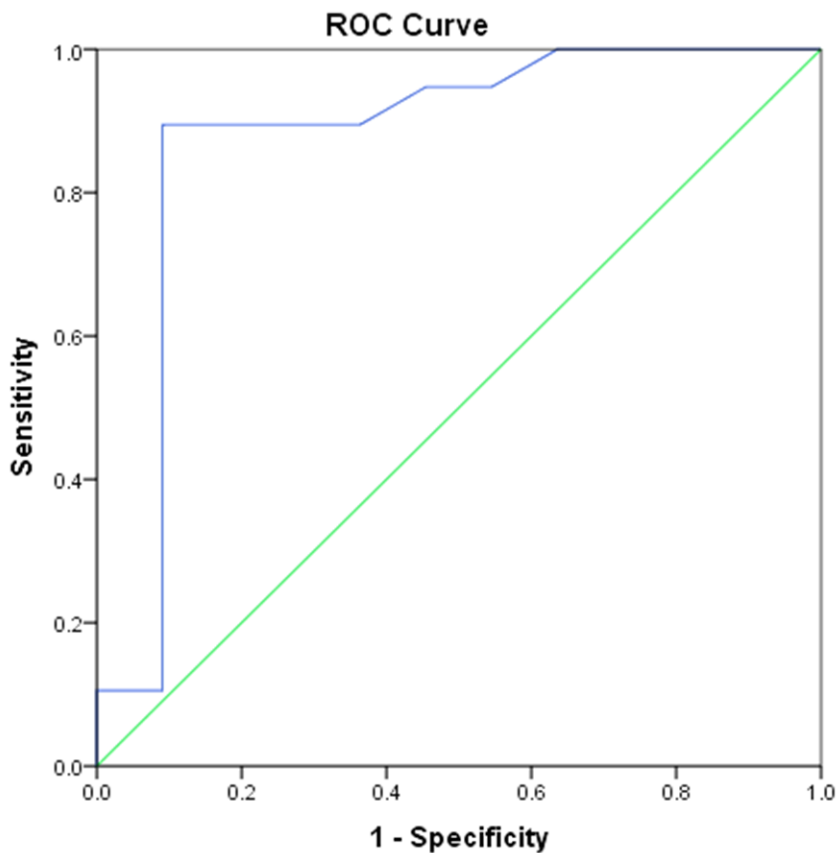


Fig 2 (A). Receiver Operation Characteristic Curve showed that vitamin D level of 28.75 ng/mL and lower is 90% sensitive and 91% specific for female pattern hair loss.

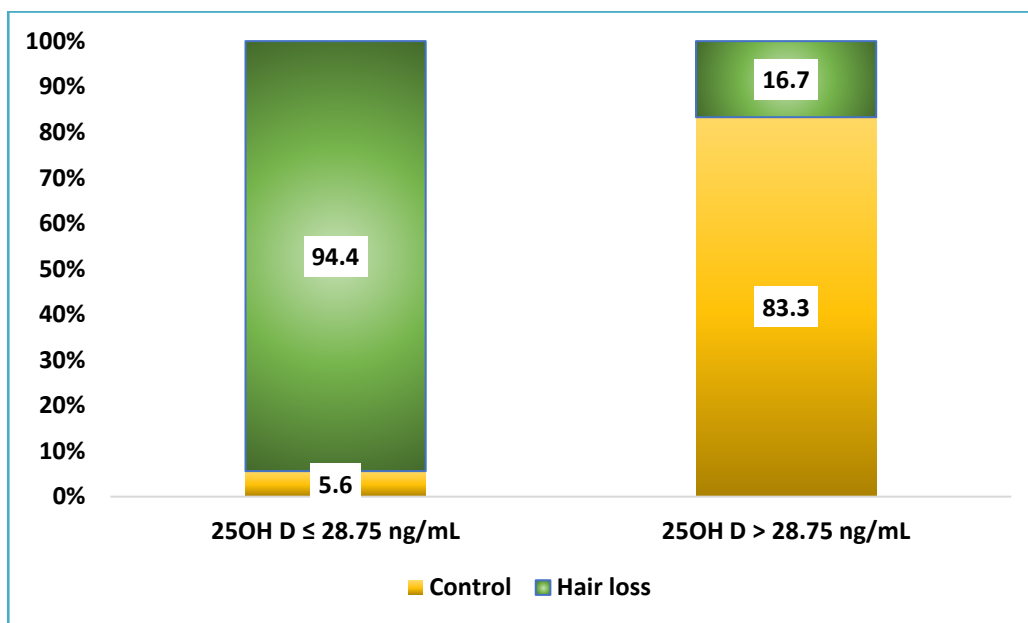


Fig 2 (B). Correlation between cutoff vitamin D level of 28.75ng/mL and FPHL and control groups.

Discussion

The results of the current study support the suggestion that the decreased hair density present in patients with FPHL is associated with altered levels of serum vitamin D. The mean level of vitamin D in patients with FPHL was lower than controls ($P < 0.001$). Deficiency rather than insufficiency, was more common among the FPHL group (58 patients, 61.1%), whereas sufficient levels were found more often among controls (63.2%), implying the possible role of vitamin D deficiency as an important prerequisite to developing hair loss. The present study matched with Hoda Moneib et al.¹⁶ and H. Rasheed et al.⁶ Accordingly, a screening test for Vitamin D level would be a useful measure in women with hair loss, and dietary supplements of Vitamin D may help to treat these patients. In our study, Ludwig grade I alopecia was found in the majority of our patients (73%), which was in line with the studies of Sarda,⁴ Zhang *et al.*,¹⁷ and Aktan *et al.*¹⁸ Although there was a small number of patients with the severe form of FPHL, we found that the level of vitamin D was significantly lower in grade III alopecia compared to grade II and I suggest that the severity of hair loss was directly correlated with the degree of vitamin D deficiency. The present study showed that vitamin D threshold level of 28.75 ng/mL and below had 90% sensitivity and 91% specificity for FPHL. And it was consistent with the finding of Rasheed, et al study.⁶ Elevated serum alkaline phosphatase (ALP) level is an essential marker for the diagnosis of vitamin D deficiency,¹⁹ and in our patients, the conspicuous and significant finding being raised serum ALP in 81% of FPHL and 87% of them had concomitant low serum level of Vitamin D (either insufficient or deficient). This observation in favor of the use of serum concentration of ALP activity as a screening test

for the status of vitamin level in women with FPHL. In our study, the association of symptoms of diffuse bone pain with a decreased level of vitamin D was found in 84.3% of cases, and this finding is closely in line with Plotnikoff and Quigley study²⁰ who reported vitamin D deficiency in 93% of patients with persistent non-specific musculoskeletal pain. There are many different pathways by which Vitamin D had influential links to bone pain including the presence of VDRs and 1- α -hydroxylase activity in the central nervous system, particularly in the hypothalamus. Vitamin D as a neuroactive steroid modulates many neurotransmitters in CNS.²¹⁻²³ Also, Vitamin D up-regulates many inflammatory pathways in chronic pain (i.e. transforming growth factor- β -1 [TGF- β -1], interleukin [IL]-4), and inhibition of prostaglandin activity. TGF- β -1 up-regulated by vitamin D will suppress IL-1, IL-2, and cytokines that are involved in chronic pain, such as tumor necrosis factor- α and interferon- γ .^{22,23} On the other hand, patients with chronic musculoskeletal pain can develop vitamin D deficiency secondary to spending less time in open environments due to depression, limited mobility, or increased fat tissue.^{26,27} We found a significant association between the degree of vitamin D deficiency and the duration of hair loss i.e the longer the duration of hair loss the more severe the vitamin D deficiency with an inverse elevation of alkaline phosphatase and being more symptomatic. This finding should encourage us to measure vitamin D level at an early stage of hair loss with the hope of reducing or preventing the progression of alopecia. It is worth mentioning that most Iraqi women are at risk of developing vitamin D deficiency due to lack of sufficient sunlight exposure and the wearing of modest clothing that covers most of

the body, in addition to the lack of eating foods rich in vitamin D. The major limitation of the study is that our data was based on the results of a single-center, southern Iraq, and more data with the inclusion of more patients from other areas are warranted. Secondly, a relationship between FPHL and low vitamin D level does not necessarily mean causality, and further studies evaluating the response of women with FPHL to vitamin D supplements are highly recommended to prove or disprove such correlation.

Conclusions

women with insufficient or deficient serum vitamin D level are at risk of developing FPHL compared to women with sufficient levels, indicating that low levels of vitamin D might have a possible role in the etiopathogenesis of this pattern of hair loss.

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دور فيتامين د في تساقط الشعر الأنثوي بين النساء العراقيات: دراسة حالة وضبط

الخلفية: قد يكون لانخفاض مستوى فيتامين د في الدم دور محتمل في التسبب في تساقط الشعر الأنثوي (FPHL).

الأهداف: تقييم مستوى فيتامين د في الدم لدى النساء العراقيات المصابات بتساقط الشعر الأنثوي ومقارنته بالتحكم الصحي الطبيعي.

الإعدادات والتصميم: تم إجراء دراسة حالة وضبط على 190 امرأة: 95 مريضاً يعانون من FPHL بعمر أقل من 15 عاماً و 95 مريضاً مع تحكم مناسب للعمر

الطرق والمواد: استند تشخيص وخطورة FPHL إلى الفحص السريري واستخدام تصنيف Ludwig. تم فحص جميع المشاركين لمعرفة مستوى فيتامين (د) والفوسفاتيز القلوي. تم جمع البيانات وتحليلها إحصائياً.

النتائج: كان متوسط مستوى SD \pm لفيتامين (د) أقل بكثير في مجموعة FPHL من مجموعة التحكم (2.6 ± 13.8 نانوغرام / مل مقابل 4.7 ± 37.6 نانوغرام / مل ، $p < 0.001$). كان لدى 82 مريضاً (86.1%) من مجموعة FPHL و 35 (36.9%) من المجموعة الضابطة مستوى منخفض من فيتامين (د). ارتفع مستوى الفوسفاتيز القلوي بشكل ملحوظ في 77 من FPHL مقارنة بالمجموعة الضابطة (81% مقابل 19% ، $p < 0.001$) ارتبط انخفاض مستوى فيتامين (د) بشكل كبير مع مدة تساقط الشعر ، وارتفاع الفوسفاتيز القلوي ، وأعراض آلام العظام.

الاستنتاجات: النساء ذوات المستويات المنخفضة من فيتامين (د) لديهن قدرة عالية على تطوير FPHL مما يشير إلى أن فيتامين D قد يكون له دور محتمل في التسبب في هذا النمط من تساقط الشعر.

الكلمات المفتاحية: فيتامين د، أنثى، شعر