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Original Research Article

Female pattern hair loss among Saudi women and hematological changes associated with it - case controlled study

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ABSTRACT

Background: Female pattern hair loss is a problematic condition. The availability of a rapid indicator is crucial. The current study compared female pattern hair loss patients with healthy controls regarding hematological parameters and vitamin D levels.
Methods: We included 78 females with female pattern hair loss and 50 healthy subjects in the control group. We collected a detailed medical history and performed a systematic clinical examination. Blood samples were collected including complete blood count, serum ferritin, and vitamin D.
Results: A significant increase in positive family history and acne among the study than the control group. Most patients had mild disease (55.1%). Female pattern hair loss was significantly associated with a reduction in red blood cell count, hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin, mean cell hemoglobin concentration, red cell distribution width, serum ferritin and serum vitamin D. Among the patient's group, the disease severity was positively correlated with disease duration and patient age. The correlation with duration was moderate (r=0.366). The disease duration was positively correlated with body mass index and negatively correlated with red blood cell count, hemoglobin concentration, hematocrit, red cell indices, ferritin and vitamin D. Disease duration was also inversely correlated with vitamin D levels.
Conclusions: Family history, body mass index, acne, hirsutism and irregular period were high among Saudi women. The disease was moderately severe. FPHL was associated with a significant reduction in hematological parameters and lower serum ferritin that indicated iron deficiency could play a crucial role in the development or progression of the disease. As a preventable etiology, restoring iron stores may provide at least an adjunct therapeutic option.

Keywords: Female pattern hair loss, Hematological parameters, Ferritin, Vitamin D, Thyroid function

INTRODUCTION

Female pattern hair loss (FPHL) or androgenic alopecia (AA) is a common disease that affects the patient's quality of life.[1] FPHL is highly prevalent, there are more than 21 million females affected in United States of America (USA). The frequency of FPHL varies among population groups. Data from the Middle East about FPHL incidence is unfortunately lacking. Hair in both females and males is associated with attractiveness and sexuality. Affected patients suffer from anxiety, depression, social phobias and stress.[2] Loss of hair has a great impact on self-image and result in low self-esteem.

FPHL has two distributions; the first is the diffuse thinning across the central scalp with a characteristic "Christmas tree" pattern witnessed along the hair midline part due to prominent thinning of the hair towards the front of the scalp with the least hairline involvement.[3,4] The frontal hairline is rarely involved. However, bitemporal thinning is common. The three-grade Ludwig scale is usually used to describe and assess the severity of the FPHL.[5] Almost

49% of women will be affected by hair loss throughout their lives, with FPHL being the most common cause of female alopecia.[6]

The diagnosis is mainly clinical. The hair-pull test is usually negative. However, it could be positive early in the disease process, mainly on the vertex or mid-frontal part of the scalp. The dermoscopic examination could reveal epidermal and dermal structures that the naked eye could not detect. It detects the hair diameter, yellow dots and pigmentation. Complete hair loss could be observed in some foci, with varying degrees of skin pigmentation.[7,8] The scalp biopsy is usually not required to reach a diagnosis, except when the clinical diagnosis is unclear or coexistent skin disease is present.[9]

The specific etiopathogenesis of FPHL is unclear. Multiple factors and conditions seem to play a role. These include deficient nutrients, hormonal, environmental and genetic factors. Its treatment (topical or systemic) is challenging, and the development of new methods is continuously underway, and effective treatments remain limited.[4] The trial of emergent drugs also restricts effective treatments that are tested only on males because length, styling, density, and patterning of hair loss vary for their female partners.[10]

The association between FPHL and different hematological parameters is not fully investigated. Thus, the current study was designed, and it proposed that FPHL is associated with abnormalities of hematological parameters. The correction of such abnormalities could share in the treatment protocol of FPHL. The current study aimed to examine the hematological parameters in the FPHL, in addition to vitamin D.

METHODS

After having ethical approval from the local IRB in the hospital, A case control study was conducted including Female patients ≥15 years of age with a history of hair loss on the crown, temporal area, or recession of hairline were included and examined clinically for hair thinning (loss of hair and/or presence of thin hair) in the department of dermatology (King Khalid University Hospital). Initially, the control group included an equal number of women, matched for age with the study group. They did not have clinical signs of hair loss and/or hyperandrogenism. They were selected from the attendants with the patients and usually of their relatives. The appropriateness of the control group was challenged by the genetic influence of FPHL. However, since the study was about hematological parameters that are not influenced by the etiopathogenesis of the disease we thought the inclusion was appropriate but not ideal.

We initially selected 100 subjects with ration of 1: 1 cases and control. However, and performed the final analysis on 78 cases to guard against the non-respondents. Among the control, 18 did not give informed consent, and 10 had one or more exclusion criteria). Thus, we included 50 subjects in the control group and 78 cases.

Inclusion criteria were patients aged 15 years or older who had FPHL (based on history, clinical basis, negative hair pull test and dermoscopy findings), with any grade according to Ludwig's classification. Patients were free from any other dermatologic or systemic medical disease that affect hair loss. On the other side, the patient was excluded if she had any other associated clinical forms of alopecia other than FPHL. If she had any other dermatologic or systemic medical diseases (especially diseases associated with hair loss such as diffuse alopecia areata, traction alopecia, trichotillomania, T. capitis, acute or chronic telogen effluvium, connective tissue disease such as lupus and dermatomyositis, hypothyroidism (TSH and T4 were done but results were not shown in the tables) and scaring alopecia. Patients on drugs known to cause hair loss such as immune suppressing drugs, warfarin, retinoids and statins. Patients with hematologic disorders or received chemotherapy. Patients received local or systemic therapy for FPHL in the last 12 months before the study enrollment. Pregnant and lactating females.

All patients were interviewed for their medical history (disease onset; course; history of stress, dieting, fevers, surgeries, breast feeding, medications, iron supplements; duration of the disease; other scalp manifestations (e.g. pain or itching); menstrual irregularities; acne; signs of hyperandrogenism and family history).

Meticulous scalp examination looking for exclamation marks suggestive of diffuse alopecia areata, or the finding of variable hair length to exclude trichotillomania or any other forms of scaring alopecias such as frontal fibrosing alopecia were sought.

A hair pull test was carried out to differentiate FPHL from telogen effluvium (TE). Approximately 60 hairs grasped between the thumb and the index and middle fingers. Then, firm, gentle traction was applied. A negative test was assigned if six or fewer hairs/less than 10% were obtained) indicating normal shedding. A negative hair pull test combined with dermoscopy findings of miniaturization, yellow dots, and pigmentation are suggestive of FPHL. On the other hand, a positive test was assigned if more than six hairs or 10% were obtained), indicating definite active hair shedding.[10] The findings of generalized hair loss associated with hair thinning, prominent hair shedding and positive hair pull test and major illness or stress were the base to consider acute or chronic TE.

Also, we performed laboratory investigations (complete blood count, serum ferritin, and vitamin D levels.

Sample size calculation

The sample size is calculated at level of confidence of 95% (type I error at %5) and power of the study of 80 (type II error at 20%). The hypothetical difference in hemoglobin

(Hb) level between cases and control is settled at more than 15 percent. The estimated sample is 50 persons for cases and 50 for control.

We decided to increase the sample size by 30 percent to guard against the non-responder or defaulters. The sample size of cases is 78, but the sample size of control is 50, as many controls refused to give blood sample.[11]

Statistical analysis of data

Collected data entered to statistical package for social science (SPSS), version 25 (IBM®SPSS® Inc., Chicago, USA). Quantitative normally distributed data were presents by the arithmetic mean (for central tendency) and standard deviation (SD) (for dispersion).

Categorical variables were presented by relative frequency and percentages. Groups were compared by independent samples, student "t" test, and Chi-square test for quantitative and categorical variables.

Pearson's correlation "r" was calculated to detect the correlation between disease severity and duration with other studied variables. A p value of 0.05 was considered significant.

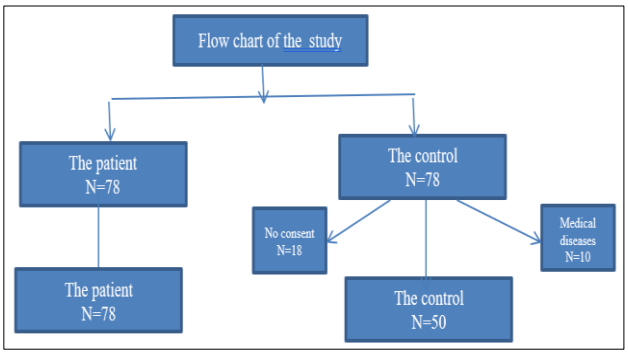

Figure 1: Flowchart of the study.

RESULTS

Demographic characters

The statistical analysis was performed on 50 subjects in the control group and 78 patients in the study group (others were excluded due to different reasons). The participants' demographics, clinical signs, disease duration and severity, are presented in Table 1. Briefly, cases and control groups were matched for age. However, there was a significant increase in the positive family history of FPHL, acne, hirsutism, and irregular period. The disease duration was less than one year, 12 months and more than a year among 5.1%, 15.4% and 79.5%, respectively. However, the majority had the mild disease (55.1%). The Ludwig grade II (moderate disease) represented 42.3% and graded III among 2.6%.

Laboratory characters

The results revealed that FPHL was significantly associated with red blood cell count, hemoglobin concentration, hematocrit percentage, mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin centration (MCHC), red cell distribution width (RDW), serum ferritin and serum vitamin D concentrations (Table 2).

Relation between severity and laboratory characters

In the study (FPHL) group, the disease severity was proportionately correlated with the disease duration and patient age. The correlation with age was mild (r<0.3) and with duration was moderate (r=0.366). The disease duration was positively and marginally correlated with body mass index (BMI). On the other side, disease severity was inversely (negatively) correlated with red blood cell count, hemoglobin concentration, hematocrit, MCV, MCH, MCHC, RDW, ferritin, and vitamin D. Disease duration also inversely correlated with vitamin D levels (Table 3).

Table 1: Demographic characteristics, family history, disease duration and disease severity among studied populations.

Variables	Study group (n=78)		Control group (n=50)		Test	P
	n	%	n	%		
Age group						
15-25	22	28.2	11	22.0	5.05	0.16
26-35	13	16.7	11	22.0		
36-45	24	30.8	15	30.0		
>45	19	24.4	13	26.0		
Positive family history	31	39.4	10	23.8	7.83	0.015*
Acne	15	19.2	4	5.0	7.56	0.006*
Hirsutism	16	20.5	2	2.5	12.69	<0.001*
Irregular period	11	14.1	3	3.8	5.24	0.022*
Disease duration (years)						
<1	4	5.1	4	8.0	2.58	0.62
1	12	15.4	4	84.0		

Continued.

Variables	Study group (n=78)		Control group (n=50)		Test	P
	n	%	n	%		
>1	62	79.5	42	8.0		
Disease severity						
Mild	43	55.1				
Moderate	33	42.3				
Severe	2	2.6				

Table 2: Comparison between study and control groups regarding hematological parameters, ESR, ferritin, and vitamin D.

Parameters	Study group		Control group		t	P
	Mean	SD	Mean	SD		
WBCs (4.0-11)×109/l	7.3397	2.40866	7.6662	2.27596	0.88	0.38
RBCs (4.25-5)×1012/l	4.2009	0.63051	4.5671	0.25670	4.81	<0.001*
Hemoglobin (120-160) (g/l)	111.11	13.31	133.23	6.68	13.25	<0.001*
Hematocrit (37-47) %	34.45	2.60	38.64	1.88	11.61	<0.001*
MCV (90-94) (fl)	80.0379	7.70338	84.1513	8.18098	3.25	0.001*
MCH (27-32) (pg)	27.4577	2.96054	29.3200	1.89312	4.72	<0.001*
MCHC (320-360) (g/l)	336.5128	10.41695	342.5625	8.29953	4.04	<0.001*
RDW (11.5-14.5)	14.6897	2.07030	13.7900	1.06005	3.45	<0.001*
Platelets (140-450)×109/l	280.3846	53.73896	279.0875	49.08535	0.29	0.87
ESR (0-17) (mm/hour)	36.7179	18.81689	35.5125	16.03319	0.46	0.67
Ferritin (13-150) (ug/l)	29.2386	21.27988	46.7278	21.77933	5.10	<0.001*
Vitamin D (75-250) (nmol/l)	19.6885	5.26273	22.7025	7.55213	2.90	0.004*

Table 3: Correlation between hematological and other parameters with disease duration and severity among the study group.

Parameters	Correlations			
	Severity		Duration	
	R	P	r	P
Severity			0.366	0.001*
Age	0.288	0.011*	0.213	0.061
Weight	0.168	0.142	0.172	0.131
Height	-0.141	0.217	-0.180	0.115
BMI	0.224	0.049*	0.242	0.033*
WBCs (4.0-11)×109/l	-0.002	0.988	0.040	0.731
RBCs (4.25-5)×1012/l	-0.263	0.020*	-0.081	0.483
Hemoglobin (120-160) (g/l)	-0.253	0.025*	-0.076	0.506
Hematocrit (37-47) %	-0.329	0.003*	-0.195	0.087
MCV (90-94) (fl)	-0.662	<0.001*	-0.211	0.064
MCH (27-32) (pg)	-0.240	0.035	-0.049	0.672
MCHC (320-360) (g/l)	-0.398	<0.001*	-0.214	0.059
RDW (11.5-14.5)	-0.379	0.001*	0.052	0.653
Platelets (140-450)×109/l	0.130	0.255	0.160	0.161
ESR (0-17) (mm/hour)	0.112	0.330	0.070	0.542
Ferritin (13-150) (ug/l)	-0.422	<0.001*	0.007	0.954
Vitamin D (75-250) (nmol/l)	-0.408	<0.001*	-0.223	0.049*

DISCUSSION

Hair loss is a devastating disorder among females. It could probably affect the patient self-esteem and be associated with poor perception of their body image. Patients usually try different treatment options (e.g. shampoos, dietary supplements, and medical treatment) with the hope of hair regrowth before seeking the advice of a dermatologist. This led to a delay between the onset of hair loss and the first dermatologic consultation visit. It could be associated with poor compliance and outcome, especially if their expectations about treatment outcomes are unrealistic.[13]

Table 4: Comparison between hematological parameters of the current study and other regional studies.

Parameters	Current study		Al-Quaiz studies[19,22]		Al-Buhairan study[25]	
	Mean	SD	Mean	SD	Mean	SD
Hemoglobin (120-160) (g/l)	111.11	13.31	120.35	10.80		
MCV (90-94) (fl)	80.0379	7.70338	79.21	12.17		
MCH (27-32) (pg)	27.4577	2.96054	26.37	6.21		
MCHC (320-360) (g/l)	336.5128	10.41695	320.36	4.91		
RDW (11.5-14.5)	14.6897	2.07030	14.84	4.65		
Ferritin (13-150) (ug/l)	29.2386	21.27988			21.20	2.20
Vitamin D (75-250) (nmol/l)	19.6885	5.26273	46.8	30.5		

The age of our patients was significantly and proportionately correlated with disease severity, and the disease is more prevalent with advanced age (except the age group from 15-25 years). Althobaiti et al from Al Taif; Saudi Arabia; stated that 75.8% was reported in females around 20-30 years old, 15.7% were between 30-40 years old, whereas 8.5% were between 40-50 years old.[14] Su et al reported that age is a risk factor for developing FPH regardless of their family history situation. It reflected the natural progression of the disease.[15]

They also reported an association between obesity (high body mass index; BMI) and the development of FPHL. These results supported the current study, as females from the study group had significantly higher BMI than control subjects. BMI also revealed a proportional and significant correlation with disease severity and duration. The age of about 47.5% of our patients lies in the age groups 26-45 years. Tandon et al reported that 53.3% were in the age group of 28-37 years, while Lee et al observed that 56.68% of 445 females were in the third decade of life.[16,17] Positive family history of FPHL was reported in 44.9% in the study group, compared to 23.8% in the control group, with a significant increase in the study than in the control group.

However, the percentage of positive family history in the control group is reported at a considerable rate. It could be referred to the fact that all control patients were selected from our attendees, who share the same social factors. Althobaiti et al from Al Taif reported that 35.9% had a positive family history in her siblings, 34% recorded positive family history in both parents, 29.5% denied any history of FPHL or thinning of hair in the family.[14] Only 0.6% of women present without a notable family history. El Samahy et al reported positive family history among 65.0% of their 20 patients.[18] However, the small number of included cases in their study could be responsible for this high percentage and controversy to the current research. Siah et al reported a positive family history of FPHL among paternal relatives of 51.0% of their patients, and 20% in maternal relatives and 24% of both paternal and maternal relatives.[19] Su et al reported that positive family history is the significant risk factor among their patients.[15]

Unfortunately, it is a non-modifiable risk factor. Tandon et al reported positive family history in 46% of patients.[16] It is in line with the current work. Al Quaiz et al from Saudi Arabia reported a mean hemoglobin of 120.35 g/l among 40% of childbearing age females and a lower-than-normal MCV and MCH levels of 79.21±12.71 and 26.37±6.21 respectively.[20] Statically significant p values of 0.0001 were observed between the two studies with regards to Hb, MCV and MCHC (Table 4).

Complete blood count showed a non-significant difference in white blood cells, platelets, and mean platelet volume. However, there was a significant decrease in red blood cells count, hemoglobin concentration, hematocrit percentage, mean cell volume, mean cell hemoglobin concentration and red cells distribution width. Comparable results were reported by Al-Asady and Al-Dulaimy.[21]

A study by Coogan et al reported that FPHL had been associated with metabolic syndrome.[22] Its harmful effects, e.g. vascular impairment due to hyperglycemia that destroys hair follicles and contributes to hair loss.

A study conducted by Al Quaiz reported vitamin D deficiency <50 nmmol/l in 64.0% of women aged between 30-75 years and 19.4% had insufficient levels of 50-75 nmol/l (Table 4) and those results are significantly higher than the results of the current study p value <0.0001.[23]

The results of the current work revealed a significant reduction of vitamin D in FPHL, and it is inversely correlated with both disease duration and severity. It indicates an important role or association with FPHL. These results coincide with Zhao et al who reported that vitamin D had a role in hair follicle cycling and its disorders and could be probably used as a treatment option to induce hair growth.[24] Rasheed et al also reported an association between low serum vitamin D and FPHL.[25]

Al Buhairan reported a serum ferritin of 21.2 µg/l and range of 7-104.5 µg/l (Table 4).[26] We found statistically significant p<0.0001 when comparing the current study to Al Buhairan,

Serum ferritin is significantly reduced in FPHL and inversely correlated with disease severity. A study done by Kantor et al reported that low serum ferritin values are associated with alopecia in females, as it might do in males.[27] Camaschella said that serum ferritin values are

often used to estimate iron reserves, and lower values indicate iron deficiency ID. Iron is included in the process of DNA synthesis, and iron deficiency affects the synthesis process.[29]

It could explain the genetic etiology of FPHL as proposed in previous work.[30] In addition, the matrix cells of the hair follicle are the most quickly dividing cells in the body, and iron deficiency may participate in hair loss via its action as a cofactor for ribonucleotide reductase the rate-limiting enzyme for the process of DNA synthesis. In addition, various genes have been recognized in the human hair follicle, and some may be regulated by iron. In addition, reversal of ID led to the restoration of hair growth.[31]

Siah et al reported a significant reduction of vitamin D and serum ferritin, but not serum zinc levels among females with FPHL than standard references for each component.[19]

Serum ferritin is a secretory form of a glycosylated protein usually reduced with depletion of tissue iron stores and increases with iron loading, inflammation, cancer, or hepatic disease. It is also an early biomarker of the iron store status. It is a specific indicator of depleted iron stores in the absence of non-specific inflammation and chronic medical diseases.[32]

We were considering the strict inclusion and exclusion criteria we used in the current study. We could ascribe ferritin deficiency and other hematological parameters due to ID, and iron deficiency could be considered to play a pathogenetic role in FPHL and other etiopathological factors.

As iron deficiency is a preventable condition, iron supplementation could be used in the treatment of FPHL. However, it is out of the area of the current research due to the long duration needed to restore iron stores (it needs six months of oral ferrous sulphate to double the stores).[33] It may be considered for future research.

Limitations

Many healthy people refuse to give sample of blood. The ratio between cases and control is not the ideal one. As the control group is among the relatives of patients may not reflect the actual population. A large-scale study will be conducted in many centers.

CONCLUSION

In conclusion, the current study has its value because it has not revealed the first direct comparison between FPHL with healthy controls matched for age. It also confirms that the reduced ferritin is due to iron deficiency anemia and supports previous literature indicating that iron deficiency could be a specific contributing factor for developing or deteriorating FPHL. Vitamin D has an important role in many diseases including FPHL. Thus, it is recommended to screen for iron deficiency and vitamin D as a routine test in cases of FPHL.

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