



## Female Pattern Hair Loss and Negative Psychological Impact: Possible Role of Brain-derived Neurotrophic Factor (BDNF)

Noha E Mohamed<sup>1</sup>, Mohamed R Soltan<sup>2</sup>, Sara A Galal<sup>3</sup>, Hassan Salem El Sayed<sup>4</sup>,  
Hadir M Hassan<sup>1</sup>, Basma HM Khater<sup>1</sup>

1 Department of Dermatology, STDs, and Andrology, Faculty of Medicine Fayoum University, Faiyum, Egypt

2 Psychiatry Department, Fayoum University, Faiyum, Egypt

3 Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt

4 Medical Biochemistry and Molecular Biology, Faculty of Medicine Fayoum University, Egypt The research was conducted in the outpatient clinic of the Department of Dermatology, STDs, and Andrology, Faculty of Medicine, Fayoum University

**Key words:** androgenetic alopecia, BDNF, psychological impact, DLQI

**Citation:** Mohamed NE, Soltan MR, Galal SA, El Sayed HS, Hassan HM, Khater BHM. Female pattern hair loss and negative psychological impact: possible role of brain-derived neurotrophic factor (BDNF). *Dermatol Pract Concept.* 2023;13(3):e2023139. DOI: <https://doi.org/10.5826/dpc.1303a139>

**Accepted:** January 2, 2023; **Published:** July 2023

**Copyright:** ©2023 Mohamed et al. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (BY-NC-4.0), <https://creativecommons.org/licenses/by-nc/4.0/>, which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.

**Funding:** None.

**Competing Interests:** None.

**Authorship:** All authors have contributed significantly to this publication.

**Corresponding Author:** Sara Ahmed Galal, Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University, 53, New Cairo, 3rd zone fifth, settlement, Cairo, Egypt Telephone number: 01008876877 Email address: [drsaragal@azhar.edu.eg](mailto:drsaragal@azhar.edu.eg)

**ABSTRACT** **Introduction:** Female Pattern Hair Loss (FPHL) is considered the most common type of hair loss in females. Women with FPHL may suffer from psychological distress and defective social functioning. Patients with psychiatric and neurodegenerative disorders almost have a deficient brain and blood brain-derived neurotrophic factor levels (BDNF). This serum BDNF level may act as a diagnostic marker for negative psychological impact in FPHL patients.

**Objectives:** Evaluate the levels of serum BDNF in patients with FPHL and correlate its level to the severity of alopecia and the degree of psychological impact.

**Methods:** Forty-six female patients with FPHL and 41 healthy age-matched female volunteers as a control were included in the study. Patients filled out a Dermatology Life Quality Index questionnaire. Both patients and controls filled Beck Depression Inventory, Beck Anxiety Inventory, and Perceived Stress Scale (PSS) questionnaires. Serum levels of BDNF were measured for all the participants using the ELISA technique.

**Results:** Patients with FPHL had significantly lower levels of BDNF and significantly higher Beck depression inventory score and PSS questionnaire scores. There is a significant negative correlation between serum levels of BDNF and Beck Depression Inventory, Beck Anxiety Inventory, and PSS questionnaire scores.

**Conclusions:** Patients with FPHL are at a high risk to develop chronic stress and depression. The serum level of BDNF is a good predictor for the assessment of chronic stress and depression in FPHL patients.

## Introduction

Female Pattern Hair Loss (FPHL) is a common cause of non-scarring alopecia in females manifested as, successive loss of terminal hairs in the vertex and frontal areas of the scalp. AGA is distinguished by follicular miniaturization which is characterized by a short anagen phase and increased vellus hairs [1].

In general, alopecia is known to be associated with many psychiatric comorbidities such as depression, anxiety, personality disorders, and drug abuse. Moreover, patients with alopecia have noticeably higher suicidal rates and get hospitalized for mental health diseases. Regarding specific types of hair loss, FPHL may be linked to many psychiatric comorbidities, especially in patients with extensive scalp affection [2].

FPHL may lead to depression and decreased life quality, poor self-esteem, and negative body image [3].

Brain-Derived Neurotrophic Factor (BDNF) is a member of the neurotrophins family which is known for its action on the growth of central and peripheral nerves. Neurotrophins show a variety of immunomodulatory impacts on non-neuronal cells especially mast cells, keratinocytes, and eosinophils [4].

BDNF controls human hair growth via tropomyosin receptors (TrkB). BDNF markedly decreases hair shaft elongation, promotes premature catagen, and decreases keratinocyte proliferation [5].

Panchaprateep et al postulated that BDNF may be essential in exerting the androgens impacts on hair follicles acting as a negative regulatory factor. This study showed that balding scalp follicles produced 12-fold more BDNF than the nonbalding scalp [6].

## Objectives

This study evaluates serum BDNF levels in patients with FPHL. We suggest that there may association between serum BDNF levels and FPHL.

Therefore, we aimed to evaluate the levels of serum BDNF in patients with FPHL and correlate its level to both the degree of psychological impact and the severity of alopecia.

## Methods

The present case-control study included 46 female patients with FPHL and 41 age-matched healthy female volunteers.

The patients were recruited from the Dermatology, STDs, and Andrology Department Clinic, during the period between May 2021 to August 2021.

All included individuals, or their families provided an informed written agreement to be included in the study. This study was conducted according to the Declaration of Helsinki and the protocol approved by the ethics committee of Würzburg University and by the Institutional Review Board of the Faculty of Medicine, Fayoum University (IRB number IRB00003613) in January 2018. An informed written Arabic consent form was signed by every participant in the presence of one of the authors.

## Patients

Female patients 15-50 years old complaining of AGA were included in this study. Patients were diagnosed and classified according to Female Pattern Hair Loss Severity Index [7].

We exclude patients suffering from any systemic or cutaneous diseases other than FPHL. We also exclude patients with a past or present history of psychiatric illness or receiving any regular psychotropic medication, antidepressants were also excluded. Pregnant and lactating women were excluded from the study.

## Control

Forty-one healthy female volunteers 15-50 years old were included in the study as a control.

## Study Design

All subjects were subjected to a Full history taking and clinical examination.

The patients were diagnosed and classified according to FPHL Severity Index [7].

Questionnaires to access the psychological state for all participants were done including Beck Depression Inventory, Beck Anxiety Inventory and Perceived Stress (PSS) Scale [8-10].

DLQI was done for the patient group only [11].

The serum level of BDNF was measured for all subjects using ELISA kits which were provided by biodiagnostic kits (Sun red Biological Technology Company). Five ml of blood were collected from the antecubital vein by venipuncture and left for 30 minutes at room temperature to allow clotting and then centrifuged for 15 minutes at 3000 rpm. Serum was separated, stored in an Eppendorf tube and kept at  $-20^{\circ}\text{C}$  until used for measurement of BDNF level.

Each female was subjected to full history, measurement of serum level of BDNF using ELISA technique.

### Statistical Analysis

Chi-square test was used for categorical variables, to compare between different groups. Fisher Exact test or Monte Carlo correction were used for correction for chi-square when more than 20% of the cells have expected count less than 5. Student t-test was used for normally distributed quantitative variables, to compare between two studied groups. Mann Whitney test was used for not normally distributed quantitative variables, to compare two studied groups. Spearman coefficient was used to correlate between two distributed not normally quantitative variables.

Kruskal Wallis test was used for not normally distributed quantitative variables, to compare between more than two studied groups. Receiver operating characteristic curve (ROC) is generated by plotting sensitivity (TP) on Y axis versus 1-specificity (FP) on X axis at different cut off values. The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. The ROC curve allows also a comparison of performance between

two tests. Logistic Regression analysis was used to detect the most independent/ affecting factor for affecting cases. Linear Regression analysis was used to detect the most independent/ affecting factor for affecting Serum BDNF.

## Results

This case-control study included 87 females, 46 female patients suffering from FPHL, and 41 age-matched healthy female subjects as a control. The participants were recruited from the Dermatology, STDs, and Andrology Department Clinic. The patients were diagnosed and classified according to FPHL Severity Index.

### Patient Group

Included 46 female patients, their ages ranged from 15 to 50 years old with a Mean  $\pm$  SD ( $29.85 \pm 9.73$ ) with a median (IQR) of 29.50 (22.0 - 38.0).

### Control Group

Included 41 healthy females, their ages ranged from 20 – 51 years with a Mean  $\pm$  SD ( $26.44 \pm 7.38$ ) with median (IQR) 26.0 (19.0 – 32.0). There was no statistically significant difference (P value  $\leq 0.05$ ) between both groups.

In the patient group 34 patients (73.9%) had positive family history of FPHL, while in the control group only 6 patients (14.9%) had positive family history.

Diet changes was reported in one patient (2.2%) in the patient group, while 4 individuals (9.8%) in the control group have diet change (Table 1).

### Clinical Parameters of the Studied Groups

In the patient group acne was reported in 11 patient (23.9%), while only 1 individual (2.4%) in the control group have acne. There was a high statistically significant difference regarding presence of acne between the case and the control groups (P value  $\leq 0.05$ ).

**Table 1. Clinical parameters of the studied group.**

	Cases (N = 46)		Control (N = 41)		$\chi^2$	P
	N	%	N	%		
Family history of FPHL						
Negative	12	26.1	35	85.4	30.669	<0.001
Positive	34	73.9	6	14.9		
Diet changes	1	2.2	4	9.8	2.301	0.183
Acne	11	23.9	1	2.4	8.407	<0.05
Hirsutism	8	17.4	4	9.8	1.063	>0.05
Signs of virilization	0	0.0	0	0.0	–	–
Menstrual irregularity	11	23.9	5	12.2	1.983	>0.05

Regarding Hirsutism of the studied patients 8 patient (17.4%) had Hirsutism, while in the control group Hirsutism was reported in 4 patient (9.8%). Signs of virilization was not reported in patients and controls. There was no statistically significant difference regarding Hirsutism, the signs of virilization and menstrual irregularity (Table 1).

### Local Examination of the Scalp of the Studied Groups

Scalp itching and soreness were reported in 34.8%, and 10.9% of the patients while in 22% and 0% in the control group respectively with no statistically significant difference.

Scalp scaling was significantly statistically higher than the control group ( $P \leq 0.05$ ). There was a high statistically significant difference ( $P = 0.001$ ) regarding hair pull test, Sinclair hair shedding scale, Sinclair hair density scale, FPHL severity index scale and FPHL severity index score between the case group and the control group (Table 2).

### Comparison Between the Two Studied Groups as Regards to the Psychological State

In the patient group PSS and Beck Depression was statistically significantly higher than the control group ( $P \leq 0.05$ ), while the Score Beck Depression Scale showed no statistically significant difference.

Regarding Beck Anxiety Score and Scale showed no statistically significant difference between both groups ( $P$  value  $> 0.05$ ) (Table 3).

### Analysis of the Dermatology Life Quality Index in the Patient Group

Only 2 cases (4.3%) had no effect on patient life, 9 cases (19.6%) with minor effect on patient's life, 20 cases (43.5%) with moderate effect on patients life, 10 cases with very great impact on patient life and 5 cases (10.9%) with extreme impact on patient life respectively.

### Serum BDNF in the Studied Groups

In the patient group serum level of BDNF was statistically significantly lower than the control group ( $P$  value  $< 0.05$ ). In patients mean  $\pm$  SD was  $0.85 \pm 1.07$ , while in the controls was  $1.07 \pm 1.26$  (Table 4).

The cut off point for serum BDNF to discriminate patients from control was  $\leq 0.714$ . The sensitivity was 76.09 and the specificity was 56.10 (Table 5 and Figure 1).

### Correlation Between Serum BDNF and Different Parameters in Patients Group

There were statistically significant positive correlations ( $P \leq 0.05$ ) between serum BDNF and FPHL duration, while there was a statistically significant negative correlation

( $P < 0.001$ ) between serum BDNF and Beck Anxiety Score, Beck Depression Score and a high statistically significant negative correlation ( $P < 0.001$ ) regarding PSS (Table 6).

### Correlation Between FPHL Severity Index Score and Different Parameters in Patient Group

There were high statistically significant positive correlations between FPHL Severity Index Score and age of patients, age of onset, duration of the FPHL and Sinclair Hair Density Scale ( $P$  value  $\leq 0.001$ ) (Table 7).

The univariate logistic regression analysis for the parameters affecting cases showed that there were statistically significant relations ( $P$  value  $\leq 0.05$ ) regarding presence of hormonal acne, presence of scaling, presence of Hair Pull test, increasing in the Perceived Stress Scale, increasing in the Beck Depression Score and increasing in the Beck Depression Scale. There was high statistically significant relation ( $p$  value  $\leq 0.001$ ) regarding presence of family history of FPHL. The multivariate logistic regression analysis showed that there was a high statistically significant relation ( $P$  value  $\leq 0.001$ ) regarding presence of family history of FPHL. There was a statistically significant relation ( $P$  value  $\leq 0.05$ ) regarding Hair Pull test (Table 8).

The univariate logistic regression analysis for the parameters affecting serum level of BDNF in the case group ( $n = 46$  vs. 41) showed that there were statistically significant relations ( $P$  value  $\leq 0.05$ ) regarding duration of FPHL, increasing in Perceived Stress Scale, increasing in Beck Anxiety Score, increasing in Beck Anxiety Scale, increasing in Beck Depression Score and increasing in Beck Depression Scale. The multivariate Logistic regression analysis showed that there was a statistically significant relation ( $P$  value  $\leq 0.05$ ) regarding increasing in Beck Depression Score (Table 9).

## Conclusions

Neurotrophins including BDNF and their receptors have role in skin hemostasias and hair growth [12].

Botchkarev et al reviewed that stress may induced hair loss, psoriasis, and other skin diseases. BDNF is a member of a family of neurotrophins [13].

This study aimed to evaluate the levels of serum BDNF in patients with FPHL and correlate its level to the severity of alopecia and the degree of psychological impact.

Our study included (87) female subjects that were divided into two groups; Group A (case group): included 46 female patients with FPHL while group B (control group): included 41 age matched healthy female volunteers as control group.

**Table 2. Local examination of the studied groups.**

		Cases (N = 46)		Control (N = 41)			
<b>Scalp</b>							
		N	%	N	%	$\chi^2$	P
Itching		16	34.8	9	22.0	1.743	>0.05
Scaling		28	60.9	15	36.6	5.114	<0.05
Erythema		0	0.0	0	0.0	–	–
Soreness		5	10.9	0	0.0	4.728	p =0.057
<b>Hair Pull test</b>							
		No.	%	No.	%	$\chi^2$	P
Negative		29	63.0	38	92.7	10.757	0.001
Positive		17	37.0	3	7.3		
<b>Sinclair Hair Shedding Scale</b>							
		No.	%	No.	%	$\chi^2$	P
Bundle with 10 hairs		27	58.7	41	100	24.494	<0.001
Bundle with 50 hairs		17	37.0	0	0.0		
Bundle with 100 hairs		2	4.3	0	0.0		
<b>Sinclair Hair Density Scale</b>							
		No.	%	No.	%	$\chi^2$	P
1		6	13.0	41	100.0	77.196*	<0.001
2		32	69.6	0	0.0		
3		8	17.4	0	0.0		
Min.– Max.		1.0– 3.0	1.0– 1.0	Min-Max.	1.0 – 3.0	123.0*	<0.001
Mean $\pm$ SD.		2.04 $\pm$ 0.56	1.0 $\pm$ 0.0	Mean $\pm$ SD	2.04 $\pm$ 0.56		
Median (IQR)		2.(2.0-2.0)	1.0 (-)	Median (IQR)	2 (2-2)		
<b>FPHL Severity Index</b>							
		No.	%	No.	%	$\chi^2$	P
FPHL unlikely		0	0.0	41	100.0	87.0	<0.001
Early FPHL		13	28.3	0	0.0		
Established FPHL		33	71.7	0	0.0		
<b>FPHL Severity Index Score</b>							
		No.	%	No.	%	$\chi^2$	P
Min. – Max.		6.0-14.0	0.0-4.0	Min.-Max.	6.0 – 14.0	t= 25.839	<0.001
Mean $\pm$ SD.		11.09 $\pm$ 2.53	0.78 $\pm$ 0.91	Mean $\pm$ SD	11.09 $\pm$ 2.53		
Median (IQR)		11(9.0-13)	1(0-1)	Median (IQR)	11(9-13)		

FPHL = Female Pattern Hair Loss; IQR = interquartile range; SD = standard deviation.

All female was subjected to full history, measurement of serum level of BDNF and Questionnaires to access the psychological state. Quality of life was accessed in the patient group only.

The patients were diagnosed and classified according to FPHL Severity Index [7]. The cases age ranged from 15 to 50 years with a mean of 29.85  $\pm$  9.73, while the control age ranged from 15 to 41 years with a mean of 26.44  $\pm$  7.38. We selected this age group as androgen effects in addition to cosmetic concerns are marked during this age group. There was

no statistically significant difference regarding age between the case and control groups as they were age matched.

There was a high statistically significant difference regarding presence of acne between the case and the control groups (P value  $\leq$  0.05).

This is due to that Female Pattern Hair Loss and hormonal acne can be due to androgen receptors hypersensitivity to circulating dihydrotestosterone or coexisted hyperandrogenic status such as virializing tumor, polycystic ovarian syndrome, or those on oral contraceptive pills that

**Table 3.** Comparison between the two studied groups according to stress, anxiety, and depression scales.

	Cases (N = 46)	Control (N = 41)	Test	P
<b>Perceived Stress Scale</b>				
Min. – Max.	13.0 – 39.0	10.0 – 35.0	2.939	<0.05
Mean ± SD.	25.17 ± 5.96	21.27 ± 6.44		
Median (IQR)	25.0 (22.0 – 29.0)	21.0 (16.0 – 27.0)		
<b>Beck Anxiety Score</b>				
Min. – Max.	12.0 – 49.0	13.0 – 53.0	0.028	>0.05
Mean ± SD.	28.83 ± 8.09	28.88 ± 9.18		
Median (IQR)	27.50 (24.0 – 35.0)	26.0 (23.0 – 36.0)		
<b>Beck Anxiety Scale</b>				
Low anxiety	6 (13%)	5 (12.2%)	0.654	>0.05
Moderate anxiety	30 (65.2%)	24 (58.5%)		
Potentially concerning level of anxiety	10 (21.7%)	12 (29.3%)		
<b>Beck Depression Score</b>				
Min. – Max.	1.0 – 36.0	6.0 – 33.0	2.347	<0.05
Mean ± SD.	20.39 ± 8.02	16.73 ± 6.29		
Median (IQR)	19.0 (15.0 – 26.0)	16.0 (11.0 – 20.0)		
<b>Beck Depression Scale</b>				
Ups and downs are normal	3 (6.5%)	6 (14.6%)	5.402	0.349
Mild depression	11 (23.9%)	15 (36.6%)		
Border line depression	13 (28.3%)	11 (26.8%)		
Moderate depression	13 (28.3%)	7 (17.1%)		
Severe depression	5 (10.9%)	2 (4.9%)		
Extreme depression	1 (2.2%)	0 (0.0%)		

IQR = interquartile range; SD = standard deviation.

**Table 4.** Comparison between the two studied groups regarding serum Brain-Derived Neurotrophic Factor.

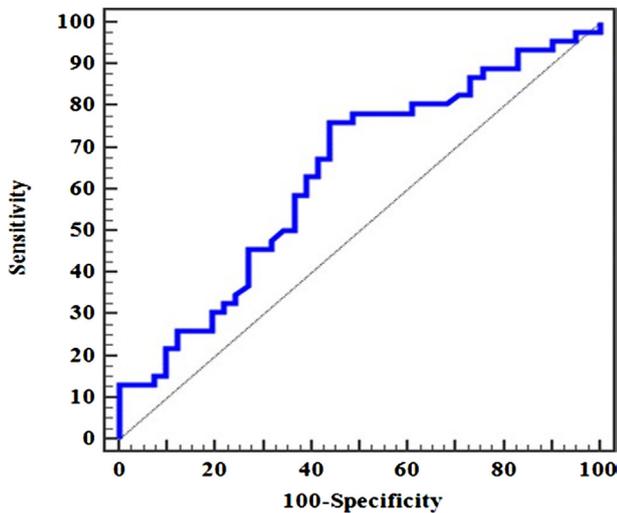
Serum BDNF	Cases (N = 46)	Control (N = 41)	U- Mann Whitney	P
Min. – Max.	0.31 – 7.68	0.47 – 7.18	688.50*	<0.05*
Mean ± SD.	0.85 ± 1.07	1.07 ± 1.26		
Median (IQR)	0.65 (0.58 – 0.71)	0.73 (63.0 – 81.0)		

BDNF = Brain-Derived Neurotrophic Factor; IQR = Inter quartile range; SD: Standard deviation.

**Table 5.** Validity for serum Brain-Derived Neurotrophic Factor to discriminate patients (N = 46) from control (N = 41).

	AUC	P	95% CI	Cut off	Sensitivity	Specificity	PPV	NPV
Serum BDNF	0.635	0.030	0.517 – 0.753	≤0.714	76.09	56.10	66.0	67.6

AUC = Area Under the Curve; BDNF = Brain-Derived Neurotrophic Factor; CI: confidence intervals; NPV = negative predictive value; PPV = positive predictive value.



**Figure 1.** Receiver operating characteristic curve for serum Brain-Derived Neurotrophic Factor to discriminate patients (N = 46) from control (N = 41).

**Table 6. Correlation between Serum BDNF and different parameters in cases group (N = 46).**

Serum BDNF vs.	$r_s$	P
Age (years)	0.038	>0.05
Age of onset of FPHL	-0.072	>0.05
Duration in years	0.293	<0.05
Sinclair hair density scale	0.036	>0.05
FPHL score	-0.050	>0.05
Perceived Stress Scale	-0.336	0.001
Beck Anxiety Score	-0.336	<0.05
Beck Depression Score	-0.328	<0.05
DLQI Score	0.228	>0.05

BDNF = Brain-Derived Neurotrophic Factor; DLQI = Dermatology Life Quality Index; FPHL = Female Pattern Hair Loss.

**Table 7. Correlation between Female Pattern Hair Loss Severity Index Score and different parameters in cases group (N = 46).**

	FPHL score	
	R	P
Age (years)	0.630	<0.001
Age of onset of FPHL	0.501	<0.001
Duration in years	0.535	<0.001
Sinclair Hair Density Scale	0.661	<0.001
Perceived Stress Scale	0.006	>0.05
Beck Anxiety Score	-0.034	>0.05
Beck Depression Score	0.117	>0.05
DLQI Score	-0.008	>0.05

DLQI = Dermatology Life Quality Index; FPHL = Female Pattern Hair Loss.

contains progesterone with a high androgenic potential such as norethindrone [14].

Bienenfeld and his colleagues stated that androgens are important in the incidence of FPHL and acne. They had essential but inadequate role in the development of, acne, and FPHL in women [15].

Regarding hirsutism, the signs of virilization and Menstrual irregularity in our study there was no statistically significant difference regarding between the patient group and the control. Carmina and his colleagues suggest that FPHL may be evident in the absence of other signs of hyperandrogenism, as it may be related to many factors, including genetic influences, androgen sensitivity and levels, and perhaps inflammation in the scalp [3]. Scalp scaling was significantly statistically higher than the control group (p-value  $\leq 0.05$ ). This can be interpreted by that the hair follicle miniaturization and apoptosis occurring in FPHL are often associated with micro-inflammation. This micro-inflammation causes destruction of the erector pili muscle and sebaceous gland hyperplasia. This led to an oily surface and scalp inflammation in form of seborrheic dermatitis. Hence, FPHL usually coexists with seborrheic dermatitis [16,17].

In our study there was a statistically significantly higher family history in the patient group (p value  $\leq 0.001$ ). Family history is an important risk factor for an early onset FPHL [18]. Our findings were in accordance with Lukasik and his colleagues who revealed that a positive history on the mother side is of great importance for FPHL incidence. Hair loss in more than one family member and in one grandparents may also indicate a higher risk of disease development [19].

In the current study the Hair Pull test, Sinclair Hair Shedding Scale, Sinclair Hair Density Scale, FPHL Severity Index scale and FPHL Severity Index score were statistically significant a higher in the patient group (P value  $\leq 0.001$ ).

FPHL has a negative psychological effect on the patients. It includes stress, depression and anxiety which are also important causes of telogen effluvium.

Brenner and Oldoni in their study reported that telogen effluvium may be the initial symptom in patients with FPHL [20].

In the patient group the Perceived Stress Scale and Beck Depression was a statistically significantly higher than the control group (P value  $\leq 0.05$ ).

This may be due to that the low self-esteem and negative body image caused by FPHL lead to deep psychological impact such as anxiety, stress and depression [3].

Our findings agree with Camacho and García-Hernández who found that AGA patients have personality changes in general and that Depression was higher in female 55% with AGA [21].

**Table 8.** Univariate and multivariate Logistic regression analysis for the parameters affecting cases (N = 46 versus. 41).

	Univariate		#Multivariate	
	P	OR (95%CI)	P	OR (95%CI)
Age (years)	0.075	1.047 (0.995 – 1.101)		
Presence of diet changes	0.165	0.206 (0.022 – 1.919)		
Presence of hirsutism	0.309	1.947 (0.540 – 7.023)		
Presence of hormonal acne	0.018	12.571 (1.544 –102.33)	0.165	8.642 (0.412 – 181.091)
Presence of menstrual irregularity	0.166	2.263 (0.713 – 7.182)		
Scalp				
Presence of itching	0.190	1.896 (0.729 – 4.936)		
Presence of scaling	0.025	2.696 (1.131 – 6.427)	0.898	0.879 (0.121 – 6.377)
Presence of family history of FPHL	<0.001	16.528 (5.570 –49.046)	<0.001	27.072(5.532 –132.498)
Presence of Hair Pull test	0.003	7.425 (1.985 – 27.771)	0.023	7.677 (1.319 – 44.696)
Increasing in Sinclair Hair Shedding Scale	0.189	0.664 (0.360 – 1.223)		
Increasing in Sinclair Hair Density Scale	0.999	–		
Increasing in FPHL score	0.990	–		
Increasing in Perceived Stress Scale	0.006	1.108 (1.029 – 1.192)	0.197	1.082 (0.960 – 1.221)
Increasing in Beck Anxiety Score	0.977	0.999 (0.951 – 1.050)		
Increasing in Beck Anxiety Scale	0.518	0.793 (0.393 – 1.602)		
Increasing in Beck Depression Score	0.026	1.074 (1.009 – 1.144)	0.270	0.915 (0.781 – 1.071)
Increasing in Beck Depression Scale	0.023	1.577 (1.066 – 2.332)	0.103	2.229 (0.851 – 5.838)
Increasing in Serum BDNF	0.625	0.911 (0.627 – 1.324)		

BDNF = Brain-Derived Neurotrophic Factor; CI = Confidence interval; FPHL = Female Pattern Hair Loss; LL = Lower limit; OR = odds ratio; UL = Upper Limit.

Regarding to quality of life most patient had impaired Dermatology Life Quality Index.

This may be caused by psychosocial problems in patients with FPHL, due to low self-esteem, altered self-image leading to depression, and less frequent positive social engagements.

Patients with AGA usually do alter their behavior peculiarly due to hair loss. Some patients use diverse haircuts or wash their hair more frequent in order to gain more volume [22]. Our study agrees with Shilpashree and his colleagues who found that most patients of FPHL suffer from moderate to severe psychosocial impact [23].

In our study the patient group serum level of BDNF was statistically significantly lower than the control group (P value < 0.05).

This can be interpreted by the relation between BDNF levels and major depressive disorders, anxiety related disorders, response to stressful events, and neurodevelopmental disorders. Most of these studies showed decreased BDNF levels with these psychiatric disorders.<sup>12</sup>

FPHL acts as a source of depression and chronic stress which leads to decrease in circulating BDNF concentration in case group [2].

On the contrary, Pancrateep and his colleagues found that in late male androgenic alopecia, mesenchymal dermal papillae cells of the balding scalp follicles produced about 12-fold more BDNF than those from the nonbalding scalp. They stated that the BDNF may be essential in mediating the impact of androgens on the hair follicles, acting as a negative regulatory factor [6].

This may be due to local production of BDNF by fibroblasts in the skin and T-lymphocytes may also produce neurotrophies in the skin [12].

In our study, there was statistically significant negative correlation regarding serum BDNF with Perceived Stress Scale, Beck Anxiety Score and Beck Depression Score respectively (P value ≤ 0.05).

Various studies have studied the link between BDNF levels and psychological disorders like major depression,

**Table 9.** Univariate and multivariate linear regression analysis for the parameters affecting serum BDNF in cases group (N = 46).

	Univariate		#Multivariate	
	P	B (95%CI)	P	B (95%CI)
Age (years)	0.383	0.014 (-0.019 – 0.048)		
Presence of diet changes	0.976	0.033 (-2.173 – 2.240)		
Presence of hirsutism	0.575	-0.237 (-1.083 – 0.608)		
Presence of hormonal acne	0.504	-0.251 (-1.001 – 0.499)		
Presence of menstrual irregularity	0.478	-0.266 (-1.016 – 0.484)		
Scalp				
Presence of itching	0.723	-0.119 (-0.794 – 0.555)		
Presence of scaling	0.108	-0.521 (-1.161 – 0.119)		
Age of onset of FPHL	0.968	-0.001 (-0.040 – 0.038)		
Duration of FPHL in years	0.009	0.117 (0.031 – 0.204)	0.362	0.030 (-0.036 – 0.096)
Presence of family history of FPHL	0.643	0.169 (-0.562 – 0.900)		
Presence of Hair Pull test	0.275	-0.361 (-1.018 – 0.297)		
Increasing in Sinclair Hair Shedding Scale	0.252	-0.315 (-0.863 – 0.232)		
Increasing in Sinclair Hair Density Scale	0.957	0.016 (-0.569 – 0.601)		
Increasing in FPHL score	0.983	0.001 (-0.127 – 0.130)		
Increasing in Perceived Stress Scale	0.010	-0.068 (-0.118 – -0.017)	0.872	0.003 (-0.038 – 0.044)
Increasing in Beck Anxiety Score	0.005	-.059 (-0.099 – -0.019)	0.080	-0.039 (-0.082 – 0.005)
Increasing in Beck Anxiety Scale	0.011	-0.675 (-1.187 – -0.163)	0.948	-0.017 (-0.554 – 0.519)
Increasing in Beck Depression Score	0.009	-.080 (-0.140 – -0.021)	0.011	-0.044 (-0.078 – -0.011)
Increasing in DLQI	0.561	-0.019 (-0.084 – 0.046)		
Increasing in Beck Depression Scale	0.024	-0.301 (-0.560 – -0.042)	0.738	-0.038 (-0.267 – 0.191)

B = Unstandardized Coefficients; BDNF = Brain-Derived Neurotrophic Factor; CI = Confidence interval; DLQI = Dermatology Life Quality Index; FPHL = Female Pattern Hair Loss; LL = Lower limit; UL = Upper Limit.

anxiety-related disorders, chronic stress, and neurodevelopmental disorders. The vast majority have reported that the development of the psychiatric diseases is associated with deficient BDNF levels. Furthermore, other studies have demonstrated that sufficient effective treatment improves the BDNF level of such patients [24].

In this study there were high statistically significant correlations between FPHL Score and age of patients, age of onset of FPHL, FPHL duration and Sinclair Hair Density Scale (P value ≤ 0.001). This may be related that woman with advancing age, there is gradually declines female sex hormones (progesterone and estrogen) and this may explain the unopposed increase of the negative impact of androgens effect on the hair follicles [25].

Patients suffering from FPHL have a high risk to develop chronic stress, anxiety and depression. The serum level of BDNF acts as a good predictor for assessment of negative psychological affection in such patients. We suggest that

a significant association between decreased serum BDNF levels and FPHL. BDNF may be an etiologic factor in its progression.

## Limitations of this Study

Was the lack of estimation of the tissue BDNF level in the balding scalp. Further studies are needed to investigate BDNF in both serum and skin.

## References

1. Tamashunas NL, Bergfeld WF. Male and female pattern hair loss: Treatable and worth treating. *Cleve Clin J Med.* 2021;88(3): 173-182. DOI: 10.3949/ccjm.88a.20014. PMID: 33648970.
2. Davis DS, Callender VD. Review of quality of life studies in women with alopecia. *Int J Womens Dermatol.* 2018;4(1):18-22. DOI: 10.1016/j.ijwd.2017.11.007. PMID: 29872671. PMCID: PMC5986111.

3. Carmina E, Azziz R, Bergfeld W, et al. Female Pattern Hair Loss and Androgen Excess: A Report From the Multidisciplinary Androgen Excess and PCOS Committee. *J Clin Endocrinol Metab.* 2019;104(7):2875-2891. DOI: 10.1210/jc.2018-02548. PMID: 30785992.
4. Kashyap MP, Roberts C, Waseem M, Tyagi P. Drug Targets in Neurotrophin Signaling in the Central and Peripheral Nervous System. *Mol Neurobiol.* 2018;55(8):6939-6955. DOI: 10.1007/s12035-018-0885-3. PMID: 29372544. PMCID: PMC7444275.
5. Peters EM, Hansen MG, Overall RW, et al. Control of human hair growth by neurotrophins: brain-derived neurotrophic factor inhibits hair shaft elongation, induces catagen, and stimulates follicular transforming growth factor beta2 expression. *J Invest Dermatol.* 2005;124(4):675-685. DOI: 10.1111/j.0022-202X.2005.23648.x. PMID: 15816823.
6. Panchaprateep R, Korkij W, Asawanonda P. Brain-derived nerve factor and neurotrophins in androgenetic alopecia. *Br J Dermatol.* 2011;165(5):997-1002. DOI: 10.1111/j.1365-2133.2011.10514.x. PMID: 21729031.
7. Harries M, Tosti A, Bergfeld W, et al. Towards a consensus on how to diagnose and quantify female pattern hair loss - The 'Female Pattern Hair Loss Severity Index (FPHL-SI)'. *J Eur Acad Dermatol Venereol.* 2016;30(4):667-676. DOI: 10.1111/jdv.13455. PMID: 26676524.
8. García-Batista ZE, Guerra-Peña K, Cano-Vindel A, Herrera-Martínez SX, Medrano LA. Validity and reliability of the Beck Depression Inventory (BDI-II) in general and hospital population of Dominican Republic. *PLoS One.* 2018;13(6):e0199750. DOI: 10.1371/journal.pone.0199750. PMID: 29958268. PMCID: PMC6025862.
9. Kaviani H, Mousavi AS. Psychometric Properties of the Persian Version of Beck Anxiety Inventory (BAI). *Tehran University Medical Journal.* 2008;66(2),136-140.
10. Cohen S, Kamarck T, Mermelstein R. Perceived stress scale. *J Health Soc Behav.* 1983;24(4):385-396. PMID: 6668417.
11. Shikar R, Harding G, Leahy M, Lennox RD. Minimal important difference (MID) of the Dermatology Life Quality Index (DLQI): results from patients with chronic idiopathic urticaria. *Health Qual Life Outcomes.* 2005;3:36. DOI: 10.1186/1477-7525-3-36. PMID: 1590721.; PMCID: PMC1180464.
12. Yanik ME, Erfan G, Albayrak Y, Aydin M, Kulac M, Kuloglu M. Reduced serum brain-derived neurotrophic factor in patients with first onset vitiligo. *Neuropsychiatr Dis Treat.* 2014;10:2361-2367. DOI: 10.2147/NDT.S74826. PMID: 25540586. PMCID: PMC4270357.
13. Botchkarev VA, Yaar M, Peters EM, et al. Neurotrophins in skin biology and pathology. *J Invest Dermatol.* 2006;126(8):1719-1727. DOI: 10.1038/sj.jid.5700270. PMID: 16845411.
14. Fabbrocini G, Cantelli M, Masarà A, Annunziata MC, Marasca C, Cacciapuoti S. Female pattern hair loss: A clinical, pathophysiologic, and therapeutic review. *Int J Women Dermatol.* 2018;4(4):203-211. DOI: 10.1016/j.ijwd.2018.05.001. PMID: 30627618. PMCID: PMC6322157.
15. Bienenfeld A, Azarchi S, Lo Sicco K, Marchbein S, Shapiro J, Nagler AR. Androgens in women: Androgen-mediated skin disease and patient evaluation. *J Am Acad Dermatol.* 2019;80(6):1497-1506. DOI: 10.1016/j.jaad.2018.08.062. PMID: 30312644.
16. Pekmezci E, Dundar C, Turkoglu M. Proprietary Herbal Extract Downregulates the Gene Expression of IL-1 $\alpha$  in HaCaT Cells: Possible Implications Against Nonscarring Alopecia. *Med Arch.* 2018;72(2):136-140. DOI: 10.5455/medarh.2018.72.136-140. PMID: 30302033. PMCID: PMC6126931.
17. Ramos PM, Brianezi G, Martins AC, da Silva MG, Marques ME, Miot HA. Apoptosis in follicles of individuals with female pattern hair loss is associated with perifollicular microinflammation. *Int J Cosmet Sci.* 2016;38(6):651-654. DOI: 10.1111/ics.12341. PMID: 27163333
18. Zhang X, Caulloo S, Zhao Y, Zhang B, Cai Z, Yang J. Female pattern hair loss: clinico-laboratory findings and trichoscopy depending on disease severity. *Int J Trichology.* 2012;4(1):23-28. DOI: 10.4103/0974-7753.96082. PMID: 22628986. PMCID: PMC3358934.
19. Łukaszik A, Kozicka K, Kłosowicz A, Jaworek A, Wojas-Pelc A. The role of family history and its influence on the onset time in female pattern hair loss. *Postepy Dermatol Alergol.* 2021;38(5):815-818. DOI: 10.5114/ada.2020.100745. PMID: 34849129. PMCID: PMC8610059.
20. Brenner FM, Oldoni C. Telogen effluvium x female pattern hair loss: is there correlation? *An Bras Dermatol.* 2019;94(4):486-487. DOI: 10.1590/abd1806-4841.20198427. PMID: 31644631. PMCID: PMC7007028.
21. Camacho FM, García-Hernández M. Psychological features of androgenetic alopecia. *J Eur Acad Dermatol Venereol.* 2002;16(5):476-480. DOI: 10.1046/j.1468-3083.2002.00475.x. PMID: 12428841.
22. Chan L, Cook DK. Female pattern hair loss. *Aust J Gen Pract.* 2018;47(7):459-464. DOI: 10.31128/AJGP-02-18-4498. PMID: 30114864.
23. Shilpashree P, Syrti Clarify, Ak Jaiswal, Shashidhar T. Impact of female pattern hair loss on the quality of life of patients *J Pak Assoc Dermatol.* 2016;26(4):347-352.
24. Autry AE, Monteggia LM. Brain-derived neurotrophic factor and neuropsychiatric disorders. *Pharmacol Rev.* 2012;64(2):238-528. DOI: 10.1124/pr.111.005108. PMID: 22407616. PMCID: PMC3310485.
25. Redler S, Messenger AG, Betz RC. Genetics and other factors in the aetiology of female pattern hair loss. *Exp Dermatol.* 2017;26(6):510-517. DOI: 10.1111/exd.13373. PMID: 28453904.