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Thyroid Functions in Patients with Diffuse Hair Loss

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ABSTRACT

Background: The function, growth, and development of every system in the body, including the hair follicle, are influenced by thyroid hormones. Numerous studies have demonstrated the expression of thyroid hormone nuclear thyroid receptors (TRs) in hair follicle cells. Thus, hair loss may be a symptom of thyroid disease, either hyperthyroidism or hypothyroidism. **Objective:** The aim of the current study is to investigate whether diffuse hair loss may be associated with thyroid dysfunctions.

Patients and methods: A cross sectional study was conducted on three groups of subjects, including 120 female patients suffering from diffuse hair loss; half of them do not have associated systemic disease or triggering factor and 60 ethnically, age and sex matched, healthy control subjects. Patients and control subjects were recruited from the Dermatology Outpatient Clinic of between March 2021 and June 2021.

Results: There was a statistical significant difference in thyroid-stimulating hormone (TSH) concentrations between 1st and 2nd group (P<0.001). TSH concentrations were higher among 2nd group than 1st group. As regard thyroxine free (FT4) levels, there was no statistical significant difference between the two groups of cases. There was a statistically significant difference in thyroid dysfunction in diffuse hair loss patients with associated disease compared to diffuse hair loss patients without associated disease and controls. None of the cases with diffuse hair loss without systemic disease (1st group) had thyroid disorders. While 16.6% of the cases with associated systemic disease (2nd group) had thyroid disorders, 3.33% were diagnosed with hyperthyroidism; 6.66% were diagnosed with overt hypothyroidism while the last 6.66% were diagnosed with subclinical hypothyroidism.

Conclusion: Abnormal thyroid functions were noted in a significant number of cases of diffuse hair loss making it mandatory to investigate them in all cases of diffuse hair loss in adult women.

Keyboards: Thyroid functions, Hair loss, TSH, Free T4.

INTRODUCTION

Both sexes and people of any age experience diffuse hair loss, a typical complaint dermatologists meet in their daily clinical practice [(1)]. However, women present more frequently than males because they take the problem of hair losing more seriously [(2)]. It lowers the patient's quality of life and causes intense emotional anguish, as well as problems with their personal, social, and professional lives [(3)].

The medical term for hair loss is alopecia. Diffuse alopecia is the medical term for alopecia that affects the scalp widely. Localized or focal alopecia, on the other hand, is characterized by patchy hair loss [(4)].

The most prevalent cause of diffuse hair losing, (a) Telogen effluvium, accounts for 30 to 50% of hair loss three months after the precipitating event and is identified by a positive pull test [(5)]. (b) Anagen effluvium is the abnormal, diffuse hair loss that occurs during the growth phase and is brought on by an occurrence that inhibits the hair follicle (HF) ability to divide, most often chemotherapy [(6)].

(c) Hair loss with a female pattern that starts only after puberty. The main issue is hair thinning [(7)]; the frontal hairline is intact; and there is no evidence of hair loss on a pull test. (d) Male pattern hair loss, which manifests as thinning hair and has no effect on a pull test. (e) Patchier distribution of diffuse alopecia areata; positive pull test. (f) Total hair loss on the scalp and/or body, also known as alopecia totalis or universalis [(7)].

Thyroid stimulating hormone (TSH), which is secreted by the thyrotrophs of the anterior pituitary in response to feedback from circulating thyroid hormones, causes the thyroid gland to produce thyroid hormones. TSH acts directly on the TSH receptor expressed on the thyroid follicular cell basolateral membrane. The sodium/iodide symporter, which is mediated by TSH, is followed by a sequence of processes required for adequate thyroid hormone synthesis and secretion [(8,9)].

Iodine atoms are a component of the structures of thyroid hormones (TH), thyroxine (T4), and the more powerful triiodothyronine (T3). Iodide is actively taken up by the sodium/iodide symporter (NIS) in the basolateral plasma membrane of thyrocytes, which is where it enters thyroid cells through the bloodstream [(10)].

In addition, thyroid hormones are essential for mammalian growth, differentiation, and metabolic equilibrium. Studies revealed that changes in human skin, hair composition, and function are related to thyroid diseases [(11)].

Thyroid hormone nuclear receptors TRs, which function as ligand-dependent transcription factors, are where the majority of the thyroid hormones' effects are mediated [(12)]. Additionally, evidence of thyroid receptors (TRs) expression in hair follicle cells suggests that thyroid hormones can directly influence hair

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follicle growth as opposed to merely regulating metabolic state [13].

Circulating T4 mostly affects peripheral organs, such as human hair follicles, after deionizing to T3 [10]. Additionally, T3 and T4 both greatly promote the production of intrafollicular melanin [14]. Important hair follicle processes include anagen phase prolongation, activation of the hair matrix, keratinocyte proliferation and pigmentation, and modulation of intracellular keratin expression are all directly influenced by T3 and T4 [15].

The aim of this study was to investigate association between the hair loss and thyroid dysfunction in Egyptian patients.

PATIENTS AND METHODS

A cross sectional study was conducted on 180 subjects (females) divided into 3 groups presented to the Dermatology Outpatient Clinic of Mansoura University Hospital between March 2021 and July 2021. Their ages were ranging between 18 and 50 years.

- 1st group includes: 60 females patients with diffuse hair loss without systemic disorders or precipitating factors for hair loss.
- 2nd group includes: 60 females patients with diffuse hair loss with systemic disorders and precipitating factors for hair loss; including diabetes mellitus, Hypertension, chronic kidney disease, hepatitis C, rheumatoid arthritis.
- 3rd Group includes: 60 females age and sex matched completely healthy controls (no diffuse hair loss and systemic disorders).

Inclusion criteria:

The patients with clinical diagnosis of diffuse hair loss (lasting for at least 6 months and resistant to medical supplements). Cases and controls recruited aged >18 years.

Exclusion criteria for 1st group of patients:

Patients with well-known causes of diffuse hair loss including: Drugs, infections, childbirth, malnutrition or crash diets, neoplasms, and systemic disorders.

All participants in this study were subjected to the following:

1. **History taking including:** age, sex, present history of the disease, treatment history, past history of the same condition (recurrence), medical history of other conditions and family history of diffuse hair loss or systemic diseases.

2. **Clinical examination including:**

- Full general examination to exclude systemic or autoimmune diseases.
- Dermatologic examination: The diagnosis of diffuse hair loss was established based on clinical examination. Clinical evaluation included a visual assessment of the pattern and extent of hair loss.

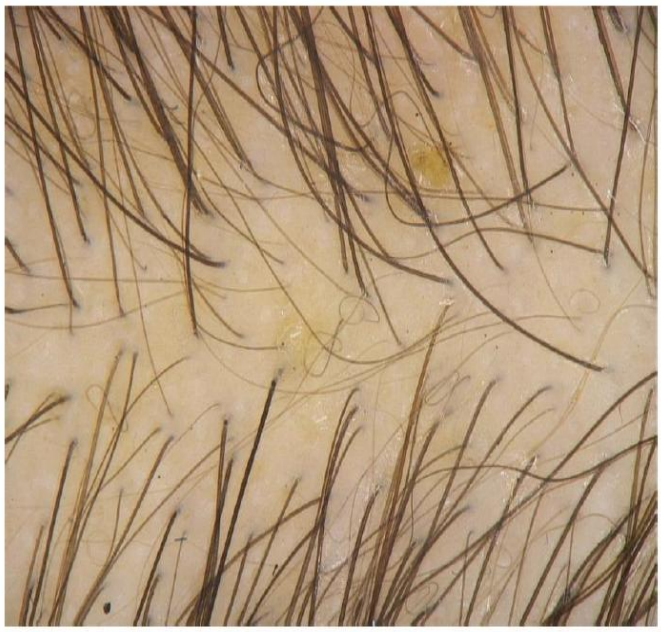

Figure (1): Trichoscopy of patient with female pattern hair loss (FPHL): Figure (1) illustrates hair diameter diversity, peripilar signs, yellow dots, and short vellus hair on the frontal scalp.

Figure (2): Trichoscopy of patient with chronic telogen effluvium (CTE): Figure (2) illustrates absence of variability and short regrowing hairs.

3. **Laboratory investigations including:**

- **Routine laboratory tests**: Complete blood count (CBC), random blood glucose level (RBG), liver function tests: albumin, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum creatinine.
- **Specific laboratory tests**: Thyroid Stimulating Hormone (TSH), free thyroxine (FT4).

Methods:

A. Specimen collection and storage:

5 ml venous blood was withdrawn from each subject under septic conditions. Thereafter, it was divided into 2 aliquots:

1. Two ml were collected into EDTA containing tubes for doing CBC.

2. Three ml were collected into plain tubes, left for 20 minutes at room temperature to clot and then centrifuged at 3000 rpm for 10 minutes. The separated serum was used for routine laboratory tests (CBC, RBG, liver function tests: albumin, bilirubin, ALT, AST and serum creatinine). The rest of serum was removed and aliquoted into eppendorf tubes and were used for determination of serum TSH, FT4 concentrations.

Samples intended for TSH and FT4 measurement were stored at -20°C for up to 1 months.

B. Routine lab investigations:

Complete blood count was performed using sysmex automated blood counter (serial no A7273). RBG level, serum creatinine level, liver function tests (albumin, bilirubin, ALT, AST) were done on automated device HITCHI 902, automated analyzer (serial no 1928013).

C. Specific lab investigations:

1. The quantitative determination of free thyroxine (FT4) by an enzyme linked immunosorbent essay (ELISA, USA).

2. The quantitative determination of thyroid stimulating hormone (TSH) by an enzyme linked immunosorbent essay (ELISA, Monocent, USA).

Ethical consent:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Number and percentage were used to describe qualitative data. After determining the normality of the data using the Kolmogrov-Smirnov test, quantitative data were reported using the median (minimum and maximum) for non-parametric data and the mean and standard deviation (SD) for parametric data.

Qualitative data:

Monte Carlo test as a Chi-Square test correction when more than 25% of cells in tables (>2*2) have counts less than 5.

Quantitative data between groups:

Parametric tests: More than two independent groups were compared using the One Way ANOVA test, and pair-wise comparisons were found using the Post Hoc Tukey test, and *Non Parametric tests:* The Mann Whitney U test was used to identify pair-wise comparisons when comparing more than two independent groups using the Kruskal Wallis test. P value $\leq$0.05 was considered significant.

RESULTS

Table 1 summarizes the age groups of the studied groups. The majority of control and 1st group and 2nd group were aged between 18-30 years.

Table (1): Age distribution of patients and controls:

Age/years	Control		1st group		2nd group	
18-30y	46	76.7%	42	70%	36	67%
>30-40	10	16.7%	22	36.6%	14	19.6%
>40-50	4	6.7%	0	0.0%	10	13.3%
>50-60	0	0.0%	0	0.0%	0	0.0%
Mean of age	28 year		28 year		29 year	

Table 2 reports that cases of 1st group (hair loss without systemic disease) had shorter disease duration (1-5 years in 96.7%) in comparison with cases of 2nd group (hair loss with systemic disease), which was mostly between (1-5 years) and (5-10 years) in 73.4% of patients.

Table (2): Incidence of duration of hair loss:

Duration of hair loss	1st group N=60(%)	2nd group N=60(%)	Statistical test
1-5 years	58(96.7%)	22(36.7%)	Monte Carlo test P<0.001*
5-10 years	2(3.3%)	22(36.7%)	
10-15 years	0	12(20.0%)	
15-20 years	0	4(6.7%)	

*Statistically significant.

Table 3 demonstrates that there is no statistical significant difference between 1st and 2nd group concerning the family history which is positive in 50% in the 1st group and 53.3% in the 2nd group (P=0.714). In addition, the majority of patients were affected by diffuse hair loss before 30 years in both groups.
There is statistical significant difference between 1st and 2nd group as regard duration of hair loss (P=0.001). The duration of the hair loss disease was longer in the 2nd group with median duration 10 years. However, the 1st group has median duration 4years.
Hair pull test was positive 40% in 1st group and 60% in the 2nd group. Hair thinning was present in 11.6% and 10 % in 1st and 2nd group. Hair density was reduced in almost all patients, 86% in 1st group, and 90% in the 2nd group.

Table (3): Comparison of different clinical presentations of hair loss between the studied cases:

Variable		1st group N=60	2nd group N=60	Statistical test
Family history of hair loss	**-ve** **+ve**	30(50.0%) 30(50.0%)	28(46.7%) 32(53.3%)	χ^2=0.133 p=0.714
Onset	**≤30** **>30**	54(90.0%) 6(10.0%)	53(88.0%) 7(12.0%)	p=0.714
Duration (years)	Median	4 years	10 years	P<0.001*
	(min-max)	(1-6)	(2-20)	
Positive hair pull test		24(40%)	36(60%)	p=0.714
Hair thinning		7(11.6%)	6(10.0%)	MC
Decreased hair density		52(86.0%)	54(90.0%)	P=0.01*

Table 4 illustrates that most of patients in the 1st and 2nd groups are affected by chronic telogen effluvium (CTE) in 83.3% and 76.7% respectively.

Table (4): Hair loss type by trichoscopy among patients:

Hair loss type	1st group	2nd group
Chronic TE Absence of variability and short regrowing hairs.	50 (83.3%)	46 (76.7%)
FPHL Hair diameter diversity, peripilar signs, yellow dots, and short vellus hair on the frontal scalp	6 (10%)	4 (6.7%)
FPHL and CTE	4 (6.7%)	10 (16.7%)

Table 5 demonstrates that there is a statistical significant difference in concentrations of TSH and FT4 in control and cases (P<0.001). TSH concentrations in cases were higher than in control, 5.07 (SD 1.22) mIU/l in cases and 2.80 (SD 0.07) mIU/l in control. FT4 concentration in control was 1.41 (SD 0.35) ng/dl and in cases 1.27 (SD 0.28) ng/dl.

Table (5): Comparison of TSH and FT4 concentrations between control and patients groups.

Variable		Control	Cases	Test of significance
TSH (mIU/L)	Median (min-max)	2.45 (1.5-7)	3.1 (0.1-21)	Mann Whitney U test <0.001*
FT4 (ng/dL)	Median (min-max)	1.4 (0.9-2.0)	1.3 (0.2-5.5)	Mann Whitney U test <0.001*

Kruskal Wallis test (Non Parametric tests), *statistically significant.

Table 6 demonstrates that there is a statistical significant difference in TSH concentrations between 1st and 2nd group (P<0.001). TSH concentrations were higher among 2nd group than 1st group. As regard FT4 levels, there was no statistical significant difference between the two groups of cases.

Table (6): Comparison of TSH and FT4 concentrations between 1st and 2nd group:

Variable		1st group	2nd group	Test of significance
TSH (mIU/L)	Median (min-max)	2.35 (0.6-6.8)	4.85 (1.0-21)	Mann Whitney U test <0.001*
FT4 (ng/dL)	Median (min-max)	1.35 (0.8-2.0)	1.1 (0.2-5.5)	Mann Whitney U test 0.238

Kruskal Wallis test (Non Parametric tests), *statistically significant.

Table 7 shows that there is statistical significant difference between control and studied patients groups regarding TSH and FT4 concentration (P<0.001). The TSH Mean ± SD values found to be 2.35±0.51 mIU/l in the 1st group, 4.85±1.2 mIU/l in the 2nd group and 2.45±0.57 mIU/l in the control group. The FT4 Mean ± SD values were 1.35±0.31 ng/dl, 1.1±0.26 ng/dl and 1.4±0.32 ng/dl in the 1st, 2nd and control respectively.

Table (7): Comparison of TSH and FT4 concentrations between all studied groups:

Variable		Control	1st group	2nd group	Test of significance
TSH (mIU/L)	Median (min-max)	2.45 (1.5-7)	2.35 (0.6-6.8)	4.85 (0.1-21.0)	**Kruskal Wallis test** <0.001*
TSH (mIU/L)	Median (min-max)	1.4 (0.9-2.0)	1.35 (0.8-2.0)	1.1 (0.2-5.5)	**Kruskal Wallis test** <0.001*

Kruskal Wallis test (Non Parametric tests), *statistically significant.

Table 8 shows that no abnormalities detected in the control and 1st group regarding TSH and FT4 levels. However, TSH level was found to be low in 2 patients, and high in 8 patients of the 2nd group. As for FT4, high and low levels were found in 2 and 4 patients respectively of the 2nd group.

Table (8): Number of hair loss patients and control groups with normal, high and low levels of serum TSH and FT4:

Variable		Control group	1st group	2nd group	test of significance
TSH	Low	0	0	2 (3.3%)	Monte Carlo test P=0.007*
	Normal	60 (100%)	60 (100%)	50 (83.3%)	
	High	0	0	8 (13.3%)	
FT4	Low	0	0	4 (6.6%)	Monte Carlo test P=0.012*
	Normal	60 (100%)	60 (100%)	54 (90%)	
	High	0	0	2 (3.3%)	

*Statistically significant.

Table 9 shows that two patients with low TSH and high FT4 are diagnosed with hyperthyroidism. Four Patients with high TSH and low FT4 were diagnosed with overt hypothyroidism, while the other 4 patients were diagnosed with subclinical hypothyroidism because they had normal FT4 and high TSH.

Table (9): Diagnosis of patients with abnormal values of TSH and FT4 of the 2nd group:

Patient number	TSH (0.4-7 MIU/L)	FT4 (0.8-2.0 ng/dl)	Diagnosis
2 patients (3.3%)	Low TSH	High FT4	**Hyperthyroidism**
4 patients (6.6%)	High TSH	Low FT4	**Overt hypothyroidism**
4 patients (6.6%)	High TSH	Normal FT4	**Subclinical hypothyroidism**

DISCUSSION

Women frequently have diffuse hair loss (DHL), a complex issue that can be difficult to manage. The most frequent cause is telogen effluvium, which is followed by female pattern hair loss and chronic telogen effluvium (CTE) [16].

Chronic hunger, acquired zinc deficiency, and other micronutrient deficits are a few of the factors that contribute to chronic telogen hair loss, as can thyroid conditions (hypo- and hyperthyroidism) [17].

The aim of this study was to find association between the hair loss and thyroid dysfunction in Egyptian female patients.

In the current study, the majority of control, 1st group and 2nd group are aged between 18-30 years. The majority of patients are affected by diffuse hair loss before 30 years in both groups. This age distribution backs up **Malkud's** [18] assertion that practically all individuals with diffuse hair loss have the condition before the age of 40. According to **Poonia *et al.*** [19], the age range of 21 to 40 years had the highest incidence of hair loss, or 70%. 11% of patients were above the age of 40, and about 19% of patients were under 20.

In the present study, patients of 1st group (hair loss without systemic disease) have shorter disease duration (1-5 years in 96.7%) in comparison with cases of 2nd group (hair loss with systemic disease), which is mostly between (1-5 years) and (5-10 years) in 73.4% of patients. There was a statistically significant difference between 1st and 2nd group as regard duration of hair loss (P=0.001). The second group's median duration of the hair loss condition is longer, at 10 years. The first group, however, had a median lifespan of 4 years. According to **Agarwal *et al.*** [16], the average length of hair loss was 18.84 (SD 25.5) months, with a range of 15 days to 2 years. In a similar vein, **Poonia *et al.*** [19] observed that the majority of patients presented within a year of the hair loss beginning, and the duration of the increasing hair loss ranged between 1 and 60 months. This is consistent with **Sadick *et al.*** [20] findings that the condition is chronically progressing.

In the current study, there was no significant difference between 1st and 2nd group concerning the family history which was positive in 50% in the 1st group and 53.3% in the 2nd group. In a similar vein, **Agarwal *et al.*** [16] discovered that 38% of the patients had a family history including a first-degree relative. According to **Phillips *et al.*** [6], who demonstrated that both maternal and paternal genetics appear to be involved in the transmission of DHL and that the mechanism of this inheritance is best understood as polygenic, the results showing a high ratio of DHL in relatives of patients were explained.

Our results showed that hair pull test was positive 40% in 1st group and 60% in the 2nd group. Hair thinning was present in 11.6% and 10 % in 1st and 2nd group respectively. Hair density was reduced in almost all patients, 86% in 1st group, and 90% in 2nd group. According to our findings, **Poonia *et al.*** [19] discovered that all patients had lower hair density on the scalp inspection, but 20% of patients had hair thinning. In 36% of patients, the hair pull test was positive.

The present study showed that most of patients in the 1st and 2nd groups are affected by chronic telogen effluvium (CTE) (83.3% and 76.7%, respectively). In agreement with this, 116 (64.44%) of the 180 patients reported by **Malkud** [18] had telogen effluvium, 28 (15.55%) had CTE, 21 (11.66%) had FPHL, and 1 (0.55%) had AE. Telogen effluvium (TE) (84, 62.2%) and female pattern hair loss (FPHL) (32, 23.7%) were the two most prevalent kinds of alopecia in **Deo *et al.*** [21] study.

In the instant study, there was a statistically significant difference between control and studied patients' groups regarding TSH and FT4 concentration (P<0.001). The TSH median values found to be 2.35 mIU/l in the 1st group, 4.85 mIU/l in the 2nd group and 2.45 mIU/l in the control group. The FT4 median values were 1.35 ng/dl, 1.1 ng/dl and 1.4 ng/dl in the 1st, 2nd and control respectively. There is also a statistical significant difference in concentrations of TSH and FT4 in control and cases (P<0.001). TSH mean level concentrations in cases were higher than in control.

Hegde and Noronha [17], in contrast to our study, discovered that there was no statistically significant difference between the patients and controls in terms of mean T4 and TSH levels.

In the study by **Jain *et al.*** [22], the mean TSH levels were 2.15mIU/mL in the patients and 2.11mIU/mL in the controls. TSH values above 7 mIU/ml were present in 8% of the individuals. In 7% of instances, the mean serum T3 levels were less than 0.07 ng/mL. The average total T4 levels were 8.14 g/dL in the controls and 8.g/dL in the patients. These results were in contrast to those of a research by **Vincent and Yogiraj** [23], which found that thyroid dysfunction was present in 23.7% of instances of hair loss.

Comparing the two group of cases (1st and 2nd group), there is a statistical significant difference in TSH mean level concentrations (P<0.001). TSH mean level concentrations are higher among 2nd group than 1st group. As regard FT4 levels, there is no statistical significant difference between the two groups of cases.

With respect to the thyroid function, our study demonstrated that no abnormalities detected in the control and 1st group regarding TSH and FT4 levels. However, 2nd group showed 10 patients (16.6%) with abnormal thyroid function. Two of them (3.33%) are diagnosed with hyperthyroidism; four patients (6.66%) are diagnosed with overt hypothyroidism while the last four patients (6.66%) are diagnosed with subclinical hypothyroidism.

Nearly the same proportion of thyroid disorders—17%, with 9.63% having hypothyroidism and 7.4% having hyperthyroidism—was found in the study carried out by **Deo *et al.*** [21]. However, in the study conducted by **Malkud** [18], 74 out of 130 patients with TE underwent a thyroid function test; only 3/74 (4.05%)

patients had hyperthyroidism, and 2/74 (2.70%) patients had subclinical hypothyroidism.

In a similar vein, **Shrivastava** [(14)] discovered a substantial difference in the incidence of aberrant thyroid function between patients and controls (TSH). When compared to the prevalence in the control group (4%), their study found a significant incidence of impaired thyroid function (11.50%).

In women with hypothyroidism, DHL was significantly associated, according to study **Poonia *et al.*** [(19)]. 11 patients (11%) were discovered to have hypothyroidism, a newly recognised thyroid condition. The frequency of hypothyroidism was similar with other research, however in study **Poonia *et al.*** [(19)], no females were reported to have hyperthyroidism.

CONCLUSION

Incidence of hair loss was found to be the highest in the 18-30 years of age group. Chronic telogen effluvium (CTE) was the most common pattern of hair loss followed by FPHL found in our study. Abnormal thyroid functions were noted in a significant number of cases of diffuse hair loss making it mandatory to investigate them in all cases of diffuse hair loss in adult women.

RECOMMENDATIONS

- Further large-scale studies including a higher number of patients with a wider age group are required to confirm our results and analyze the pathogenic mechanisms underlying the correlation between DHL occurrence and thyroid disorders.
- More studies are needed to establish the association between chronic diffuse hair loss with thyroid dysfunction and if it can be an important therapeutic target to treat chronic diffuse hair loss.
- Women suffering from recalcitrant hair loss should undergo thyroid function tests to reveal subclinical thyroid disorders.

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