Low Iron stores as one of the risk factors for hair loss

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Abstract:

Introduction: Hair loss affects a large part of the population with up to 50 percent of men
and women throughout their lives.
Objectives: To assess iron status in patients who complained of hair loss and had either
telogen effluvium (TE) or androgenic alopecia (AA) ,and evaluate risk factors associated with
 hair loss.**Methods**: This study included 100 patients with hair loss, 40 healthy persons as
control, all patients were subjected to a questionnaire for assessment of hair loss,
dermatologic evaluation and biochemical analysis for blood count (RBCs), serum iron, serum
ferritin and erythrocyte sedimentation rate (ESR).
Results: Significant lower means of serum iron , serum ferritin , RBCs count and
Hemoglobin levels were reported between cases relative to controls. As regard to amount of
hair loss "moderate hair loss"was found in (48%) of patients and "excessive hair loss"was
found in (52%). Among the patients affected by excessive hair loss, a larger proportion   had
clinical picture of anemia and low iron stores
(< 40 µg/L) (73.1%) ,(86.5%) respectively,compared to (47.9%),(70.8%) in patients with
moderate hair loss.   It is found that, positive history of emotional stress, positive family
history, use of hair conditioner, presence of dandruff in scalp, use of hair heat iron, use of
coloring agents, more frequent hair comb/day, frequent hair wash/week and seasonal variation
had deleterious effect on hair loss. **Conclusion:** Iron deficiency is one of the potential risk
factors for hair loss.
Key words: hair loss, risk factors, serum ferritin,serum iron .

Introduction:

Hair loss affects a large part of the
population with up to 50 percent men
and women throughout their lives[1] .
Diffuse hair loss can affect both sexes
at any age, but usually recognized
more readily by women than men.
Androgenic Alopecia (AGA) and
Telogen Effluvium (TE) account for
almost all cases of diffuse alopecia [2].

TE, or hair shedding, results from the
synchronous transition of hair follicles
from the growing stage of the hair
cycle (anagen) to the resting stage of
the hair cycle (telogen) [3]. Common
precipitating events include childbirth,

fever, and medications, although
precipitating factors are often not
discernable [4].TE lasting greater than
6 months is referred to as "chronic
TE"[5]. Because hormonal changes in
the postpartum period are common
causes of telogen effluvium, women
may have a greater tendency to
experience this condition, also, women
tend to find the hair shedding more
troublesome than men do [6].

As regard to AGA, Hamilton, 1942,
established that male pattern hai
loss is a physiologic process induced
in genetically predisposed hair

follicles under the influence of androgens [7]. Female pattern hair loss (FPHL) has emerged as the preferred term for androgenic alopecia in females owing to uncertain relationship between androgens and this

entity [8].In AGA, the duration of the anagen phase decreases with each passage through the hair cycle, because the duration of the anagen phase is the main determinant of hair length, the maximum length of the new anagen hair is shorter than its predecessor.The main histological characteristic of AGA is the miniaturization of terminal hair follicles and their transformation to vellus-like follicles [9].

Iron deficiency has been suspected to represent one of the possible cause of excessive hair loss [10]. The relationship between iron body status and different types of hair loss has been investigated in a number of studies, however with relatively discrepant findings [11]. Centres for Disease Control(CDC) (1998) divided iron into three compartments:
Functional iron (hemoglobin, myoglobin),storage iron (ferrittin and hemosiderin) and transport iron(transferrin) [12].
Trost et al (2006) described the degree of deficiency into:
1. Low iron store: body iron stores are reduced (serum ferritin <40μg/L) and functional iron remains normal.
2. Iron deficiency without anemia: both storage and transport iron are decreased (serum ferritin <40μg/L- serum iron <50μg/L), but functional iron remains normal. Red blood cell production is diminished, resulting in insufficient iron for growth and function.
3. Iron deficiency anemia: storage, transport, and functional iron are severely decreased (serum ferritin <40μg/L- serum iron <50μg/L ,

HB<12 g/dL for female & <13 g/dL for male) and can lead to impairment of function of multiple organs [13].

Aim of the work:
To assess the impact of iron status of the patients with hair loss and to evaluate risk factors associated with hair loss.

Patients and methods:
This study was conducted at the department of Dermatology ,venereology and andrology ,with collaboration with clinical pathology department, Sohag university hospital during the period from January 2010 to end of June 2010.
The study included 100 patients with hair loss with the diagnosis of either TE or AGA, recruited from the outpatient's clinic of the Dermatology department, in addition to 40 sex and age matched healthy volunteers(with no subjective or objective hair loss) as controls. Written informed consents were obtained from all enrollees. Approval of research ethics committee of Sohag University hospital was obtained before the start of the study.

exclusion criteria Study:
All cases with local scalp disease, cicatricial alopecia and alopecia areata. Patients who have medical diseases known to be associated with hair loss, e.g. chronic renal failure, hepatic failure or thyroid disorders.
Patients who receive specific drugs known to be associated with hair loss e.g. hormonal contraceptive, anticoagulants, cytotoxic agents, chemicals or toxins associated with hair loss. Pregnant females and postpartum ones within 6 months.
All patients were subjected to: full history taking, general examination to asses signs of anemia, local scalp examination to exclude local disorders, detect type and severity of hair loss.
Pulling test: a negative test (≤6 hairs obtained) indicates normal

shedding, whereas positive test (>6 hairs obtained) indicates active hair shedding[6]. All diagnoses were made by history and physical examination.

The diagnosis of TE was made if the patients had increased shedding by history or physical examination .
Androgenic alopecia was diagnosed according to Norwood classification for men[14] and Ludwig's scale for women[15].   Regarding iron stores, patients were classified by Trost et al (2006) classification (mentioned above) [13].

- Hair loss assessment:

Hair loss was assessed with help of a set of descriptive questions extracted from a self-assessment questionnaire [10] .
Multiple correspondence analysis and hierarchical cluster analysis (HCA) were used to group the answers with similar expression patterns.

A.Hair loss questionnaire:
1. Do you feel involved by hair loss?
- Yes   - No
2. Currently, during hair washing, how much do you estimate hair loss?
- Many hairs.   – few   - very few or none
3. Currently, drying your hair with a bath towel, how much do you estimate your hair loss?
- Many hairs   - few hairs   - very few or none
4. Currently, during hair brushing, how much do you estimate your hair loss?
- Many hairs   - few hairs   - very few or none
5. Currently, after a night's sleep, how much do you estimate your hair loss on the pillow?
- Many hairs   - few hairs   - very few or none
6. Currently, during a day how much do you estimate your hair loss on your clothes?
- Many hairs   - few hairs   - very few or none

B. Hair loss classification according to descriptive questions, table.1:(Deloche et al, 2007) [10].

Cluster 1. absence of hair loss	Cluster 2. Moderate hair loss	Cluster 3.Excessive hair loss
Not concerned by hair loss	Hair loss self –perceived as normal hair loss	Hair loss self-perceived as abnormal hair loss
No hair loss or little during the washi	Lose a few hairs during the washing	Lose a lot of hairs during washing
No hair loss or a little during hair brushing	Lose a few hairs during hair brushing	Lose a lot of hairs during hair brushing
No hair loss or a little on the bath towel	Lose a few hairs on the bath towel	Lose a lot of hairs on the bath towel
No hair loss or a little on the pillow	Lose a few or a lot of hairs on the pillow	Lose a few or a lot of hairs on the pillow

No hair loss or a little on the clothes	Lose a few or a lot of hairs on the clothes	Lose a few or a lot of hairs on the clothes

- laboratory investigations: complete blood count, serum
iron, serum ferritin and erythrocyte Sedimentation Rate (ESR) were done to exclude
non specific inflammation if (ESR>30mm per h) may indicate non specific
inflammation that also raises ferritin and invalidates its use as a marker of iron
status(As ferritin is also an acute phase reactant, this means its level can increase
during infection or inflammation) [13].
Statistical analysis: results were tabulated and analyzed using SPSS package
programm version 17,T-test and Chi-square tests were used for comparison.

Table.2: comparison between cases with hair loss and control group according to risk factors for hair loss.

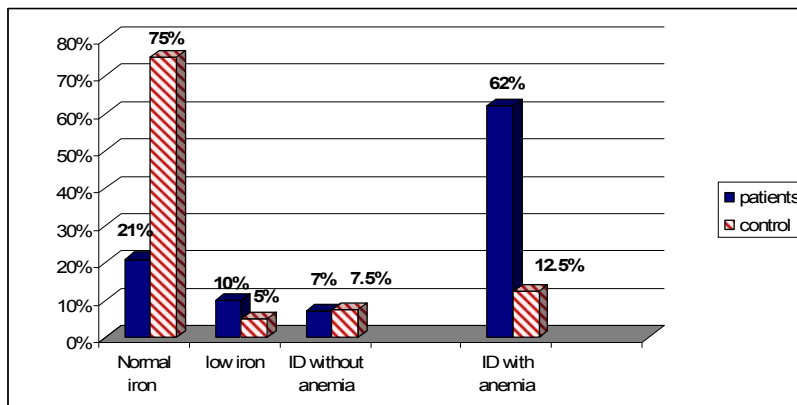| Variables		Cases with hair loss		Control group		P.value	Risk (Odd ratio)
		N=100	100%	N=40	100%		
Family history of HL	+ve	48	48%	6	15%	** 0.000	5.2
	- ve	52	52%	34	85%		
History of emotional sress	+ve	71	71%	6	15%	** 0.000	13.8
	- ve	29	29%	34	85%		
Use of hair heat iron	Yes	37	37%	4	10%	* 0.02	5.3
	No	63	63%	36	90%		
Use of hair conditioner	Yes	55	55%	10	25%	** 0.001	3.7
	No	45	45%	30	75%		
Use of coloring agent	Yes	54	54%	14	35%	* 0.03	1.5
	No	46	46%	26	65%		
Dandruff in scalp	present	53	53%	9	22.5%	** 0.001	3.9
	absent	47	47%	31	77.5%		
Frequency of hair comb/day	≤ 1/d	29	29%	31	77.5%	* 0.05	2.6
	≥ 2/d	71	71%	9	22.5%		
Seasonal variation	present	45	45%	9	22.5%	* 0.01	2.8
	absent	55	55%	31	77.5%		
Source of water supply	wells	42	42%	9	22.5%	* 0.03	2.4
	running	58	58%	31	77.5%		
Use of hair covers	Yes	48	48%	21	52.5%	0.63	0.8
	No	52	52%	19	47.5%		
Frequency of hair wash/week	≤ 2/w	74	74%	27	67.5%	0.5	1.3
	>2/w	26	26%	13	32.5%		
Lice/nets in scalp	present	23	23%	6	15%	0.43	1.6
	absent	77	77%	34	85%		

Table.3: comparison between male and female patients in relation to risk factors for hair loss.

Variables		Male		Female		P.value	Risk (Odd ratio)
		N=30	100%	N=70	100%		
Family history of HL	+ve	22	73.3%	26	37.1%	** 0.001	4.7
	- ve	8	26.7%	44	62.9%		
History of emotional sress	+ve	22	73.3%	49	70%	0.7	1.2
	- ve	8	26.7%	21	30%		
Type of hair loss	AGA	24	80%	19	27.1%	** 0.000	7.2
	TE	6	20%	51	72.9%		
Symptoms& Signs of anaemia	Present	12	40%	49	70%	** 0.005	0.3
	Absent	18	60%	21	30%		
Use of hair heat iron	Yes	2	6.7%	35	50%	** 0.000	0.1
	No	28	93.3%	35	50%		
Use of hair conditioner	Yes	10	33.3%	45	64.3%	** 0.004	0.3
	No	20	66.7%	25	35.7%		
Use of hair coloring agents	Yes	17	56.7%	29	41.4%	* 0.03	1.8
	No	13	43.3%	41	58.6%		
Pulling test	+ve	2	6.7%	45	64.3%	** 0.000	0.4
	-ve	28	93.3%	25	35.7%		
Lice/nets in the scalp	Present	1	3.3%	22	30.7%	* 0.03	1.5
	Absent	29	96.7%	48	69.3%		
Frequency of hair comb/day	≤1/d	27	90%	63	90%	1	1
	≥2/d	3	10%	7	10%		
Frequency of hair wash/week	< 2/w	20	66.7%	54	77.1%	0.3	0.6
	>2/w	10	33.3%	16	22.9%		
Use of hair covers	Yes	15	50%	33	47.1%	0.79	1.1
	NO	15	50%	37	52.9%		
Dandruff in the scalp	Present	15	50%	38	54.3%	0.69	0.8
	Absent	15	50%	32	45.7%		

Table.4: Comparison between male and female patients regards iron status.

Variables	Males		Females		P.value	Odd ratio
	N= 30	100%	N=70	100%		
Iron abnormalities: Normal iron status	13	43.3%	8	11.4%	0.000 *	5.9
Abnormal iron [a]	17	56.7%	62	88.6%		
Iron status: 1.Normal iron status	13	43.3%	8	11.4%		
2.Low iron store	1	3.3%	9	12.9%	0.002 *	
3.Iron deficiency without anaemia	3	10%	4	5.7%		
4.Iron deficiency with anemia.	13	43.3%	49	70%		

[a] based on level of serum ferritin.

Figure.1: Iron status between cases with hair loss and control
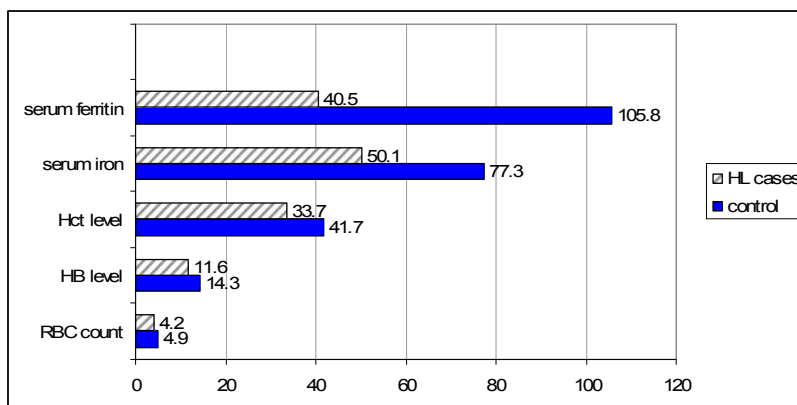
Fig.2: Comparison between hematological parameters in cases
with hair loss and control group.
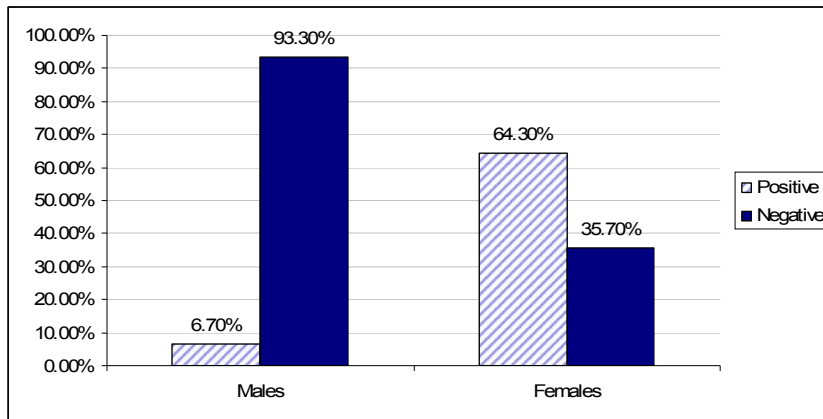
Fig.3: Pulling test between male and female patients.
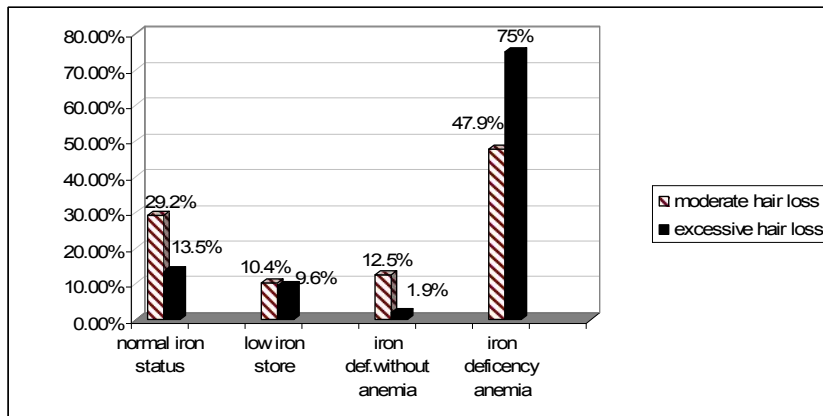
Fig.4: The relation between iron status and amount of hair loss

Results:

In this study, 100 patients with diffuse hair loss were examined,
investigated and clinically diagnosed, 70 of them were females, with
  43 patients had AGA and 57 had TE, in addition 40 healthy persons
were selected as controls.
The age of cases ranged between (12-55ys) with a mean of 25.3± 9.8years. The age of
control group ranged between (15-59ys) with a mean of 27.6± 11.8 years.
Among AGA patients, 24 were males and 19 were females, in T E,
 6 were males and 51were females.
**1 .Comparison between cases with hair loss and control group according to risk
factors for hair loss.**
This is shown in (table2 ,fig.1) with positive history of emotional stress,
use of hair conditioner, presence of dandruff in scalp ,low iron status and presence of
clinical features of anemia, showed highly significant increase among cases relative to
control.
**2.Comparison between cases with hair loss and control regarding to
Clinical features of iron deficiency anemia(IDA), iron status and hematological
parameters**
According to fig.1, clinical features of anemia were more prevalent
among cases (61%) relative to (10%) in control group with highly
significant differences (P value < 0.001), also a highly significant
low iron status was detected among cases (79%) relative to (25%)

of control group.
As demonstrated in fig.2, all hematological parameters had significant
lower means among cases compared to control group, the mean of serum
 iron and serum ferritin were (50.1± 12.1) , (40.5±14.6) µg/L respectively among
cases in comparison to (77.3±9.2), (105.8±28.8) in control group.

3- Comparison between male and female patients according to risk factors for hair loss

 Family history of hair loss was significantly more prevalent among males(73.7%),
while use of hair heat iron, frequent hair Comb/day, use of hair conditioner, presence
of symptoms and signs of anemia were significantly higher in female group (Table3)
and low iron status was also significantly higher in female patients as shown in
(Table4).

  TE was more prevalent in females affecting (72.9%), while AGA affected males
more (80% of them). Low iron status was significantly lower in TE patients than
AGA patients. Pulling test was positive in 64.3% of female group relative to 6.7%
only in male group, Fig.3

4.Comparison between amounts of hair loss according to iron status

Fig.4 shows cases with excessive hair loss had high prevalence of low
iron store relative to those with moderate degree with insignificant
difference (P value =0.05), regarding iron status, cases with excessive
hair loss had iron deficiency anemia in 75% relative to 47.9% of cases
with moderate degree, with significant difference (P value=0.02)

Discussion:

Loss of hair follicles and alterations in hair fiber production in humans is generally not a life threatening events but does have a dramatic impact on quality of life and emotional well being, as such hair disorders are a significant issue for many individuals[16].

The relationship between iron body status and different types of hair loss has been investigated in a number of studies, however, with relatively discrepant findings [11].

In this work, the factors impacting hair loss were analyzed, focusing upon iron status as one of the important risk factors for diffuse hair loss. In this study, females are more affected with hair loss than males, this coincides with Thai and Sinclair (2002) who reported that TE predominantly affects women between 30-60ys old[17].

Regarding the type of hair loss, the present findings showed that higher prevalence of AGA among male patients, while TE showed significant female affection .These findings matched with Rebora et al (2005) who reported that about 90% of TE affected women, whereas 60% of AGA affected men [18].

In the present study , clinical features of anemia were more
prevalent among female cases with hair loss relative to male cases,
complete blood count (CBC) analysis of cases with hair loss showed
lower means of RBCs count/dl, HB level g/dl and Htc% than controls.

Also, significant lower means of serum iron<50 µg/l and serum ferritin levels<40 µg/l.compared to control group were reported in this study.

The clear significant statistical relationship between hair loss and iron

status at multiple levels and by various parameters that been identified in the current study, are in agreement with many studies (Deloche et al . 2007, Gonul and Cakmaelk, 2009)[10,19] . Also, agreed with result of

Moeinvaziri and Mansoori (2009) who reported that the mean ferritin level and transferrin saturation were statistically significantly lower in patients with diffuse telogen hair loss than in subjects without hair loss [11].

Our results support the "threshold hypothesis" [20], which states that decreased iron stores lower the threshold for developing different types of alopecia.

On the contrary , Boffa et al (1995) analyzed serum iron in 32 patients with hair loss (21 females, 11 males) and defined iron deficiency as serum ferritin > 15 μg/L, analysis of their data revealed no increased incidence of iron deficiency in patients with hair loss[21].

Also, Aydingoz et al (1999) were unable to demonstrate significant difference in serum ferritin levels among 43 women with diffuse alopecia and female pattern alopecia compared to 46 healthy controls[22].

This discrepancy could be explained by differences in the design of the studies. Nevertheless, additional studies with larger sample size are required to better understand the biological significance of the critical iron status level in the etiology of hair loss.

In hair follicles, iron is implicated as a metabolic factor. Iron is also a main constituent for hemoglobin, and iron depletion leads to anemia.

From a biologic point of view, hair follicle matrix cells are some of the most rapidly proliferating cells in the body. At the cellular level, ferritin levels are increased in nondividing cells, such as stem cells and terminally differentiated cells, whereas rapidly proliferating cells appear to have lower levels of ferritin and higher levels of free iron [23,24,25] . This balance of ferritin and iron is at least partially controlled by the transcription factor c-myc [25]. Overexpression of c-myc in the cutaneous epithelium results in loss of follicular differentiation and a decrease in stem cells[26], but whether this phenotype is related to abnormal iron metabolism remains to be determined. Another likely mechanism for iron's possible effect on hair growth stems from its requirement as a cofactor for ribonucleotide reductase, the rate-limiting enzyme for DNA synthesis. The depletion of iron could prevent proper functioning of this enzyme resulting in inhibition of proliferation [27]. Inhibition of other iron-dependent enzymes, such as stearyl CoA desaturase, when mutated causes hair loss in mice [28] and is also present in the human hair follicle [29] , could contribute to hair loss as well.

The current study also evaluated other risk factors associated with diffuse hair loss and reported a significant statistical difference between cases with hair loss and control group as regard history of emotional stress. This finding agreed with Arck et al. (2003) and Peters et al. (2004) who reported that chronic stress in human was associated with significant inhibition of hair growth, increased mast cell degranulation and perifollicular inflammation[30,31] , on the contrary,Harrison and Sinclair (2002) reported that evidence for this association appears to be weak and everyday stresses are likely not enough to trigger hair loss[32].

In this study there was a statistically significant increase in hair loss in late summer in cases than controls this agreed with Randall and Ebling (1991) who reported that seasonal variation of hair loss is caused by raised summer

androgens that amplify a biannual cycle by stimulating growth rate to superimpose a single cycle [33].

The present study reported a significant percentage of dandruff among cases with hair loss, particularly among those with an excessive degree with no gender differences, these agreed with study of Pie`rard–Franchimont et al. (2000) who detected that presence of dandruff preceded or accompanied TE[34].

In this study, there were a significant loss of hair between cases compared to controls ,and in female patients compared to male

Conclusion:

Hemoglobin concentration can be used to screen for iron deficiency, while serum ferritin concentration can be used to confirm iron deficiency.

Low iron status, presence of clinical features of anemia, positive history of emotional stress, use of hair conditioner, presence of dandruff in scalp positive family history, use of hair heat iron, use of hair coloring agents, more frequent hair comb/day, frequency of hair wash/week and seasonal variation, all had deleterious effect on hair loss.

regarding use of hair dryer, hair heat iron, use of hair shampoo, hair conditioner and shower jell.

These results coincide with Ruetsch and Kamath (2004) who found that using hair dryers or curling irons is associated with structural changes of hair[35] .Also these results match with Masukawa et al (2005) who mentioned that frequent shampooing, efficiently cleanses hair of its natural sebum,increase the prevalence of hair falling where leave the hair dry, statically charged and more exposed to friction and thus to weather [36].

Recommendations:

All patients with diffuse hair loss must be screened for iron status, especially if the patient has clinical features (symptoms and signs) of anemia, or has history of blood loss .An excessive hair loss supports the need to check serum ferritin levels. The cause of iron deficiency must be identified. Iron supplementation is highly recommended, for all cases with hair loss associated with iron deficiency (identified clinically and/or confirmed by laboratory tests) and recommended for those found to have low iron stores.

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الملخص العربى

نقص مستويات الحديد كاحد عوامل الخطر لمرض سقوط الشعر

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يعتبر سقوط الشعر شكوى عامة ، ومع ذلك يعد تقييمها و علاجها صعبا للان ، فالمريض يلاحظ تساقط كثير من الشعر على الاكتاف او اثناء التسريح او على الوسادة اثناء النوم ومع ان السقوط العام لشعر الراس ذو اسباب كثيرة و متعددة الا انه فى كثير من المرضى يصعب تحديد السبب. و حديثا بدا ينظر لنقص الحديد كاحد اسباب السقوط الشديد للشعر.

الهدف من البحث:

- تعيين نسبة الحديد بالدم فى مرضى سقوط الشعر و دراسة ما اذا كان لها علاقة بهذه المشكلة.

- تقييم العوامل الاخرى المصاحبة لسقوط الشعر.

منهج البحث:

اجريت هذه الدراسة على مائه مريض ممن يعانون من سقوط الشعر من المترددين على عياده الامراض الجلدية بمستشفى كليه طب سوهاج و عشرين اخرين اصحاء كعينه ضابطه من كلا الجنسين و تتروح اعمارهم من عشر الى ستين عاما.

نتائج البحث:

- زياده نسبه سقوط الشعر لدى السيدات بنسبة اكبر من الرجال. وجد ان الاستعمال العنيف و المتكرر لفرشاة الشعر هما عاملا الخطر المرتبطين احصائيا مع زياده نسبه حالات سقوط الشعر.

- زياده نسبه الحالات المصابه بسقوط الشعر بدلالات احصائية واضحه فى الحالات التى تستعمل مكواه الشعر و الصبغات الاصطناعية و الجل و مثبتات الشعر مقارنه بالاشخاص الاصحاء فى الدراسه.

- زياده نسبه سقوط الشعر لدى الحالات التى لها تاريخ اسرى بالنسبه لهذا المرض، والحالات التى تعانى من قشره بفروة الراس وكذلك الذين يعانون من الضغوط النفسيه و التوتر و القلق.

- استعمال تقنيه قياس انيميا فقر الدم اكثر حساسيه عن قياس الدلالات الكيميائيه فى تقييم حالات سقوط الشعر و هى نسبه الفريتين بالدم.

- وجد ان نسبه (الهيموجلوبين و نسبه الحديد و نسبه الفريتين بالدم) هم الادله الكيميائيه ذات الاختلاف الاحصائى بين الحالات التى تعانى من مرض سقوط الشعر

و الاشخاص الاصحاء.

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