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Original Article

Dermatology Section

A Hospital-based Study to Determine Causes of Diffuse Hair Loss in Women

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ABSTRACT

Background: Diffuse hair loss is a common complaint encountered by dermatologists in their daily clinical practice. Hair loss in women is a distressing condition. Various underlying factors individually or in combination contribute to the pathogenesis.

Objectives: To determine causes of diffuse hair loss in women and to find the association between probable causes and relevant laboratory parameters, wherever applicable.

Materials and Methods: One hundred and eighty women with diffuse hair loss were included in the study. Detailed history and clinical examination including hair pull test and hair microscopy were done in all study subjects. Specific laboratory investigations for determining iron deficiency anaemia, thyroid dysfunction and parasitic infestation were done.

Results: Among 180 patients, 116 (64.44%) had telogen effluvium, 28 (15.55%) had CTE, 21 (11.66%) had FPHL and 1 (0.55%) had AE. Fourteen patients (7.77%) had more than one aetiological diagnosis of diffuse hair loss. TE was the commonest type of diffuse hair loss. Incidence of TE and FPHL were highest in the age group of 21-30 years, whereas CTE in 30-40 years. Psychological stress and iron deficiency anaemia were the most common underlying aetiological factors for TE, which is statistically significant ($p<0.05$). Out of 130 patients with TE, more than one aetiological factor was recorded in 10 cases whereas in 32 cases probable aetiological factors could not be elicited from history. Most cases of CTE were idiopathic. No significant relationship was observed between CTE, haemoglobin level and serum ferritin level. Out of 35 patients with FPHL, low haemoglobin level was observed in 6/20 (30%) and low serum ferritin level in 14/17 (82.35%).

Conclusion: Diffuse hair loss is a multifactorial condition. A detailed history, thorough clinical examination and appropriate investigations help to identify the causative factors and treat them accordingly.

Keywords: Anagen effluvium, Chronic telogen effluvium, Female pattern hair loss, Telogen effluvium

INTRODUCTION

Hair is an ectodermal structure with great cosmetic importance. It helps an individual to maintain self-image and carry on healthy and meaningful social interactions [1]. Hair loss is a matter of concern in any individual irrespective of age and gender, more so in females [2]. Normal hair cycle results in replacement of every hair on the scalp by 3-5 years [3].

Hair is essential in identity of many women. Femininity, sexuality, attractiveness, and personality are symbolically linked to woman's hair rather than in men. Women are more likely to have lowered quality of life and restrict social contacts as compared to men as a result of hair loss [2]. Psychiatric disorders are more prevalent in patients with alopecia than in general population, suggesting that those with alopecia may be at higher risk for developing a serious depressive episodes, anxiety disorders, social phobia, or paranoid disorder [1].

Diffuse hair loss is a common complaint encountered by dermatologists in their daily clinical practice [4]. Women present more frequently with this complaint [5]. Diffuse hair loss usually occurs without any inflammation or scarring [3]. There are various causes for diffuse hair loss, which include telogen effluvium (TE), female pattern hair loss (FPHL), chronic telogen effluvium (CTE), anagen effluvium (AE), loose anagen hair syndrome and diffuse type of alopecia areata. True incidence of telogen effluvium is not well determined due to lack of data, especially of subclinical cases [6-8]. Although diffuse hair loss is a commonly encountered problem, there are only few studies conducted in India and other countries exploring the causes of diffuse hair loss [9,10].

However, hair loss should not be looked upon as merely a complaint of cosmetic concern. This may be a pointer to various systemic illnesses like anaemia, hypothyroidism, hyperthyroidism, chronic infectious diseases, etc. Hence determining the cause of diffuse hair loss is mandatory in all cases [4]. This study has been conducted with an aim to detect various causes of diffuse alopecia among Indian women and their association with relevant laboratory parameters.

MATERIALS AND METHODS

This was a hospital-based study conducted during the period of October 2011 to September 2013. Prior approval of institutional ethical committee was undertaken. All adolescent girls and women, who presented with diffuse hair loss to the outpatient section of the Department of Dermatology of a tertiary care institution during the study period, were included. Patients with alopecia areata/alopecia universalis and cicatricial alopecia were excluded.

A total of 180 patients were enrolled for the study during this period. Patients were explained about the non-invasive methods of hair examination which would be followed during the study. Informed consent was taken from all patients or parents, in case of teen-aged girls. Detailed history was taken from all study subjects with special queries regarding major febrile illness, psychological stress or any surgery and child birth in the recent past (3 months prior to the onset of hair loss). History of chronic blood loss, crash diet and any drug intake was also recorded.

Specific signs of anaemia, jaundice, and thyroid swelling were looked for during general clinical examination. Type of hair loss, hair thinning and temporal recession was noted during scalp examination. Hair pull test, tug test and trichoscopy were done in all patients. Patients with FPHL were categorized into three subgroups based on Ludwig scale (Types I, II, and III). Hair pull test was performed by pulling 20-60 hairs between thumb, index and middle finger. Test was considered positive if more than 10% of pulled hair away from scalp [11]. Laboratory investigations including haemoglobin level, peripheral blood smear, complete blood count, serum ferritin level, thyroid stimulating hormone (TSH), T3, T4 and stool examination were done for all patients.

The observations pertaining to the parameters under study group were expressed in percentage. Collected data was presented with mean ± 2SD. Chi-square test and Fischer exact test were applied to find the association between diffuse hair loss and various laboratory parameters.

RESULTS

A total of 180 patients with diffuse hair loss were examined during the study period. Out of 180 patients 116 (64.44%) had telogen effluvium, 28 (15.55%) had CTE, 21 (11.66%) had FPHL and 1 (0.55%) had AE. Fourteen patients (7.77%) had more than one aetiological diagnosis of diffuse hair loss. Various clinical types of hair loss in different age groups have been presented in [Table/Fig-1].

The age of the patients with TE ranged from 12 to 54 years (mean age 25.9 ± 7.99 years). Incidence of TE was highest in the age group of 21-30 years. Duration of hair loss spanned between 7 days to 6 months. Psychological stress was the commonest probable aetiological factor (n=48, p<0.05) followed by preceding febrile illness in 16 cases, drug intake in 12 cases, topical application of various commercial hair products in 8 cases, crash diet in 8 cases, child birth in 7 cases, chronic blood loss in 6 cases, preceding surgery in 3 cases [Table/Fig-2]. Based on history, no probable aetiological factor could be elicited in 32 (24.61%) patients and more than one factor was recorded in 10 (7.69%) cases. On scalp examination, hair thinning was seen in 46 (35.38%) patients. Hair pull test was positive in 54 (41.53%) patients. Positive tug test and bitemporal recession was observed in 13 (10%) and 16 (12.30%) patients respectively. On microscopic examination telogen hair was seen in all the patients (100%).

Clinical types	Age-groups in years					
	10-20	21-30	31-40	41-50	51-60	Total
TE	24	62	23	5	2	116
CTE	6	7	13	2	0	28
FPHL	1	7	6	5	2	21
AE	0	0	1	0	0	01
TE + FPHL	0	6	4	3	1	14
Total						180

[Table/Fig-1]: Clinical types of hair loss among various age groups of patients

Sl.No	Probable aetiological causes	No of patients	%
1	Febrile illness	16	12.30
2	Psychological stress	48	36.92
3	Child birth	7	5.38
4	Crash diet	8	6.15
5	Surgical operation	3	2.30
6	Chronic blood loss	6	4.61
7	Drug intake	12	9.23
8	Topical application	8	6.15

[Table/Fig-2]: Probable aetiological causes of telogen effluvium in the study subjects (based on history)

Complete haemogram was done in 83 out of 130 patients. Low haemoglobin (<12gm/dl) was observed in 50/83 (60.24%) patients (p<0.05). Peripheral smear examination revealed microcytic hypochromic smear in 21/83 (25.30%) patients, normocytic hypochromic smear in 4/83 (4.87%) patients, dimorphic and macrocytic anaemia in 1/83 (1.21%) patient each [Table/Fig-3]. Serum ferritin level estimation was done in 74 out of 130 patients with TE. Serum ferritin level <70µg/l was seen in 69/74 (93.24%) patients (p >0.05) [Table/Fig-4]. Thyroid function test was done in 74 out of 130 patients with TE; hyperthyroidism was recorded in 3/74 (4.05%) patients and subclinical hypothyroidism in 2/74 (2.70%) patients. Stool examination was done in 33 patients; evidence of parasitic infestation was seen in 2 (6.06%) patients.

Total 35 patients were diagnosed as FPHL. The age of onset of female pattern hair loss varied from 20-55 years. Age of the patient with FPHL type I ranged from 20 to 55 years (mean age 28.87±8.81 years) and age range of patients with FPHL type II was 22 to 55 years (mean age 36.75±8.60 years) but none had type III FPHL.

Diagnosis	Hemoglobin level (gm%)		Peripheral blood smear				
	<12	>12	MCHC	NCHC	MC	DM	NCNC
TE (n=83)	50 (60.2%)	33 (39.7%)	21	4	1	1	56
FPHL(n=20)	6 (30%)	14 (70%)	2	2	-	-	16
CTE (n=20)	10 (50%)	10 (50%)	5	2	-	-	13

[Table/Fig-3]: Haemoglobin level and peripheral blood smear findings in patients with telogen effluvium, chronic telogen effluvium and female pattern hair loss(MCHC- microcytic hypochromic, NCHC- normocytic hypochromic, MC- macrocytic anemia, DM- dimorphic anaemia, NCNC- normocytic normochromic)

Diagnosis	Serum ferritin level			
	<12 µg/l	12-20 µg/l	20-70 µg/l	>70 µg/l
TE (n=74)	25 (33.78%)	17 (22.97%)	27 (34.48%)	5 (6.75%)
FPHL(n=17)	5 (29.41%)	3 (17.64%)	6 (35.29%)	3 (17.64%)
CTE (n=17)	2 (11.76%)	2 (11.76%)	8 (47.05%)	5 (29.41%)

[Table/Fig-4]: Serum ferritin level in patients with telogen effluvium, female pattern hair loss and chronic telogen effluvium

Family history of patterned baldness was noted in 14 (38.8%) patients. Incidence of FPHL was highest in the age group of 21 to 30 years. On examination, bitemporal recession was noted in 3 (8.33%) patients. Positive hair pull test was seen in 13 (36.11%) patients. On microscopic examination telogen hair was seen in all patients (100%).

Complete haemogram was done in 20 out of 35 patients. Low haemoglobin level was observed in 6/20 (30%) patients (p<0.05). Peripheral blood smear examination showed microcytic hypochromic and normocytic hypochromic picture, each in 2 (10%) patients [Table/Fig-3]. Out of 35, 17 patients underwent serum ferritin estimation. Serum ferritin level <70µg/l was seen in 14 cases (p >0.05) [Table/Fig-4]. Thyroid function test was undertaken in 17 out of 35 patients. Biochemical evidence of subclinical hypothyroidism and hyperthyroidism was recorded in 1 patient each.

Among 180 patients with diffuse hair loss, 28 (15.55%) patients were diagnosed as CTE with age of the patients ranging from 15-45 years (mean age 26.74 years). Incidence of CTE was highest in the 30-40 years of age group. Out of the 28 patients with CTE, 5 gave history in favor of probable aetiological causes of CTE. These were drug intake (n=1, 3.57%), diabetes (n=2, 7.14%), protein energy malnutrition (n=1, 3.57%) and zinc deficiency (n=1, 3.57%).

On scalp examination, thinning of hair was noted in 5 (17.8%) patients and bitemporal recession in 5 (17.85%) patients. Hair pull test was positive in 10 (35.71%) patients. Complete haemogram was done in 20 out of 28 patients; low haemoglobin (<12gm/dl) level was seen in 10 patients (p >0.05). On peripheral blood smear examination, microcytic hypochromic anaemia was seen in 5 patients, and normocytic hypochromic smear in 2 patients [Table/Fig-3]. Serum ferritin level was estimated in 17 out of 28 patients. Serum ferritin level <70µg/l was seen in 12 cases (p >0.05) [Table/Fig-4]. Thyroid function test was undertaken in 17 out of 28 patients but all of them were found to be euthyroid. One of the 180 patients presented with AE. She was on chemotherapy (cyclophosphamide, adriamycin, 5-flurouracil) for carcinoma of breast. On examination, hair pull test and tug test were positive. On microscopic examination, dystrophic anagen hairs were observed.

DISCUSSION

Dermatologists are frequently confronted with hair disorders in day-to-day practice. Hair loss has little or no physically harmful effects, but may lead to psychological consequences, including high level of anxiety and depression [12]. Hair loss is a common disorder, with an estimated life-time prevalence of 1.7%; however, this figure is not a reliable estimate, as very few epidemiological studies have been published in this regard, owing partly to under-reporting [1].

The association of low serum ferritin level and hair loss has been debated over the years. There has been controversy over the cut-off

level of serum ferritin, below which it can be defined as nutritional deficiency, triggering hair loss [13]. Serum ferritin is directly related to intracellular ferritin and thus to total body iron stores. Only iron deficiency causes very low serum ferritin concentrations; therefore, a low ferritin concentration is very specific for iron deficiency [14].

Using serum ferritin level as a marker for iron storage deficiency, the definition of iron deficiency (but not specifically iron deficiency anaemia) in various studies has ranged from a serum ferritin level of ≤15µg/l to <70µg/l. According to World Health Organization (WHO), anaemia is defined as serum haemoglobin level <12gm/dl [15].

Telogen effluvium

Out of 180 patients, 116 were diagnosed as TE and 14 were TE with FPHL [Table/Fig-5]. Jain et al., studied 100 cases of diffuse hair loss and observed TE in 92% cases; febrile illness was the most common underlying cause (33%) [9]. In the present study, psychological stress was the commonest cause of TE (36.92%) and there was a statistically significant association (p <0.05) between these two variables. Rustom et al., studied 50 cases of TE and also found that psychological stress was the most common underlying cause (42%) [10]. Low haemoglobin level was recorded in 50% cases with TE in their study [10]; in the present study it was found in 60.24% patients, and there was a statistically significant association (p <0.05) between these two variables. On routine stool examination gastrointestinal parasitic infestation was found in 12 cases in the above study [10]. In the present study parasitic infestations were seen in 2 cases. Authors did not record concomitant drug intake or endocrinopathy as an aetiological factor of TE, whereas in the present study, drug intake, hyperthyroidism and hypothyroidism were encountered as probable causes of telogen effluvium in 9.23%, 4.05% and 2.70% cases respectively. Based on history, Rustom et al., could not find any probable aetiological causes of diffuse hair loss in 30% patients [10]; as compared to the present study, where in 24.61% patients did not give any history pertaining to probable causes of TE.

[Table/Fig-5]: A case of telogen effluvium with hand-full of shed hair

In a prospective cohort study by Sinclair R, in 194 female subjects aged 11 to 72 years with TE, 12 (6%) were found to have serum ferritin level ≤20µg/l [13]. All these patients had normal haemoglobin concentration [13]. In the present study serum ferritin level <70µg/l was seen in 69/74 patients, which was statistically non-significant (p >0.05). Kantor et al., compared the serum ferritin level of female patients with hair loss of varied aetiology, e.g., telogen effluvium, androgenetic alopecia, alopecia areata and alopecia totalis/universalis with healthy control group [16]. The mean serum ferritin levels were lower in subjects with androgenetic alopecia and alopecia areata as compared to healthy control subjects, but not so when compared to those with TE or alopecia totalis/universalis [16].

Female pattern hair loss

Fewer than 45% of women have a head full of hair throughout the life [2]. FPHL is characterized by a reduction in hair density over the crown and frontal scalp with retention of frontal hair line. Prevalence of FPHL increases with advancing age. Affected women may experience psychological distress and impaired social interaction. In most of the cases the diagnosis can be made clinically and medical management is possible.

Out of 180 patients, 21 were diagnosed as FPHL and 14 were FPHL with TE. Among them 15 patients had type I and 20 patients had type II FPHL. Gan et al., noted increased prevalence of FPHL with increasing age, from approximately 12% among women aged between 20 to 29 years to over 50% among women above the age of 80 [17]. In a study by Birch et al., 337 women aged 18-99 years, who presented to a general dermatology clinic with other complaints, 6% of the women aged less than 50 years were diagnosed as having FPHL [18]. This incidence increased to 38% in women above 70 years [18]. In contrast to the above studies, present study records a lower incidence of FPHL in the older age group. This may be due to reduced concern regarding hair loss in the older age group in this population, who were mostly rural. Mean age of onset of FPHL in our study was 31.60 years as compared to 34.4 years reported by Zhang et al., [19]. FPHL type III or Sinclair grade 5 is a severe form which is uncommon and affects less than 1% of women [2]. In our study, we did not record any case of FPHL type III. In a study of 60 female patients of patterned baldness, family history of androgenetic alopecia among male members was present in 27/60 (45%) patients [19]; in the present study such history was noted in 14/35 (38.8%) patients. Mean duration of hair loss in our patients was 1.5 years, as compared to 4.49 years in another study [19].

Low haemoglobin level (<12gm/dl) was recorded in 6/20 (30%) patients in the present study as compared to 8.3% in another study [19]. Only 2/20 patients showed microcytic hypochromic peripheral blood smear in the present study.Out of 17 patients, 2 had thyroid dysfunction of which one had subclinical hypothyroidism and the other had hyperthyroidism. In the study by Zhang et al., of the 17 patients with FPHL, slight deviation of TSH level was recorded in 2(11.76%) patients, but T3, T4 levels were within normal limits [19].

In this study patients were categorized based on their serum ferritin levels into 4 groups:

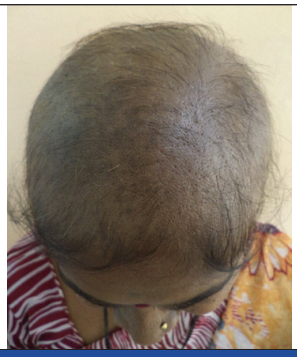
- <12µg/l (iron deficiency)
- 12-20 µg/l (iron depletion)
- 20-70 µg/l (serum ferritin level lower than required for normal hair cycle)
- >70 µg/l (normal ferritin level)

Serum ferritin levels were estimated in 17 out of 35 patients with FPHL. Fourteen (82.35%) out of these 17 patients had serum ferritin level < 70 µg/l. This is higher compared to the findings of the study by Zhang et al., [19], where only 35% of the FPHL patients had serum ferritin level <70 µg/l. In our study we did not find significant association between FPHL and serum ferritin levels. This is similar to the findings of the study by Zhang et al., [19]. Olsen et al., studied 285 women with FPHL, of which 215(75.4%) showed serum ferritin level < 70 µg/l [14] as compared to 82.35% in our study. The mean haemoglobin and serum ferritin level was 11.2gm/dl and 36.11 µg/l respectively, as compared to the values 13.64gm/dl and 61.01µg/l in study by Olsen et al., [14].

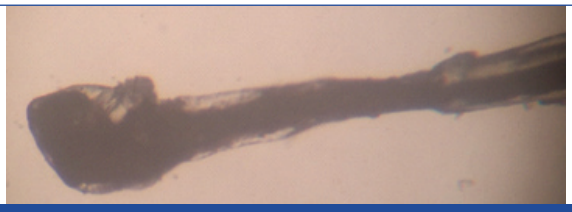
In another case-controlled study by Aydingoz et al., the authors compared 10 female subjects with FPHL and 46 healthy controls [20]. There was no difference in the prevalence of depleted iron stores or iron deficiency anaemia in both the groups.

Chronic telogen effluvium

CTE is a diffuse, generalized form of hair loss of unknown cause that is common in middle aged women. It affects the entire scalp, often starts abruptly and is alarming to the patient as large number of hairs are shed [21]. In the present study, among 180 patients with diffuse hair loss, 28 were diagnosed as CTE. Duration of hair loss in these patients varied from 6 months to 8 years. Incidence of CTE was highest in 31-40 (46.42%) years of age group. Pre-menopausal women (96.4%) were most commonly affected, in contrast to the study by Garcia-Hernandez, in which it was predominantly seen among post-menopausal women (67%) [21]. Olsen et al., studied



[Table/Fig-6]: A case of anagen effluvium 3 weeks after initiation of chemotherapy for carcinoma of breast



[Table/Fig-7]: Photomicrograph showing shed anagen hair (10X), in a case of anagen effluvium

96 women of CTE, of whom 58 (60%) were pre-menopausal and 38(40%) were post-menopausal [14].

In this study, probable aetiological causes of CTE, based on history were drug intake in 1(3.57%) patient, diabetes in 2(7.14%) patients, protein energy malnutrition in 1(3.57%) patient, and zinc deficiency in 1 (3.57%) patient. On scalp examination hair thinning was noted in 5 (17.8%) patients, bitemporal recession in 5 (17.85%) patients and hair pull test was positive in 10 (35.71%) patients.

Of the 28 patients with CTE in this study, 20 underwent haemoglobin estimation, and 10 (50%) of them were found to have a low level (<12gm/dl), which was not statistically significant (p >0.05). Serum ferritin level was estimated in 17 patients and 15 had serum ferritin value <70µg/l, which was statistically non-significant (p >0.05). In the study by Olsen et al., [14], 72 out of 96 (75%) patients had serum ferritin level <70µg/l, as compared to 88.23% patients in our study. Mean serum ferritin level of the patients with CTE in our study was 39.39µg/l, as compared to 51.81µg/l in the study by Olsen et al., [14]. Rushton et al., studied 200 women with CTE out of which 95% had serum ferritin level less than 70µg/l [22]. Thyroid profile was also done in 17 of the 28 patients in our study and showed no abnormal values.

Anagen effluvium

In AE hair shedding usually begins at 1-3 weeks after initiation of chemotherapy. Severity of hair loss depends on the route as well as the dose and frequency of administration of the drugs. Due to long anagen phase, scalp is the most common location for hair loss, while other terminal hairs are variably affected depending on the percentage of hairs in anagen phase. AE is typically reversible [23].

Out of 180 patients only one was diagnosed as AE [Table/Fig-6]. The patient was started on cyclophosphamide, adriamycin and 5-flurouracil regimen for carcinoma of the breast. After 3 weeks of initiation of chemotherapy she noticed hair loss. On scalp examination, diffuse hair loss was seen. On microscopic examination, dystrophic anagen hairs were observed [Table/Fig-7]. The World Health Organization criteria for anagen effluvium is grade 0 = no loss, grade 1 = mild hair loss, and grade 2 = pronounced or complete hair loss. According to WHO criteria, the present case belonged to grade 2 [23].

CONCLUSION

Diffuse hair loss is a common clinical condition. The diagnosis can be established with a history, with particular focus on the chronology of events, examination of the shed hair-bulbs, and a few simple screening laboratory tests. Once the diagnosis is established, appropriate treatment according to the diagnosis is likely to arrest the hair loss in all cases except CTE. Patients with CTE can however be reassured that the condition is non-progressive and self-limiting.

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