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Original article

Screening of Helicobacter Pylori Infection in Patients with Telogen Effluvium

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Abstract:

Background: Background: Telogen effluvium (TE) is a scalp condition characterized by hair shedding that is diffuse and does not leave scars. Helicobacter pylorus (H. pylori) is a microaerophilic gram-negative bacterium that colonizes the gastric mucosa and is found in around 50% of the global population. Aim: To screen for the presence of H. pylori in patients with TE. **Methods:** The study comprised 50 female patients with TE and 30 apparently healthy age-matched females as controls. Laboratory tests were performed, including a complete blood count, serum ferritin, and stool analysis for H. pylori Ag. **Results:** Hemoglobin (Hb), hematocrit (HCT), serum ferritin levels were significantly lower in cases compared to controls ($p=0.002$, <0.001, <0.001, respectively). The mean level of Hb and HCT differed substantially between categories of TE severity ($p = 0.008$, 0.009, respectively). H. pylori was detected with statistical significance in cases compared to controls ($p<0.001$). Serum ferritin, Hb and HCT levels were substantially lower in individuals with positive H. pylori Ag than those with negative H. pylori Ag ($p=0.02$, 0.004, 0.004, respectively). Serum ferritin levels less than 75.5 ng/ml can be used as a cutoff point to predict the development of TE ($p<0.001$). **Conclusion:** H. pylori should be tested in TE patients, particularly those with iron insufficiency.

Keywords: Helicobacter pylori; Hair loss; Ferritin; Telogen Effluvium.

Introduction

The loss of hair is a widespread disorder with many different manifestations. Telogen effluvium (TE) is a scalp condition that causes diffuse, non-scarring hair loss. Several hypotheses were proposed addressing the pathophysiology of TE. It is believed that several functional types of TE exist based on changes throughout specific stages of the follicular cycle. TE has been linked to a variety of insults, including physical, mental, and chemical [(1)].

Acute TE is characterized by hair loss that occurs three months following the triggering incident [(2)]. However, chronic TE can be defined as idiopathic, extensive falling of telogen hairs from the scalp for more than six months [(3)]. The hair thickness seems normal, with shorter re-growing hairs, and hair pull examination is typically helpful in diagnosis [(4)]. Many studies looked into the association between iron deficiency and hair loss. The majority of them targeted women, and several claimed that iron deficiency, even in the absence of anemia, might cause TE [(5)].

Iron insufficiency is frequent among women who experience hair loss [(6)]. Nonetheless, the link between hair loss and low serum ferritin levels has been contested for years. There is ongoing debate over whether low serum ferritin levels should be classified as a dietary deficiency causing hair loss (mostly TE) [(7)]. Menstruation is the leading cause of iron deficiency among otherwise healthy premenopausal women. Hemoglobin and ferritin reference ranges for women of reproductive age are frequently reported to be lower than those for men of the same age [(8)].

Helicobacter pylori (H. pylori) are a microaerophilic gram-negative bacterium that colonizes the stomach mucosa and is found in around 50% of the global population. The prevalence of H. pylori infection is 60.9% in children under the age of 12 and 77.2% in adults [(9)].

Infection with H. pylori has been linked to gastrointestinal disorders such as active chronic gastritis, peptic ulcers, and gastric cancer [(10)]. It has also been linked to extra-gastric symptoms such as thrombocytopenic purpura, reduced growth velocity, and iron shortage and/or anemia [(11)]. Some investigations have found that by eliminating H. pylori bacteria, indices of iron nutritional status recover to normal levels, eliminating the need for iron supplementation [(12)].

The goal of this study was to screen for the presence of H. pylori infection in TE patients.

Patients and methods

The present study was a cross-sectional case-control research. Fifty female patients with TE were included. In addition, 30 apparently healthy, age-matched volunteer females served as the control group. The study took place in the Dermatology, Andrology, and Venereology Department of Benha University Hospitals from October 2021 to January 2023.

Female patients over the age of 18 who suffered from hair loss and met the TE criteria were enrolled. However, patients older than 18 years old, receiving drugs that cause hair fall, such as antikeratinizing, anticoagulant, antithyroid, anticonvalsant, and hormones were excluded from the study. Other types of hair loss, such as alopecia areata, tractional alopecia, or female pattern hair loss; patients under treatment for H. pylori; history of polycystic ovary or menstrual irregularities; postmenopausal or pregnant women; acute inflammatory conditions or infections; and chronic liver, renal, heart, or autoimmune diseases, were not eligible to share in the study.

Ethical considerations:

The study was carried out following approval by the Research Ethics Committee of Benha Faculty of Medicine, Benha University (MS.27.9.2021). Each subject provided informed written consent.

Each participant was given a secret code number and an explanation of the study's objective.

Methodology:

All participants were asked to provide a comprehensive background, including their age, length of hair loss, drug use, and chronic systemic illnesses. In addition, a general examination was performed, with body mass index (BMI) estimated as weight (kilogram) / height (square meter).

Dermatologic examination was performed, with the patients seated on a chair rather than an examination table for better visualization. The entire scalp (back, front, top, and sides) was checked under good illumination.

The hair pull test was used to assess the severity of TE [(13)]. The procedure involved picking 50 to 60 hairs and holding the bundle close to the scalp between the thumb, index finger, and middle finger before firmly tugging the bundle with slow traction as the fingers travelled down the hair shaft. It was done on the vertex, two parietal areas, and the occipital region of the scalp.

Next, pulled hairs were counted. When > 10% of the hairs in each bundle are pulled from a scalp location, the hair pull test is positive. If < 10% of the hair is gone, the loss is probably caused by natural shedding. The current study used three levels of severity for the pull test: mild if it is positive in one scalp location, moderate if it is positive in two areas and severe if it is positive in more than two.

Trichoscopy was also performed using a manual dermoscope, Dermlite 4 (DL4) (3Gen Inc., USA), to confirm the diagnosis. TE was distinguished by observations such as decreased hair density in the presence of empty follicles. On the other hand, female-pattern hair loss is characterized by follicular miniaturization.

A complete blood count, serum ferritin measurement, and H. pylori stool antigen test (HpSAg) were all conducted in the laboratory. The enzyme-linked immunosorbent assay (ELISA) (KaiBiLi H. Pylori Antigen Rapid Test) was used to detect HpSAg. To rule out individuals with inflammatory disorders, C-reactive protein levels were measured before the study began.

Statistical analysis

The data was analyzed using IBM SPSS v26 (IBM Corp., Armonk, New York, USA). Descriptive statistical methods for numerical data included mean and standard deviation, while frequency and percentage were employed for non-numerical data. The student's t-test was used to determine significance for parametric data, whereas the Mann-Whitney U-test was employed for non-parametric data. Multiple groups were compared using ANOVA and Kruskal-Wallis tests. To compare categorical data, the chi square test (X2-value) was applied. A ROC curve analysis was performed to determine the optimum cutoff point and indicative power of the test. P-values < 0.05 imply statistical significance.

Results

The mean serum ferritin, hemoglobin (Hb), and hematocrit (HCT) levels were considerably lower in patients than controls. H. pylori Ag was positive in 60%, 20% of patients, and controls, respectively (p<0.001) (Table 1).

In terms of TE severity, the current study found that patients were classified as moderate (62%), severe (26%), or mild (12%) based on the pull test (Table 1).

There were statistically significant differences in Hb and HCT levels among different grades of TE, with the lowest levels in severe cases (p =0.008, 0.009, respectively). However, no significant change was found in serum ferritin (p = *0.6*) (Table 2).

Serum ferritin, Hb, and HCT levels were significantly lower in those with positive H. pylori Ag versus those with negative H. pylori Ag (Table 3).

According to existing data, a serum ferritin level of less than 75.5 ng/mL can indicate TE with 75% specificity and 80% sensitivity (Table 4, Figure 1).

Table 1: Comparison between studied groups regarding clinical and laboratory findings.

Characteristics	**Case (n=50)**		**Control (n=30)**		**t**	***P***
	Mean	**± SD**	**Mean**	**± SD**		
Age (Year)	26.60	6.34	25.20	4.89	1.1	0.3
Age range	18-42		18-34			
BMI (kg/m^2)	23.76	3.22	22.50	2.24	1.9	0.06
RBCs (N=3.5-5 million/ųl)	4.41	0.30	4.47	0.30	0.9	0.4
Hb (N=11.5–15 g/dl)	11.22	1.01	11.83	0.64	3.3	0.002*
HCT (N=34-44 %)	35.33	2.82	37.48	2.11	3.9	<0.001*
MCH (N=26–34 pg)	25.76	2.22	26.39	1.80	1.3	0.2
MCV (N=73 – 98 fl)	80.30	5.74	82.32	5.59	1.5	0.1
WBCs (N=4–11 10^3 /ųl)	7.44	2.32	7.25	1.88	0.4	0.7
Platelets (N=150–450 10^3/ųl)	296.86	68.94	316.87	95.16	1.1	0.3
Serum ferritin(N=6-150 ng/ml)	41.22	29.49	75.40	22.97	5.8	<0.001*
H. pylori Ag	**No.**	**%**	**No.**	**%**	**X^2**	***P***
Negative	20	40	24	80	12.1	<0.001*
Positive	30	60	6	20		
TE severity	**No.**	%				
Mild	6	12				
Moderate	31	62				
Severe	13	26				

BMI = Body mass index; RBCs = Red blood cells; Hb= Haemoglobin; HCT=Hematocrit; MCH= mean corpuscular Haemoglobin; MCV= Mean corpuscular volume; WBCs = White blood cells; TE= Telogen effluvium; H. pylori Ag = Helicobacter pylori antigen; t= student t test; SD= standard deviation; X^2=Chi square test; *significant <0.05.

Table 2: Serum ferritin, Hb, and HCT levels in relation to TE severity.

		n	**Mean**	**± SD**	**Test of significance**	***P***
Serum ferritin	Mild	6	52.00	22.27	z =0.5	0.6
(N=6-159 ng/ml)	Moderate	31	39.26	29.41		
	Severe	13	40.92	33.39		
Hb	Mild	6	12.1333	0.99	f = 5.27	0 .008*
(N=11.5–15 g/dl)	Moderate	31	11.2839	0.98		
	Severe	13	10.6615	0.77		
HCT	Mild	6	37.8333	2.42	f =5.16	0.009*
(N=34-44 %)	Moderate	31	35.5194	2.76		
	Severe	13	33.7769	2.28		

Hb= Haemoglobin; HCT=Hematocrit; z =Kruskal Wallis test; f=Anova test; SD= standard deviation; *significant <0.05.

Table 3: Serum ferritin, Hb and HCT in relation to H. Pylori Ag.

Characteristics	**Negative H. Pylori (n=44)**		**Positive H. Pylori (n=36)**		**Test of significance**	***P***
	Mean	**SD**	**Mean**	**SD**		
Serum ferritin (N=6 -159 ng/ml)	61.68	31.56	44.69	29.89	U=2.5	0.02*
Hb (N=11.5–15 g/dl)	11.7	0.86	11.1	0.90	t = 2.9	0.004*
HCT (N=34-44 %)	36.93	2.56	35.16	2.73	t=2.9	0.004*

Hb= Hemoglobin; HCT=Hematocrit; H. pylori Ag = Helicobacter pylori antigen; U=Mann Whitney U test; t= student t test; SD= standard deviation; *significant <0.05.

Table 4: Receiver Operating Characteristic (ROC) curve analysis of the cutoff values of serum ferritin for prediction of TE.

Variable	Cutoff value	AUC	95% CI	Sensitivity	Specificity	*P*
Serum ferritin (N=6–159 ng/ml)	<75.5	0.81	0.72 - 0.91	80	75	<0.001*

AUC= Area under the Curve; *significant <0.05.

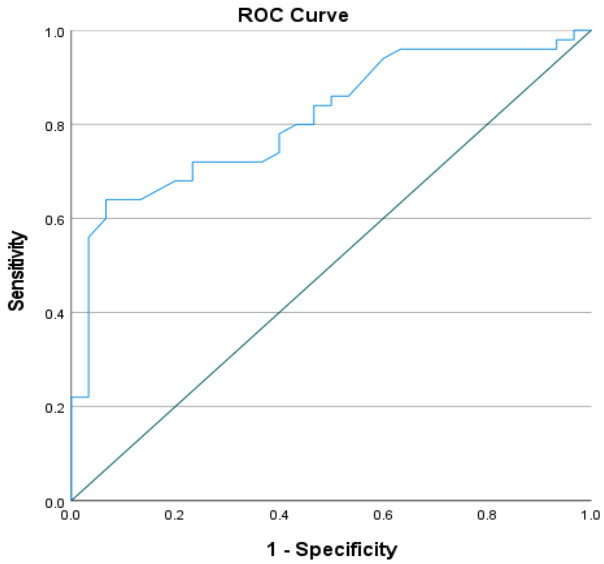

Figure 1: ROC curve analysis of the cutoff values of serum ferritin for prediction of TE

Discussion

Telogen effluvium (TE) is a result of a disruption in the normal growth cycle of hair that occurs for a variety of reasons. It was hypothesized that regardless of the source of hair loss, the follicle tends to exhibit premature anagen termination. Afterwards, the follicle enters catagen and rests, simulating telogen [14].

Iron is involved in DNA synthesis. In the bulge area, gene expression is iron-regulated [7, 15]. The reduced ferritin level in TE patients could be attributed to a variety of causes [16]. Several investigations reported blood ferritin concentrations ranging from 15 to 70 ng/ml in cases of iron insufficiency [17]. To restore severe TE-related hair loss, several publications advocated keeping ferritin levels > 40ng/ml [18] or 70ng/ml [19].

Some studies have identified reduced serum iron in TE patients, whereas others have found no link. The association between serum ferritin and hair loss is a contentious issue [20].

In the current study, patients showed considerably lower levels of Hb, HCT, and serum ferritin than the control group, however there was no significant relationship between ferritin levels and the severity of TE.

Elethawi and Jabbar found that individuals with chronic TE had significantly lower blood ferritin levels (17.6ng/ml) compared to control group (41.2ng/ml). However, Hb levels did not differ significantly between both groups [21].

The findings of the present work are consistent with previous studies, which found that TE patients had significantly lower levels of iron parameters such as

serum iron, Hb, and ferritin, as well as significantly higher levels of serum iron binding capacity than controls [22-25].

In contrast, several investigators found that ferritin and Hb levels in TE patients were not substantially different from those of control persons [26-28]. Furthermore, Bregy and Trueb discovered no link between ferritin levels and telogen ratios [29].

Sinclair found that 12 patients with TE having serum ferritin less than 20µg/l received iron supplementation for 3 months; four patients still had low ferritin levels and required further iron administration for another 3months. Despite the increased serum ferritin in all patients, the therapy did not improve hair shedding or density. Accordingly, they recommended that low iron levels did not promote hair loss [30].

We think variation in ferritin and Hb levels between trials can be ascribed to a variety of factors. The findings may differ depending on social lifestyle practices such as insufficient iron intake and poor iron absorption due to excessive tea drinking. Although ferritin is a reliable indicator of iron deficiency, it may be unreliable in cases of chronic inflammation and infection.

The current research discovered a significant difference in H. pylori Ag results between the studied subjects (positive in 60% of cases, 20% of controls). Furthermore, patients with positive H. pylori Ag had significantly lower serum ferritin, Hb, and HCT levels than those with negative H. pylori Ag.

H. pylori infection may be linked to anaemia by reducing iron absorption due to chronic gastritis, which induces stomach hypochlorhydria, resulting in an impaired conversion of dietary iron from ferric to ferrous form [31].

Other researchers reported low levels of ferritin in 14.5% and 8.6% of H. pylori positive and negative subjects, respectively [32-34], which is consistent with our findings.

It was found that H. pylori eradication treatment with iron supplementation is more effective than iron administration alone in the management of iron deficiency anaemia (IDA) [35].

Several meta-analyses confirmed a substantial relationship between H. pylori infection and IDA [36]. IDA during H. pylori infection is primarily caused by gastric bleeding, diminished iron absorption, and the increase in hepcidin levels [37].

Our findings contradict other finding of considerably higher blood ferritin levels in H. pylori infection [38]. The disparity could be explained by differences in sample sizes, participant ages, and associations.

In addition, the link between H. pylori infection and iron in children with upper gastrointestinal symptoms was investigated. They found no significant difference between negative and positive H. pylori status-related ferritin and Hb levels [39].

Conclusion

The current study suggests H. pylori testing in TE patients, mainly those with iron deficiency.

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