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Original Article

Tracing the Connection of Iron and Copper in Chronic Telogen Effluvium

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ABSTRACT

Chronic Telogen Effluvium (CTE) is a common non- scarring, diffuse type of hair loss, affecting a significant proportion of population. The purpose of the current study is to assess the relationship between CTE and trace metal levels, specifically copper and iron. **Objective:** To collect hair and serum samples from both control group and patients with CTE and to analyze the association between hair copper and iron content and serum copper and iron levels in both groups. **Methods:** The Dow University Hospital (DUHS) in Karachi, Sindh, Pakistan, served as the site of this case control research. The duration of study was one year. The study population encompassed hundred individuals, categorized into 50 cases with CTE and 50 healthy controls. Using non probability sampling technique (convenient sampling), the sample size was determined. Diagnostic criteria a positive hair pull test. Hair and serum samples were collected from both groups for trace metal analysis. Analysis was carried out using ab Atomic Absorption Spectrophotometer (Perkin Elmer Analyst 800, located in Waltham, MA, USA). Data analysis was carried out using SPSS® software for Windows® version 16.0. **Results:** Results showed that hair samples from patients had considerably lower iron levels than those from controls ($p<0.001$), while there was no significant difference in copper levels ($p=0.713$). Additionally, the CTE group showed noticeably greater copper levels ($p<0.001$) and significantly lower serum iron levels ($p<0.001$). **Conclusions:** The study identified a positive association between iron deficiency and hair loss.

INTRODUCTION

Alopecia is a common concern among men and women and is often a cause of distress [1]. Among the myriad factors contributing to occurrence of alopecia, Telogen Effluvium (TE) has emerged as a common cause [1]. It is a non-scarring form of alopecia, characterized by simultaneous diffuse shedding of a considerable amount of hair in telogen phase [1]. Alterations in the hair follicle cycle, particularly prolonged or reduced anagen and telogen phases as well as synchronous hair follicle cycling resulting in fallout of hair shafts in telogen, can be attributed to telogen effluvium [2]. It occurs as a response to metabolic or physiological stresses [1]. No racial inclination for this condition has been observed. However, the rate of occurrence among females is greater than males [3]. Acute Telogen Effluvium (ATE) and Chronic Telogen Effluvium (CTE) are the two subtypes of TE that are distinguished by the duration of the illness. Where majority of cases of ATE resolve within a span of 6 months, in some cases the hair loss continues longer beyond this duration. Under these circumstances the condition is defined as CTE [1]. CTE typically exhibits an intermittent pattern, characterized by alternative episodes of spontaneous remissions and relapses [1]. Usually, conditions like severe iron deficiency anemia, idiopathic thyroid disorders, acrodermatitis, malnutrition etc. are linked with CTE [3]. Hair growth and structure can both be impacted by nutritional deficiencies [1]. Among these Copper and iron are significant contributors to metalloenzymatic processes including

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cellular processes and hair follicle cycle [1]. Where copper is found to be an important player in proliferation and differentiation of a specialized type of fibroblasts (dermal papilla cell), which are involved in growth of hair follicles, Iron levels have also been found to be an essential factor affecting hair loss [1].

The rationale is systemic illnesses and CTE are strongly correlated with metals deficiency like iron and copper. Because of the poor nutritional state, it is vital to research the role of metals. In order to compare the Copper and iron contents of hair samples from patients with Chronic Telogen Effluvium (CTE) and controls with their corresponding serum copper and iron levels. The aim of the study was to explore the relationship between these two parameters.

METHODS

From April 2017 to May 2018, the case-control study was carried out at DUHS following Institutional Ethical Review Board Approval (IRB-842/DUHS/Approval/2017/57). Open Source Epidemiologic Statistics for Public Health was used to calculate the sample size with 80% power and a 95% Confidence Interval (CI) using non-probability sampling (convenient sampling) technique [1]. 50 subjects with CTE who attended the dermatology outpatient clinic, DUHS, were enrolled as cases. The diagnostic criteria for CTE were positive hair pull test. About sixty hairs were pulled gently using middle finger and thumb from all four quadrants including bi temporal. Falling of ≥10 strands was deemed indicative of a positive pull test, 50 healthy controls were sourced from the students and faculty of DUHS [1]. CTE individuals between the ages of 18 and 35 met the inclusion criteria for cases. Inclusion criteria for control group were a negative hair pull test. Exclusion criteria encompassed individuals who had undergone scalp surgery, those with systemic disorders, receiving medications for systemic disorders, currently undergoing copper and/or iron treatment or experiencing any hormonal abnormality. For trace element analysis in hair, hair samples were obtained from the nape of neck, with the help of stainless-steel scissors [1]. The samples measuring about 3-4 cm in length and 0.5-1 g in weight were then washed with ultra-pure water. Subsequently the washed sample was treated with methanol and afterwards, subjected to an ultrasonic bath. Following this the hair samples were dried and preserved in a desiccator until analysis. These samples then underwent microwave assisted digestion for analysis. Additionally, a venous blood sample of 3 ml was taken from both groups' determination of Trace metal levels in serum. The blood samples were centrifuged and stored for further analysis. An Atomic Absorption Spectrophotometer (AAS) equipped with hollow cathode lamps was used to measure the quantities of iron and copper in serum and hair samples. Flame mode was used for the analysis. The Perkin Elmer Analyst 800, based in Waltham, MA, USA, was the instrument used. The Statistical Package for Social Sciences (SPSS®) software for Windows® version 16.0 was used to analysed the data. The mean was calculated using descriptive analysis, and the mean values were compared using an independent sample t-test. P = 0.001 was maintained as the significance level.

RESULTS

The study sample comprised of 100 individuals, categorized into, age and sex matched, case and control group. With a mean age of 27.46 ± 4.98 years, 50 (50%) of the 100 participants were cases, and 50 (50%) were controls, with a mean age of 28.34 ± 4.92 years (p-value 0.502)(Table 1).

Table 1: Mean Age of the Controls and Cases

Study Variables	Controls (n=50) (Mean ± SD)	Cases (n=50) (Mean ± SD)	p-Value
Age (Years)	28.34 ± 4.92	27.46 ± 4.98	0.502

SD=Standard Deviation

56% of the subjects in the cases were men, and 44% were women (Figure 1A).

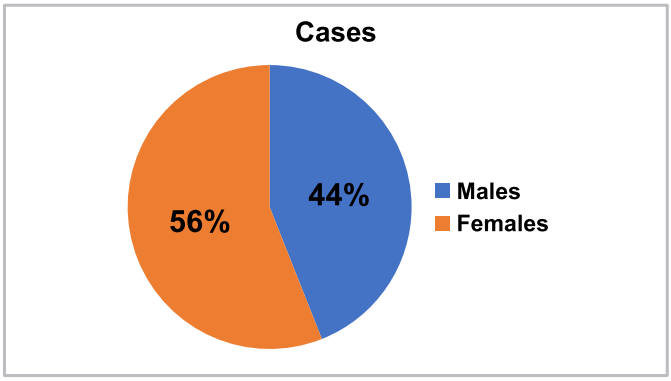

Figure 1: Gender Distribution of Cases

Among controls 48% of the subjects were male and 52% of the subjects were female. The p value was found to be 0.423 (Figure 1B).

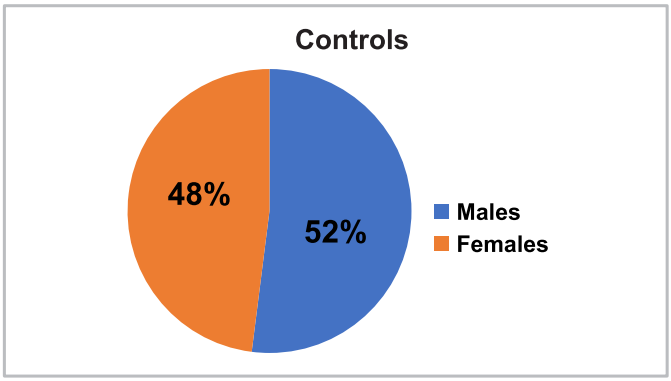

Figure 1B: Gender Distribution of Controls

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Trace metal analysis of the hair samples revealed significantly lower iron levels (p<0.001) in cases as compared to controls. However, copper levels in hair samples did not exhibit a significant difference (p=0.713) (Table 2).

Table 2: Comparison of Iron and Copper Levels in Hair between CTE Cases and Control Samples

Biochemical Parameters	Controls (n=50) (Mean ± SD)	Cases (n=50) (Mean ± SD)	p-Value
Copper (µg/g)	27.36 ± 2.51	26.90 ± 8.47	0.713
Iron (µg/g)	32.34 ± 10.88	24.56 ± 10.27	<0.001*

The Mann-Whitney U test and Independent T-test were used to assess the statistical differences between controls and cases. The data were reported as mean and standard deviation; *(p<0.05) is regarded a significant difference, and ** (p<0.01) is deemed highly significant. Moreover, CTE group exhibited significantly lower serum iron levels (p<0.001), whereas coper levels were significantly higher in this group (Table 3). The Mann-Whitney U test and Independent T-test were used to assess the statistical differences between controls and cases. The data were reported as mean and standard deviation; *(p<0.05) is regarded a significant difference, and **(p<0.01) is considered highly significant.

Table 3: Comparison of Serum Levels of Copper and Iron between CTE Cases and Control Samples

Biochemical Parameters	Controls (n=50) (Mean ± SD)	Cases (n=50) (Mean ± SD)	p-Value
Copper (µg/dl)	110.30 ± 6.40	120.36 ± 18.79	0.001*
Iron (µg/dl)	134.96 ± 9.86	122.14 ± 10.98	<0.001*

DISCUSSION

Considering, that hair is the foremost defining feature of human appearance, hair loss or alopecia have a profound effect on an individual's quality of life and influences a person's psychological as well as emotional state [1-14]. A kind of noncicatricial hair loss known as TE is characterized by a noticeable daily increase in hair loss [13]. Iron deficiency is one of the most prevalent forms of malnutrition worldwide and is a contributing factor to TE [1]. The purpose of this case-control study was to compare the levels of iron and copper in serum and hair samples from CTE patients and normal controls. Copper ion levels may be involved in hair loss. Dermofibroblasts are involved in formation of Vascular Endothelial Growth Factor (VGEF) which in turn facilities formation of new capillaries. These dermofibroblasts are stimulated by copper ions, which is possibly why the hair follicle receives an appropriate blood supply [1-2]. Compared to previous research where blood levels of copper were shown to be much lower in cases, the current study's mean serum levels of copper were significantly higher in cases than in controls [1-4]. However other studies have reported that serum copper levels did not show any significant differences in patients with alopecia, indicating that hair loss might not be affected by serum copper levels [1-2]. Additionally, this study reported significantly lower serum iron levels in the control group. These results were consistent with the findings of previous studies [1-10]. Additionally, another study further supported the role of low iron stores in the body by highlighting the strong negative correlation between decreased ferritin levels and hair fall in patients of TE [1]. These findings can be explained by the fact that iron is essential for the oxygen and electron transfer that occurs in hair cells. Iron also functions as a cofactor for the ribonucleotide reductase enzyme, which is an enzyme involved in DNA synthesis. Due to these functions presence of iron is essential for proliferation of hair follicles and deficiency would therefore disrupt the process [20]. Hair's structure, particularly the presence of sulphur rich keratin, makes it more likely to bind metal cations [21]. This affinity for metal binding and its slow growth makes hair a potential long term indicator of metal ion levels. While there was no discernible change in the quantities of copper ions, the CTE group's hair samples had much lower iron levels in the current investigation [22]. These conclusions run counter to those of an earlier study [4]. The evidence supporting the potential involvement of these metals in the aetiology of CTE is provided by the variations in the levels of these trace elements between the case and control groups.

CONCLUSIONS

Based upon the findings of current investigation, a positive association was found between occurrence of CTE and low levels of iron in serum as well as hair samples of the affected individuals.

Authors Contribution

Conceptualization: SN
Methodology: SZ, AB
Formal analysis: SZ
Writing, review and editing: FN, EA, SR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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