

A comparative study on the association of serum ferritin and vitamin D, and B12 levels among individuals with hair loss

Estudo comparativo sobre a associação dos níveis séricos de ferritina, vitamina D e B12 em indivíduos com queda de cabelo

Akshay J. Salecha^{a*}, Akula V. Sai-Sameer^b, Leepika Annamreddy^c, Vobbalareddy P. Siva-Priyanka^d, Senthil Kumar-AL^e, and D.V.S.B. Rama-Murthy^f

Department of D.V.L, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India

ORCID: ^a0009-0009-8286-5000; ^b0009-0009-3507-5700; ^c0009-0004-8725-9062; ^d0009-0001-0746-4137; ^e0000-0003-2796-9199; ^f0009-0003-6475-5031

Abstract

Objectives: The objective of this study was to study the most frequent type of hair loss in different age groups, and the prevalent micronutrient deficiency linked to hair loss and to compare the association of serum ferritin, vitamin D, and vitamin B12 levels with hair loss among cases and controls. **Methods:** This was a cross-sectional study which included a total of 100 subjects with 50 hair loss cases and 50 age and sex-matched controls. Serum levels of vitamin D, vitamin B12, and ferritin were measured in all subjects. **Results:** Most of the subjects were between 20 and 30 years of age. There was a predominance of telogen effluvium followed by male androgenetic alopecia in all age groups. Females had considerably lower levels of serum ferritin compared to males among cases, with p-value of 0.0001. Vitamin D, vitamin B12, and serum ferritin were significantly low among cases compared to controls, with p-values of 0.0001, 0.01, and 0.006, respectively. **Conclusion:** This study suggests that low levels of serum vitamin B12 and serum ferritin and particularly vitamin D might play an appreciable role in hair loss especially telogen effluvium among females. Evaluation of these parameters could aid the clinician in opting for a more precise therapeutic modality, but identification of the exact etiology remains a primary concern as it is multifactorial, which paves path to appropriate and effective treatment.

Keywords: Hair loss. Vit D. Vit B12. Serum ferritin.

Resumo

Objetivos: Estudar o tipo de queda de cabelo mais frequente em diferentes faixas etárias e a deficiência prevalente de micronutrientes associada à queda de cabelo. Comparar a associação dos níveis séricos de ferritina, vitamina D e vitamina B12 com queda de cabelo entre casos e controles. **Métodos:** Este foi um estudo transversal que incluiu um total de 100 indivíduos com 50 casos de queda de cabelo e 50 controles pareados por idade e sexo. Os níveis séricos de vitamina D, vitamina B12 e ferritina foram medidos em todos os indivíduos. **Resultados:** A maioria dos sujeitos tinha entre 20 e 30 anos de idade. Houve predomínio do eflúvio telógeno seguido da alopecia androgenética masculina em todas as faixas etárias. As mulheres apresentaram níveis consideravelmente mais baixos de ferritina sérica em comparação aos homens entre os casos, com valor p de 0,0001. A vitamina D, a vitamina B12 e a ferritina sérica foram significativamente baixas entre os casos em comparação aos controles, com valores de p de 0,0001, 0,01 e 0,006, respectivamente. **Conclusão:** Este estudo sugere que baixos níveis séricos de vitamina B12 e ferritina sérica e particularmente vitamina D podem desempenhar um papel apreciável

*Correspondence:

Akshay Jain-Salecha

E-mail: akshaysalecha92@gmail.com

2795-501X / © 2023 Portuguese Society of Dermatology and Venereology. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Received: 14-10-2023

Accepted: 15-12-2023

DOI: 10.24875/PJDV.23000082

Available online: 06-03-2024

Port J Dermatol and Venereol. 2023;81(4):44-48

www.portuguesejournalofdermatology.com

na perda de cabelo, especialmente no eflúvio telógeno entre as mulheres. A avaliação destes parâmetros poderia ajudar o médico a optar por uma modalidade terapêutica mais precisa, mas a identificação da etiologia exacta continua a ser uma preocupação primordial, uma vez que é multifactorial, o que abre o caminho para um tratamento adequado e eficaz.

Palavras-chave: Perda de cabelo. Vit D. Vit B12. Ferritina sérica.

Introduction

Diffuse hair loss is not an infrequent complaint encountered by dermatologists globally, which can be disquieting to patients. Hair loss or alopecia has a diversity of causes which can be due to genetics, hormone imbalances, diet, drugs, stress, infections, or other systemic conditions.

Micronutrients are crucial elements in the hair follicle cycle, playing a pivotal role in cellular turnover, within the matrix cells in the follicle bulb¹.

Vitamin D, a fat-soluble vitamin, is synthesized mainly by epidermal keratinocytes and dermal papillary cells through UVB-mediated conversion of 7-dehydrocholesterol to cholecalciferol in the skin, followed by further hydroxylation in the liver and kidney to 1, 25-dihydroxy vitamin D(1,25[OH]₂D), the active form^{2,3}.

Vitamin D exerts its action through the vitamin D receptor (VDR), whose expression is required for hair follicle differentiation but not for proliferation, and its deficiency can inhibit keratinocyte differentiation and disturb the normal hair follicle cycle⁴. VDR is also required for anagen initiation⁵.

Vitamin B12 has two active forms, methylcobalamin and 5 deoxyadenosyl cobalamin. It is a requisite for DNA synthesis, the formation of red blood cells, and neurological function⁶.

Data suggest that vitamin B12 supports the transition of the hair follicle into anagen by increasing transcription of β -catenin through Wnt signaling and reducing transcription of glycogen synthase kinase-3, which is an inhibitor of Wnt signalling⁷. Hence, it plays a role in hair follicle proliferation.

Iron deficiency is considered the leading nutritional deficiency affecting all age groups, especially women. An abnormal balance between cellular ferritin and free iron has been suspected as a mechanism for abnormal hair growth⁸, as dividing cells require higher ferritin. Serum ferritin level can be used as an early marker of iron deficiency as it is a main iron-binding protein in non-erythroid cells reflecting total body iron stores⁹.

Nutrition and diet can be harnessed to treat hair loss, which represents a vital area of exploration. Studies regarding the association of deficiency of micronutrients

and hair loss are still a matter of ongoing research. Providing insights into the role of micronutrients in hair loss opens better therapeutic options.

Our study aims to study the type of hair loss in different age groups and to identify the prevalent micronutrient deficiency linked to hair loss to validate their supplementation in patients with hair loss. To seek to shed light on their connection, we compared serum ferritin, vitamin D, and vitamin B12 levels in individuals with hair loss among and control cases.

Methods

This is a cross-sectional study which included 50 cases of hair loss and 50 healthy age and sex-matched controls who presented to the Dermatology Outpatient Clinic of Katuri Medical College. Cases and controls between the age group of 18-50 years who were inclined to participate were included in the study after obtaining due informed consent. Pregnancy, breastfeeding, patients with chronic medical illness, and patients not willing to participate in the study were excluded from the study. All patients were subjected to detailed clinical history, and the diagnosis was made based on a detailed physical examination by a dermatologist in the department.

Under sterile conditions with minimum atmosphere, venous blood samples were collected from an accessible vein and sent for analysis. The levels of vitamin D, vitamin B12, and serum ferritin were measured by MAGLUMI 2000 Plus Fully Automated Hormone Analyzer using the Flash Chemiluminescent Immunoassay Nanotechnology method. The normal reference intervals were 30-100 ng/mL for vitamin D, 200-1100 pg/mL for vitamin B12, and, for serum ferritin 25-350 ng/ml in males and 13-232 ng/ml in females.

Data obtained were tabulated and assessed by IBM SPSS V20 software. Continuous variables are outlined using frequency, mean, and standard deviation, while categorical variables are summarized using frequency and percentage. Means among groups were compared using an independent t-test, and proportions were compared using the Chi-square test. $P < 0.05$ was considered statistically significant.

Results

Our study included 50 cases (25 females/25 males) and 50 age and sex-matched controls between the 18 and 50 years age group. The mean age of distribution among cases was 29.68 ± 7.32 , and the majority of cases (56%) affected by hair loss were found to be in the 21-30 years age group (Table 1).

Out of different causes of hair loss, telogen effluvium was diagnosed in 30 patients (60%), followed by androgenetic alopecia, 18 cases in male patients (36%), and 2 in female (4%). The distribution of diagnosis was similar.

In all age groups, females had a greater predominance of telogen effluvium, while males had a greater predominance of androgenetic alopecia.

Vitamin D, vitamin B12, and serum ferritin were significantly low among cases compared to controls, as shown in figure 1. Females had considerably low levels of serum ferritin compared to males cases ($p = 0.0001$), while no such difference was seen with vitamin D ($p = 0.185$), and vitamin B12 ($p = 0.802$), as depicted in table 2.

We observed low serum vitamin D levels in 62% (31 patients) of cases compared to 22% (11 patients) in controls with vitamin D level remarkably lower in cases than in controls ($p = 0.0001$), as shown in table 3.

Serum vitamin B12 was found to be deficient in 46% (23 patients) of cases compared to 26% (13 patients) in controls, with statistically significant lower levels in cases compared to controls ($p = 0.01$), as depicted in table 3.

Serum ferritin levels were low in 30% (15 patients) of cases compared to 10% (five patients) in controls, and the difference between case and control values was statistically significant ($p = 0.006$) (Table 3).

Out of 30 telogen effluvium cases, 20 (66%) had low vitamin D levels, 16 (53%) had low vitamin B12, and 14 (46%) had low serum ferritin levels.

Among the 18 cases of male androgenetic alopecia, 9 (50%) had low vitamin D, 7 (38%) had low vitamin B12, and 1 (5.5%) had low serum ferritin levels. On the other hand, the 2 (100%) cases of female androgenetic alopecia had low vitamin D levels, normal vitamin B12, and serum ferritin.

Discussion

Vitamin D, vitamin B12, and iron may be related to hair loss through several ascribed mechanisms. VDR activation plays a key role in the hair follicle cycle⁵ and

Table 1. Sociodemographic profile among cases and controls

Sociodemographic profile	Cases	Controls
Gender		
Male	25 (50%)	28 (56%)
Female	25 (50%)	22 (44%)
Age		
< 20	4 (8%)	3 (6%)
21-30	28 (56%)	29 (58%)
31-40	13 (26%)	16 (32%)
40-50	5 (10%)	2 (4%)
Age (mean \pm SD)	29.68 ± 7.32	28.9 ± 5.02
Vitamin D	24.23 ± 12.45	34.78 ± 9.64
Vitamin B12	194.61 ± 72.75	248.38 ± 103.10
Serum ferritin	26.07 ± 13.92	32.01 ± 14.20

Table 2. Mean values of vitamin D, vitamin B12, and serum ferritin among males and females

Cases	Gender		t-value	p-value
	Male (mean \pm SD)	Female (mean \pm SD)		
Vitamin D	26.58 ± 13.43	21.88 ± 11.17	1.346	0.185
Vitamin B12	192 ± 72.38	197.23 ± 74.51	0.252	0.802
Serum ferritin	35.65 ± 11.31	16.50 ± 8.77	6.69	0.0001

SD: standard deviation.

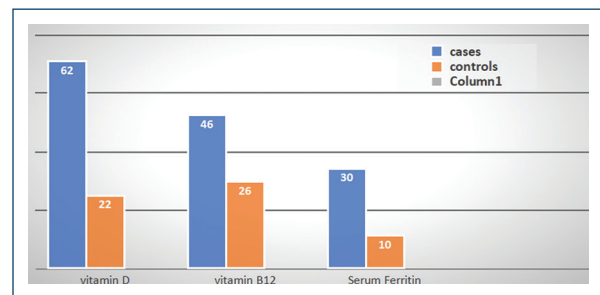


Figure 1. Comparison of percentage of vitamin D, vitamin B12, and serum ferritin deficit among cases and controls.

its role in hair loss needs to be emphasized. To date, iron deficiency runs the most reported nutritional cause of hair loss. Evaluation of low iron stores is done through serum ferritin levels. Vitamin B12 association with hair loss stays an ongoing debate for years.

Table 3. Vitamin D, vitamin B12, and serum ferritin percentages among cases and controls

	Vitamin D				Chi-square value	p-value
	Normal	Percentage	Deficit	Percentage		
Cases	19	38	31	62	16.42	0.0001
Controls	39	78	11	22		
	Vitamin B12				Chi-square value	p-value
	Normal	Percentage	Deficit	Percentage		
Cases	27	54	23	46	4.34	0.01
Controls	37	74	13	26		
	Serum ferritin				Chi-square value	p-value
	Normal	Percentage	Deficit	Percentage		
Cases	35	70	15	30	6.25	0.006
Controls	45	90	5	10		

After exploring all contrasting reports regarding micronutrients and hair loss, we chalked out a strategy to evaluate serum vitamin D, vitamin B12, and serum ferritin levels in all patients with hair loss.

The age of disease distribution was between 18 and 45 years, most frequently 21-30 years, with a mean age of 29.68 ± 7.32 years. The common cause of hair loss according to our study, was telogen effluvium (60%), similar to the study by Rasheed et al.¹⁰ which included 80 female patients with a similar mean age (29.8 ± 9.3), of which 50% were telogen effluvium cases.

In this study, serum vitamin D, vitamin B12, and serum ferritin levels were significantly lower in cases with hair loss in accordance with Farah et al.⁸.

There is a significant difference between cases and controls (62% vs. 22%, $p = 0.0001$) considering serum vitamin D, which is in accordance with a study by Rasheed et al.¹⁰ who compared serum 25(OH)D levels in female patients with chronic telogen effluvium, female androgenetic alopecia, and healthy controls and also reported significantly lower serum 25(OH)D levels compared to the control group.

Similarly, Moneib et al.¹¹ reported significantly lower serum 25(OH) D levels in patients with female androgenetic alopecia than in controls, and Samar et al.¹² reported significantly lower vitamin D levels in male androgenetic alopecia cases.

Contrary to these studies, Karadag et al.¹³ found significantly higher serum 25(OH)D levels in patients with telogen effluvium than in controls.

Our study showed significantly low levels of vitamin B12 among cases than controls (46% vs. 26%, $p = 0.01$), consistent with results reported by Ebru et al.¹⁴, whereas Özden et al.¹⁵ found low vitamin B12 levels in only 2% of 100 individuals with diffuse hair loss.

The present study displays a significant correlation between hair loss and serum ferritin levels when compared with controls (30% vs. 10%, $p = 0.006$). These low serum ferritin levels were noted specially among females when compared to males (35.65 ± 11.31 vs. 16.50 ± 8.77 , $p = 0.0001$).

Rasheed et al.¹⁰ also reported significantly low serum ferritin levels in both telogen effluvium and female androgenetic alopecia patients compared to controls and Tamer et al.¹⁶ also found that hair loss is associated with low serum ferritin levels in 54 patients with hair loss compared to controls. However, on the contrary, Bregy and Trueb¹⁷ found no association between serum ferritin level and hair loss.

Our study has certain limitations, such as a relatively small sample size (none of the pediatric age range, post-menopausal women, or elderly males are included), the absence of other types of hair loss (alopecia areata, frontal fibrosing alopecia, etc.), and the diagnosis being based only on the board-certified dermatologists' clinical experience. The study would have been more valuable if these components had been included from the study.

Conclusion

This study suggests that low levels of serum vitamin B12 and serum ferritin and particularly serum vitamin D may play

a role in hair loss, especially in telogen effluvium among females. The identification of exact etiology of hair loss remains a primary concern as it is multifactorial, which paves the path to appropriate and effective treatment, evaluation of serum levels of these nutrients could aid the clinician in opting for a more precise complementary therapeutic modality, patient-wise.

Acknowledgments

We acknowledge the Indian Council of Medical Research- Short-term studentship-2022 (ICMR-STs) for the grant.

Funding

Indian Council of Medical Research.

Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text.

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Almohanna HM, Ahmed AA, Tsatalis JP, Tosti A. The role of vitamins and minerals in hair loss: a review. *Dermatol Ther (Heidelb)*. 2019;9:51-70.
2. D'Aurizio F, Villalta D, Metus P, Doretto P, Tozzoli R. Is vitamin D a player or not in the pathophysiology of autoimmune thyroid diseases? *Autoimmun Rev*. 2015;14:363-9.
3. Thompson JM, Mirza MA, Park MK, Qureshi AA, Cho E. The role of micronutrients in alopecia areata: a review. *Am J Clin Dermatol*. 2017;18:663-79.
4. Gerkowicz A, Chyl-Surdacka K, Krasowska D, Chodorowska G. The role of Vitamin D in non-scarring alopecia. *Int J Mol Sci*. 2017;18:2653.
5. Mostafa WZ, Hegazy RA. Vitamin D and the skin: focus on a complex relationship: a review. *J Adv Res*. 2015;6:793-804.
6. Institute of Medicine, Food and Nutrition Board. *Dietary Reference Intakes: Thiamin, Riboflavin, Niacin, Vitamin b6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press; 1998.
7. Krugluger W, Stiefsohn K, Laciak K, Moser K, Moser C. Vitamin B12 activates the wnt-pathway in human hair follicle cells by induction of beta-catenin and inhibition of glycogen synthase Kinase-3 transcription. *J Cosmet Dermatol Sci Appl*. 2011;1:25-9.
8. Farah HS, Hajleh AM, Shalan N, Assi GA, Alqaisi T. The association between the levels of Ferritin, TSH, Zinc, Hb, vitamin B12, vitamin D and the hair loss among different age groups of women: a retrospective study. 2021;13:143-8.
9. Park SY, Na SY, Kim JH, Cho S, Lee JH. Iron plays a certain role in patterned hair loss. *J Korean Med Sci*. 2013;28:934-8.
10. Rasheed H, Mahgoub D, Hegazy R, El-Komy M, Abdel Hay R, Hamid MA, et al. Serum ferritin and vitamin d in female hair loss: do they play a role? *Skin Pharmacol Physiol*. 2013;26:101-7.
11. Moneib H, Fathy G, Ouda A. Possible association of female-pattern hair loss with alteration in serum 25-hydroxyvitamin D levels. *Egypt J Dermatol Venerol*. 2014;34:15-20.
12. Samar SM, Alkhayat MA, Ali H, Samhoud EA. Serum Vitamin D and serum ferritin levels in male pattern hair loss: Is there a role? *Fayoum Univ Med J*. 2021;7:1-8.
13. Karadag AS, Ertugrul DT, Tatal E, Akin KO. The role of anemia and Vitamin D levels in acute and chronic telogen effluvium. *Turk J Med Sci*. 2011;41:827-33.
14. Ertug EY, Yilmaz RA. Reduced ferritin, folate, and vitamin B12 levels in female patients diagnosed with telogen effluvium. *Int J Med Biochem*. 2018;1:111-4.
15. Özden MG, Öztaş MO, Gülekon A, Güler MA. Diffuse hair loss in females and associating findings [Article in Turkish]. *O M Ü Tip Dergisi*. 2008;25:50-6.
16. Tamer F, Yuksel ME, Karabag Y. Serum ferritin and vitamin D levels should be evaluated in patients with diffuse hair loss prior to treatment. *Postepy Dermatol Alergol*. 2020;37:407-11.
17. Bregy A, Trueb RM. No association between serum ferritin levels >10 microg/l and hair loss activity in women. *Dermatology*. 2008;217:1-6.