ARAŞTIRMA YAZISI / RESEARCH ARTICLE SAÇ DÖKÜLMESİ: LABORATUAR İNCELEMELERİ KİME GEREKLİ?

HAİR LOSS: WHO NEEDS LABORATORY INVESTIGATIONS?

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ÖΖ

ABSTRACT

AMAÇ: Bu çalışmanın amacı saç dökülmesi şikâyetiyle başvuran hastalarda öykü ve fizik muayenenin önemini vurgulamak, hangi hastalarda laboratuvar tetkilerinin gerekli olduğunu ortaya koymaktır.

GEREÇ VE YÖNTEM: Çalışmaya Karabük Eğitim ve Araştırma Hastanesi Dermatoloji Polikliniğine Nisan 2017-Nisan 2018 tarihleri arasında saç dökülmesi şikayeti ile başvuran 622 hasta dâhil edildi. Hastane veri tabanındaki elektronik dosyalar yardımıyla herhangi bir saç dökülme türüne ait tanı alan hastaların tanı ve tedavi süreci içinde istenen tam kan sayımı, serum glukoz, vitamin B12, vitamin D, TSH, serum demir, demir bağlama kapasitesi sonuçları, eşlik eden hastalıkları kaydedildi. Bu veriler hastaların demografik özellikleriyle ve literatürle karşılaştırıldı.

BULGULAR: 622 hastanın 339'u (%55) kadın, 283'ünü (%45) erkek idi. Saç dökülmesi yakınmasıyla başvuran hastaların 321'ini (%51) yaygın saç dökülmesi, 210'unu (%33) alopesi areata, 72'sini (%12) androgenetik alopesi tanısı alan hastalar oluşturdu. Skarla sonuçlanmış saç kaybı yakınması olan hasta sayısı 14, saç dökülmesi yakınması nedeniyle başvurup tinea capitis tanısı alan hasta sayısı da 5 olarák belirlendi. Yaygın saç dökülmesi yakınmasıyla başvuran kadın hastaların %10'unda demir eksikliği anemisi, %30'unda Vitamin D eksikliği saptandı. Yaygın dökülme yakınması olan kadın hastaların %10'unda görülen demir eksikliği dışında, alopesi areata, androgenetik alopesi ve skatrisyel alopesili kadın hastalarda anormal labaratuar bulgusu saptanmadı. Saç dökülmesi ile başvuran tüm erkek hastalarda da sac dökülmesiyle iliskilendirilebilecek anormal labaratuar bulgusu saptanmadı.

SONUÇ: Sonuç olarak saç dökülmesi şikâyeti ile başvuran bazı hastalarda laboratuar tetkikleri, saç dökülmesinin nedeni hakkında fikir vermektedir. İyi bir anamnez ve fizik muayene hangi hastada hangi testlerin istenmesi gerektiği konusunda yol gösterici olabilmektedir.

ANAHTAR KELİMELER: Saç dökülmesi, alopesi areata, androgenetik alopesi, anemi, vitamin eksikliği

OBJECTIVE: The aim of this study was to emphasize the importance of history and physical examination in patients presenting with hair loss, and to determine in which patients laboratory tests are necessary.

MATERIAL AND METHODS: 622 patients with hair loss complaint, who applied to Karabük Training and Research Hospital Dermatology Clinic between April 2017 and April 2018 were included. The required complete blood count, serum glucose, vitamin B12, vitamin D, TSH, serum iron, iron binding capacity, and ferritin results and accompanying diseases were recorded in the patients diagnosed with any hair loss in the hospital database.

RESULTS: Of the 622 patients, 339 (55%) were female and 283 (45%) were male. 321 (51%) of the patients had diffuse hair loss, 210 of them (33%) alopecia areata, 72 of them (12%) were diagnosed with androgenetic alopecia. The number of patients with scarring hair loss complaints was 14, and the number of patients with tinea capitis diagnosed with hair loss complaints was 5. Iron deficiency anemia was detected in 10% of female patients who complained of diffuse hair loss and Vitamin D deficiency was detected in 30% of patients. It was 34 in scarring alopecia patients. There were no abnormal laboratory findings in women with alopecia areata, androgenetic alopecia and scatricial alopecia except iron deficiency seen in 10% of women with diffuse hair loss.No abnormal laboratory findings could be associated with hair loss in all male patients presenting with hair loss.

CONCLUSIONS: Our findings showed that laboratory examination of patients who presented with hair loss complaints did not give information about the cause except for selected patients. It will be a time and economic impact of not wanting unnecessary tests with a good anamnesis.

KEYWORDS: Hair loss, alopecia areata, androgenetic alopecia, anemia, vitamin deficiency.

Geliş Tarihi / Received: 06.03.2019 Kabul Tarihi / Accepted:27.05.2019 Yazışma Adresi / Correspondence: Dr.Öğr.Üyesi Habibullah AKTAŞ Karabuk Üniversitesi Tıp Fakültesi, Dermatoloji Anabilim Dalı E-mail: aktashabib@hotmail.com Orcid No: 0000-0001-9239-1659 Hair is an important cosmetic figure that completes the human phenotype and has a major role in terms of quality of life. Hair loss is a common complaint referring to dermatologists, family physicians and internal medicine specialists in all age groups, from newborn to older ages. Hair loss is defined as very different characteristics ranging from the telogen effluvium, which can be accepted as a part of physiology in a way that comes after the birth, to scarring hair loss caused by malignant or inflammatory skin diseases. As well as temporary hair loss due to drug-induced or mild malnutrition, there is also hair loss due to severe problems such as hypothyroidism, anemia and polycystic ovary syndrome. Even a malignant condition may have caused hair loss as a first symptom. Physical examination and a rigorous story take the first place to evaluate hair loss dermatologically. Diseases such as androgenetic alopecia (AGA), alopecia areata (AA), and telogen effluvium are clinically easily identifiable (1-3).

It is important to learn the history of drug use in diffuse hair loss, the patient's past medical history, or any other accompanying illness. Skin biopsies are required for accurate diagnosis of scarring alopecia such as lichen planopilaris, discoid lupus erythematosus (4). Several methods have been developed to bring out the cause of diagnosis in patients who present with complaints of hair loss. In addition to hematological and biochemical tests, trichogram, potassium hydroxide (KOH), electron microscopy and dermatoscopy are also used as diagnostic methods (5).

In this study, we reviewed the diagnoses, the laboratory tests performed and the results obtained in patients who applied with hair loss. We examined the relationship between hair loss types and test results and questioned the necessity of tests.

MATERIALS AND METHODS

We conducted a retrospective research of patients with hair loss complaint admitting to Dermatology Outpatient Clinic at Karabuk Training and Research Hospital between April 2017 and April 2018. The hospital database was used to obtain the patient data. The patients' age, gender, original diagnoses for the hair loss, the laboratory tests performed and accompanying diseases were recorded. Patients whose diagnosis was not confirmed in the records, and whose primary complaint was not hair loss were not included in the study. Complete blood count, glucose level, serum vitamin B12, vitamin D, TSH, iron, iron binding capacity, ferritin levels were evaluated. Patients with hair loss were evaluated in 5 groups as AA, AGA, scarring alopecia, non-scarring diffuse alopecia and tinea capitis according to clinical diagnosis, biopsy, and KOH examination results. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 21.0 package program (SPSS software, SPSS Inc., Chicago, IL, USA). For descriptive statistics, percent, mean, standard deviation (SD), median, minimum and maximum values were presented.

ETHICAL APPROVAL

The study was approved by Ethics committee of Karabük University (2018: 6/7).

RESULTS

The results of 622 patients aged 1-75 were analised. 339 (54.5%) of the patients were female and 283 (45.5%) were male. Five different diagnoses were made for complaints of hair loss: Diffuse alopecia, AA, AGA, scarring alopecia and tinea capitis. The age and gender distribution according to the diagnosis of hair loss is given in **(Table 1)**.

Table 1 : The age and gender distribution according to

 the diagnosis of hair loss

Hair loss		Male		Female		Total
type	$Mean \pm SD$	n	%	n	%	n
Diffuse alopecia	27,9 ± 12,5	63	19.6	258	79.8	321
Alopecia areata	29,5 ± 13,4	157	74.8	53	25.2	210
Androgenetic alopecia	29,0 ± 12,2	55	76.4	17	23.6	72
Scarring alopecia	34,2 ± 10,6	4	28.5	10	71.5	14
Tinea capitis	7,0 ± 2,3	4	80.0	1	20.0	5
Total		283	45.5	339	54.5	622

Blood tests were performed on 193 of 258 female patients with diffuse alopecia, and 103 patients had completely normal results. Detected abnormalities were as follows: Iron deficiency anemia in 21 patients, Vitamin D deficiency in

57 patients, vitamin B12 deficiency in 13 patients, hypothyroidism in 6 patients and hyperthyroidism in 4 patients. Of the 63 male patients with the same diagnosis, 41 were found to have blood tests and results were those: vitamin D and vitamin B12 deficiency in 6 patients for each and hypothyroidism in 1 patient. None of the male patients had anemia of iron deficiency. 28 male patients had completely normal blood test results. An abnormality in 14 patients was found in 27 patients with female AA patients who underwent blood tests. These were iron deficiency anemia in 4 patients, (all four patients were between 45 and 54 years old) vitamin D deficiency in 9 patients, B12 deficiency in 2 patients, diabetes in 1 patient. A few abnormalities were observed in some patients. Of the 157 male patients with AA, 37 were requested to be tested, only 7 patients had abnormal findings: 4 vit D deficiency, 2 hypothyroidism and 1 diabetes. No anemia or vitamin B12 deficiency in a single male patient was observed.

Seventeen female patients who were diagnosed with AGA were asked to undergo a test of 11 in, and 4 of them had abnormal results. In 55 male patients with AGA, 17 patients were asked to be tested and from these, 5 patients with vitamin D deficiency, 3 patients with vitamin B12 deficiency, 1 patient with polycythemia were found. There were no iron deficiency or thyroid disorders in all 28 AGA patients who were done blood tests. No blood tests were performed on the causes of hair loss in any of the 10 female, 4 male patients who received a scarring alopecia diagnosis. Five of these patients were clinically diagnosed with pseudopelade, 2 posttraumatic scarring alopecia, 6 lichen planopilaris with skin biopsy and 1 already diagnosed as discoid lupus erythematosus before admitted. Pathological laboratory test results rates according to hair loss type are given in (Table 2).

Table 2 : Pathological laboratory test results rates according to hair loss type

Hair loss	Male Female		le	Total		
type	n	%	n	%	n	%
Diffuse alopecia	13 / 28	46.4	90 / 193	46.6	103 / 211	48.8
Alopecia areata	7 / 37	18.9	14 / 27	51.8	21 / 64	32.8
Androgenetic alopecia	4 / 11	36.3	5 / 17	29.4	9 / 28	32.1
Total	24 / 76	31.5	109 / 237	46.0	133 / 303	43.9

DISCUSSION

Patients who complain of hair loss do not only refer to dermatology outpatient clinics but also to departments such as family medicine and internal medicine. Some patients worrying their hair loss to a possible internal disease require extensive laboratory tests. Physical examination and a rigorous history are key to proper care as well as unnecessary testing, avoiding time loss and economic burden. The present study showed that important abnormalities were detected in a number of patients who applied with hair loss. There are few studies regarding the causes of hair loss in large patient groups. Our study demonstrated that most of the patients with hair loss complaints got a diagnosis of diffuse hair loss (51.6%), followed by AA (33.8%) and AGA (11.6%) (Tablo 3).

Table 3 : Number of hair loss patients with anormal laboratory lests

	Male (n=283) Hair Loss Types			F			
Concomitant	Diffus e	Alope cia	Androgen etic	Diffuse alopecia	Alopec ia	Androgenet ic alopecia	Total
illness	alopec	areata	alopecia	atopeeta	areata	ie alopeela	rotai
	ia						
Iron		-	-	21	4	-	25
deficiency	-						
anemia Vitamin D	6	4	5	57	9	_	79
deficiency	0	•	2	57	-		
Vitamin B12	6	-	3	13	2	-	24
deficiency							
Hypothyroidis	1	2	-	6	-	-	9
m							
Hyperthyroidi sm	-	-	-	4	-	-	4
Diabetes		1	_	_	1	_	2
Other		•	1			4	5
	-	-	1	-	-		
No illness	28	30	8	103	13	7	189

In a study conducted in South Korea, 312 patients with hair loss were examined (6). The patients were divided into 4 groups as AA, male and female type of AGA and telogen effluvium. The mean ages were between 33 to 37 in that study, and 31% of all patients were AA, 50% were AGA and 16% were diffuse hair loss. The average age of the patient group in our study is slightly younger (mean ages of our patients for diffuse hair loss, AA and AGA were between 27.9 and 29.5). This difference may be due to genetic, environmental factors and nutrition. Our AA ratio is around 33% similar to Korean study. However, there is a big difference between diffuse hair loss and AGA. We assume that a significant portion of our diffuse hair loss patients may have been mixed with AGA. It is known that patients with AGA begin with diffuse shedding before being converted to the classical pattern Gowda et al. (7) showed that diffuse hair loss was more common among women

in their study, that iron deficiency was common in female patients with diffuse hair loss, that vitamin B12 deficiency was not common or that it was not significant in patients with AGA. Our findings also concur with this study.

In a study conducted in women suffering from hair loss in India, it was reported that diffuse hair loss is the most common type, that 75% of the women who experience such hair loss have iron deficiency anemia (8). AGA was the second common hair loss type in that study and incidence of thyroid disorders was not different from the normal population (8). In our study, the most common abnormality was the anemia of iron deficiency, but about 25% of the patients were found. There may be a number of reasons for this difference, including methodological differences in the diagnosis of iron deficiency, ethnic differences, accompanying nutritional disorders etc. A study again performed in female patients with diffuse hair loss reported low hemoglobin level in 57% patients, vitamin B12 deficiency in 76% cases and vitamin D3 < 30 ng/mL in 81% cases. Subclinical hypothyroidism was present in 11% of cases (9). These outcomes are very different from ours and other studies concerning vitamin B12 levels. In that study group, the vitamin B12 deficiency must be searched for a possible internal cause vitamin D and thyroid disorder rates are somehow similar when considered a low number of patients in both studies.

The role of certain vitamins and elements in AA etiology was examined in some studies. In a retrospective study conducted by Kılınç et al. on 110 patients with AA, iron deficiency was detected in 24 patients (10). The results of this study, in which the male to female ratio is not given, does not match our data. We have found only 4 anemia in 27 female AA patients. Among 37 male patients whose test results were obtained, no anemia was seen in a single patient. In Thomas's study, 8% of iron deficiency anemia and 3% of vitamin B12 deficiency were found in AA patients (11). Two of our 64 AA patients (3%) were found to have the vitamin B12 deficiency. The overall iron deficiency anemia rate was detected in 4% of patients, as roughly consistent with Thomas's data. AA and zinc relations

are also controversial. In a double-blind study, it was reported that oral zinc treatment in AA patients did not improve despite increased serum zinc level (12), whereas Park et al. (13) showed that zinc replacement is beneficial in AA patients with low zinc levels. There was no correlation between AA and vitamin B12, iron and ferritin deficiency (14, 15). Thyroid disorders were reported to be frequent in new-onset AA patients (16), but hypothyroidism was detected in only 2 of our 64 patients.

Vitamin D deficiency is another controversial issue for many diseases, not just for hair loss. Even when we set to cut off to 15 ng/ml, we have seen vitamin D deficiency in many of our hair loss patients. There are studies linking AA to vitamin D deficiency but there is no difference between the control groups (17, 18). Assuming that vitamin D deficiency may develop secondary to hair loss depending on the main etiology, replacement of vitamin D and observation is the best approach in such patients (19).

In a study done by Park et al. (20) from South Korea, hemoglobin level was found to be in the normal range in male and female patients with AGA. These results are exactly the same as our data. A significant association between AGA and the metabolic syndrome has been noted (21). In our patients, only 1 patient had DM, 2 patients had hypertension and 2 patients had hirsutism, implying a metabolic syndrome association.

The fact that the vast majority of our study group is below the age of 40 and the average age is 29 can explain this low rate. Serum zinc levels in diffuse hair loss and AGA patients were found to be lower than healthy controls and healing of hair loss was observed with the use of zinc (6). In the same study, serum copper levels were not different in patients with and without hair loss. In a study conducted in our country, AGA was found to have low levels of zinc and copper in the hair of patients and normal in serum and urine samples. They suggest that zinc and copper in the hair are more accurate for treatment planning. In that study, it has been suggested that the patient group is more obese than the healthy group, which may interfere with copper and zinc utilization (22).

Conversely, Yavuz et al. reported that chronic diffuse hair loss is not associated with zinc, but may be associated with some heavy metal exposure (23). Ayhan and colleagues showed that a 7-year-old boy who applied with a complaint of hair loss improved with biotin replacement. There was a lack of biotinidase enzyme playing role in biotin synthesis and eczema-like rash on the skin of the patient (24).

There are also studies suggesting that empirical biotin replacement is not beneficial in diffuse hair loss (25). Biotin treatment can work if any enzyme deficiency is detected. In our patients who applied with hair loss, since the elements such as heavy metals, zinc copper were not routinely required, we could not obtain their values in the patients in our study group. So we can not compare it with other studies.

Tinea capitis was categorized as a type of hair loss because the primary complaint of the patients was hair loss. Patients who were diagnosed as scarring hair loss and tinea capitis were not required blood tests.

Our study has some limitations. If a long follow-up would be, we could have seen that some diffuse hair loss patients could evolve AGA pattern in the future. In addition, some trace elements and vitamins such as zinc and biotin, which are thought to be important in hair loss, may have been tested for better evaluation.

Hematologic and biochemical abnormalities, which are considered to be the most frequently associated with hair loss in practice and in the literature, are thyroid disorders in both men and women, and iron deficiency anemia especially for female patients (26, 27). Generally, our data were compatible with the findings of previous studies.

In conclusion, we showed that laboratory investigation, particularly in women patients with diffuse hair loss, could detect the cause of alopecia. A good history and physical examination of patients with necessary laboratory tests are mandatory for patients with hair loss complaint.

REFERENCES

1. Mubki T, Rudnicka L, Olszewska M, Shapiro J. Evaluation and diagnosis of the hair loss patient: part I. History and clinical examination. J Am Acad Dermatol 2014;71(3):415. e1-415.e15.

2. Jose N, Isac CM, Kunjumani S, Vilasinlamma L. Sarcomatoid lung carcinoma presenting as alopecia neoplastica. Indian J Dermatol Venereol Leprol 2018;84(2):188-90.

3. Lause M, Kamboj A, Fernandez Faith E. Dermatologic manifestations of endocrine disorders. Transl Pediatr 2017;6(4):300-12.

4. Knopp E.The scalp biopsy for hair loss and its interpretation. Semin Cutan Med Surg 2015;34(2):57-66.

5. Lacarrubba F, Micali G, Tosti A. Scalp dermoscopy or trichoscopy. Curr Probl Dermatol 2015;47:21-32.

6. Kill MS, Kim CW, Kim SS. Analysis of serum zinc and copper concentrations in hair loss. Ann Dermatol 2013;25(4):405-9.

7. Gowda D, Premalatha W, Imtiyaz DB. Prevalence of nutritional deficiencies in hair loss among Indian participants: results of a cross-sectional study. Int J Trichology 2017;9(3):101-4.

8. Deo K, Sharma YK, Wadhokar M, Tyagi N. Clinicoepidemiological observational study of acquired alopecias in females correlating with anemia and thyroid function. Dermatol Res Pract 2016;2016:6279108.

9. Poonia K, Thami GP, Bhalla M, Jaiswal S, Sandhu J. Nonscarring diffuse hair loss in women: a clinico-etiological study from tertiary care center in North-West India. J Cosmet Dermatol 2018;May 17. doi: 10.1111/jocd.12559.

10. Kilinc I, Alper S, Ceylan C, Ünal İ. Patent profile of alopecia areata: a retrospective study. Ege Tip Dergisi 2002;41(1):25-7.

11. Thomas E, Kadyan RS. Alopecia areata and autoimmunity: a clinical study. Indian J Dermatol. 2008;53(2):70-4.

12. Ead RD. Oral zinc sulphate in alopacia areata-a double blind trial. Br J Dermatol 1981;104(4):483-4.

13. Park H, Kim CW, Kim SS, Park CW. The therapeutic effect and the changed serum zinc level after zinc supplementation in alopecia areata patients who had a low serum zinc level. Ann Dermatol 2009;21(2):142-6.

14. Ertugrul DT, Karadag AS, Takci Z, et al. Serum holotranscobalamine, vitamin B12, folic acid and homocysteine levels in alopecia areata patients. Cutan Ocul Toxicol 2013;32(1):1-3.

15. Gonul M, Cakmak SK, Soylu S, Kilic A, Gul U. Serum vitamin B12, folate, ferritin, and iron levels in Turkish patients with alopecia areata. Indian J Dermatol Venereol Leprol. 2009;75(5):552.

16. Lyakhovitsky A, Shemer A, Amichai B. Increased prevalence of thyroid disorders in patients with new onset alopecia areata. Australas J Dermatol 2015;56(2):103-6.

17. Aksu Cerman A, Sarıkaya Solak S, Kıvanç Altunay I. Vitamin D deficiency in alopecia areata. Br J Dermatol 2014;170(6):1299-304.

18. Erpolat S, Sarifakioglu E, Ayyildiz A. 25-hydroxyvitamin D status in patients with alopecia areata. Postepy Dermatol Alergol 2017;34(3):248-52.

19. Gerkowicz A, Chyl-Surdacka K, Krasowska D, Chodorowska G. The role of vitamin D in non-scarring alopecia. Int J Mol Sci 2017;18(12):2653.

20. Park SY, Na SY, Kim HJ, Cho S, Lee JH. Iron plays a certain role in patterned hair loss. J Korean Med Sci 2013;28(6):934-8.

21. Lie C, Liew CF, Oon HH. Alopecia and the metabolic syndrome. Clin Dermatol 2018;36(1):54-61.

22. Ozturk P, Kurutas E, Ataseven A, et al. BMI and levels of zinc, copper in hair, serum and urine of Turkish male patients with androgenetic alopecia. J Trace Elem Med Biol. 2014 Jul;28(3):266-70.

23. Yavuz IH, Yavuz GO, Bilgili SG, Demir H, Demir C. Assessment of Heavy Metal and Trace Element Levels in Patients with Telogen Effluvium. Indian J Dermatol 2018;63(3):246-50.

24. Ayhan E, Kivrak A, Aytekin S. Biotinidase Deficiency Accompanying Hair Changes and Periorificial Lesions: A Case Report. Turk J Dermatol 2011;5:79-81.

25. Patel DP, Swink SM, Castelo-Soccio L. A review of the use of biotin for hair loss. Skin Appendage Disord. 2017;3(3):166-9.

26. Güler Özden M, Öztaş MO, Gülekon A, Gürer MA. Kadın Olgularda Yaygın Saç Kaybı ve Eşlik Eden Bulgular. O.M.Ü. Tıp Dergisi 2008;25(2):50-6.

27. Aksoy GG. Diffuse alopecia; nutritional factors and supplements. Türkderm 2014;48: Özel Sayı 1:45-7.

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