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Evaluation of Vitamin D and Hematological Parameters in Pediatric Non-Scarring Alopecias

Pediatrik Non-Skatrisyel Alopesilerde Vitamin D ve Hematolojik Parametrelerin Değerlendirilmesi

Betül ŞEREFLİCAN
0000-0001-9947-7690
Merve DİLCAN
0000-0001-9870-4767
Mualla POLAT
0000-0001-9226-5134

Department of Dermatology, Bolu Abant İzzet Baysal University Faculty of Medicine, Bolu, Türkiye

Corresponding Author
Sorumlu Yazar
Betül ŞEREFLİCAN
ozbetul@yahoo.com

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ABSTRACT

Aim: Vitamin D is an important factor for the hair follicle cycle. Alopecia areata (AA), androgenetic alopecia (AGA), and telogen effluvium (TE) are the most common forms of non-scarring alopecia. This study aimed to define vitamin D levels and hemogram parameters in children and adolescents with non-cicatricial alopecia.

Material and Methods: A total of 157 patients under the age of 18 and diagnosed with AA, AGA, and TE were included in this retrospective study. Vitamin D levels, and neutrophil/lymphocyte (neu/lym) and platelet/lymphocyte (plt/lym) ratios were evaluated. Vitamin D levels were examined in four different groups according to the admission period as autumn, winter, spring, and summer.

Results: Of the patients, 30 were diagnosed with AA, 11 with AGA, and 116 with TE. Vitamin D deficiency was detected in 128 of 153 patients, of whom vitamin D levels were examined, insufficiency in 20, and sufficiency in 5. There was no statistically significant difference in vitamin D levels between groups (p=0.114). Also, no statistically significant difference was found between the groups in terms of vitamin D deficiency and insufficiency (p=0.403). Vitamin D levels were significantly higher in males than in females (p<0.001), and in autumn than in winter (p=0.043). The ratio of neu/lym in patients with TE was significantly higher than the patients in the AA group (p=0.005).

Conclusion: Vitamin D deficiency was seen in a very high percentage of all non-cicatricial alopecia. Neu/lym ratio may be a more appropriate inflammatory marker for patients with TE than the other nonscarring alopecia.

Keywords: Alopecia; alopecia areata; androgenetic alopecia; vitamin D.

ÖZ

Amaç: D vitamini saç folikülü döngüsü için önemli bir faktördür. Alopesi areata (AA), androgenetik alopesi (AGA) ve telogen effluvium (TE) skarsız alopesilerin en sık görülen formlarıdır. Bu çalışmada non-skatrisyel alopesisi olan çocuk ve adölesanlarda D vitamini düzeylerinin ve hemogram parametrelerininin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu geriye dönük çalışmaya AA, AGA ve TE tanısı almış ve 18 yaş altı olan toplam 157 hasta dahil edildi. D vitamini düzeyleri ile nötrofil/lenfosit (neu/lym) ve platelet/lenfosit (plt/lym) oranları değerlendirildi. D vitamini düzeyleri başvuru dönemine göre sonbahar, kış, ilkbahar ve yaz olmak üzere dört farklı grupta incelendi.

Bulgular: Tüm hastaların 30'u AA, 11'i AGA ve 116'sı TE tanısı aldı. D vitamini düzeylerine bakılmış olan 153 hastanın 128'inde D vitamini eksikliği, 20'sinde yetersizlik, 5'inde ise yeterlilik saptandı. Gruplar arasında D vitamini düzeyleri açısından istatistiksel olarak anlamlı bir farklılık yoktu (p=0,114). Ayrıca, gruplar arasında D vitamini eksikliği ve yetersizliği açısından da istatistiksel olarak anlamlı bir fark bulunmadı (p=0,403). D vitamini düzeyleri erkeklerde kadınlara göre (p<0,001) ve sonbaharda kışa göre (p=0,043) anlamlı olarak daha yüksekti. Neu/lym oranı, TE hastalarında AA grubundaki hastalara göre anlamlı olarak daha yüksekti (p=0,005).

Sonuç: Tüm non-skatrisyel alopesilerin çok yüksek bir yüzdesinde D vitamini eksikliği görüldü. Neu/lym oranı TE'li hastalar için diğer non-skatrisyel alopesilerden daha uygun bir inflamatuar belirteç olabilir.

Anahtar kelimeler: Alopesi; alopesi areata; androgenetik alopesi; D vitamini.

INTRODUCTION

Hair loss is a clinical condition that is frequently seen in dermatology clinics and affects the quality of life of patients. There are two major categories of hair loss: scarring alopecia and non-scarring alopecia. Alopecia areata (AA), androgenetic alopecia (AGA), and telogen effluvium (TE) exemplify the three most common patterns of non-scarring alopecia (1,2).

Vitamin D is a fat resolvable vitamin and plays a considerable role in bone metabolism, adjustment of the immune system, keratinocyte differentiation, and hair follicle cycle. Vitamin D is generated in the skin and involved in the etiopathogenesis of various diseases, including hair loss (3).

Low vitamin D levels have been shown in patients with non-cicatricial alopecia in several studies (4). However, there are not enough studies in the pediatric age group to understand the effects of vitamin D on non-cicatricial alopecia in childhood.

Neutrophils (neu), lymphocytes (lym), and platelets (plt) play a role in the inflammatory response of the body, and their levels vary depending on the severity of systemic inflammation. Recent studies have shown that the plt/lym and neu/lym ratios can be used as new inflammatory parameters associated with many inflammatory diseases, cardiovascular system diseases, and malignancies (5). AA, AGA, and TE may result from inflammatory conditions (6-8).

The objective of this study was to investigate the levels of vitamin D in patients with AA, AGA, and TE, as well as to evaluate the plt/lym and neu/lym ratios in these patient groups.

MATERIAL AND METHODS

The study included patients under the age of 18 who were referred to the dermatology outpatient clinic of Bolu Abant İzzet Baysal University İzzet Baysal Training and Research Hospital between January 2012 and December 2019 and were diagnosed with AA, AGA, and TE.

In this retrospective study, laboratory information of the patients was evaluated based on their first admission to the dermatology outpatient clinic. Vitamin D levels, plt, lym, and neu counts in the complete blood examination were recorded based on the laboratory values of the patients. Vitamin D values were examined in four different groups according to the admission period: autumn, winter, spring, and summer.

Following the Endocrine Society Clinical Practice Guideline, serum 25 (OH) vitamin D levels ≥30 ng/ml were considered adequate, levels of 20-29 ng/ml indicate vitamin D insufficiency, and levels below 20 ng/ml indicate vitamin D deficiency (9).

The study was approved by the Bolu Abant İzzet Baysal University Faculty of Medicine Ethics Committee with the decision dated 19.12.2023 and numbered 2023/459.

Statistical Analysis

R v.4.3.0 software was used in statistical analyses. Prior to undertaking any statistical analysis, the Shapiro-Wilk test was employed to ascertain whether the data exhibited a normal distribution. For variables not showing normal distribution, median, 25^{th}-75^{th} percentiles, minimum, and maximum were used as descriptive statistics. Comparison between groups was made with the Kruskal-Wallis test. Mann-Whitney U test with Bonferroni correction was utilized as a post-hoc test to detect the significantly different groups. Cross-tabulations containing absolute frequencies were created for categorical variables, and a chi-squared test was used for statistical analysis, but Fisher's exact test was used where the expected count was less than 5 in a cell. A p-value of <0.05 was determined as the statistical significance level.

RESULTS

Data for 157 patients were obtained. The median age of all patients was 15 (range, 1-17) years. Of the patients, 129 were female and 28 were male. There were 17 females and 13 males in patients with AA, 3 females and 8 males in patients with AGA, and 109 females and 7 males in patients with TE. The details for demographic data and hemogram values according to patient groups were presented in Table 1.

The distribution of plt/lym and neu/lym ratios according to patient groups was shown in Table 1. No significant difference was found in the plt/lym ratios between the groups (p=0.271). A significant difference was observed in neu/lym ratios between the patient groups (p=0.006). The ratio of neu/lym in patients with TE was found to be significantly higher than in the AA group (p=0.005) according to the post hoc test results.

Vitamin D levels were examined in 153 patients, of whom 127 were female and 26 were male. Among them, 29 patients were diagnosed with AA, 10 with AGA, and 114 with TE. While 57 of these patients applied in the autumn, 34 in the winter, 26 in the spring, and 36 in the summer. Vitamin D deficiency was detected in 128 of these patients, insufficiency in 20 patients, and sufficiency in 5 patients. The median vitamin D levels of the patients were

Table 1. Demographic data and hemogram values according to patient groups

	AA (n=30)	AGA (n=11)	TE (n=116)	p
Age (years)	9.5 (5-15) [1-17][a]	16 (15-17) [12-17][b]	16 (14-17) [2-17][b]	**<0.001**
Plt (K/uL)	299 (252-358) [118-573]	254 (225-268) [178-306]	270 (234-318) [162-415]	0.060
Lym (K/uL)	2.5 (2.0-3.4) [1.1-8.7]	2.2 (2.0-3.0) [1.9-3.3]	2.3 (1.9-2.8) [1.0-6.0]	0.227
Neu (K/uL)	3.6 (2.8-4.3) [1.8-8.0]	3.8 (3.2-5.2) [2.7-6.8]	4.2 (3.5-5.5) [1.3-10.3]	0.087
Plt/Lym	115.3 (88.9-146.8) [31.2-301.9]	104.6 (77.6-127.6) [68.6-145.6]	120.4 (95.0-144.6) [38.7-240.9]	0.271
Neu/Lym	1.4 (1.0-1.7) [0.4-4.0][a]	1.7 (1.5-2.0) [1.0-3.0][b]	1.9 (1.3-2.6) [0.4-5.5][b]	**0.006**

AA: alopecia areata, AGA: androgenetic alopecia, TE: telogen effluvium, Plt: platelet, Lym: lymphocyte, Neu: neutrophil, values not sharing a common superscript within each row are significantly different as determined by Bonferroni corrected Mann-Whitney U test, values were presented as median (25^{th}-75^{th} percentile) [minimum-maximum]

found to be 13.4 (range, 4.1-29.2) ng/ml in AA patients, while 15.9 (range, 6.3-25.1) ng/ml in AGA patients, and 11.3 (range, 3.1-35.3) ng/ml in TE patients (Figure 1). No significant difference was observed in vitamin D levels between the groups (p=0.114).

Median vitamin D levels were found significantly higher in males at 17.6 (range, 7.7-29.2) ng/ml, compared to females at 10.5 (range, 3.1-35.3) ng/ml (p<0.001).

The vitamin D levels of the patient groups according to seasons were presented in Table 2. Vitamin D levels showed a significant difference across seasons (p=0.043). Post hoc test with Bonferroni correction showed that vitamin D levels in autumn were significantly higher than those observed in winter.

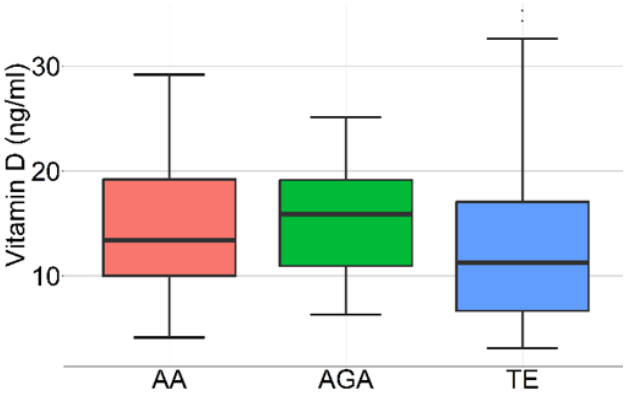

Figure 1. Vitamin D levels in patient groups

Table 2. The vitamin D levels according to the seasons*

	Autumn (n=57)	Winter (n=34)	Spring (n=26)	Summer (n=36)	p
VitD (ng/ml)	13.9 (9.3-18.6) [3.1-32.6]^{a}	9.6 (5.5-14.2) [3.3-31.9]^{b}	11.3 (6.3-18.2) [4.1-29.2]^{ab}	10.7 (6.9-19.2) [3.4-35.3]^{ab}	**0.043**

VitD: vitamin D, *: vitamin D levels were examined in 153 patients, values not sharing a common superscript within each row are significantly different as determined by Bonferroni corrected Mann-Whitney U test, values were presented as median (25th-75th percentile) [minimum-maximum]

The distribution of vitamin D status according to patient groups was as indicated in Table 3. There was no significant difference between the groups in terms of vitamin D deficiency and insufficiency (p=0.403).

The distribution of patient groups according to the season of admission to the hospital was presented in Table 4. No statistically significant difference was found between the patient groups according to the seasons admitted to the hospital (p=0.582).

Table 3. Vitamin D status according to patient groups

	AA (n=29)	AGA (n=10)	TE (n=114)	p
VitD, n (%)				
Deficiency	23 (79.3%)	9 (90.0%)	96 (84.2%)	
Insufficient	6 (20.7%)	1 (10.0%)	13 (11.4%)	0.403
Sufficient	0 (0.0%)	0 (0.0%)	5 (4.4%)	

VitD: vitamin D, AA: alopecia areata, AGA: androgenetic alopecia, TE: telogen effluvium, *: vitamin D levels were examined in 153 patients

Table 4. Patient groups by seasons

	AA (n=30)	AGA (n=11)	TE (n=116)	p
Season, n (%)				
Autumn	7 (23.3%)	4 (36.4%)	47 (40.5%)	
Spring	8 (26.7%)	2 (18.2%)	17 (14.7%)	
Summer	7 (23.3%)	3 (27.3%)	28 (24.1%)	0.582
Winter	8 (26.7%)	2 (18.2%)	24 (20.7%)	

AA: alopecia areata, AGA: androgenetic alopecia, TE: telogen effluvium

DISCUSSION

Vitamin D levels were shown to be linked to different dermatological diseases, such as atopic dermatitis, psoriasis, vitiligo, and systemic sclerosis (10).

In the study of Gade et al. (11), significant systemic inflammation and vitamin D deficiency were found in patients with AA compared to healthy controls. In the study of Bhat et al. (12), levels of 25(OH)D were lower in AA patients than in the controls. A few studies have failed to identify a significant association between AA and vitamin D (13,14). In a meta-analysis by Liu et al. (15) on 1585 AA patients, a deficiency of serum 25(OH)D level was found. So a relationship between vitamin D and AA can be mentioned (16). In the present study, 79.3% of patients with AA exhibited vitamin D deficiency, with no patients demonstrating sufficient vitamin D levels within this patient group.

Although there are studies examining the relationship between AA and vitamin D levels in adults, there are few studies examining this relationship in the pediatric patient group.

In pediatric AA cases evaluated by Siddappe et al. (17) and Kundak et al. (18), 25(OH)D levels were determined to be lower, and vitamin D deficiency incidence was higher than the controls. In the study conducted by Lim et al. (19), to determine the predictors of vitamin D insufficiency in child and adolescent AA patients, insufficiency was found in 60.4%, and deficiency was found in 38.2% of the patients.

In the study of Unal et al. (20), lower serum 25(OH)D levels in the pediatric AA patients than the controls were detected, but there was no significant difference.

The present study represents low vitamin D levels in AA in the pediatric age group, parallel to the few studies conducted on pediatric AA patients in the literature.

In the study of Tran et al. (21), AA patients had a significantly lower mean vitamin D level than the other alopecias, including cicatricial and noncicatricial. In the study of Öner et al. (22), vitamin D levels in nonscarring alopecia, including AA, TE, and AGA in the pediatric age group and adults, were evaluated. The mean vitamin D levels in all groups indicate vitamin D deficiency. The incidence of patients with vitamin D deficiency was higher in the TE group. In the present study, there was no significant difference in median vitamin D levels between the patient groups.

AGA in pediatric patients is rarely reported in the literature (23). In one study by Losoya-Jaquez et al. (24), 145 AGA patients in the pediatric age group were analyzed, and vitamin D deficiency was found in 84% of the patients. In the present study, vitamin D deficiency was detected in 90% of the patients in a smaller group.

There are studies in the literature showing low levels of vitamin D regarding TE, as well as studies stating the opposite (25-27). In a study conducted on pediatric TE patients, it was reported that the vitamin D deficiency seen in this group of patients was similar to the general pediatric population (28).

The study of Conic et al. (3) evaluated the prevalence of vitamin D deficiency in scarring and nonscarring alopecia. They found vitamin D deficiency in 64.8% of all the patients. TE patients were 3.7 times more likely to have severe vitamin D deficiency than those with AA.

In a recent meta-analysis assessing serum 25(OH)D levels in non-scarring alopecia, decreased serum 25(OH)D levels and increased incidence of vitamin D deficiency were found (4). So, we can say that although there are a few opposite results, in general, low vitamin D levels can be expected in non-cicatricial alopecia.

In the study of Lim et al. (19), children and adolescents with AA showed significantly increased odds of vitamin D insufficiency in the non-summer season. In a meta-analysis by Chen et al. (4) examining non-scarring alopecia in all age groups, there is a study in which vitamin D deficiency was observed in AA patients, particularly in winter and autumn, and one study in which deficiency was observed in almost all seasons. In the present study, vitamin D levels in patients were found to be higher in autumn than in winter. This result can be explained as the result of exposure to sunlight throughout summer and continuing sun exposure in autumn.

Neu/lym ratio and plt/lym ratio are strong predictors of inflammation used in a great deal of diseases (29). However, there are few studies investigating the relationship of these markers with hair diseases. In two studies examining neu/lym ratio and plt/lym ratio in patients with AA and control groups, no significant difference was found (30,31). In one study, the plt/lym ratio was higher in patients with AA than in controls, but there was no difference in the neu/lym ratio (32). In the study of El-Taweel et al. (33), neu/lym and plt/lym ratios were found to be significantly higher in AGA patients compared to controls. To our knowledge, there was no study in patients with TE regarding the relationship with these inflammatory markers.

In the study of Öner et al. (22), the number of patients with the highest differences in all laboratory parameters, including vitamin D, vitamin B12, ferritin, hemoglobin deficiency, and thyroid dysfunction, was observed in TE compared to AA and AGA. In the present study, the neu/lym ratio was highest in the TE group, and the ratio of neu/lym in patients with TE was significantly higher than that of patients in AA, but there was no difference in the plt/lym ratios between patient groups.

Limitations of this study were that a control group could not be formed as there was no homogeneous distribution in the groups, the study was conducted in one center, and the relatively small number of patients.

CONCLUSION

Vitamin D deficiency was seen in a very high percentage of all non-cicatricial alopecia in our study. But no subgroup stands out in terms of low vitamin D levels. Neu/lym ratio is one of the constantly used markers to determine inflammation in many diseases, including dermatological ones. It can be considered that the neu/lym ratio may be a more appropriate inflammatory marker for patients with TE than other nonscarring alopecias. Multicenter studies conducted with control groups will contribute more objective results.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Bolu Abant İzzet Baysal University (19.12.2023, 459).

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