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The role of autoimmune thyroid disorders in patients with alopecia areata

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ABSTRACT

Objectives: The aim of this study was to investigate the association of thyroid autoimmunity with alopecia areata (AA) by examining thyroid stimulating hormone (TSH) and thyroid autoantibody levels. In addition, to compare the epidemiologic data obtained with the data of our country.

Methods: Our study was organized as a cross-sectional, retrospective study. The study was performed on patients between the ages of 2-65 years who were admitted to our outpatient clinic between 01.01.2008 and 31.12.2011, who were clinically or histopathological diagnosed with AA, examined for etiology and thyroid autoantibodies were requested. Patients under two years of age and over 65 years of age, patients with no thyroid autoantibodies and pregnant patients were excluded. Results were expressed as mean±standard deviation and median values. Mann-Whitney U test was used to compare TSH, anti-TG antibody (Anti-TG) and anti-TPO (Anti-TPO) antibody values in the variables of nail involvement, psychiatry, comorbidity and family history. Spearman correlation analysis was used to examine the relationships between age and disease duration and TSH, Anti-TPO and Anti-TG variables.

Results: In our study, 65 (42.8%) of 152 patients were female and 87 (57.2%) were male. The age of the patients was 26.5±14.6 years. The mean age of females was 27.5±14.4 and 25.7±14.9 in males. Elevated thyroid autoantibodies were found in a total of 29 patients, 21 of whom were female and 8 of whom were male. Of these 29 patients, 10 had hypothyroidism, 2 had chronic thyroiditis and 3 had toxic multinodular goiter. 14 patients did not return after the examination at the internal medicine outpatient clinic, so the diagnosis of thyroid disease could not be reached. The mean TSH, Anti-TG and Anti-TPO values were 2.27±1.57, 29.2±99 and 71.5±2.2, respectively. When these values were analyzed separately as men and women, they were found to be 2.6±2.02, 41.8±1.23 and 134±2.8 in women and 1.99±1.03, 19.8±75.6 and 24.5±1.32 in men. There was a significant difference between men and women in terms of Anti-TG and Anti-TPO values (p=0.011 and p=0.001, respectively). A significant correlation was found between disease duration and Anti-TPO positivity (p=0.045); however, a similar relationship was not found between disease duration and Anti-TG positivity (p=0.34).

Conclusions: As a result of this study, although there was a significant correlation between anti-TPO and duration of AA, the association between thyroid autoimmunity and AA was not found to be statistically significant. This may be due to the fact that humoral autoimmunity plays a role in thyroid autoimmunity and primarily cellular autoimmunity plays a role in AA. In addition, the epidemiologic data of our study were similar to the data of studies conducted in our country.

Keywords: Alopecia areata, thyroid autoantibodies, autoimmune thyroid disorders, autoimmune diseases, dermatology, skin and venereal diseases

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Alopecia areata (AA), a complex, multifactorial and autoimmune disease, is the second most common form of scarless hair loss after androgenetic alopecia. AA appears as sharply circumscribed round or oval areas with no visible inflammation on the skin, appearing suddenly on hair anywhere on the body, especially on the scalp. It may regress spontaneously or progress and affect the entire scalp and other body hair. The prevalence of the disease is 1 in 1000 worldwide, and this rate increases to 1-2% in those who apply to dermatology outpatient clinics. It affects 147 million people worldwide. The lifetime incidence is 2%. Most patients are younger than 30 years of age and only 20% are 40 years or older. It can occur at any age, regardless of race or gender, but is more common in young adults. AA leads to a reduced quality of life. It increases many psychosocial problems, especially in family and work life. The likelihood of autoimmune and systemic diseases is higher in patients with AA. Common cytokine response, similar immune cell types and similar genetic structures are thought to play a role in this.[1-5] The etiopathogenesis of AA has been linked to genetics, epigenetics, oxidative stress, immunology, microbiota, microbiome and allergy.[6] There is a lymphocytic infiltration involving the peribulbar anagen terminal hairs, which is described histopathologically as a "swarm of bees", but in the chronic phase almost all the follicles are in the telogen phase.[6]

AA was associated with increased odds of the following overall categories of disease in descending order: ocular (OR 3.15), thyroid (OR 3.13), connective tissue and autoimmune (OR 2.28), neurologic (OR 2.06), dermatologic (OR 1.94), atopic (OR 1.82). Alopecia Areata has been shown to be associated with vitamin D deficiency. As in Behcet's disease, a chronic vasculitis of unknown cause, and other autoimmune diseases.[7-10]

AA was associated with lower rates of irritable bowel syndrome, acne vulgaris and some cancers (colorectal, non-melanoma skin cancers, bladder, hepatocellular, stomach) compared to healthy volunteers. However, data on these conditions were obtained from a small number of studies.[9]

The possible association of AA with autoimmune diseases comes to mind; it's possible that there is an association with thyroid disease, which is also known to be associated with autoimmunity. There are some studies in the literature on this subject, but there is a new need for screening in both patient groups to investigate the association of AA with thyroid diseases and to raise awareness. The aim of this study was to investigate the association of thyroid autoimmunity with AA by examining thyroid stimulating hormone (TSH) and thyroid autoantibody levels. In addition, to compare the epidemiologic data obtained with the data of our country.

METHODS

Our study was organized as a cross-sectional, retrospective study. Approval was obtained from Trakya University Faculty of Medicine Ethics Committee on 21.12.2011 with decision number 14/138 and protocol number 15789. SPSS 19 statistical package program was used for statistical analysis. The study was performed on patients between the ages of 2-65 years who were admitted to our outpatient clinic between 01.01.2008 and 31.12.2011, who were clinically or histopathological diagnosed with AA, examined for etiology and thyroid autoantibodies were requested. Patients under two years of age and over 65 years of age, patients with no thyroid autoantibodies and pregnant patients were excluded. 37,000 patients were screened. Three hundred forty-three AA patients were identified. A total of 152 patients who met these conditions were included in this study.

Results were expressed as mean ± standard deviation and median values. Mann-Whitney U test was used to compare TSH, anti-TG antibody (Anti-TG) and anti-TPO (Anti-TPO) antibody values in the variables of nail involvement, psychiatry, comorbidity and family history. Spearman correlation analysis was used to examine the relationships between age and disease duration and TSH, Anti-TPO and Anti-TG variables.

RESULTS

In our study, 65 (42.8%) of 152 patients were female and 87 (57.2%) were male. Elevated thyroid autoantibodies were found in a total of 29 patients, 21 of whom were female and 8 of whom were male. Of these 29 patients, 10 had hypothyroidism, 2 had chronic thyroiditis and 3 had toxic multinodular goiter. 14 patients did not return after the examination at the internal medicine outpatient clinic, so the diagnosis of thyroid disease could not be reached.

The ages of the patients ranged between 2-64 years

and the mean age was 26.5±14.6 years. The mean age of females was 27.5±14.4 and 25.7±14.9 in males (figure 1).

Patch type AA was seen in 150 cases and alopecia totalis (AT) was present in 2 cases. One of the AT patients was female and one was male. Scalp was involved in 115 patients (74.7%), beard in 18, scalp and beard in 8, scalp and eyebrows or eyelashes in 6, and only eyebrows or eyelashes in 5. Nail involvement was found in only 12 (7.9%) patients, but not in 140 (92.1%) patients.

While 51 (33.6%) of the patients had comorbidities, 101 (63.4%) did not. Of those with comorbidities, 31 had psychiatric, 15 thyroid, 2 acne vulgaris, 2 vitiligo, and one had both psychiatric and thyroid diseases. Family history was present in 17 (11.2%) and absent in 135 (88.8%) of 152 patients. Ophiasis was present in 5 patients and both ophiasis and nevus flammeus were present in 1 patient.

The mean TSH, Anti-TG and Anti-TPO values were 2.27±1.57, 29.2±99 and 71.5±2.2, respectively. When these values were analyzed separately as men and women, they were found to be 2.6±2.02, 41.8±1.23 and 134±2.8 in women and 1.99±1.03, 19.8±75.6 and 24.5±1.32 in men. There was a significant difference between men and women in terms of Anti-TG and Anti-TPO values (p=0.011 and p=0.001, respectively).

Mann-Whitney U test showed no significant association between nail involvement and TSH, Anti-TG and Anti-TPO (p=0.65, p=0.49 and p=0.38, respectively). No significant association was observed between comorbidities and TSH and Anti-TG (p=0.172 and p=0.226, respectively). However, there was a statistically significant relationship between comorbidities and Anti-TPO (p=0.016). No significant correlation was observed between the presence of family history and TSH, Anti-TG and anti-TPO (p=0.68, p=0.60 and p=0.22, respectively). Thirty-one (20.4%) patients had psychiatric illness, while 121 (79.6%) did not. No significant correlation was observed between the presence of psychiatric disease and TSH, Anti-TG and Anti-TPO (p=0.78, p=0.59 and p=0.17, respectively) (Table 1).

There was no significant correlation between age and disease duration and Anti-TG, Anti-TPO (p=0.069, p=0.633 and p=0.205, respectively) (Spearman's correlation test).

A significant correlation was found between disease duration and Anti-TPO positivity (p=0.045); however, a similar relationship was not found between disease duration and Anti-TG positivity (p=0.34) (Table 2).

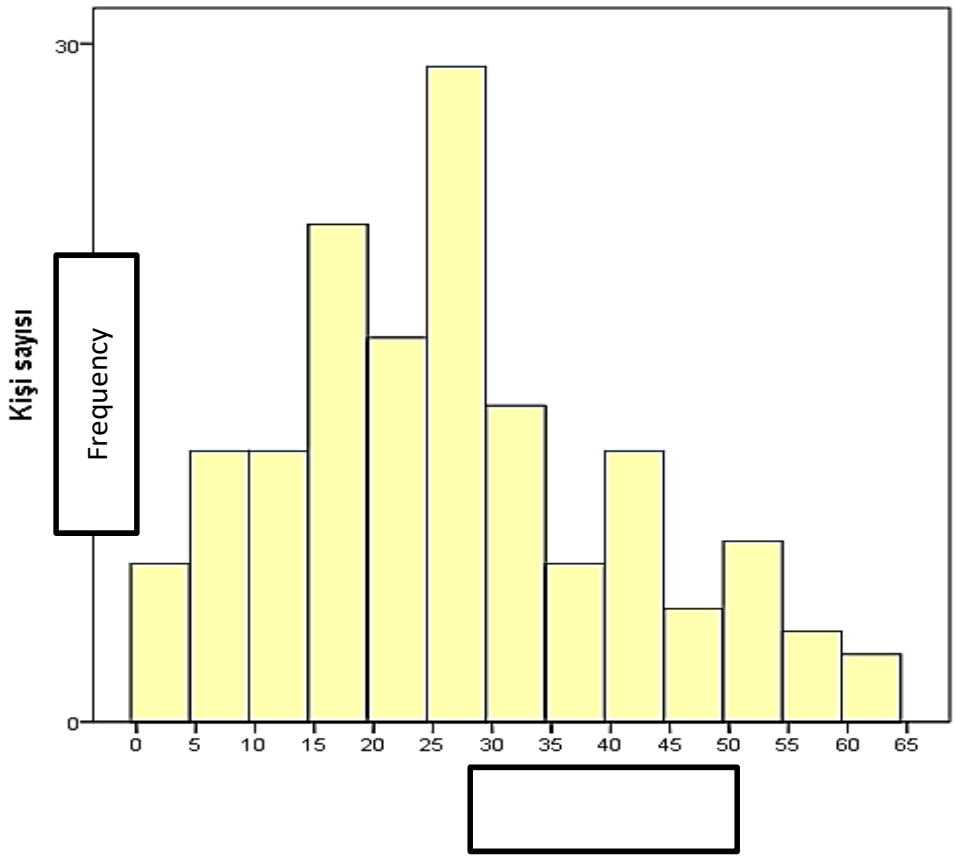

Figure 1. Patient frequency according to age

Table 1. Comparison of TSH, Anti-TG and Anti TPO with Nail Involvement, Comorbidity, Psychiatric Disease and Family History

			TSH	*p*	Anti-TG	*p*	Anti-TPO	*p*
Nail Involvement	**Yes**	**Mean±SD**	2.3±1.21	0.650	63.7±1.98	0.490	67.7±2.13	0.380
	No	**Mean±SD**	2.28±1.60		26.2±86		116±2.94	
Comorbidity	**Yes**	**Mean±SD**	2.78±2.18	0.172	62.2±1.5	0.226	178±3.31	**0.016**
	No	**Mean±SD**	2.02±1.06		12.5±48.9		17.3±97.7	
Psychiatric Disease	**Yes**	**Mean±SD**	2.32±1.44	0.780	86.3±184	0.590	67±222	0.170
	No	**Mean±SD**	2.27±1.6		29.9±86.1		102.2±227	
Family History	**Yes**	**Mean±SD**	2.09±1.3	0.680	18.5±47.9	0.600	132±276.9	0.220
	No	**Mean±SD**	2.31±1.6		47.3±125.8		66.2±215	

TSH: Thyroid-stimulating hormone: **Anti-TG:** Anti-Thyroglobulin antibody; **Anti-TPO:** Anti-Thyroid peroxidase antibody

Table 2. The Relationship Between Anti-TPO and Anti-TG and Disease Duration (Median)

	Anti-TPO		Anti-TG	
	Positive	**Negative**	**Positive**	**Negative**
Disease duration (days) (median)	365	90	272	90

Anti-TG: Anti-Thyroglobulin antibody; **Anti-TPO:** Anti-Thyroid peroxidase antibody

DISCUSSION

Alopecia areata is a disease that occurs at a young age, most commonly between the 2nd and 4th decades, with a prevalence reported to be 0.1%. Finner et al. reported that 66% of the patients were under the age of 30 years and the disease was very rare under the age of 3 years.[11] In a study performed in Iran, 69.9% of the patients were seen in the first two decades and the mean age was 24.05±9.98 years.[10] In studies conducted in Turkey, the age of disease was found to be 32.4±8.32, 25.87±12.57, 26.72±12.91.[12-14] In our study, the age range of the patients was 2-64 years and the mean age was 26.5±14.6 years. The mean age was 27.5±14.4 years in women and 25.7±14.9 years in men. There were only three patients under the age of three years. The majority of the patients between the ages of 25-30 years constituted the largest age group with a rate of 21.7%. 68.4% of the patients were under 30 years of age and 21% were over 40 years of age. These findings were found to be consistent with the literature.

In a study conducted in Greece in which 637 patients participated, it was reported that male patients were more common, which was compatible with the data of studies in France, Italy and Spain.[15] The study data in Turkey are mixed, and in addition to the publications with a higher proportion of women (52.7% of the patients were women and 47.3% were men in the study by Kılınç et al.), 2 separate studies, one of which was multicenter (38.2% of the patients were women and 61.8% were men in the study by Kavak et al.), reported a higher proportion of men.[16-18] Contrary to the literature, AA was found to be higher in men in our study. However, this is a cosmetic problem and may be more common in women because they are more concerned about their appearance. As our study did not include patients without thyroid autoantibodies, the sex distribution may be different for all AA patients, and this may explain why our study found AA predominantly in men.

In terms of the type and pattern of involvement of AA, Polat et al. reported 90.2% of cases as AA, 5.5% as AU and 4.1% as AT. In the same study, 75.3% scalp, 20% beard, 0.77% scalp and eyebrow, 3.8% eyebrow or eyelash involvement were found.[13] Kyriakis et al. reported 50.5% beard, 39.3% scalp, 9.2% scalp and beard, and 1% eyebrows in male patients, but no rate was given for female patients.[15] Finner found patch type in 75% of patients with AA and 10-20% AT.[11] In the study by Kılınç et al. 63% of the patients were AA, 11% were AT and 36% were AU.[18] In our study, 74.7% of the patients had patch-type involvement, which is consistent with the studies discussed above.

Nail changes in alopecia areata have been found to be 10%, 9%, 20% in various studies.[11,18] The result in our study was 7.9%, which is lower than the literature. The fact that the study was retrospective and nail changes developed later may be a factor in this.

Lutz et al. found diffuse goiter in 70% and nodular goiter in 12% of 120 patients with AA aged 7-60 years; 115 (96%) of these patients were euthyroid,

three (2.5%) had subclinical hypothyroidism, two (1.66%) had subclinical hyperthyroidism and one (0.83%) had Hashimoto's thyroiditis.[19] In addition, thyroid dysfunction was found to be 24.4% and 20.2% in 2 separate studies conducted in children under 16 years of age.[20] In another study in a group of 80 pediatric patients under 12 years of age, thyroid dysfunction was similarly found to be 17.5%. In the same study, thyroid autoantibody levels were found to be 14%.[21] In our study, children under 16 years of age constituted 27.6% of the patients with AA and thyroid dysfunction was found in 17.2% and thyroid autoantibody elevation in 13.7%. It was consistent with the literature.

In this study, thyroid autoantibody elevation was found in 19% of all patients and this value was not statistically significant. In addition, the mean TSH value was calculated as 3.58 in this autoantibody elevated group. This value was higher than the TSH value of 2.2 found by Baars et al. in AA patients with thyroid autoantibody positivity; in the same study, the TSH value was 1.6 in the group without thyroid autoantibody positivity.[22] In addition, in our study, 35% of women had thyroid autoantibody positivity whereas only 6.8% of men had antibody positivity. This result suggests that autoimmunity is affected by gender in accordance with the literature.[17,23]

When the family history of patients with alopecia areata was analyzed, family history was found to be 4-42%, 10-20%, 29.6%, 42%.[24] Gönül et al. 2011, they found family history to be 15.9%; and found a correlation between the length of disease duration and thyroid otonticor positivity.[17] In our study, family history was present in 17 (11.2%) patients with AA. In addition, among the tests indicating thyroid autoimmunity, only Anti-TPO was significantly associated with the duration of AA. A similar relationship could not be demonstrated with Anti-TG.

In our study, elevated levels of at least one of anti-TG and anti-TPO were found in 29 (19.07%) patients with AA. In this group of patients with elevated autoantibodies, 15 (9.8%) patients were diagnosed with thyroid disease and recorded. We could not find any information about the disease in the remaining 14 patients because they stopped their follow-up. In a study conducted in Iran, a high rate of association was found between impaired thyroid function and elevated serum autoantibody levels in patients with AA. This was explained by the high number of female patients included in the study (-thyroid diseases are more common in the female gender).[10] In our study, the association with thyroid disease may not have been found to be high due to the high number of male patients. When similar studies were analyzed, the prevalence of thyroid disease was found between 1-20% and 8-28% [10, 24].

The prevalence of vitiligo in AA patients was found to be between 1.5% and 4% in studies.[11,17,25] In our study, vitiligo was detected in 2 (3.8%) of the participants. No different results were found from other studies.

The effect of stress in patients with alopecia areata has been examined in many studies with different results. Psychopathology was shown to be associated with 17.7% of 132 patients with AA in our country.[17] In Belgium, it was shown that psychological and traumatic events were more frequent in people with AA than in healthy controls.[26] In a study conducted in pediatric AA patients, emotional stress was reported to be present in 57% of patients [21]. In our results, we could not show a significant correlation between the presence of psychiatric disease and TSH, Anti-TG and Anti-TPO in patients with AA. We found a significant correlation only between all types of diseases accompanying AA and Anti-TPO, but not with Anti-TG.

The epidemiologic data of our study were similar to those of other studies conducted in our country. The limitations of our study include the inaccessibility of all data since the cases were screened retrospectively, not representing the entire AA population since it was a single-center study in which patients in our outpatient clinic were examined cross-sectionally, and the lack of genetic findings. As a result of this study, although there was a significant correlation between anti-TPO and the duration of AA, the association between thyroid autoimmunity and AA was not statistically significant. . In our study, no correlation was found between AA and autoimmune thyroiditis, suggesting that cellular immunity rather than humoral immunity is predominant in the etiology of AA. Again, considering that autoimmune mechanisms are more predominant in female patients compared to male patients and considering that the number of female patients in our study was less than the number of male patients, it can be considered as one of the reasons for the lack of statistical significance between thyroid autoimmunity and AA.[17,23,27]

CONCLUSION

In our study, patch type AA was found in 98.6% and alopecia totalis in 1.4%. The scalp was involved in 74.7% and the beard in 11.8%. Nail involvement was seen in only 7.9% of patients. Elevated thyroid autoantibodies were found in 19.0%, of whom 10 had hypothyroidism, 2 had chronic thyroiditis and 3 had toxic multinodular goiter. Although there was a significant correlation between anti-TPO and duration of AA, the association between thyroid autoimmunity and AA was not found to be statistically significant. This may be due to the fact that humoral autoimmunity plays a role in thyroid autoimmunity and primarily cellular autoimmunity plays a role in AA. In addition, the epidemiologic data of our study were similar to the data of studies conducted in our country

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Trakya University Faculty of Medicine, Edirne, Turkey. (Decision number: 3-15, date: 11.01.2012).

Authors' Contribution

Study Conception: HNŞ, AG; Study Design: HNŞ, AG; Supervision; HNŞ, AG; Funding: HNŞ, AG; Materials: HNŞ; Data Collection and/or Processing: HNŞ; Analysis and/or Data Interpretation: HNŞ, AG; Literature Review: HNŞ, AG; Critical Review: HNŞ, AG; Manuscript preparing: HNŞ, AG.

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