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Association between Alopecia Areata and Thyroid Disorders

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ABSTRACT

Background & Objective: Alopecia areata (AA) is an autoimmune disorder characterized by patches of non-scarring alopecia affecting the scalp and body hair. Previous epidemiological studies suggest a potential positive association between alopecia areata (AA) and several autoimmune diseases, including autoimmune thyroid disorders. The present study was therefore undertaken to determine the association between AA and thyroid disorder.

Methods: This cross-sectional case-control study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka over a period of 1 year from July 2021 to June 2022. A total of 40 clinically diagnosed patients of AA (case) of both sexes with age ≥18 years were taken from the Outpatient Department of Dermatology and Venereology, Dhaka Medical College Hospital (DMCH), Dhaka. An equal number (n = 40) of age-matched (with cases) apparently healthy subjects were taken as controls for comparison. In order to assess thyroid function status, five variables were measured. These were free tri-iodothyronine (FT_3), free thyroxine (FT_4), thyroid stimulating hormone (TSH), thyroglobulin antibody (TgAb), and thyroid peroxidase antibody (TPOAb or TmAb). Thyroid disorders were evaluated in terms of hypothyroidism, subclinical hypothyroidism, hyperthyroidism, subclinical hyperthyroidism, etc.

Result: In the present study, the baseline demographic and clinical characteristics were almost similar between cases and controls. The male-to-female ratio of AA patients was 1:1. The mean age was 29.9 ± 10.5 years for the case group and 29.9 ± 10.4 years for the control group. Most of the patients with AA had mild disease (45%) followed by moderate (42.5%) and severe (12.5%) diseases. The study demonstrated the prevalence of thyroid dysfunction to be significantly higher in the case group (20%) than that in the control group (5%) with a risk of developing thyroid disorder in patients with AA being 4.7(95% CI = 0.9 – 23.9) times higher than that in the control group (p = 0.043). There were significant differences between cases and controls in terms of levels of TSH, FT_3 and FT_4. The present study demonstrated a significant difference between cases (AA patients) and controls with respect to thyroid auto-antibodies (Tg-Ab, TPO-Ab) as well. Tg-Ab and TPO-Ab were also found positive in 12 euthyroid alopecia areata patients.

Conclusion: The prevalence of thyroid disorders is comparatively high in alopecia areata patients as opposed to healthy individuals of similar age and sex. The serum levels of TSH, TPO-Ab and Tg-Ab are significantly elevated, and the levels of free T_3 and free T_4 are significantly dropped in patients of alopecia areata compared to their healthy counterparts. However, Tg-Ab and TPO-Ab may be present in euthyroid alopecia areata patients.

Keywords: Alopecia areata, thyroid disorders, thyroid function, autoimmune disease, etc.

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INTRODUCTION:

Alopecia areata (AA) is a common, non-cicatricial form of hair loss that can affect the scalp and other hair-bearing areas. There is significant variation in clinical presentation ranging from small well-demarcated patches to complete loss of scalp or body hair.[1] Worldwide, the estimated lifetime prevalence of alopecia areata (AA) in the general population is 2%.[2] The frequency of AA ranges from 0.7-3.8% of patients attending dermatology clinics.[3,4] Clinically, alopecia areata (AA) may present as a single well-demarcated patch of hair loss, multiple patches, ophiasis (Snake-shaped plaques extending to the scalp border, or loss of hair in the shape of a wave at the circumference of the head), sisapho (entire scalp except for occipital area) or extensive hair loss in the form of total loss of scalp hair (alopecia totalis) or loss of entire scalp and body hair (alopecia universalis).[5,6]

Previous epidemiological studies suggest a potential positive association between AA and several autoimmune diseases, including autoimmune thyroid disorders, vitiligo, psoriasis, lupus erythematosus, diabetes mellitus, and pernicious anemia.[7-10] Goh & associates[11] reported that autoimmune diseases are found in 56% of AA patients in which thyroid disease is the most common association (19%) after atopy. Different studies have shown that the prevalence of thyroid disorders in patients with AA ranges from 8 to 28% with the highest prevalence (24%) being observed in an Australian study.[12-14] Hypothyroidism and hyperthyroidism are the two main types of thyroid disorders that are found in AA.[15] Thomas & Kadyan[6] described the association between thyroid autoimmunity and AA by the formation of organ-specific autoantibodies which play a pathogenic role in both disorders. There is an increased number of activated T lymphocytes in the peripheral blood of patients with AA and autoimmune thyroid disease which highlights not only the participation of these lymphocytes in the pathogenesis of these diseases but also in their inter-relationship.[16] Ahmed & associates[13] conducted a cross-sectional study on 112 patients of AA and found 10(8.9%) patients with thyroid disorders; of them 90% were hypothyroid. Similar types of findings were reported in previous studies.[11,17-19]

As autoimmunity is a major factor that involves in the pathogenesis of thyroid disorders,[20] evaluation of the relationship between AA and thyroid disorders may yield novel findings.[21] Although several studies have been conducted to investigate the association between thyroid disorders & alopecia areata in different countries, there is a lack of studies on this topic in Bangladesh. The present study was, therefore, intended to evaluate the association between AA and thyroid disorder. The findings derived from the study could be of immense value to raise awareness among physicians and patients with alopecia areata (AA).

METHODS:

This cross-sectional study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka over a period of 1 year from July 2021 to June 2022. The study was carried out after obtaining clearance from the Research Review Committee of the Department of Physiology and Ethical Review Committee of Dhaka Medical College, Dhaka. A total of 40 clinically diagnosed patients of AA (case) of both sexes with age ≥18 years were taken from the Outpatient Department of Dermatology and Venereology, Dhaka Medical College Hospital (DMCH). An equal number (n = 40) of age-matched (with cases) apparently healthy subjects were taken as controls for comparison. However, cases of AA suffering from systemic diseases like diabetes, malignancy, chronic liver disease, chronic renal disease, thyroid disorders, or from any autoimmune disorders, or under medications like lithium, amiodarone, dopamine, levodopa, bromocriptine, an oral contraceptive pill for the last six months (that may interfere with thyroid functions) or pregnant and lactating women with AA were excluded from the study.

In order to assess thyroid function status, five variables were measured. These were free tri-iodothyronine (FT_3), b) free thyroxine (FT_4), c) Thyroid stimulating hormone (TSH), d) Thyroglobulin antibody (TgAb), and e) Thyroid peroxidase antibody (TPOAb or TmAb). Data were analyzed using SPSS (Statistical Package for Social Sciences), version 25.0. The quantitative data were expressed as

mean ± standard deviation (mean ± SD), median (IQR), and range, and the qualitative data were expressed as the frequency with corresponding percentages. Unpaired t-Test and Chi-squared (χ^2) Test were performed to compare data between case and control groups. The level of significance was set at 5% and a p-value of < 0.05 was considered significant.

RESULTS:

No statistical differences were observed between the case and control groups in terms of age and sex, for controls were selected matched with the age and sex of cases. The mean BMI for the case and control groups were 22.3 ± 1.1 and 21.9 ± 1.3 kg/m^2 respectively (p = 0.421). The mean systolic blood pressure in the case and the control groups were 118.5 ± 6.4 mmHg and 118 ± 5.3 mmHg respectively (p = 0.507). Likewise, the mean diastolic blood pressures of the case and control groups were 78.1±4.19 mmHg and 77.4± 5.43 mmHg respectively (p = 0.511).

Table I. General characteristics of the subjects in both groups

Baseline characteristics	Group		p-value
	Case (n=40)	Control (n=40)	
Age* (years)			
21 – 30	27(67.5)	27(67.5)	
31 – 40	8(20.0)	8(20.0)	0.997
> 40	5(12.5)	5(12.5)	
Gender*			
Female	20(50.0)	20(50.0)	0.998
Male	20(50.0)	20(50.0)	
BMI# (kg/m^2)	22.3 ±1.13	21.9 ± 1.29	0.421
Systolic blood pressure# (mmHg)	118.5 ± 6.40	118 ± 5.31	0.507
Diastolic blood pressure# (mmHg)	78.1 ± 4.19	77.4 ± 5.43	0.511

*Data were analyzed using **Chi-squared** (χ^2) **Test** and were presented as **n**(%).
#Data were analyzed using **Unpaired t-Test** and were presented as **mean ± SD.**

Clinical profile of the cases of AA

Table II describes the clinical profile of patients with alopecia areata. Almost half of the cases (45%) had mild AA, 43% had moderate AA and only 12.5% had severe AA. Over one-third (35%) of the patients had positive family histories for AA. The average age of onset of AA was 29.8 ± 10.6. In the majority (92.5%) of the cases, the duration of the disease was <1 year, and in 3(7.5%) cases only, the disease duration was > 1 year. More than half of the cases (57.5%) had a history of recurrence and in the rest (42.5%), the present attack was the 1st attack. Over half (57.5%) had multiple patches of AA, 25% had a single patch and 10% had alopecia totalis (AT), 5% ophiasis and only 1(2.5%) had alopecia universalis (AU). The scalp was the predominant area of involvement (72.5%), followed by body hair involvement (17.5%) and both scalp and body hair (10%). One-fifth (20%) had nail involvement. A comparison of thyroid function tests between case and control groups revealed that free FT_3 and FT_4 were significantly lower in the case group compared to those in the control group (p < 0.001 and p=0.001 respectively), while serum TSH was significantly higher in the former group than that in the latter group (p = 0.011). Fifty percent of the cases demonstrated the presence of TPO-Ab as compared to 15% of the control group (p = 0.002). The presence of Tg-Ab was also staggeringly higher in the former group than that in the latter group (p=0.002) (Table III).

Table II. Distribution of cases by their clinical profile of (n = 40)

Clinical Profile	Frequency	Percentage	Mean ± SD
Severity of alopecia areata			
Mild	18	45.0	--
Moderate	17	42.5	--
Severe	5	12.5	--
Family History	14	35.0	--
Age at onset	--	--	29.8 ± 10.6
Duration of alopecia areata			
<1	37	92.5	--
>1	3	7.5	--
Recurrence, n (%)	23	57.5	--
Pattern of alopecia areata			
Single patch	10	25.0	--
Multiple patches	23	57.5	--
AT	4	10.0	--
AU	1	2.5	--
Ophiasis	2	5.0	--
Site of hair loss			
Scalp	29	72.5	--
Body hair	7	17.5	--
Both body hair and scalp	4	10.0	--
Nail Changes	8	20.0	--

Thyroid disorders:

Eighty percent of the cases were euthyroid as compared to 95% of the controls. Subclinical hypothyroidism was higher in the case group

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(12.5%) than that in the control group (5%). A few cases had hypothyroidism & hyperthyroidism as well, while none of the control group had these disorders. (Table IV). Overall, thyroid dysfunction was much higher in the case group than that in the control group with a risk of having thyroid disorder in patients with AA was estimated to be 4.7(95% CI=0.9–23.9) times higher than that in the control group (p = 0.043) (Table V).

Table III. Comparison of thyroid function parameters between the study groups

Thyroid function-related variables	Group		p-value
	Case (n=40)	Control (n=40)	
FT3# (pmol/L)	4.0 ± 0.9	4.6 ± 0.7	< 0.001
FT4# (pmol/L	13.9 ± 2.8	15.1 ± 2.4	0.011
TSH# (mIU/L)	4.8 ± 4.6	2.8 ± 2.2	0.011
Presence of TPO-Ab*	20(50.0)	7(17.5)	0.002
Presence of Tg-Ab*	19(47.5)	6(15.0)	0.002

*Data were analyzed using **Chi-squared** (χ^2) **Test** and were presented as **n**(%).
#Data were analyzed using **Unpaired t-Test** and were presented as **mean ± SD.**

Table IV. Distribution of thyroid function status between groups

Thyroid function status	Case (n=40)	Control (n=40)
Euthyroid	32(80.0)	38(95.0)
Subclinical hypothyroidism	5(12.5)	2(5.0)
Hypothyroidism	2(5.0)	0(0.0)
Hyperthyroidism	1(2.5)	0(0.0)

Figures in the parenthesis denote the corresponding percentage.

Table V. Association between thyroid disorder and alopecia areata

Thyroid disorder	Case (n=40)	Control (n=40)	Odds Ratio (95% CI of OR)	p-value*
Present	8(20.0)	2(5.0)	4.7(0.9 – 23.9)	0.043
Absent	32(80.0)	38(95.0)		

*Data were analyzed using **Chi-squared** (χ^2) **Test;** data were analyzed using **Fisher's Exact Test.** Figures in the parenthesis denote the corresponding percentage.

DISCUSSION:

The present study was undertaken to determine whether thyroid disorders were associated with alopecia areata. In the present study, the baseline demographic and clinical characteristics were almost similar between cases and controls. The mean age was 29.9 ± 10.5 years for the case group and 29.9 ± 10.4 years for the control group. Consistent with this finding, Marahatta and associates[3] in a similar study in Nepal demonstrated mean ages for the case and control groups to be 29.4 ± 9.9 and 28.9 ± 9.9 years respectively. In the present study, males and females were equal in number. Shahzadi and colleagues[18] also reported an almost equal male-female ratio (1:1). Kurtev and Iliev[16] also claimed an equal frequency of both sexes in alopecia areata. However, Ahmed et al.[13] reported a female preponderance in their study. Most of the patients with alopecia areata in this study were suffering from mild disease (45%) followed by moderate (42.5%) and severe (12.5%) types of disease. A similar type of observation was reported by Asgher et al[22] and Marahatta[3] et al.

The current study demonstrated the prevalence of thyroid dysfunction to be significantly higher in the case group (20%) compared to that in the control group (5%). Alopecia areata patients carry a > 4-fold greater risk of acquiring thyroid disorder than do the euthyroid subjects. Similar to this study several studies[3,6,14] also reported thyroid disorders ranging from 17.3 - 24% in patients with alopecia areata. Conversely, Puavilai et al.[23] reported a low prevalence of thyroid disease (7.2%) in patients with alopecia areata with an insignificant difference between cases and controls. In this study out of 8 alopecia areata patients with thyroid disorders, 7(17.5%) had hypothyroidism (5 subclinical hypothyroidism, 2 hypothyroidism), and only one patient (2.5%) had hyperthyroidism. There were significant differences between cases and controls regarding levels of TSH, free T_3, and free T_4. These results were in agreement with a clinical study done by Bakry et al.[24] who reported that among the thyroid disorders hypothyroidism was the most frequent form of thyroid function abnormalities associated with alopecia areata. Moreover, several studies[3,6,13] also demonstrated that thyroid function abnormality in the form of hypothyroidism was found to range from as low as 14.1 to as high as 90% in patients with alopecia areata.

The present study demonstrated a significant difference between cases (alopecia areata patients) and controls with respect to thyroid auto-antibodies (Tg-Ab, TPO-Ab).

The result was fairly comparable to the observations of Kurtev and Ilev[16] and Nanda et al'[25]s study. They reported a significant increase in serum Tg-Ab (14%) in children with alopecia areata. Bin Saif[26] also reported a significantly higher frequency of thyroid auto-antibodies in patients with alopecia areata (27%) than in healthy controls (4%). Conversely, Puavilai et al[23] stated that there were no significant differences between alopecia areata patients and control subjects in terms of Tg-Ab and TPO-Ab. The higher frequency of thyroid autoantibody Tg-Ab and TPO-Ab in alopecia areata patients compared to the healthy control supported the potential susceptibility of alopecia areata patients to autoimmune thyroid disorders,[27] which, in turn, emphasizes the autoimmune background of both the disorders.

In our study, Tg-Ab and TPO-Ab were positive in 12 euthyroid alopecia areata patients as well. A similar type of result was found in a study conducted by Bakry et al[24], where Tg-Ab and TPO-Ab were positive in 15 and 19 euthyroid patients respectively. The presence of TPO-Ab was strongly associated with thyroid failure during 20 years of follow-up of TPO-Ab-positive thyroid individuals[28] indicating that TPO-Ab strongly correlates with altered thyroid functions than Tg-Ab does. Hence, this auto-antibody should be followed up for early detection of thyroid dysfunction in euthyroid alopecia areata patients.

Limitations:

Despite taking all-out measures to overcome limitations, there remain some limitations, which deserve mention.

1. The study population was selected from a single tertiary care center in Dhaka city, which does not represent the entire study population of the country.
2. The sample was taken purposively. So, there may be a scope of sampling bias that can influence the findings of the study.
3. Differen torgan-system-specific symptoms of thyroid dysfunction were not evaluated in this study.

CONCLUSION:

The prevalence of thyroid disorders is significantly higher in alopecia areata patients as compared to the healthy controls of similar age and sex. Alopecia areata patients tend to carry a significantly higher risk of acquiring thyroid disorder than their euthyroid counterparts do. While the serum levels of TSH, TPO-Ab, and Tg-Ab are significantly elevated, the levels of free T_3 and free T_4 are significantly declined in patients of alopecia areata compared to healthy individuals. However, Tg-Ab and TPO-Ab may be present in euthyroid alopecia areata patients who require careful follow-up, for they may develop thyroid disorders in the long run.

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