Evaluation of prevalence of thyroid autoimmunity and alopecia areata in children with atopic dermatitis

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Background: Atopic dermatitis is a chronic relapsing inflammatory skin disease that has possible associations with other diseases such as allergic conditions, autoimmune skin diseases, and systemic diseases. We evaluated the prevalence of alopecia areata and thyroid autoimmunity in children with atopic dermatitis.

Methods: This was a cross-sectional study on 124 children (62 children with atopic dermatitis and 62 healthy children). Demographic features of the participants and duration of disease in children with atopic dermatitis were recorded. Antithyroid peroxidase and thyroid stimulating hormone were evaluated in both groups. Odds ratio (OR) and 95% confidence interval (CI) were calculated to estimate relative risk. The chi-squared test and analysis of variance test (ANOVA) were used to evaluate the association of thyroid autoimmunity with the demographic and clinical features of patients.

Results: Thyroid autoimmunity was only detected in atopic dermatitis children and not in the control group, and the difference was statistically significant [OR = 4.32, 95% CI = 2.15–10.81, $P = 0.04$). Furthermore, overt thyroid disease was significantly more common in the atopic dermatitis group compared with the control group (OR = 4.46, 95% CI = 1.15–17.24, $P = 0.03$). A personal history of alopecia areata was also significantly more common in the atopic dermatitis group (OR = 4.46, CI = 1.17–15.29, $P = 0.030$). In addition, there was no significant difference between thyroid autoimmunity and overt thyroid disease in the patients' severity of atopic dermatitis and demographic features ($P > 0.05$).

Conclusion: Patients with atopic dermatitis had a significantly higher percentage of thyroid autoimmunity, overt thyroid disease, and alopecia areata than the control group.

Keywords: atopic dermatitis, thyroid, autoimmunity, alopecia areata

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INTRODUCTION

Atopic dermatitis is a chronic relapsing inflammatory skin disease that affects 20% of children worldwide [1]. The prevalence of atopic dermatitis in Iran has been estimated at 9.1% [2]. Currently, the literature supports an association of atopic dermatitis with other diseases such as allergic conditions (asthma, allergic rhinitis, and chronic urticaria), autoimmune skin diseases (vitiligo and lupus erythematosus), gastrointestinal disease (eosinophilic gastroenteritis, and inflammatory bowel disease), renal disease (idiopathic nephritic syndrome), metabolic syndrome (hyperlipidemia

and diabetes mellitus type 1), cardiovascular disease, and cancer [3-5].

Acute atopic dermatitis is associated with increased levels of Th2 cytokines [interleukin (IL)-4, IL-5, and IL-13], while chronic atopic dermatitis is associated with increased levels of Th1 cytokines [IL-2, IL-12, tumor necrosis factor (TNF)-α, and interferon (IFN)-gamma].

Thyroid autoimmunity is associated with increased levels of Th2 cytokines. Increased levels of cytokines associated with Th17 (IL-17, IL-21, and IL-22), as well as a reduction in T regulatory cells and an increase in decoy receptor 3 (belonging to the TNF receptor family), lead to an imbalance of the immune system in atopic dermatitis and thyroid autoimmunity, possibly linking the two diseases [6-8].

Alopecia areata is an autoimmune disease that targets hair follicles. Previous studies reported the association of alopecia areata with allergic conditions (chronic urticaria, asthma, and allergic rhinitis). In addition, it has been proposed that patients with concurrent atopic dermatitis and alopecia areata have a poor prognosis [9,10]. In this study, we evaluated the prevalence of alopecia areata and thyroid autoimmunity in children with atopic dermatitis in comparison with controls.

PARTICIPANTS AND METHODS

This was a cross-sectional study on 124 children (62 children with atopic dermatitis, 62 healthy children) less than 18 years old in Afzalipour Hospital in Kerman, Iran. After obtaining informed consent from parents and from both parents and children in those older than 12, demographic features of participants (age and sex), family history of atopy (atopic dermatitis, allergic rhinitis, asthma, and food allergy), family history, and personal history of thyroid autoimmunity and alopecia areata, as well as the duration of disease and location of skin lesions in children with atopic dermatitis, were recorded. Diagnosis of atopic dermatitis was according to Hannifin and Rajka [11] criteria, and the severity of the disease was assessed based on the SCORatopic dermatitis index [12]. Then, antithyroid peroxidase (anti-TPO) and thyroid-stimulating hormone (TSH) levels were evaluated in the two groups. Serum levels of TSH from 4 to 6.2 μUI/ml (Roche, Germany) and anti-TPO less than 50 Ul/ml (Aesku, Iran) were considered normal. Thyroid autoimmunity was defined as a level of anti-TPO antibody higher than the reference range [13]. Finally, the prevalence of thyroid autoimmunity and alopecia areata was evaluated in the groups; also, the prevalence of autoimmune diseases was assessed in children with atopic dermatitis according to the disease severity and demographic features.

Statistical analysis

Data were analyzed using SPSS 16 (IBM, Armonk, NY, USA). Quantitative and qualitative data were described by mean ± standard deviation and frequency, respectively. Logistic regression analysis was used for risk assessment of the occurrence of thyroid autoimmunity, subclinical thyroid disease, and overt thyroid disease in atopic dermatitis patients compared with the control group. The chi-squared test and analysis of variance (ANOVA) were used to evaluate the association of thyroid autoimmunity with the demographic features of patients and the duration and severity of atopic dermatitis. P-values below 0.05 were regarded as significant.

RESULTS

In this study, 124 participants (57.3% male, 42.7% female) including 62 children with atopic dermatitis and 62 healthy ones (as the control group) were enrolled (Table 1). The locations of skin lesions in children with atopic dermatitis were the upper limb (40.3%), head and neck (25.8%), lower limb (17.7%), and trunk (16.1%). The severity of atopic dermatitis based on SCORatopic dermatitis was mostly mild (67.7%), followed by moderate (25.8%) and severe (6.5%).

There was no significant difference between atopic dermatitis and control groups regarding demographic features including age and sex (Table 1). Personal history of atopy and alopecia areata, as well as family history of atopy and autoimmune diseases (thyroid autoimmunity and alopecia areata), were significantly more common in the atopic dermatitis group ($P < 0.05$) (Table 1). Thyroid autoimmunity was only detected in children with atopic dermatitis and not in healthy controls; the difference was statistically significant [OR = 4.32, 95% CI = 2.15–10.81, $P = 0.04$) (Table 2). Furthermore, overt thyroid disease

Table 1. Demographic features of participants in atopic dermatitis and control groups

Variables	Atopic dermatitis	Control	OR	95% CI	*P*-value
Age (mean ± SD)	6.54 ± 3.93	6.72 ± 4.55	1.01	0.92–1.09	0.81
Sex					
Male	36 (58.1%)	35 (56.5%)	1.06	0.52–2.17	0.85
Female	26 (41.9%)	27 (43.5%)			
Family history of atopy					
Atopic dermatitis	12 (19.4%)	2 (3.2%)	1.38	1.03–1.85	0.02
Allergic rhinitis	8 (12.9%)	6 (9.7%)			
Food allergy	4 (6.5%)	2 (3.2%)			
Family history of autoimmune disease					
Thyroid autoimmunity	17 (27.4%)	10 (16.1%)	1.62	1.4–2.54	0.03
Alopecia areata	7 (11.3%)	1 (1.6%)			
Personal history of atopy					
Asthma	25 (40.3%)	0 (0%)	0.74	0.49–1.10	0.01
Allergic rhinitis	7 (11.3%)	5 (8.1%)			
Food allergy	5 (8.1%)	3 (4.8%)			
Personal history of alopecia areata	7 (11.3%)	0 (0%)	4.46	1.17–15.29	0.030

Abbreviations: OR, odds ratio; CI, confidence interval; SD, standard deviation

Table 2. Comparison between thyroid-stimulating hormone (TSH) and anti-thyroid peroxidase (anti-TPO) in the two groups

Variables	Atopic dermatitis	Control	OR	95% CI	*P*-value
TSH (mean ± SD)	3.71 ± 2.22	3.49 ± 2.18	0.95	0.80–1.11	0.54
Anti-TPO					
Positive	3 (4.8%)	0 (0%)	4.32	2.15–10.81	0.04
Negative	59 (95.2%)	62 (100%)			
Subclinical thyroid disease					
Hyperthyroidism	8 (12.9%)	7 (11.3%)	0.92	0.43–1.98	0.84
Hypothyroidism	2 (3.2%)	2 (3.2%)			
Overt thyroid disease	4 (6.5%)	1 (1.6%)	4.46	1.15–17.29	0.03

Abbreviations: TSH, thyroid-stimulating hormone; TPO, thyroid peroxidase; OR, odds ratio; CI, confidence interval; SD, standard deviation

was significantly more common in children with atopic dermatitis relative to controls (OR = 4.46, 95% CI = 1.15–17.24, $P = 0.03$). Subclinical thyroid disease was observed to be nearly equal in both groups, with no significant difference between them ($P = 0.84$) (Table 2). In addition, there was no significant difference between the presence of thyroid autoimmunity, overt thyroid disease, and personal history of alopecia areata in factors including the severity of atopic dermatitis, age and sex of patients, and duration of disease ($P > 0.05$) (Table 3).

Table 3. Association between demographic features of patients and duration and severity of atopic dermatitis and personal history of alopecia areata and thyroid autoimmunity

Variables	Anti-TPO antibody		Overt thyroid disease	Personal history of alopecia areata	*P*-value
	Positive	Negative			
Age (years)	4.66 ± 0.66	6.64 ± 0.52	7.25 ± 1.70	6.28 ± 2.17	0.07
Sex N (%)					
Male	2 (66.7)	34 (57.6)	2 (50)	4 (57.1)	>0.05
Female	1 (33.3)	25 (42.4)	2 (50)	3 (42.9)	
Severity of atopic dermatitis N (%)					
Mild	3 (7.1)	39 (92.9)	3 (7.1)	6 (14.3)	>0.05
Moderate	0 (0)	16 (100)	1 (6.2)	1 (6.2)	
Severe	0 (0)	4 (100)	0 (0)	0 (0)	
Duration (months)	5.0 ± 0.57	10.77 ± 1.26	15.0 ± 5.09	6.85 ± 3.15	0.96

Abbreviations: TPO, thyroid peroxidase; N, number.

DISCUSSION

In this study, thyroid autoimmunity and overt thyroid disease were significantly more prevalent in children with atopic dermatitis than in the control group. In the study of Pedullá *et al.* in Italy, 9.52% of children with atopic dermatitis had thyroid autoimmunity; the difference was statistically significant. The higher prevalence of thyroid autoimmunity in that study can be due to the assessment of both antithyroglobulin (anti-TG) and anti-TPO antibodies, whereas we only assessed the anti-TPO antibody [13]. In a study by Andersen *et al.*, similar to our study, the prevalence of thyroid autoimmunity was higher in the atopic dermatitis group (1.33%) than in the control group (0.91%); however, the result was not statistically significant ($P > 0.05$) [14].

In the present study, although atopic dermatitis patients with thyroid autoimmunity were younger than those without thyroid autoimmunity, the difference was not statistically significant. In Taiwan, Wu *et al.* evaluated the prevalence of autoimmune disease in atopic dermatitis patients according to age. They found no significant relationship between the age of the patients and autoimmune diseases, except for lupus erythematosus in atopic dermatitis patients less than 18 years old [4].

In the current study, there was no significant correlation between thyroid autoimmunity and alopecia areata with the severity of atopic dermatitis (SCORAD index) [4]. No other studies have evaluated the association between SCORAD and autoimmunity. Still, Pedullá *et al.* demonstrated a higher prevalence of thyroid autoimmunity in children with IgE-mediated atopic dermatitis compared with non-IgE-mediated atopic dermatitis. Considering the association between IgE and severity of atopic dermatitis, it can be concluded that a higher percentage of thyroid autoimmunity was detected in more severe cases of atopic dermatitis [13].

In the current study, children with atopic dermatitis significantly had a higher prevalence of alopecia areata than the control group, similar to the Pedullá *et al.* study (13.67% vs. 2.67%, OR = 5.76; 95% CI = 1.71–19.35) [15]. Augustin *et al.* in 2015 showed that the risk of development of alopecia areata in children with atopic dermatitis was 2.34 times that of those without atopic dermatitis (95% CI = 1.77–3.08) [16]. Similar results were obtained in adults with atopic dermatitis by Barahmani *et al.* in Florida (OR = 2.00, 95% CI = 1.50–2.54) and Andersen *et al.* in Denmark (OR = 29.89, 95% CI = 16.60–53.82) [9,14]. In a study by Chu *et al.* in Taiwan, a higher risk of atopic dermatitis was demonstrated in patients with alopecia areata (OR = 3.82, 95% CI = 2.67–5.45) [17]. The exact mechanism behind the association between alopecia areata and atopic dermatitis remains elusive. In both alopecia areata and atopic dermatitis, TH1, TH2, and the RANTES (regulated upon activation, normal T-cell expressed and secreted) chemokine are involved. Furthermore, an association with human leukocyte antigen (HLA) class II has been demonstrated in both diseases. Therefore, these diseases have some shared pathways in their pathogenesis, which may explain their association [9].

In the present study, positive family history of thyroid autoimmunity and atopy was significantly more common in children with atopic dermatitis than in the control group, and it was nearly consistent with the Pedullá *et al.* study (22 and 48.7% in atopic dermatitis vs. 16 and 26% in controls, respectively). In our study, a personal history of atopy was reported in approximately half of the children with atopic dermatitis, similar to that reported by Pedullá *et al.* (64.6%) [13]. Similar results were observed by Augustin *et al.* (38.68% in atopic dermatitis vs. 14.60% in controls) and Wu *et al.* (29.46% in atopic dermatitis vs.15.92% in controls) [4,16]. In addition, in our study, food allergy was significantly more common in children with atopic dermatitis (8.1%) than in the control group (4.8%). Similar to our study, Pedullá *et al.* found a higher rate of food allergy in children with atopic dermatitis (61%) relative to controls (0%). However, they assessed food allergy using the skin prick test, but our assessment was based on patient history. Therefore, this can explain the disparity between the two studies [13].

CONCLUSION

In the current study, patients with atopic dermatitis had a significantly higher prevalence of thyroid autoimmunity, alopecia areata, and family history of atopy, thyroid autoimmunity, and alopecia areata compared with the control group.

Conflict of interest: None declared.

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