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Original Investigation

Evaluating of Thyroid Function Tests and Thyroid Autoantibodies in Patients with Allergic Rhinitis

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Abstract

Introduction: Allergic rhinitis is a common chronic allergic disease. The effects of allergic diseases on autoimmune diseases are not known. The patients are predisposed to react to exogenic antigens in allergic diseases and they can more easily react to endogenous antigens. Therefore, autoantibody prevalence studies are required. In this study, we attempted to prove the possible relation between the thyroid function tests, thyroid autoantibodies and allergic rhinitis.

Methods: A total of 319 patients, with 193 (60%) with allergic rhinitis between June 2015 and October 2015 and 126 (40%) as the control group were included in the study; 38% of the patient group was male and 62% was female; and 44% of the control group was male and 56% was female.

Results: No significant difference was found in the antithyroglobuline (anti-Tg; p=0.295) and antithyroid peroxidase (anti-TPO; p=0.224) and thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) (p>0.05) values between the patient and control groups. In our study, autoantibody positivity ratios in the patients with allergic rhinitis were specified as 15.6% (anti-Tg) and 11.5% (anti-TPO). In addition, a weak positive relationship was found between the age and anti-Tg values (p<0.001; r=0.268).

Conclusion: Allergic and autoimmune diseases together find are not common phenomena in an individual. This can be explained to usually managed by different processing of the Th1 and Th2 pathways. Although we did not find a statistical significance in our study, the thyroid autoantibodies were higher in the allergic rhinitis group with compared to controls . We believe that these patients should be closely monitored in terms of clinical and laboratory parameters and should be followed in terms of thyroid disease development.

Keywords: Allergic rhinitis, thyroid, autoantibody

Introduction

Allergic rhinitis is a common chronic allergic disease. It is responsible for at least 2.5% of all the doctor visits (1). The incidence in the population is estimated to be between 10% and 25% and between 11% and 17.6% in Turkey (2). Rhinitis is diagnosed completely the presence of at least two of the following nasal symptoms: nasal obstruction continuing for more than 1 hour per day, sneezing, nasal itching, and decrease in the sense of smell (3, 4).

Rhinitis is commonly examined in three groups as allergic, infectious and noninfectious, and nonallergic (5). In epidemiological studies, it was found that approximately 50% of chronic rhinitis cases are of allergic origin (6, 7). Hormonal rhinitis is examined in the noninfectious and nonallergic rhinitis group. Hypothyroidism, pregnancy, puberty, acromegaly, and oral contraceptives are considered causes for hormonal allergic rhinitis (8). In literature, there are a limited number of studies indicating that hypothyroidism may cause nasal complaints. Rhinitis is experienced in 2%-3% of the patients with hypothyroidism (9). In these studies, histological and physiological changes were observed in the nasal submucosa in hypothyroidism (10). Hypothyroidism causes some changes that can be clinically defined in the otorhinolaryngeal area. Lack of hearing in the ear is the primary symptom (11). In the patients with hypothyroidism, this disease causes some clinical changes in the ear-nose-throat area as it affects all the body systems. Nasal obstruction and rhinorrhea are frequent rhinitis symptoms in patients with hypothyroidism (12).

Allergic disease prevalence has increased globally. However, its effects on the clinical course of autoimmune diseases are not known (13). Thus, autoantibody prevalence studies among the allergic patients will be beneficial. The patients are predisposed to react to exogenic antigens in allergic diseases and they can more easily react to endogenous antigens. Therefore, autoantibody prevalence studies are required (14). Due to a high risk of accompanying autoimmunologic or allergic disorders, the patients with autoimmune thyroid disorders should be strictly controlled (15). Besides, in the patients who present with rhinitis symptoms, other tests, including thyroid function tests, should also be conducted (16).

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The patients are predisposed to react to exogenic antigens in allergic diseases and they can more easily react to endogenous antigens. Therefore, autoantibody prevalence studies are required. In this study, we attempted to prove the possible relation between the thyroid function tests, thyroid autoantibodies and allergic rhinitis.

Materials and Methods

A total of 319 patients, with 193 (60%) with allergic rhinitis between June 2015 and October 2015 and 126 (40%) as the control group were included in the study; 38% of the patient group was male and 62% was female; and 44% of the control group was male and 56% was female. The ethics committee approval for this research was given by the ethics committee at Bursa Training and Research Hospital. Verbal informed consent was obtained from patients and control group.

Skin prick tests were conducted using the Allergopharma Skin Prick Test solution. Thyroid function tests and thyroid autoantibody tests were performed using the Siemens Advia Centaur XP Immunoassay System kits and direct chemiluminescence method.

Statistical Analysis

Descriptive statistics were provided using frequency, ratio, mean, standard deviation (SD), and median, minimum (min), and maximum (max) values. In the analysis of the relations between categorical variables, Fisher's Exact Test or Pearson Chi-Square test were used. In the normality test, Shapiro 85 Wilks test was used when the sample quantity was <50, and the Kolmogorov-Smirnov test was used when the sample quantity was >50. In the analysis of the difference between the measurement values of both groups, the Mann-Whitney U test was used when the measurement values did not show normal distribution, and independent samples t-test was used if data showed normal distribution. In the nonparametric comparison of three groups, Kruskal-Wallis test was used, and for the significant cases, Bonferroni-Dunn test was used as the posthoc test. The Spearman Correlation test was used to evaluate the relationship between the ordinal variables and age. A p value <0.05 was considered statistically significant. Analyses were performed using the Statistical Package for Social Sciences version 22.0 (IBM Corp.; Armonk, NY, USA).

Results

In total, 319 patients were included in the study, with 193 (60%) in the allergic rhinitis group and 126 (40%) in the control group included 126 Of the allergic rhinitis patients, 49% was allergic to pollen, 30% to house dust mite and pollen, and 17% to only allergic to house dust mite; 7 of the remaining 11 patients were allergic to house dust mite+pollen+fungi, 2 were allergic to house dust mite and fungi, and 2 were allergic to pollen + fungi. The differences of both groups according to gender, age, antithyroglobuline (anti-Tg), anti thyroid peroxidase (anti-TPO), thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4) values are shown in Table 1; There was no significant difference in age between allergic rhinitis and control groups. (p=0.131). No significant difference was found between the patient and control groups when excluded according to the anti-Tg (p=0.295) and anti-TPO values (p=0.224). There was no significant difference between patient and control groups in terms of TSH, FT3, and FT4 values (p>0.05).

Differences in females and males according to age, anti-Tg, anti-TPO, TSH, FT3, and FT4 values are shown in Table 2. No significant difference was found between the ages of females and males included in the study (p=0.095). Statistically significant relationship was found between gender and anti-Tg status (p=0.002). The anti-Tg value was found to be less than 15 U/mL in 49.6% males and in 31.9% females and over 60 U/mL in 7.8% males and 17.6% females. A low anti-Tg ratio in males and high anti-Tg ratio in females were detected (p<0.05 with Bonferroni Correction). No significant difference was found between males and females according to their anti-TPO, TSH, FT3, and FT4 values (p>0.05).

The age differences according to anti-Tg, anti-TPO, TSH, FT3, and FT4 values are shown in Table 3. At least one age value of the anti-Tg groups was found different from the other group (p<0.001). According to the posthoc test, this difference was due to the median of age value of anti-Tg <15 U/mL group was 25,5 years (18-55) and it was lower than the median value of Anti-Tg 15-60 U/mL group (32 years [17-55]) and anti-Tg >60 U/mL group (35 years [18-55]; (p<0.001 with Bonferroni Correction; Table3).The age value of at least one of the anti-TPO groups was found to be different from the other group (p<0.027). According to the posthoc test, it was seen that this difference was due to the age median of the group with an anti-TPO value between 28 and 60 U/mL which was 28 (18-55) because it was lower than the age median value of anti-TPO >60 U/mL group which was 36 (18-55) (p=0.02 with Bonferroni Correction). No significant difference was found between the ages of the groups with TSH, FT3, and FT4 values within and out of the normal range (p>0.05). The relations between the age values and the ordinal values of anti-Tg, anti-TPO, TSH, FT3, and FT4 situations were evaluated using the correlation analysis. Accordingly, a positive but weak relationship was found between the age value and the anti-Tg values (p<0.001; r=0.268). A negative weak relationship was observed between the age and the FT4 value (p=0.023; r=-0.127). No significant relationship was found between age and anti-TPO, TSH, and FT3 values (p>0.05).

Discussion

The prevalence of allergic diseases has been increased worldwide. However, its effects on the clinical course of autoimmune diseases are not known (13). Allergic disorders are the inappropriate reactions of the immune system to the external antigens. On the contrary, autoimmune diseases are direct reactions against autoantigens and they result with different types of diseases depending on its effects on the organs (14). Our knowledge on the relationship between the thyroid diseases and allergic diseases is also very limited (17).

The immune system regulates the immune response through the T lymphocytes. T-cell numbers are maintained normal by the immune system to protect health. Suppressor T cells and autoreactive cells help to prevent tumor development. A decrease in the number of T suppressor cells in autoimmune diseases, such as Graves' disease is a defect in protective immunity, which causes uncontrolled progression in autoimmune reactions. During the allergic reactions, normal regulating mechanisms have shown to

Table 1. Differences of allergic rhinitis and control group according to the gender, age, anti-Tg, anti-TPO, TSH, FT3, and FT4 values

		Allergic rhinitis group		Healthy group		
Variables	**Group**	**n**	**Ratio**	**n**	**Ratio**	**p**
Gender[1]	Female	120	62%	70	56%	0.239
	Male	73	38%	56	44%	
Age, years[2]		31.65±9.97	31 (17-55)	30.13±10.10	27(18-55)	0.131
Anti-Tg[1]	<15 U/mL	70	36.5%	54	43.2%	0.295
	15-60 U/mL	92	47.9%	58	46.4%	
	>60 U/mL	30	15.6%	13	10.4%	
Anti-TPO[1]	<28 U/mL	35	18.2%	31	24.6%	0.224
	28-60 U/mL	135	70.3%	86	68.3%	
	>60 U/mL	22	11.5%	9	7.1%	
TSH[1]	Below normal value	5	2.6%	5	4.0%	0,968
	Normal value	184	95.3%	120	95.2%	
	Above normal value	4	2.1%	1	0.8%	
FT3[3]	Below normal value	1	0.5%	2	1.6%	0,441
	Normal value	190	98.4%	122	96.8%	
	Above normal value	2	1.0%	2	1.6%	
FT4[3]	Below normal value	2	1.0%	4	3.2%	0,117
	Normal value	191	99.0%	121	96.0%	
	Above normal value	0	0.0%	1	0.8%	
Allergy	Pollen allergy	94	48.7%	-	-	-
	House dust allergy	31	16.1%	-	-	
	House dust+polen allergy	57	29.5%	-	-	
	House dust+fungi allergy	2	1.0%	-	-	
	Pollen+fungi allergy	2	1.0%	-	-	
	House dust+pollen+fungi allergy	7	3.6%	-	-	

[1]Pearson Chi-Square Test; [2]Mann-Whitney U Test presented with mean±standard deviation and median (min-max); [3]Fisher's Exact Test
anti-Tg: antithyroglobuline; anti-TPO: antithyroid peroxidase; TSH: thyroid stimulating hormone; FT3: free triiodothyronine; FT4: free thyroxine

permit the production of autoantibodies with T cells that are not completely functional (18). Each direct effect of the autoimmune thyroid disease and allergic rhinitis evidently suggests the activation of other systemic processes. While the relationship between the upregulation of T1-induced cytokines is related with painless thyroiditis and active phase Hashimoto, T2 upregulation was found in Graves' disease. It is known that the excess activation pattern of T2 cytokines is a dominant feature of allergic rhinitis. Moenset et al. (19) considered that there is a defect in suppressor T-cell response in the atopic disease and thyroid autoimmunity. In this condition, Th2 response is increased and need to IL4, IL5 and IL13 and stimulate B cells to secrete thyroid antibodies. This subsequently causes a decrease in the thyroid hormone synthesis and secretion (20). It is suggested that suppressor T-cell defect has caused both atopic syndrome and autoimmune thyroid disease (19).

Takeoka et al. (13) have indicated that seasonal allergic rhinitis has exacerbated the clinical course of Graves' disease. They have presented that allergic rhinitis has increased the serum antithyroid autoantibody and pollen-specific immunoglobulin E (IgE) concentrations. It is known that Japanese cedar wood pollen allergy also contributes to the Graves' disease. In the USA, ragweed-related pollen allergies and food allergies contribute to the Graves' disease. Exposure to allergic reactions causes the development of Graves' disease worldwide and exacerbates the disease in the patients on antithyroid drugs. Currently, recovery in Graves' disease is related to the allergic triggering factors. Allergic triggers in Graves' disease can be shown through the blood tests.

Hidaka et al. (21) have observed that Graves disease is exacerbated and relapsed after seasonal allergic rhinitis attacks. There was more association with Graves' disease in pollen allergies (22). In our study, among the patients in the rhinitis group, 48.7% has seasonal allergic rhinitis; 16.1% were allergic to perennial house dust mite; and the remaining 35.1% were allergic to house dust mite and/or fungi and/or pollen. Generally, pollen allergy is less common than house dust mite sensitivity. Since our tests were conducted during the pollen season and soon after (June to October), the high rates may be justified. Among a total of 319 patients included in our study, 193 (60.5%) were in the allergic rhinitis group and 126 (39.5%) in the healthy control group. In both groups, there is no previously diagnosed thyroid pathology. In the rhinitis group, we determined the aeroallergen sensitivities by applying a skin prick test. None of our patients received immunotherapy. No significant difference was found between the groups that were separated ac-

Table 2. Differences of males and females according to age, anti-Tg, anti-TPO, TSH, FT3, and FT4 values

		Female		Male		
Variables	**Group**	**n**	**Ratio**	**n**	**Ratio**	**p**
Age. years[2]		31.93±10.45	30 (17-55)	29.75±9.28	28 (18-55)	0.095
Anti-Tg[1]	<15 U/mL*	60	31.9%	64	49.6%	0.002*
	15-60 U/mL	95	50.5%	55	42.6%	
	>60 U/mL*	33	17.6%	10	7.8%	
Anti-TPO[1]	<28 U/mL	37	19.5%	29	22.7%	0.711
	28-60 U/mL	133	70.0%	88	68.8%	
	>60 U/mL	20	10.5%	11	8.6%	
TSH[1]	Below normal value	8	4.2%	2	1.6%	0.566
	Normal value	180	94.7%	124	96.1%	
	Above normal value	2	1.1%	3	2.3%	
FT3[3]	Below normal value	2	1.1%	1	.8%	0.999
	Normal value	186	97.9%	126	97.7%	
	Above normal value	2	1.1%	2	1.6%	
FT4[3]	Below normal value	5	2.6%	1	.8%	0.705
	Normal value	185	97.4%	127	98.4%	
	Above normal value	0	0.0%	1	.8%	
Allergy	Pollen	56	46.7%	38	52.1%	-
	House dust	22	18.3%	9	12.3%	
	House dust+pollen	34	28.3%	23	31.5%	
	House dust+fungi	2	1.7%	0	0.0%	
	Pollen+fungi	2	1.7%	0	0.0%	
	House dust+pollen+fungi	4	3.3%	3	4.1%	

[1]Pearson Chi-Square Test; [2]Mann-Whitney U Test presented with mean±standard deviation and median (min-max); [3]Fisher's Exact Test (Values below normal and above are combined); *p<0.05

cording to the anti-Tg (p=0.295) and anti-TPO values (p=0.224) of the patient and control groups. However, there was a proportional difference between the patient group (15.6%) and the healthy control group (10.4%) in terms of anti-Tg antibodies. Similar difference was also valid for anti-TPO. anti-TPO values were high (11.5%) in the patient group and in the healthy control group (7.1%). There was no significant difference between patient and control groups in terms of TSH, FT3, and FT4 values (p>0.05). Lindberg et al. (14) found high anti-TPO levels in with allergic asthma. Our patients have only allergic rhinitis and patients with allergic asthma were not included in the study.

In a study by Değirmenci et al. (23) the relationship between allergic rhinitis and autoimmune thyroid disease was investigated. In the general population, the prevalence of Hashimato thyroiditis was detected 1,5% and allergic rhinitis was observed in 16,3% patients. In patients with allergic rhinitis, high incidence of Hashimato thyroiditis was found as related to the dominant Th2 response. Graves' disease patients were not included in the study.

In our study, we did not investigate TSH receptor antibodies, which are known to be more related to Graves' disease. Other thyroid autoantibodies are found only 50% in Graves. This may be a limitation of our study. There was no known thyroid disease in the allergic rhinitis and healthy groups.

Hamilton and Atkinson did report statistically significant IgE levels between the patients with allergic rhinitis and bronchial asthma (24). IgE levels were high in 40% of the patients with allergic asthma and in 60% of the patients with bronchial asthma. However, no statistically significant difference was found in FT3, FT4, and TSH levels between the patients with bronchial asthma and those with allergic rhinitis in this study (p>0.05). Anti-Tg and anti-TPO levels were not also significant between the two allergic disease groups (p>0.05). Among the patients with severe bronchial asthma, anti-TPO and anti-Tg levels are found to be high. These results suggest that environmental antigens do not only stimulate local allergic reactions; at the same time, they also stimulate Th2 cell proliferation in Graves' disease and exacerbate autoimmune thyroid reactions and Th2-related autoimmune thyroid diseases (13).

In a study of El Aziz et al. (25) they have found that there is no difference in the thyroid function tests between the healthy group and the patient group, and thyroid autoantibodies are significantly higher in the patient group compared to the healthy group. El Aziz et al. (25) could not find a statistically significant difference between FT3, FT4, and TSH levels both in the allergic groups and in the healthy group. In the study by El Aziz et al., both anti-TPO and anti-Tg antibodies were statistically higher in patients with bronchial asthma and allergic rhinitis when compared to the healthy group (p<0.01). In our study, there is no significant difference

Table 3. Age differences according to anti-Tg, anti-TPO, TSH, FT3, and FT4 values

Variables	Group	n	Mean±SD	Median (Min-Max)	p	Spearman Correlation
Antitiroglobulin[1]	<15 U/mL	124	27.68 ± 8.4	25.50 (18-55)	<0.001*	p<0.001*
	15-60 U/mL	150	32.75 ± 10.42	32.00 (17-55)		r=0.268
	>60 U/mL	43	34.47 ± 10.21	35.00 (18-55)		
ATPO[1]	<28 U/mL	66	30.67 ± 10.22	28.00 (17-54)	0.027*	p=0.088
	28-60 U/mL	221	30.62 ±10.10	28.00 (18-55)		r=0.096
	>60 U/mL	31	34.94 ±8.70	36.00 (18-55)		
TSH[2]	Normal value	304	30.83 ±9.98	28.50 (17-55)	0.073	p = 0.536
	Abnormal value	15	35.53 ± 10.37	35.00 (20-50)		r = -0.035
FT3[2]	Normal value	312	30.92 ± 9.94	29.00 (17-55)	0.21	p = 0.108
	Abnormal value	7	37.00 ± 13.14	35.00 (21-55)		r = -0.090
FT4[2]	Normal value	312	30.88 ± 9.96	29.00 (17-55)	0.061	p=0.023*
	Abnormal value	7	38.57 ± 11.13	38.00 (25-51)		r= - 0.127

[1]Kruskal Wallis Test with Bonferroni-Dunn Test; [2]Mann-Whitney U Test; *p<0.05

between the FT4, FT3, and TSH and anti-Tg and anti-TPO values between the healthy and rhinitis groups. Diversely, there were no asthma patients in our study. The allergic group included rhinitis patients. Our patient and control groups are numerically higher (El Aziz's study: 20/20; our study: 193/126).

Akkoca et al. (26) could find any significant difference between the allergic rhinitis group and the healthy group in terms of the thyroid function tests. These results are concordant to the results of our study. In our study, no significant difference was found between the ages of the males and females included in the study (p=0.095). In our study, no significant difference was found between the ages of the groups in and out of the normal range of TSH, FT3, and FT4 values (p>0.05). The relation between ages and the ordinal values of anti-Tg, anti-TPO, TSH, FT3, and FT4 situations are evaluated using the correlation analysis. Accordingly, a positive weak relation was found between the age and anti-Tg values (p<0.001; r=0.268). A negative weak relation was found between the age and the FT4 value (p=0.023; r=-0.127). No significant relationship was found between age and anti-TPO, TSH, and FT3 values (p>0.05). These results are concordant to the increase in the incidence of thyroid autoantibodies in allergic rhinitis and/or bronchial asthma patients defined by Lindberg et al.(14) and Amino et al. (27).

Biscaldi et al. (28) have reported that FT3 and FT4 levels are higher in asthma patients compared to the control group. However, the presence of the thyroid hormone levels of asthma patients within the reference ratios suggests that asthma is not related to the thyroid function changes .The reports show that autoimmune thyroid disease in females is dominantly higher. In a study, the male/female ratio was found to be 6.67/1. This difference is probably related to estrogen. In some patients, the histories of the patient and known additional diseases have taken as a basis for the diagnosis (29). In our study, allergic patient group included only rhinitis patients. The patients with a history of asthma and thyroid diseases were excluded from the study. A statistically significant relationship was found between gender and the anti-Tg status. (p=0.002). It was found that The anti-Tg value was found to be under 15 U/mL in 49.6% males and 31.9% females and over 60 U/mL in 7.8% males and 17.6% females. A low anti-Tg ratio was found in males and high anti-Tg ratio was found in females (p<0.05 with Bonferroni Correction). No significant difference was found between the males and females according to their anti-TPO, TSH, FT3, and FT4 situations (p>0.05).

Conclusion

Allergic and autoimmune diseases together find are not common phenomena in an individual. This can be explained to usually managed by different processing of the Th1 and Th2 pathways. Although we did not find a statistical significance in our study, the thyroid autoantibodies were higher in the allergic rhinitis group with compared to controls . We believe that these patients should be closely monitored in terms of clinical and laboratory parameters and should be followed in terms of thyroid disease development.

Ethics Committee Approval: The ethics committee approval was received for this study from the ethics committee at Bursa Training and Research Hospital.

Informed Consent: Verbal informed consent was obtained from the patients and control group who participated in this study.

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