# Study of Thyroid Auto-Antibodies in Patients with Bronchial Asthma and Allergic Rhinitis

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***Abstract.*** **Background:** Authors of a few reports have stated that autoimmunity increases the frequency of Grave's disease in some patients with allergic rhinitis. Also, seasonal allergic rhinitis has been reported to be more frequent in Grave's disease but rare in painless thyroiditis. However, little is known about the relation between thyroid disease and allergic diseases. **Aim of Our Work:** Our aim was to study the coexistence of thyroid auto-antibodies in patients with bronchial asthma and allergic rhinitis. **Methods:** Forty patients with allergic diseases (20 patients with bronchial asthma [BA] and 20 patients with allergic rhinitis [AR]) and 20 healthy control subjects were included in the study. We measured the free triiodothyronine ($FT_3$), free thyroxin ($FT_4$) by radioimmunoassay (RIA), and thyroid stimulating hormone (TSH); thyroid auto-antibodies (anti-thyroid peroxidase [anti-TPO] and anti-thyroglobulin [anti-TG]) by Enzyme-linked Immunosorbent Assay (ELISA); the complete blood picture; allergic skin tests; and peak expiratory flow rate measured by spirometry. **Results:** Thyroid auto-antibodies levels were higher in patients with BA and AR compared to healthy subjects ($P < 0.05$). However, thyroid function test results ($FT_3$, $FT_4$, and TSH) did not significantly differ between patients and controls. Also, thyroid auto-antibodies levels did not significantly differ between patients with BA and those with AR ($P > 0.05$). **Conclusion:** Thyroid auto-immunity was associated with allergic disease but was not reflected in changed thyroid biochemical profiles.

***Keywords*** • Anti-thyroglobulin • Anti-thyroid peroxidase antibody • Allergic diseases • thyroid hormones IgE

## *Introduction*

Allergic disorders are diseases in which the immune system reacts inappropriately to exogenous antigens. In contrast, in autoimmune diseases, reactions are directed against auto-antigens, resulting in different kinds of diseases, depending on which organs are affected. The prevalence of auto-antibodies among allergic patients needs to be studied, since patients prone to react against exogenous antigens may also react more readily to endogenous antigens.[1]

The prevalence of allergic disease is increasing allover the world, but its influence on the clinical course of autoimmune disease in unknown.[2] Also, little is known about the relation between thyroid disease and allergic diseases.[3] Little is also known about the influence of allergic rhinitis, the production of auto-antibodies, and the clinical course of autoimmune disease.

Takeoka and colleagues[3] concluded that seasonal allergic rhinitis aggravated the clinical course of Grave's disease. They wrote that the allergic rhinitis increased both serum anti-thyroid auto-antibodies and the concentration of pollen-specific IgE. Hidaka and co-workers[4] observed that Grave's thyrotoxicosis

**Table 1.** Comparison between bronchial asthma (BA) versus allergic rhinitis patients (AR) as regard total IgE, thyroid profile and thyroid auto-antibodies by student t-test and Mann Whitney test (#)

| Variables | BA (n = 20) (Mean±SD) | AR (N = 20) (Mean±SD) | t | *p* - value |
|---|---|---|---|---|
| **Free T3** (pg/mL) | 2.3 ± 0.7 | 2.05 ± 0.6 | 1.1 | >0.05 (NS*) |
| **Free T4** (ng/mL) | 1.2 ± 0.3 | 1.3 ± 0.3 | 1 | >0.05 (NS) |
| **TSH** (MIU/mL) | 1.7 ± 1.6 | 1.7 ± 1.0 | 0.1# | >0.05 (NS) |
| **Total IgE** | 192 ± 101 | 189 ±144 | 0.16# | >0.05 (NS) |
| **Anti-thyroglobulin Antibody** | 20.4 ± 10 | 16.8 ± 9 | 1.12# | >0.05 (NS) |
| **Anti-thyroid peroxidase Antibody** | 15 ± 7.9 | 15 ± 0.4 | 5.2 | >0.05 (NS) |

[1]BA: Bronchial asthma; [2]AR: Allergic rhinitis; [3]NS: nonsignificant.

frequently relapsed or was aggravated after attacks of seasonal allergic rhinitis. Furthermore, Lindberg and coworkers[1] found higher thyroid peroxidase antibodies in children with allergic asthma.

Knowledge of the presence of thyroid disease in patients with bronchial asthma is important. The reason is that hypothyroidism may coexist with allergic diseases such as bronchial asthma,[1] while hyperthyroidism may be associated with a lower incidence of allergies. The association of thyroid disease and allergic diseases may be useful to clinicians who are alerted to the association. To add to the available knowledge base, the aim of our study, was to determine whether thyroid auto-antibodies coexist in patients with bronchial asthma and allergic rhinitis.

## *Methods and Materials*

Our case-control study included 40 patients with different allergic diseases. Twenty patients had bronchial asthma, and 20 patients had allergic rhinitis. We also included 20 healthy controls. All patients abstained from steroid therapy for at least one month before collection of laboratory samples. Each subjects provided a full history and underwent a clinical examination.

Fasting serum samples were collected from all patients and processed within 30 minutes. The samples were kept frozen at -20°C. We assayed levels of free triiodothyronine ($FT_3$), free thyroxine ($FT_4$) by using $T_3$ and $T_4$ Accubind ELISA Microwells (Monobind, Inc. Lake Forest, CA (92630) USA).

For $FT_3$, values between 1.4 and 4.2 ng/dL were considered normal, and for $FT_4$, 0.8 and 2.5 ng/dL were considered normal.

Serum TSH, anti-TG antibodies and anti-TPO antibodies were assessed by using TSH, anti-TG and anti-TPO Accubind ELISA Microwells (Monobind, Inc. Costa Mesa, CA (92627) USA). Values between 0.28 and 5.6 mU/L were consider normal for the TSH. Test results for thyroid autoimmunity were considered positive if anti-TG antibody levels were greater than 125 IU/mL, and for anti-TPO antibody levels greater than 40 IU/mL.

Allergic evaluation included two methods. First was the total serum IgE by ELISA based on the sandwich principle, assessed according to Engvall et al.[5] Second was skin tests using common, environmental, and food antigens on the volar surface of forearm. Grading of the skin prick test was performed according to Saxon.[6]

For each subject, we also included a complete blood picture and neck ultrasonography. Asthmatic patients underwent peak expiratory flow rate measurements according to the method of Haydu et al.[7] and Dworin.[8] Before a subject was included in the study, an informed consent was obtained from each patient. Our study protocol was reviewed and approved by our local institutional human research committee as conforming to the ethical guidelines of the 1975 Declaration of Helsinki.

**Statistical analysis.** Analysis of data was done by IBM computer using SPSS (statistical program for social science, version 12). The following statistical methods were used:

**Table 2.** Comparison between BA versus controls as regard total IgE, thyroid profile and thyroid auto-antibodies by student t-test and Mann Whitney test (#)

| Variables | BA (n = 20) (Mean±SD) | Controls (N = 20) (Mean±SD) | t | *p* - value |
|---|---|---|---|---|
| **$FT_3$** (pg/mL) | 2.3 ± 1.1 | 1.5 ± 0.4 | 1.4 | > 0.05 ($NS^2$) |
| **$FT_4$** (ng/mL) | 1.2 ± 0.3 | 1.3 ± 0.4 | 0.7 | > 0.05 (NS) |
| **TSH** (MIU/mL) | 1.7 ± 1.6 | 1.7 ± 0.5 | 0.9# | > 0.05 (NS) |
| **Total IgE** | 180 ± 144 | 14.2 ± 7 | 5.3# | < 0.01 ($HS^3$) |
| **Anti-thyroglobulin Antibody** | 16.84 ± 9 | 10.3 ± 2.7 | 3# | < 0.01 (HS) |
| **Anti-thyroperoxidase Antibody** | 15 ± 5.2 | 8.3 ± 2.2 | 5.5 | < 0.01 (HS) |

[1]BA: bronchial asthma; [2]NS: Nonsignificant; [3]HS: Highly significant.

Description of quantitative variables as means, SDs, and ranges; description of qualitative variables as numbers and percentages; chi-square test for com parisons of qualitative variables between groups; unpaired t-tests to compare two groups, and ANOVA to compare more than two groups regarding quantitative variables in parametric data; the Mann-Whitney Wilcoxon test instead of unpaired t-tests with non-parametric data; Spearman correlation coefficient to rank different variables as either positive or inverse.

The results were considered to be statistically significant at a $p$ value < 0.05, highly significant at a $p$ value < 0.001, and insignificant at a $p$ value > 0.05.

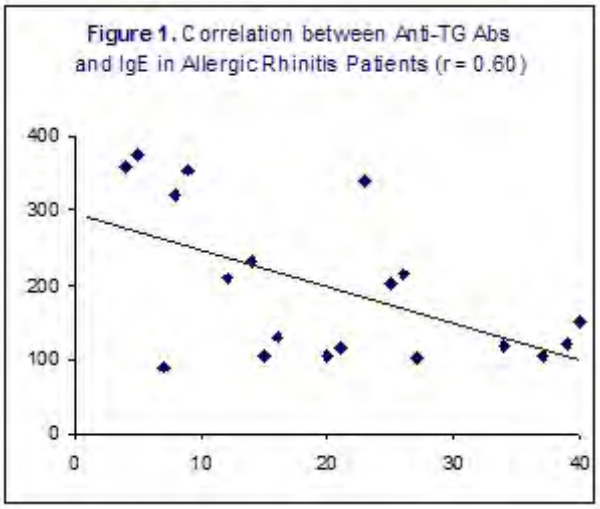
### *Results*

The sixty subjects included in this study were matched by age and gender; the three groups did not significantly differ on these matching variables ($p$ > 0.05).

As shown in Table 1, the TSH, $FT_3$, $FT_4$, thyroid auto-antibodies and total IgE results of patients with bronchial asthma and allergic rhinitis did not significantly differ ($p$ > 0.05). Also, as shown in Tables 2 and 3, there was no significant difference in the TSH, $FT_3$, $FT_4$ levels between the two patients groups and the healthy controls healthy subjects ($p$ > 0.05).

However, IgE, anti-TG, and anti-TPO antibody levels were significantly higher in patients with allergic diseases than in healthy subjects ($p$ < 0.01). The mean anti-TG antibody level was significantly positively correlated with the total IgE level (IU/mL) in bronchial asthma patients ($r$ = 0.54, $p$ < 0.05). Similarly, the mean anti-thyroglobulin antibody level was significantly positively correlated with the total IgE level (IU/mL) in allergic rhinitis patients ($r$ = 0.60, $p$ < 0.01), as shown in Figure 1.

In bronchial asthma patients, anti-TG antibody and anti-TPO antibody levels did not significantly correlate with the peak expiratory flow rate (L/m), ($r$ = 0.08, $p$ > 0.05) and ($r$ = 0.18, $p$ > 0.05).




Anti-TPO antibody level significantly negatively correlated with the total IgE in allergic rhinitis patients ($r$ = -0.56, $p$ < 0.05), as shown in Figure 2. But peroxidase antibodies did not correlate with the total IgE in bronchial asthma patients ($r$ = 0.13, $p$ > 0.05).

The duration of allergic diseases and anti-TG antibody did not correlate among both patients with bronchial asthma ($r$ = -0.31, $p$ > 0.05) and those with al-

**Table 3.** Comparison between AR versus controls as regard total IgE, thyroid profile and thyroid autoantibodies by student t-test and Mann Whitney test (#)

| Variables | AR (n = 20) (Mean ± SD | Controls (N = 20) (Mean±SD) | t | *p* - value |
|---|---|---|---|---|
| **$FT_3$** (pg/mL) | 2.05 ± 0.6 | 1.5 ± 0.4 | 1.9 | > 0.05 (NS) |
| **$FT_4$** (ng/mL) | 1.3 ± 0.3 | 1.3 ± 0.4 | 0.12 | > 0.05 (NS) |
| **TSH** (MIU/mL) | 1.7 ± 1.0 | 1.7 ± 0.5 | 0.04# | > 0.05 (NS) |
| **Total IgE** | 180 ± 144 | 14.2 ± 7 | 5.3# | < 0.01 (HS[3]) |
| **Anti-thyroglobulin Antibody** | 16.84 ± 9 | 10.3 ± 2.7 | 3# | < 0.01 (HS) |
| **Anti-thyperoxidase Antibody** | 15 ± 5.2 | 8.3 ± 2.2 | 5.5 | < 0.01 (HS) |

[1]AR: Allergic rhinitis; NS: [2]Nonssignificant; [3]HS: Highly significant.

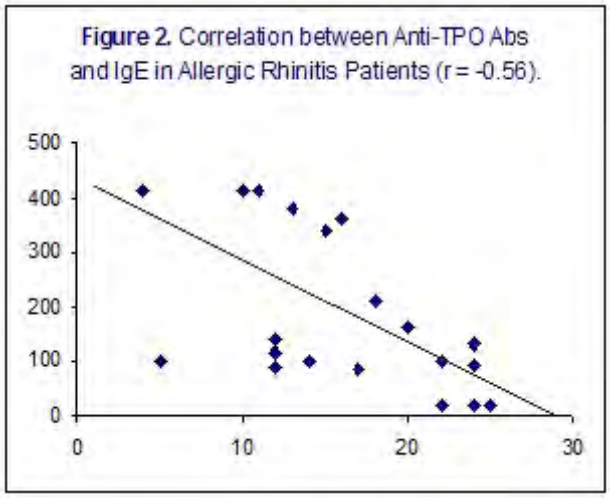
lergic rhinitis ($r$ = -0.21, $p > 0.05$). The duration of allergic disease significantly negatively correlated with anti-TPO ($r$ = -0.42, $p < 0.05$) in patients with bronchial asthma, but did not correlate in patients with allergic rhinitis ($r$ = -0.2, $p > 0.05$). The anti-TG antibody level significantly positively correlated with the TSH in both bronchial asthma patients ($r$ = 0.45, $p < 0.05$) and allergic rhinitis patients ($r$ = 0.25, $p < 0.05$). Anti-TPO antibody levels did not significantly correlate with the TSH level of either patients with bronchial asthma ($r$ = 0.13, $p > 0.05$) or allergic rhinitis ($r$ = 0.11, $p > 0.05$).

## *Discussion*

The prevalence of auto-antibodies among allergic patients merits study. The reason is that patients who are prone to react to exogenous antigens may also react more readily to endogenous antigens.[1]

In the present study, there was a significant statistical difference between the serum total IgE level of healthy subjects and those of patients with bronchial asthma and allergic rhinitis ($p < 0.01$). But no statistically significant difference was found between patients with bronchial asthma and those with allergic rhinitis ($p > 0.05$). These results agree with those of Takeoka and colleagues[2] who recorded a statistically significant elevation of serum total IgE in allergic patients. In addition, Hamilton and Adkinson[9] reported finding no statistically significant difference between the IgE levels was patients with bronchial asthma and those with allergic rhinitis. IgE levels were elevated in 40% of allergic rhinitis patients and 60% of bronchial asthma patients.

On the other hand, in our study, we did not find a significant statistical difference between the $FT_3$, $FT_4$, and TSH levels of patients with bronchial asthma and those with allergic rhinitis ($p > 0.05$). Also, the thyroglobulin and peroxidase antibody levels between the two groups of patients with allergic diseases did not significantly ($p > 0.05$).




Among patients with severe bronchial asthma, thyroglobulin and peroxidase antibodies were elevated. This result suggests that environmental antigens may induce not only local allergic reactions but also stimulate thyroid autoimmune reactions with stimulation of Th2 proliferation in Graves' patients and an aggravation of their Th2-dependent autoimmune thyroid disease.[2]

Anti-TPO and anti-TG antibodies in both our bronchial asthma patients and allergic rhinitis patients were statistically higher than in healthy subjects ($p < 0.01$). These results were in agreement with Lindberg et al.,[1] and Amino et al.[10] who described an increased incidence of thyroid auto-antibodies in patients with bronchial asthma and/or allergic rhinitis. The explanation was that the Th2 response enhanced antibodies as in allergies, and involved IL4, IL5, and IL13 that stimulate B cells to secrete thyroid antibodies, which in turn decrease thyroid hormone synthesis and secretion.[11]

In our study, however, we found no statistically significant difference ($p > 0.05$) between the $FT_3$, $FT_4$, and TSH levels of the two allergic groups and healthy subjects. This finding is contrary to that of Landyshev et al.[12] who reported that thyroid function undergoes biphasic changes in bronchial asthma patients. The also reported that as patients with mild bronchial asthma progressed to paroxysmal exacerbation of their asthma, hypofunction of the patients' thyroid glands developed.[12] Biscaldi et al.[13] reported that $FT_3$ and $T_4$ levels were higher in a control group than in asthmatic patients; but still, the asthmatic patients' thyroid hormone levels were within the reference range, suggesting that asthma was not associated with changes in thyroid function.

## Conclusion

From our study results, thyroid auto-antibody levels were higher in patients with bronchial asthma and allergic rhinitis. But we found no statistically significant difference between the $FT_3$, $FT_4$, and TSH levels of the two groups of allergic patients and those of our healthy control subjects. Our results suggest that thyroid autoimmune processes may be associated with allergic disease, but the processes do not induce changes in TSH and thyroid hormone profile. We recommend larger studies for further evaluation.

## Coauthors' Participation

All authors of this report shared equally in patient selection, definitions of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review.

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