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Ustekinumab May Have Therapeutic Effects on Autoimmune Thyroid Disease

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Abstract

Interleukin (IL)-12 and IL-23 play crucial roles in initiating and maintaining autoimmunity, which is implicated in autoimmune thyroid disease (AITD). This study evaluated the effect of ustekinumab, a biologic agent targeting IL-12/23, on AITD in patients with inflammatory bowel disease (IBD). A total of 203 IBD patients and 58 age- and sex-matched healthy controls underwent comprehensive thyroid examinations including biochemical tests and sonography. Among the IBD patients, 127 received biologic therapy and 76 did not; 91 were treated with infliximab, 26 with adalimumab, and 10 with ustekinumab. Compared with healthy controls, patients with IBD exhibited impaired thyroid structure and a higher incidence of AITD. The incidence of AITD was lower and thyroid structure was better preserved in IBD patients receiving biologic therapy than in those not receiving it. When thyroid findings were analyzed by biologic type, ustekinumab-treated patients had the lowest AITD incidence, lower anti-thyroid peroxidase levels, and more favorable sonographic features compared with adalimumab and infliximab groups. These findings suggest that ustekinumab may have a protective or therapeutic effect on the thyroid gland and may be a potential treatment option in patients with AITD.

Keywords: Autoimmune thyroid disease, inflammatory bowel disease, interleukin-12, interleukin-23, ustekinumab

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Introduction

Autoimmune thyroid disease (AITD) is the most common autoimmune disease leading to thyroid gland damage and subsequent dysfunction [1]. It results from complex genetic and environmental factors, culminating in the production and accumulation of autoantigens in the thyroid gland, followed by the infiltration of autoreactive immune cells [2]. Ultimately, this process leads to irreversible gland dysfunction characterized by progressive loss of thyroid follicular cells, lymphocytic infiltration, and fibrosis. The underlying autoimmune mechanisms involve upregulation of T helper (Th) 1 and Th 17 lymphocytes [3], with interleukin (IL)-23, a member of the interleukin IL-12 family, known to drive T lymphocytes towards the Th-17 phenotype [4]. Elevated IL-23 levels have been observed in individuals with AITD [5]. Cytokine–chemokine networks orchestrate intrathyroidal immune cell recruitment and effector functions in AITD. IL-12 and IL-23 promote Th1/Th17 polarization, sustaining interferon-γ/TNF-α–driven inflammation, while the CXCR3 axis (CXCL9, CXCL10, CXCL11) recruits Th1 lymphocytes and amplifies local immune activation [6]. These pathways have been implicated across Hashimoto's thyroiditis and Graves' disease and are considered potential therapeutic targets. In this context, modulating the IL-12/23 axis (e.g., with ustekinumab) could attenuate upstream drivers that also shape chemokine signaling in thyroid autoimmunity.

Inflammatory bowel disease (IBD) is a chronic inflammation that affects various parts of the gastrointestinal tract and is due to an excessive immune response to multiple antigens or environmental triggers [7]. This disease manifests with symptoms that affect

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numerous extraintestinal organs and systems [8], including the thyroid gland. Studies have shown that AITD is more common in patients with IBD [9-11]. Corticosteroids, aminosalicylates, and biological agents are commonly used to treat IBD [12], among which ustekinumab, a human monoclonal antibody (MAB) of the immunoglobulin (Ig)-G1 structure targeting IL-12/23, plays a prominent role [13].

In this context, our study aimed to investigate thyroid gland health and the influencing factors in patients with IBD who are particularly predisposed to AITD and frequently treated with biological agents.

Materials and Methods

Study Design and Participants

This single-center, cross-sectional, observational study was conducted in a tertiary care hospital's endocrinology and gastroenterology departments. Patients presenting to the IBD outpatient clinic of the gastroenterology department between January 2023 and September 2023 were included in the study. Patients were eligible if they had either a previous or newly diagnosed IBD, and their diagnosis was confirmed by endoscopic and laboratory tests [14]. Exclusion criteria were patients who had undergone imaging with iodinated contrast agents in the previous six weeks [15], those taking medications such as amiodarone known to interfere with thyroid function [16], and patients who had undergone thyroidectomy, had previously been treated with radioactive iodine or had undergone radiotherapy to the neck. Pregnant women and patients with conditions such as heart failure and liver cirrhosis that could affect thyroid function and measurements were also excluded [17, 18]. In addition, those who were diagnosed with thyroid disease or who had started treatment for thyroid disease before the diagnosis of IBD were excluded from the study.

Subsequently, the patients with IBD were compared with a healthy control group selected consecutively from individuals who were registered for routine examinations at our center.

Procedures

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To determine whether the incidence of AITD is increased in patients with IBD, both patients and healthy controls underwent a comprehensive thyroid examination. This examination included thyroid function tests, measurement of thyroid autoantibodies, and an ultrasound examination of the thyroid gland. The results of these examinations were then compared in the two groups.

After this initial comparison, the thyroid examination results in patients with IBD were further analyzed using biological agents. This allowed an assessment of possible associations between the use of biologics and thyroid dysfunction in these patients.

Finally, the thyroid examination results in the subgroup of patients treated with ustekinumab were compared with those treated with other biological agents. This comparison aimed to identify differences in thyroid function and autoimmunity outcomes associated with the different biological treatments. The study flowchart outlining these analyses is shown in Figure 1.

Data Collected, Examination Procedures and Definitions

The biometric and clinical data of the patients were taken from the follow-up cards of the IBD outpatient clinics. All treatments taken by patients are recorded both in the physical follow-up files and on the website (https://medeczane.sgk.gov.tr/doktor/login.jsp), the government's digital database containing information on the course of prescription medication, including intake, duration, dose, and intervals. The relevant data were examined. Afterward, the blood sample was drawn from each participant for thyroid function tests and thyroid autoantibodies in addition to routine tests for IBD follow-up. Since the use of iodine in table salt has been mandatory in our country since 1998, cases of iodine deficiency are no longer observed [19]. For this reason, the participants were not tested for their iodine status, and all were considered iodine-sufficient.

When free triiodothyronine (FT3) and free thyroxine (FT4) levels were within the normal range, levels above the reference range for thyroid stimulating hormone (TSH) were considered subclinical hypothyroidism [20]; when FT3 and FT4 were below the reference range, and TSH was above the reference range, this was regarded as overt

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hypothyroidism [21]. If FT3 and FT4 were within the normal range and TSH was below the reference range, this was referred to as subclinical hyperthyroidism; if FT3 and FT4 were above the reference range and TSH was below the reference range, this was referred to as overt hyperthyroidism [22]. While anti-thyroglobulin (TG) and anti-thyroid peroxidase (TPO) antibodies in serum were measured in all patients, thyroid-stimulating hormone receptor antibody (TRAb) levels were only measured in patients with overt and subclinical hyperthyroidism.

The measurement results for anti-TG and anti-TPO in serum were classified as positive if they exceeded 115 IU/mL and 34 IU/mL, respectively. Values above 1.5 IU/mL in the TRAb measurement were positive results.

The presence of AITD was defined as the presence of Hashimoto's thyroiditis and Graves' disease. While Hashimoto's thyroiditis was defined as anti-TPO or anti-TG positivity, Graves' disease was defined as TRAb positivity.

Sonographic Examination

All sonographic examinations were performed by an endocrinologist (AND) with three years of experience, blinded to the patients' clinical information, using the same ultrasound machine. First, the patients were positioned with their necks hyperextended. Then, each thyroid lobe was scanned separately in three planes with LOGIQ e Ultrasound (software version R9.1.2; General Electric Company, China, 2016). A linear 6–12 MHz transducer was used. In combination with color Doppler ultrasonography, B-mode ultrasonography was used to assess vascular conditions. The thyroid volume was calculated according to the ellipsoidal formula: Volume (mL): depth (cm) x width (cm) x length (cm) x π/6 [23]. Normal thyroid volume was defined as <15 mL [24]. Sonography is a non-invasive diagnostic imaging technique that provides information about the degree of inflammatory activity. Significantly reduced echogenicity, heterogeneity, and multifocal pseudonodular hypoechoic infiltration are signs of high inflammatory activity [25]. The parenchymal structure was evaluated according to the sonographic classification system VESINC (Volume, Echogenicity, Sonographic structure, Pseudonodular Infiltration, Nodules, and Cysts) [26].

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Calculation of Thyroid Secretory Capacity

The secretory capacity of the thyroid gland provides an estimate of its maximum secretion rate under stimulated conditions. For this purpose, a physiological index approach (SPINA-GT) was used for calculation [27]. Calculations were performed using the SimThyr 4.0 application with measured hormone concentrations. 1.4 to 8.7 pmol/s were defined as the reference range [28]. SPINA-GT significantly increased in toxic adenomas and Graves' disease, while it significantly decreased in Hashimoto's thyroiditis [27, 28].

Biochemical Assays

All patients fasting blood samples were taken between 08.00 and 09.00 am. TSH was measured by sandwich method with two different monoclonal antibodies labeled with biotin or a ruthenium complex; FT3 and FT4 were measured by electrochemiluminescence immunoassay (ECLIA) with a specific monoclonal antibody labeled with a ruthenium complex, using a competitive technique. These parameters were analyzed using Elecsys test kits on Roche Cobas e 602 systems. In addition, TRAb, anti-TPO, and anti-TG were measured using a competitive technique using the ECLIA method. These parameters were analyzed using Roche/Hitachi Cobas c systems (Roche Diagnostics GmbH, Mannheim, Germany).

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Statistical Analysis

Statistical analyses were done using the Statistical Package for the Social Sciences (SPSS) software (version 21.0). The data were first analyzed for normality using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± standard deviation (SD) and/or median (interquartile range [IQR]). Student’s t-tests or analyses of variance (ANOVA) were used to compare means between groups with normal data distribution. Medians were compared using the Mann-Whitney U test and the Kruskal-Wallis test. The Spearman rank and Pearson correlation tests were used to calculate the correlation coefficients between continuous variables. Frequencies were compared using the Pearson test and Fisher's exact test. Patients with a prior or current diagnosis of AITD were included in the prevalence analyses but excluded from comparisons of continuous thyroid

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function parameters (TSH, FT3, FT4, SPINA-GT) to minimize treatment-related bias. The results were evaluated within a 95% confidence interval, and a p-value < 0.05 was considered statistically significant. A priori power analysis (G*Power v3.1) was conducted for the primary comparison between IBD patients and healthy controls on continuous thyroid parameters using a two-sample, two-tailed t-test (α = 0.05, power = 0.95), assuming a moderate standardized effect size (Cohen's d = 0.5). Under the planned unequal allocation, the required total sample size was 250, which was achieved with 261 participants (IBD n = 203; controls n = 58). Subgroup analyses by biologic agent type were exploratory and not formally powered.

Results

General Characteristics of Participants

The study included 203 patients with IBD and 58 healthy controls. There was no significant difference between the general characteristics of patients and controls (Table 1). One hundred twenty (59.1 %) patients had Crohn's disease (CD), and 83 (40.9 %) had ulcerative colitis (UC). The detailed characteristics of patients with IBD and a comparison of the characteristics of patients with CD and UC can be found in Supplementary Table 1. The median disease duration of patients with IBD was 6 [4-11] years. While 127 (62.6%) of the patients received biological treatment, 76 (37.4%) did not. Of those who received biologic treatment, 91 (71.7%) were treated with infliximab, 26 (20.5%) with adalimumab, and 10 (7.8%) with ustekinumab. The median duration of biological treatment was 40 [28-50] months for infliximab, 38 [30-46] months for adalimumab, and 42 [34-52] months for ustekinumab (p = 0.815).

Comparison of Thyroid Examination Findings Between Patients With Inflammatory Bowel Disease and Healthy Controls

A comparison of the thyroid examination results of patients with IBD and healthy controls is shown in Table 2. Ten of the patients were diagnosed with AITD after the diagnosis of IBD but before our investigation. Eight patients were receiving L-thyroxine treatment for Hashimoto's thyroiditis, and two patients were taking methimazole for Graves' disease.

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The calculation excluded the TSH, FT3, FT4, and SPINA-GT values of 10 patients diagnosed with AITD from the statistical analysis. TSH, FT3, FT4, SPINA-GT, and anti-TG levels were similar in patients and controls ($p > 0.05$ for all). Anti-TPO levels were significantly higher in patients with IBD than in controls ($p = 0.048$). When sonographic findings were examined, patients with IBD had a larger glandular volume, hypoechoic and heterogeneous structure of the glandular parenchyma, and increased nodule frequency compared to controls ($p < 0.05$ for all). After the evaluation, none of the patients with IBD were newly diagnosed with Graves' disease, while 32 patients were newly diagnosed with Hashimoto's thyroiditis. Finally, the incidence of AITD was 20.7% ($n = 42$) in patients with IBD and 13.8% in controls ($p = 0.041$). These percentages include all patients meeting AITD diagnostic criteria regardless of current treatment status. In addition, patients with UC and CD were compared regarding thyroid findings; the results are shown in Supplementary Table 2. There was no difference between the two groups regarding thyroid findings and AITD frequency. The distribution of AITD according to diagnostic criteria is presented in Supplementary Table 3.

Comparison of Thyroid Examination Findings of Patients Who Received Biologic Treatment and Patients Who Did Not in Inflammatory Bowel Disease

After showing that the incidence of AITD was increased and thyroid structure was impaired in patients with IBD compared to healthy controls, thyroid examination results were evaluated according to the use of biologic treatment. While 127 (62.6%) patients received biologic treatment, 76 (37.4%) did not. A comparison of the thyroid examination results of the two groups is shown in Table 3. Four patients who did not receive biologic treatment were treated for Hashimoto's thyroiditis, and six of the patients who received biologic treatment were diagnosed with AITD after starting treatment. At the time of evaluation, four patients treated with biologics were being treated for Hashimoto's thyroiditis, and two patients were being treated for Graves' disease. TSH, FT3, FT4, and SPINA-GT values of patients diagnosed with AITD and currently receiving treatment were excluded from statistical analysis. Thyroid function tests and thyroid secretory capacity were similar in patients receiving biological therapy and in patients who did not. Although

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the thyroid autoantibody levels of patients who received biologic treatment were lower than those of patients who did not, there was no significant difference. The thyroid gland of the patients who received biological treatment was more isoechoic than those who did not ($p = 0.038$). Heterogeneous glandular structure, pseudonodular hypoechoic infiltration, and nodules and cysts were lower in patients receiving biologic treatment than in those not receiving biologic treatment but did not reach statistical significance. Finally, the incidence of AITD was lower in patients who received biologic treatment than in those who did not ($p = 0.011$).

Comparison of Thyroid Examination Findings According to Biologic Agent Type in Inflammatory Bowel Disease

After finding that IBD patients who received biologic treatment had relatively better thyroid structure and a lower incidence of AITD than patients who did not, the effects of the biologic treatments were compared. Three of the patients treated with infliximab were diagnosed with Hashimoto's thyroiditis and one with Graves' disease before evaluation. One of the patients treated with adalimumab was diagnosed with Hashimoto's thyroiditis, and one with Graves' disease before evaluation. None of the patients treated with ustekinumab were diagnosed with AITD before evaluation. TSH, FT3, FT4, and SPINA-GT values of patients diagnosed with AITD and currently being treated were excluded from the statistical analysis. The results are shown in Table 4. It was found that patients treated with ustekinumab had a lower anti-TPO level, an isoechoic and more homogeneous glandular structure, and a lower rate of AITD than patients treated with infliximab and adalimumab ($p < 0.05$ for all).

Discussion

This study investigated the effects of biologic treatments on thyroid health and AITD. For this purpose, more than 200 IBD patients and more than 50 healthy controls underwent a detailed thyroid examination. The thyroid structure was disturbed in patients with IBD, and the incidence of AITD was higher than in healthy controls. Subsequently, the results of patients with IBD who received biologic treatment were compared with those of patients who did not. The results showed that the incidence of AITD was lower in patients

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with IBD who received biologic treatment than in those who did not and that thyroid structure was better. Finally, thyroid structure and the incidence of AITD were evaluated according to the type of biologic treatment. It was found that ustekinumab, an anti-IL12/23 MAB, was the biologic that had the most positive effect on thyroid health and the lowest incidence of AITD.

First, the frequency of AITD in IBD was investigated. In the literature, their study of 31 patients, Bianchi et al. reported that there are changes in thyroid volume and function in IBD, even in the absence of clinically detectable thyroid disease, and that IBD coexists with thyroid disorders [29]. Messina et al. followed 41 patients with IBD prospectively for one year and reported that thyroid involvement is joint in IBD along with morphologic, hormonal, and immunologic abnormalities [9]. Neubauer et al. examined 199 patients with IBD sonographically and reported a significantly larger thyroid volume, i.e., goiter, in the patients compared to healthy patients [10]. Shizuma reported an increased concurrence of UC and AITD and an increased concurrence of CD and amyloid goiter [11]. Our study found that the thyroid structure was more hypoechoic and heterogeneous in patients with IBD than in healthy controls, and the frequency of nodular goiter increased. In addition, the incidence of AITD was increased in patients with IBD compared to controls. Our results suggest that thyroid structure and dysfunction is not only an extraintestinal finding of IBD due to increased inflammatory activity in patients with IBD but also the coexistence of IBD and AITD as concurrent autoimmune diseases. In this context, it is consistent with the literature. Although there is no definitive evidence yet for the coincidence of IBD and thyroid disease, autoimmune and immunologic factors may partially explain the pathogenic mechanism underlying both diseases. Further work on this topic is needed.

Following the finding that the incidence of AITD is increasing in patients with IBD, the effect of the use of biologics on the incidence of AITD was investigated. Many patients with IBD are now treated with biologic agents that target proinflammatory cytokines [30]. These anti-TNF and anti-IL therapies suppress auto-inflammation by blocking ILs and TNF [31]. The effect of these treatment agents on the thyroid is not known with certainty, but

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recent studies show a positive impact on thyroid health and AITD both clinically and experimentally [32]. In their study of 41 patients with IBD, Paschou et al. reported a lower rate of AITD in patients with IBD who received anti-TNF therapy compared to patients who did not receive therapy [33]. However, thyroid morphology was not examined in their study. In addition, patients receiving anti-IL therapy were excluded from the analysis. In their research compiling reports of thyroid disease in patients with rheumatoid arthritis treated with biologic agents, Bliddal et al. reported that 311 patients treated with biologic agents had lower AITD and antibody titers [34]. However, the use of anti-IL treatments in patients with IBD is relatively new, and no studies are reporting on the effects of this treatment on the thyroid gland. This study found that patients who received biologic treatment had a healthier thyroid structure, lower anti-TPO titers, and a lower incidence of AITD than patients who did not. This result confirms what has been previously reported in the literature.

Interestingly, the prevalence of ultrasound-defined AITD in our cohort exceeded that of antibody-positive disease. This discrepancy likely reflects several overlapping mechanisms. First, the relatively stringent serologic thresholds used in our laboratory (anti-TPO > 34 IU/mL and anti-TG > 115 IU/mL) may have underestimated patients with low-titer autoantibody positivity, as also reported in “seronegative” or “low-titer” variants of autoimmune thyroiditis [35,36]. Second, inflammatory bowel disease itself may predispose to a form of thyroid autoimmunity that is primarily T-cell–mediated rather than antibody-driven. In such patients, intrathyroidal lymphocytic infiltration and cytokine-driven damage may occur in the absence of circulating antibodies, a phenomenon increasingly recognized in other systemic autoimmune conditions [37–40]. Chronic immune activation in IBD, particularly through the IL-12/23–Th1/Th17 axis, may contribute to this seronegative pattern by promoting cellular cytotoxicity and interferon-γ–dependent thyroidal inflammation [38,40]. In addition, long-term exposure to immunosuppressive drugs commonly used in IBD—such as corticosteroids, azathioprine, methotrexate, and anti-TNF agents—can suppress B-cell activity and reduce circulating antibody levels [34,41]. This pharmacologic effect may partially explain why some patients show clear sonographic evidence of autoimmune thyroiditis but remain antibody-negative.

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Taken together, these mechanisms suggest that IBD-associated thyroid autoimmunity may represent a unique clinical–immunological phenotype characterized by predominant cellular immune activation and attenuated humoral response. If confirmed in larger mechanistic studies, this seronegative pattern could help refine our understanding of thyroid involvement in systemic autoimmune diseases and identify subgroups that might benefit from targeted cytokine inhibition, such as IL-12/23 blockade with ustekinumab.

Having demonstrated the beneficial effects of biologics on the thyroid gland in patients with IBD and their association with a lower incidence of AITD, it was time to examine these effects in detail according to the type of biologic. Biological agents aim to suppress various cytokines and mediators that play a role in initiating and maintaining inflammation. IL-12 and IL-23 are known to be critical proinflammatory cytokines in the pathogenesis of IBD [42]. Ustekinumab, a human IgG1 MAB targeting the p40 subunit of IL-12 and IL-23, is increasingly used to treat IBD [43]. Ustekinumab is well tolerated and successfully induces and maintains remission in patients with moderate to severe IBD who are clinically responsive to induction therapy, with no significant side effects or adverse events observed [44]. Recent studies have reconfirmed the critical role of elevated IL-12 and IL-23 in developing AITD [5, 45]. We aimed to investigate whether ustekinumab, which targets these elevated cytokines directly, could be therapeutically effective in AITD. Indeed, our results showed better thyroid morphology, lower anti-TPO titers, and less frequent occurrence of AITD in patients with IBD treated with ustekinumab. The suppression of proinflammatory IL-12 and IL-23 by ustekinumab results in lower thyroid autoimmunity, less inflammation of the glandular structure, and lower anti-TPO antibody titers.

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Of note, mean BMI was in the overweight range in both IBD and control groups, which is consistent with national prevalence data for Turkey; moreover, in IBD, prior glucocorticoid exposure and contemporary treatment patterns (including biologic therapy) have been associated with weight gain in subsets of patients [46].

This study has some limitations. It was purely observational, and patients were evaluated during their ongoing treatments without any interventional design or pre- and

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post-treatment follow-up. Therefore, temporal causality between biologic exposure and thyroid outcomes cannot be inferred. As a cross-sectional study, patients were recruited and evaluated at different disease stages, which further limits the ability to establish cause-and-effect relationships. A prospective longitudinal design with baseline and post-treatment assessments would provide more meaningful results. Nevertheless, the results were robust due to the inclusion of a large number of patients, the application of strict exclusion criteria, and the use of appropriate group comparisons. Another limitation is the lack of pathological and molecular-level confirmation. However, extensive thyroid function tests, antibody measurements, and detailed sonographic examinations performed according to a strict protocol and by a single operator supported reliable pathophysiological interpretation of the findings. Although the number of patients treated with ustekinumab was relatively small, and none fulfilled the diagnostic criteria for AITD, the results were internally consistent and support a potential mechanistic link between IL-12/23 inhibition and reduced thyroid autoimmunity. However, prospective studies with a larger number of patients are needed to generalize the results.

Conclusion

This study confirms the increased incidence of AITD in patients with IBD. It also showed a healthier thyroid structure, lower anti-TPO titer, and the presence of lower AITD in patients treated with the previously reported biologic agents compared to patients who did not receive biologic agents. However, this study was the first to demonstrate the therapeutic effect of ustekinumab on the thyroid gland and AITD. Ustekinumab, a biological agent that explicitly targets IL-12 and IL-23, which play a crucial role in initiating and maintaining autoimmunity in AITD, could be a potential therapeutic target for AITD.

Declarations

Conflict of interest

The authors have no relevant financial or nonfinancial interests and declare no conflicts of interest.

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Ethical Statement

The study was conducted in accordance with the 1964 Helsinki Declaration. The Ethics Committee of Istanbul University-Cerrahpaşa approved the study (No: 602785). Trial registration was not applicable because the study did not prospectively assign individuals to a health-related intervention. The article was prepared in accordance with the Improving Quality and Transparency of Health Research (EQUATOR) Network guidelines for observational studies (STROBE).

Informed Consent

Signed informed consent was obtained from all study participants.

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Author Contribution

Mustafa Sait Gonen and Ali Ibrahim Hatemi contributed to the conceptualization of the study. Ahmet Numan Demir and Suleyman Sami Guzel were responsible for the methodological design. Suleyman Sami Guzel, Tugce Eskazan, and Ahmet Numan Demir conducted the investigation and data collection. Data curation was performed by Suleyman Sami Guzel and Tugce Eskazan. Formal analysis and visualization were carried out by Ahmet Numan Demir. The original draft was written by Suleyman Sami Guzel and Ahmet Numan Demir, and the manuscript was reviewed and edited by Mustafa Sait Gonen and Ahmet Numan Demir. The study was supervised by Mustafa Sait Gonen. All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement

This article and its tables include all data obtained or analyzed in this study. The data archive can be made available on request. Further requests can be directed to the corresponding author.

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Legends of Table and Figure

Table

Table 1. General characteristics of patients with inflammatory bowel disease and healthy controls

Table 2. Comparison of thyroid examination findings of patients with inflammatory bowel disease and healthy controls

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Table 3. Comparison of thyroid examination findings of patients who received biologic treatment and patients who did not in inflammatory bowel disease

Table 4. Comparison of thyroid examination findings according to biologic agent type in inflammatory bowel disease

Figure

Figure. Study flow chart

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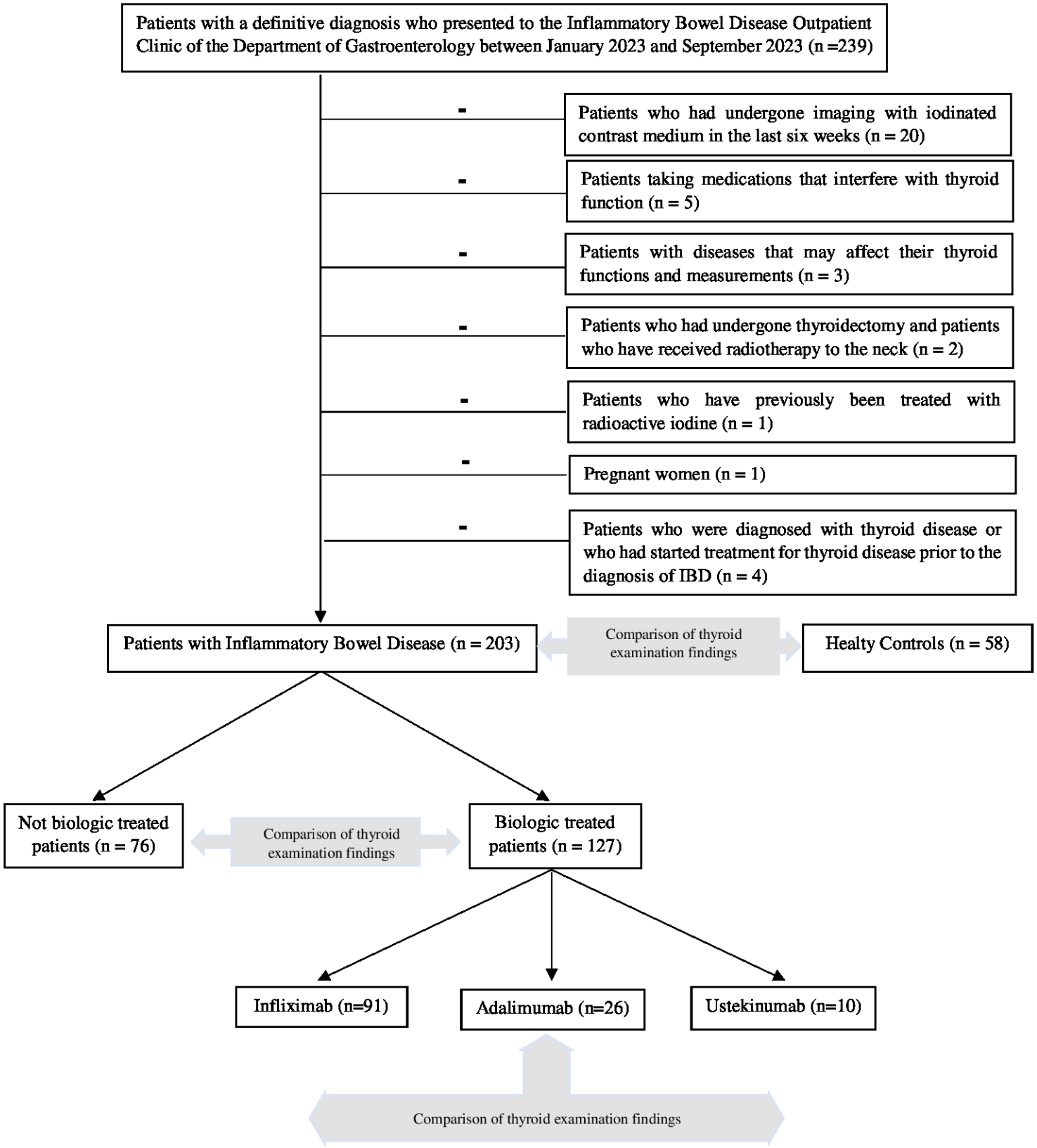

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Table 1. General characteristics of patients with inflammatory bowel disease and healthy controls

Characteristics	**Patients with IBD (n = 203)**	**Healthy Controls (n = 58)**	**P-value**
Age, year, mean ± SD	43.9 ± 13.5	43.9 ± 9.4	0.990
Sex, female, n (%)	107 (52.7)	30 (51.7)	0.551
Height, cm, mean ± SD	167.5 ± 8.9	164.5 ± 8.7	0.226
Body mass index, kg/m^2, mean ± SD	25.5 ± 4.7	26.3 ± 4.5	0.248
Smoking, yes, n (%)	66 (32.5)	19 (32.8)	0.122

IBD, Inflammatory bowel disease; SD, Standard deviation

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Table 2. Comparison of thyroid examination findings of patients with inflammatory bowel disease and healthy controls

Findings	Patients with IBD (n = 203)	Healthy Controls (n = 58)	P-value
TSH, μIU/mL, mean ± SD	2.0 ± 1.1	1.9 ± 0.9	0.944
FT4, ng/dL, mean ± SD	1.3 ± 0.9	1.2 ± 0.2	0.411
FT3, pg/mL, mean ± SD	3.2 ± 0.6	3.3 ± 0.5	0.226
Anti-TPO, IU/mL, median [IQR]	27.9 [17.3-68.8]	13.0 [8.6-17.8]	0.048
Anti-TG, IU/mL, median [IQR]	15.9 [13.9-18.5]	12.9 [10.0-18.2]	0.256
SPINA-GT, pmol/s, mean ± SD	3.8 ± 2.1	3.3 ± 1.6	0.395
Thyroid sonography examination			
Volume, cm^3, mean ± SD	12.2 ± 4.9	8.9 ± 5.2	<0.001
Echogenicity, n, (%)			<0.001
Isoechoic	74 (36.5)	44 (75.9)	
Moderately hypoechoic	114 (56.2)	13 (22.4)	
Hypoechoic	15 (7.4)	1 (1.7)	
Sonographic structure, n (%)			<0.001
Homogeneous	108 (53.2)	45 (77.6)	
Heterogeneous	95 (46.8)	13 (22.4)	
Pseudonodular hypoechoic infiltration, n (%)	29 (14.3)	8 (13.8)	0.925
Nodule, n (%)	43 (21.2)	2 (3.4)	0.002
Cyst, n (%)	26 (12.8)	8 (13.8)	0.843
AITD, n (%)	42 (20.7)	8 (13.8)	0.041

AITD, Autoimmune thyroid disease; Anti-TG, Anti-thyroglobulin; Anti-TPO, Anti-thyroid peroxidase; IBD, Inflammatory bowel disease; IQR, Interquartile range; SD, Standard deviation; FT3, Free triiodothyronine; FT4, Free thyroxine; TSH, Thyroid-stimulating hormone

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Table 3. Comparison of thyroid examination findings of patients who received biologic treatment and patients who did not in inflammatory bowel disease

Findings	**Biologic treated patients (n = 127)**	**Not biologic treated patients (n = 76)**	**p-value**
TSH, μIU/mL, mean ± SD	1.9 ± 1.0	2.2 ± 1.1	0.751
FT4, ng/dL, mean ± SD	1.4 ± 0.8	1.1 ± 0.3	0.382
FT3, pg/mL, mean ± SD	3.4 ± 0.7	3.0 ± 0.9	0.637
Anti-TPO, IU/mL, median [IQR]	17.9 [12.3-38.8]	23.0 [10.6-29.8]	0.428
Anti-TG, IU/mL, median [IQR]	13.1 [11.8-14.3]	19.4 [11.3-29.1]	0.612
SPINA-GT, pmol/s, mean ± SD	3.9 ± 2.1	3.5 ± 1.7	0.511
Thyroid sonography examination			
Volume, cm^3, mean ± SD	11.9 ± 3.8	12.6 ± 6.1	0.859
Echogenicity, n, (%)			0.038
Isoechoic	51 (40.2)	23 (30.3)	
Moderately hypoechoic	68 (53.5)	46 (60.5)	
Hypoechoic	8 (6.3)	7 (9.2)	
Sonographic structure, n (%)			0.312
Homogeneous	69 (54.3)	39 (51.3)	
Heterogeneous	58 (45.7)	37 (48.7)	
Pseudonodular hypoechoic infiltration, n (%)	17 (13.4)	12 (15.8)	0.925
Nodule, n (%)	23 (18.1)	21 (27.6)	0.119
Cyst, n (%)	13 (10.2)	13 (17.1)	0.243
AITD, n (%)	16 (12.6)	26 (34.2)	0.011

AITD, Autoimmune thyroid disease; Anti-TG, Anti-thyroglobulin; Anti-TPO, Anti-thyroid peroxidase; IQR, Interquartile range; SD, Standard deviation; FT3, Free triiodothyronine; FT4, Free thyroxine; TSH, Thyroid-stimulating hormone

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Table 4. Comparison of thyroid examination findings according to biological agent type in inflammatory bowel disease

Findings	Infliximab (n=91)	Adalimumab (n=26)	Ustekinumab (n=10)	P-value
TSH, μIU/mL, mean ± SD	2.2 ± 1.2	1.7 ± 0.9	1.8 ± 0.8	0.199
FT4, ng/dL, mean ± SD	1.4 ± 0.4	1.3 ± 0.4	1.3 ± 0.2	0.872
FT3, pg/mL, mean ± SD	3.3 ± 0.5	3.1 ± 0.7	3.4 ± 0.6	0.182
Anti-TPO, IU/mL, median [IQR]	25.9 [5.2-46.6]	27.4 [3.4-58.9]	13.4 [7.4-28.1]	0.024
Anti-TG, IU/mL, median [IQR]	14.2 [10.3-31.4]	16.7 [11.3-49.1]	11.9 [8.5-30.3]	0.675
SPINA-GT, pmol/s, mean ± SD	4.1 ± 2.1	3.5 ± 1.3	3.6 ± 1.2	0.846
Thyroid sonography examination				
Volume, cm^3, mean ± SD	12.8 ± 5.0	10.8 ± 3.5	11.1 ± 5.7	0.116
Echogenicity, n, (%)				0.022
Isoechoic	40 (43.9)	5 (19.2)	6 (60.0)	
Moderately hypoechoic	46 (50.5)	18 (69.2)	4 (40.0)	
Hypoechoic	5 (5.6)	3 (11.6)	0 (0)	
Sonographic structure, n (%)				0.037
Homogeneous	49 (53.8)	13 (50.0)	7 (70.0)	
Heterogeneous	42 (46.2)	13 (50.0)	3 (30.0)	
Pseudonodular hypoechoic infiltration, n (%)	13 (14.3)	3 (11.5)	1 (10.0)	0.087
Nodule, n (%)	15 (16.4)	6 (23.1)	2 (20.0)	0.890
Cyst, n (%)	9 (9.9)	4 (15.4)	0 (0)	0.641
AITD, n (%)	12 (13.2)	4 (15.4)	0 (0)	0.024

AITD, Autoimmune thyroid disease; Anti-TG, Anti-thyroglobulin; Anti-TPO, Anti-thyroid peroxidase; IQR, Interquartile range; SD, Standard deviation; FT3, Free triiodothyronine; FT4, Free thyroxine; TSH, Thyroid-stimulating hormone

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