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Original research article

THE LEVEL OF ANTI-TPO ANTIBODIES IN IBD PATIENTS: A CASE SERIES

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Abstract: *Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are chronic conditions characterized by intestinal inflammation. Autoimmune thyroid diseases (AITDs), such as those involving anti-thyroid peroxidase (anti-TPO) antibodies, have been noted as common comorbidities in IBD patients. Despite this, comprehensive data on anti-TPO antibodies' prevalence and clinical significance in IBD, particularly about disease type and location, remain limited.* ***Objective:*** *This study aims to determine the prevalence of anti-TPO antibodies among patients with IBD, primarily focusing on UC, and to compare these findings with the prevalence of anti-TPO antibodies in the general Iranian population.* ***Methods:*** *A cross-sectional study was conducted at Amir Alam Hospital, Tehran University of Medical Sciences, in 2022. The study included 98 patients diagnosed with IBD, using convenient sampling. Gender, age, anti-TPO levels, Free T4, and TSH were measured through questionnaires, serological tests, and imaging. Statistical analyses involved descriptive statistics, Chi-square tests, Pearson correlation coefficients, independent samples t-tests, and ANOVA, performed using SPSS software.* ***Results:*** *No significant differences were observed in anti-TPO levels between genders ($p = 0.844$). Additionally, no significant difference was found in Free T4 and TSH levels based on gender ($p = 0.396$ and $p = 0.260$, respectively). A significant correlation was identified between TSH levels and disease location ($p < 0.05$), while anti-TPO levels showed no significant correlation with disease type or location.* ***Conclusion:*** *The prevalence of anti-TPO antibodies in IBD patients was notable, with no significant differences observed between UC and CD or between genders. The study underscores the importance of regular thyroid function monitoring in IBD patients, particularly considering the significant association between TSH levels and disease location. Further research is needed to explore the underlying mechanisms and clinical implications of thyroid dysfunction in IBD.*

Keywords: Anti-TPO Antibodies, Crohn's Disease, Inflammatory Bowel Diseases, Thyroid Function, Ulcerative Colitis.

Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) are the two most prevalent forms of inflammatory bowel disease (IBD), characterized by chronic recurrent inflammation of the intestines. These conditions may arise due to environmental, genetic, and immunological factors. While CD can affect any part of the gastrointestinal tract, UC is confined to the large intestine. Microscopically, CD involves inflammation of the entire bowel wall, whereas UC is limited to the epithelial lining of the gut (1). Although the association of IBD with extraintestinal manifestations and autoimmune disorders is well documented, the coexistence of IBD and thyroid diseases, particularly autoimmune thyroid diseases (AITDs), has not been extensively studied. A recent systematic review has highlighted an increasing trend in the incidence and prevalence of IBDs globally over the past four to five decades. UC incidence rates range from 0.6 to 24.3 per 100,000 individuals in Europe, 0.1 to 6.3 in Asia and the Middle East, and 0 to 19.2 in North America. CD incidence rates range from 0.3 to 12.7 in Europe, 0.04 to 5.0 in Asia and the Middle East, and 0 to 20.2 in North America. The prevalence of UC ranges from 4.9 to 505 per 100,000 persons in Europe, 4.9 to 168.3 in Asia and the Middle East, and 37.5 to 248.6 in North America. Similarly, the prevalence of CD ranges from 0.6 to 322 per 100,000 persons in Europe, 0.88 to 67.9 in Asia and the Middle East, and 16.7 to 318.5 in North America (2).

In Iran, gender-specific assessments reveal male-to-female ratios of 1.6:1 for UC and 1.4:1 for CD, indicating a female predominance in UC and a male predominance in CD (3). Autoimmune diseases (ADs), characterized by the production of antibodies against self-antigens and the cytotoxic action of T cells, include conditions such as Graves' disease (GD), Hashimoto's thyroiditis (HT), rheumatoid arthritis (RA), type 1 diabetes mellitus (T1DM), Crohn's disease (CD), multiple sclerosis (MS), and Sjögren's disease (SD) (4). Autoimmune thyroid diseases, including GD and HT, are frequently accompanied by the presence of anti-thyroid peroxidase (TPO), anti-thyroglobulin (Tg), and anti-thyroid-stimulating hormone receptor (TSHR) antibodies. Other antibodies against thyroid antigens, such as carbonic anhydrase 2, megalin, T3 and T4, sodium iodide symporter (NIS), and pendrin, are less commonly detected (5, 6).

Epidemiological studies have demonstrated a two- to fourfold increase in the prevalence of thyroid dysfunction in UC patients compared to the general population (7). For instance, Jarnerot et al. reported a significantly higher prevalence of hyperthyroidism in UC patients compared to controls (3.7% versus 0.8%; $p < 0.01$) (8). Despite these observations, the literature on the relationship between anti-

TPO antibodies and IBD outcomes remains sparse and inconclusive.

Given the limited data, there is a pressing need for more precise and comprehensive research on the prevalence and implications of anti-TPO antibodies in IBD patients. This study aims to bridge this gap by investigating the prevalence of anti-TPO antibodies among IBD patients, particularly those with UC, referred to Amir Alam Hospital of Tehran University of Medical Sciences. Furthermore, it seeks to compare the prevalence of anti-TPO antibodies in this cohort with that of the general Iranian population.

Methodology

This cross-sectional study was conducted on patients presenting with inflammatory bowel diseases (IBD) at the gastrointestinal department of Amir Alam Hospital in 2022. The study included patients diagnosed with IBD, confirmed through preoperative diagnosis, intraoperative parameters, and pathology. Patients with undiagnosed IBD were excluded from the study. The study population comprised all IBD cases retrieved from the Amir Alam Hospital, with approximately 55% of the subjects being female. All medical workups were performed within the same department.

Convenient sampling was employed to recruit patients. All patients diagnosed with IBD who met the inclusion criteria were included, while those who did not were excluded. The variables measured in the study included gender, age, anti-thyroid peroxidase antibodies (Anti-TPO), type of disease (either ulcerative colitis or Crohn's disease), disease severity, presence of past medical disease, location of the disease, free thyroxine (FreeT4), and thyroid-stimulating hormone (TSH).

Gender was determined based on the phenotype of the patient, measured through a questionnaire with options for male and female. Age was recorded as the individual's chronological age in solar years. Anti-TPO levels, free T4, and TSH levels were measured in IU/ml using serology lab tests. The type of disease was categorized as either ulcerative colitis or Crohn's disease, diagnosed through patient history, lab findings, and imaging. Disease severity was evaluated based on the presence of alarm signs such as toxic megacolon, perianal abscesses, fistulas, and bowel obstruction, as assessed by a physician. The presence of any past medical diseases was determined based on the patient's medical history. The location of colon involvement was identified through colonoscopy.

Data were collected from 98 patients using various methods. Demographic data, including gender and age, were collected through questionnaires. Clinical presentation and physical examination data were obtained from patient records, including the type of IBD, severity, and past medical history. Serology data on Anti-TPO, FreeT4, and TSH levels were measured in the lab. Imaging and colonoscopy results provided data on the location of the disease. The Tehran University of Medical Sciences ethics committee approved the research protocol. All patients provided written informed consent before participation.

Data analysis was performed using SPSS software. Descriptive statistics were calculated for all variables. Chi-square tests and Pearson correlation coefficients were used to evaluate relationships between categorical and continuous variables. Independent samples t-tests and ANOVA were employed to compare means across groups.

Results

In total, 98 patients were included in the study, with 54 (55.1%) females and 44 (44.9%) males. (Figure 1)

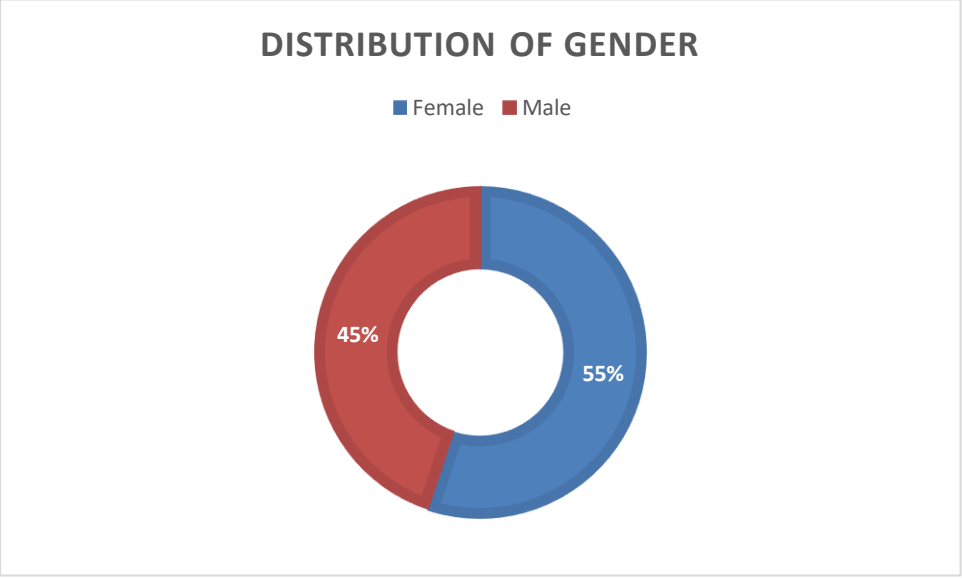

Figure 1: Distribution of gender among the study population

Among the 98 participants, 88 (89.8%) were diagnosed with ulcerative colitis, 9 (9.2%) with Crohn's disease, and one patient had missing data. The missing data for the patient was credited with the mode (most common value) of ulcerative colitis. (Table 1)

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Table 1: Type of Disease

Type of Disease	Frequency	Percent	Valid Percent
Ulcerative Colitis	89	90.8	90.8
Crohn's Disease	9	9.2	9.2
Total	98	100.0	100.0

Based on the location of the disease, pancolitis had the highest number of patients (41, 41.8%), followed by left colitis (24, 24.5%), with rectum and rectosigmoid recording the lowest (15.3% and 9.2%, respectively). The missing data was filled in using the mode pancolitis. (Table 2). A large majority (96.9%) did not have a past medical history, while a small fraction (3.1%) did.

Table 2: Location of Disease

Location of Disease	Frequency	Percent	Valid Percent
Left Colitis	24	24.5	24.5
Pancolitis	50	51.0	51.0
Rectum	15	15.3	15.3
Rectosigmoid	9	9.2	9.2
Total	98	100.0	100.0

Table 3 presents the descriptive statistics for age, anti-TPO, TSH, and Free T4 levels among the study participants. The mean age was 41.98 years, with a mean anti-TPO level of 57.47, a mean TSH of 2.40, and a mean Free T4 of 3.59.

Table 3: Descriptive Statistics of TSH, Anti-TPO, and Free T4

Variable	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	98	93	18	111	41.98	14.697
Level of Anti TPO	98	848	1	849	57.47	128.975
TSH	98	9	0	9	2.40	2.015
Free T4	98	213	1	214	3.59	21.754

Table 4: Comparison of Past Medical History by Gender

Past Medical History	Males	Females	Total	p-value
No	43	52	95	0.683
Yes	1	2	3	-
Total	44	54	98	-

Table 5 compares the types of diseases by gender. There was no significant relationship between the kind of disease and gender (p = 0.954).

Table 5: Comparison of Type of Disease by Gender

Type of Disease	Males	Females	Total	p-value
Ulcerative Colitis	40	49	89	0.954
Crohn's Disease	4	5	9	-
Total	44	54	98	-

Table 6 compares the location of the disease by gender. There was no significant relationship between gender and the location of the disease (p = 0.580).

Table 6: Comparison of Location of Disease by Gender

Location of Disease	Males	Females	Total	p-value
Left Colitis	13	11	24	0.580
Pancolitis	20	30	50	-
Rectum	6	9	15	-
Rectosigmoid	5	4	9	-
Total	44	54	98	-

Table 7 shows the ANOVA results for age, Anti-TPO, Free T4, and TSH by gender. No significant relationships were found between these variables and gender.

Table 7: ANOVA for Age, Anti-TPO, Free T4, and TSH by Gender

Variable	Sum of Squares	df	Mean Square	F	Sig.	p-value
Age	57.580	1	57.580	0.340	0.561	0.561
Level of Anti TPO	652.666	1	652.666	0.039	0.844	0.844
Free T4	345.144	1	345.144	0.727	0.396	0.396
TSH	5.192	1	5.192	1.283	0.260	0.260

Table 8 shows the ANOVA results for the location of disease, Anti-TPO, Free T4, and TSH. A significant relationship was found between the location of the disease and TSH levels (p = 0.026).

Table 8: ANOVA for Location of Disease, Anti-TPO, Free T4, and TSH

Variable	Sum of Squares	df	Mean Square	F	Sig.	p-value
Level of Anti TPO	71053.296	3	23684.432	1.577	0.201	0.201
Free T4	543.854	3	181.285	0.339	0.797	0.797
TSH	36.842	3	12.281	3.240	0.026	0.026

Table 9: Independent T-Test for Gender and Levels of Anti-TPO, Free T4, and TSH

Variable	Gender	N	Mean	Std. Deviation	Std. Error Mean	p-value
Level of Anti TPO	Males	43	60.37	125.810	19.186	0.844
	Females	55	57.47	128.975	17.387	-
Free T4	Males	43	1.48	2.067	0.315	0.396
	Females	55	3.59	21.754	2.931	-
TSH	Males	43	2.14	1.853	0.283	0.260
	Females	55	2.61	2.132	0.287	-

Table 9 shows the independent t-test results for gender and Anti-TPO, Free T4, and TSH levels. No significant differences were found between gender and Anti-TPO levels (p = 0.844), Free T4 levels (p = 0.396), and TSH levels (p = 0.260). A Pearson correlation coefficient was performed to evaluate the relationship between anti-TPO

and the type of disease. The result indicated that the relationship was not significant.

Discussion

The results of this study provide insights into the prevalence and clinical implications of anti-TPO antibodies among patients with inflammatory bowel diseases (IBD), particularly ulcerative colitis (UC) and Crohn's disease (CD). Our findings revealed no significant gender differences in anti-TPO, Free T4, and TSH levels among the study participants. Additionally, an important relationship was observed between the location of the disease and TSH levels. In contrast, no significant correlations were found between anti-TPO levels and the type or location of the disease. The prevalence of thyroid dysfunction among IBD patients has been a subject of interest in recent studies. Our findings align with those of a survey by Cañas et al. (2017), which reported that thyroid disorders are relatively common in patients with IBD, with no significant difference in the prevalence between UC and CD patients (9). This suggests that the presence of thyroid dysfunction is a common comorbidity in IBD, regardless of the specific type of bowel disease. In contrast, a study by Viget et al. (2018) found a higher prevalence of thyroid disorders in UC patients than in CD patients, highlighting the need for regular thyroid function monitoring in UC patients (10). Our study, however, did not find a significant difference in anti-TPO levels between UC and CD patients, which may be due to variations in study populations and methodologies.

The significant relationship between TSH levels and the location of the disease in our study is a novel finding. Previous studies have not extensively explored this aspect. A possible explanation could be the varying degrees of inflammation and its systemic effects on thyroid function depending on the extent and location of bowel involvement. Future research should aim to elucidate the mechanisms underlying this association.

Our study also contributes to the growing body of literature on the prevalence of autoimmune thyroid diseases (AITDs) in IBD patients. Recent studies, such as the one by Witek et al. (2018), have reported a higher prevalence of AITDs in IBD patients compared to the general population, with anti-TPO antibodies being a common marker (11). This supports our findings of a notable prevalence of anti-TPO antibodies among IBD patients.

Furthermore, the absence of significant gender differences in anti-TPO, Free T4, and TSH levels in our study aligns with the findings of a survey by Triantafillidis et al. (2019), which reported no significant gender-based differences in the prevalence of thyroid dysfunction among IBD patients (12). This suggests that gender may not be a major determinant of thyroid dysfunction risk in the context of IBD.

However, it is important to consider our study's limitations. The cross-sectional design limits the ability to infer causality, and the relatively small sample size may affect the generalizability of the findings. The study population was also limited to a single hospital, which may not fully represent the broader IBD patient population.

In conclusion, our study highlights the need for regular thyroid function monitoring in IBD patients, given the significant prevalence of thyroid dysfunction and the observed association between TSH levels and disease location. Future research should explore the underlying mechanisms of this association and the potential clinical implications of thyroid dysfunction in managing IBD. Enhanced understanding of these relationships could inform better diagnostic and therapeutic strategies, ultimately improving patient outcomes.

Conclusion

According to our results, the presence of anti-TPO antibodies was not significantly associated with IBD patients. However, we found some significant correlations between some parameters, including the propensity of UC in the female populations and the presence of relatively higher levels of anti-TPO antibodies in IBD patients with a past medical history.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
Approved by the department concerned.
Consent for publication
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Conflict of interest

The authors declared an absence of conflict of interest.

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