

Thyroid Disorders in Patients with Inflammatory Bowel Diseases

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ABSTRACT

Background: The rate of thyroid disorders is reported to be increased in patients with Ulcerative Colitis (UC) and Crohn's disease (CD) than the normal population. The purpose of this study is to evaluate the prevalence of Thyroid disorders in a group of patients with inflammatory bowel diseases (IBD). **Material and Methods:** 146 IBD patients (113 UC and 33 CD patients) and 66 healthy control subjects were enrolled into the study. Serum free T4 (FT4), free T3 (FT3), TSH and anti TPO levels of the patients were analyzed retrospectively and compared with a control group. These cases were also investigated with thyroid ultrasound and nuclear (scintigraphy) imaging. **Results:** The mean age of IBD patients (76 women) was 42.9 ± 12.4 years. Among the control group 42 were female and their mean age was 40.9 ± 12.1 years. Thyroid gland disease was found in 14 (9.5%, 8 female, 6 male) of 146 IBD patients. The frequency of thyroid disorders has been found to be higher than the control group in patients with control group (14/146 vs. 1/66, $p = 0.042$). No statistically significant difference has been observed at the thyroid disorder rates between the UC and CD patients (11/113 vs. 3/33, $p = 0.912$). Hashimoto thyroiditis has been found at 4 (2.7%) of the IBD patients. **Conclusion:** In accordance with several works published in literature, we have found a higher rate of thyroid disease appearance at IBD patients.

Keywords: Ulcerative Colitis, Crohn's Disease, Thyroid Disorders

1. Introduction

Inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD) are diseases that is caused by dysregulation of immune system in patients with genetic predisposition and characterized by chronic inflammation with relapse and remission periods. Ulcerative colitis and CD are associated with a wide range of extraintestinal complications that influence the course and therapy of the disease. Although extraintestinal complications of IBD including rheumatologic, ocular, dermatologic and hepatobiliary complications are well understood, the data regarding the relationship between IBD and thyroid disorders are not completely established [1-3]. Epidemiological investigations showed an increased prevalence of hyperthyroidism and IBD. In previous studies, the relationship between UC and thyroid diseases is well established. The rate of thyroid diseases is reported to be higher in UC and CD patients compared to normal population [3-5]. The incidence of thyrotoxicosis is reported as 0.8% - 3.7% in UC patients [2,3,6-8]. However, the rate of thyroid diseases in CD patients has been

considered in less number of studies than that of UC patients. The aim of this study was to evaluate the prevalence of thyroid disorders in patients with UC and CD.

2. Material and Methods

In this retrospective study, a total of 146 patients diagnosed as having inflammatory bowel diseases (113 UC, 33 CD) were enrolled into the study. All patients had the diagnosis of IBD according to clinical, laboratory, endoscopic and histopathological findings. Medical records of all patients were investigated for their demographic profiles, types of IBD, disease and localisation, and laboratory parameters especially including serum free T4, free T3, TSH and antiTPO levels. Patients were analyzed retrospectively in terms of age, gender, UC or CD localisation. Disease localisation was considered as proctite, left-sided colon involvement, extensive type and pancolitis in UC patients and ileal involvement, colon involvement and ileocolonic involvement in CD patients. Serum free T4 (FT4), free T3 (FT3), TSH and anti TPO levels of both the patients and the control group were

analyzed. Patients and control group were diagnosed as having hyperthyroidism, hypothyroidism, subclinical hyperthyroidism, subclinical hypothyroidism and autoimmune thyroiditis based on their thyroid hormone profile and TSH levels, and antithyroid antibody-positivity. These cases were also investigated with thyroid ultrasound and nuclear (scintigraphy) imaging. Serum free T4 (FT4), free T3 (FT3), TSH and anti TPO levels were determined by using radioimmunoassay method. The normal ranges for hormone levels were as follows: TSH: 0.34 - 5.6 micro IU/ml FT4: 7 - 16 pikomol/L, FT3: 7-16 pikomol/L and anti-TPO: 0 - 9 IU/ml.

Data were analyzed with the Statistical Package for Social Sciences (SPSS; version 11.0; SPSS Inc. Chicago, IL) for Windows software. For statistical comparison the Fisher's exact test were used whenever appropriate. Student's t-test was used to compare quantitative variables. Results were expressed a mean \pm SD and percentages. A value of $p < 0.05$ was regarded as significant.

3. Results

Patients' demographic characteristics and disease localisation are shown in **Tables 1** and **2**. The mean age of IBD patients was 42.9 ± 12.4 years. No statistically difference has been observed between the mean ages ($p = 0.357$) and gender distribution ($p = 0.136$) of patients and control group. Patients and control group's thyroid hor-

mon profiles and antibody levels are shown in **Table 3**. When mean FT3 FT4 and TSH levels are taken into consideration, no significant difference was observed between the IBD patients and the control group.

Thyroid gland disease was found in 14 (11 UC, 3 CD) of 146 IBD patients. Number and rates of thyroid diseases found in IBD, UC and CD patients were listed in **Table 4**. The frequency of appearance of thyroid disease has been found to be higher in IBD patients compared to control group (14/146 vs. 1/66, $p = 0.042$). Five patients had hyperthyroidism and 2 patients had subclinical hyperthyroidism in patients with UC (5/113, 4.4% and 2/113, 1.7%). As for CD patients, 3 patients were diagnosed as having subclinical hyperthyroidism. No statistically meaningful difference has been observed in the thyroid disorder rates between the CD and UC patients (11/113 vs. 3/33, $p = 0.912$). Hashimoto thyroiditis has been found in 4 (2.7%) of the IBD patients and all of them were UC patients. One of the four patients identified with Hashimoto thyroiditis had hypothyroidism and thyroid hormone treatment was started. Another patient with Hashimoto thyroiditis had rheumatoid arthritis as well. One individual in the control group who was identified as having thyroid disorder had Hashimoto thyroiditis. The frequency of Hashimoto thyroiditis was similar in IBD patients and in the control group (2.7% vs. 1.5%, $p = 0.596$).

Table 1. Baseline characteristics of patients.

Variables	IBD Patients	UC Patients	CD Patients	Control Group
<i>n</i> (%)	<i>n</i> = 146	<i>n</i> = 113 (77.3%)	<i>n</i> = 33 (22.6%)	<i>n</i> = 66
Age (years)	42.9 \pm 12.4	43.6 \pm 11.5	41.9 \pm 13,	40.9 \pm 12.1
Sex	70 male 76 female	50 male 63 female	20 male 13 female	24 male 42 female

Table 2. Distribution of the patients.

	Crohn's Disease (<i>n</i> = 33)	Ulcerative Colitis (<i>n</i> = 113)
Location	Terminal Ileum (62%)	Distal UC (28.2%)
	Colon (0%)	Left-sided UC (44.7%)
	Ileocolon (38%)	Extensive UC (12.9%)
	Upper GI (0%)	Pancolitis (14.1%)

Table 3. Patients and control group's thyroid hormone profiles and antithyroid antibody levels.

	Free T3 (picomol/L)	Free T4 (picomol/L)	TSH (micro IU/ml)	Anti TPO (IU/ml)
IBD	4.4 \pm 1.27	14.4 \pm 4.01	2.1 \pm 3.6	14.1 \pm 29.1
UC	4.5 \pm 1.42	14.3 \pm 4.015	1.8 \pm 2.13	14.2 \pm 30.25
CD	4.3 \pm 0.89	14.46 \pm 3.81	2.7 \pm 5.59	14.07 \pm 28.35
Control Group	4.8 \pm 0.85	15.04 \pm 2.9	4 \pm 15.3	22.4 \pm 82.6

Table 4. The rate of thyroid disease in IBD patients.

	IBD (n = 146)	UC (n = 113)	CD (n = 33)	Control Group (n = 66)
Thyroid Disease	14 (9.5%)	11 (9.7%)	3 (9.0%)	1 (1.5%)
Hyperthyroidism	5 (3.4%)	5 (4.4%)	0 (0%)	0 (0%)
Hypothyroidism	1 (0.06 %)*	0 (0%)	0 (0%)	0 (0%)
Subclinical Hypothyroidism	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Subclinical Hyperthyroidism	5 (3.4%)	2 (1.7%)	3 (9.0%)	0 (0%)
Thyroiditis	4 (2.7%)	4 (3.5%)	0 (0%)	1 (1.5%)

4. Discussion

In the present study, 146 patients with IBD, among which 113 were UC and 33 were CD, were evaluated. It has been observed that thyroid disease occurrence rate is higher than that of the control group (9.5% vs 1.5%). Thyroid disorders were observed in 9.7% of the patients with UC and in 9.0% of the patients with CD. The incidence of hyperthyroidism and subclinical hyperthyroidism was found to be higher in IBD patients compared to the control group. However, hypothyroidism and thyroiditis frequencies were similar to that of the control group (2.7% vs. 1.5%, $p = 0.596$). However, no significant difference has been observed in patients with UC compared to patients with CD patients.

In some studies, occurrence of thyroid disorders in IBD patients is reported to be at similar frequencies compared to normal population. In a population based study performed in Canada in which 8,072 IBD patients were evaluated, thyroiditis rate was 0.23% in UC patients and 0.19% in CD patients (versus 0.15% - 0.20% in controls). In this study thyroid disease frequency is found to be similar to that of normal population [9]. In a study performed in our country in which 25 ulcerative colitis patients were evaluated, thyroid disease frequency is reported to be similar to that of control group [10]. In a study performed in Italy, in which 162 UC patients were evaluated thyroid disorders (hyper- and hypothyroidism) are reported at the rate of 2.5%. In the same geographic region, the rate has been reported as 7.5% in normal population [6]. In a recent study performed in Italy in which 909 IBD patients are evaluated thyroid disorder rates are reported as 6.6% in all IBD patients, 6.89% in CD patients and 6.29% in UC patients. In this study Hashimoto thyroiditis rates are reported as 1.98% in all IBD patients, 2.15% in CD patients and 1.8% in UC patients. As a result of this study it has been concluded that thyroid disorder rate is twice in IBD patients than that in healthy European population [3]. Subclinical hyperthyroidism also has been reported in patients with ulcerative colitis [11]. Though in most studies thyroid disorders are

associated with only UC, in a limited number of cases thyroid diseases has been reported also in patients with CD [12,13]. In some studies $tT4$ level is reported to decrease in CD patients. Also in these studies it has been shown that frequency of antithyroglobulin and antithyroid microsomal/peroxidase antibodies increases in IBD patients [13,14]. It is reported that making laboratory tests for hyperthyroidism in patients with ulcerative colitis is necessary [15,16].

Some of the advantages and shortcomings of this study can be listed as follows: in the present study CD patients, which are studied less in the literature, as well are evaluated together with UC patients. The rates of thyroid diseases observed in IBD patients are classified according to thyroid disease groups (thyroiditis, hyper- thyroidism, hypothyroidism, subclinical hyperthyroidism, subclinical hypothyroidism). Number of patients is large enough in this field and comparisons are made with a control group. The weakness of the study is that, this was a retrospective study and population based evaluation has not been performed.

In conclusion, although the thyroid disease prevalence in IBD patients is reported to be similar to that in normal population in some studies, we have found an increased rate of thyroid diseases in IBD patients in accordance with most of the studies. It is necessary to make laboratory tests for hyperthyroidism in patients with ulcerative colitis in which treatment-resistant and/or enlarged thyroid gland is observed. Early diagnosis of thyroid diseases is important because thyroid diseases may worsen the course and symptoms of IBH.

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