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İnflamatuar Bağırsak Hastalarında Tiroid Bozukluklarının Değerlendirilmesi

Assessment of Thyroid Disorders in Patients with Inflammatory Bowel Diseases

Eda Demir Önal[1], Zeki Islamoğlu[2], Ayça Eroğlu Haktanır[2], Gökhan Dindar[2]

[1] Kocaeli Şehir Hastanesi, Endokrinoloji Bölümü, Kocaeli, Türkiye.

[2] Kocaeli Şehir Hastanesi, Gastroenteroloji Bölümü, Kocaeli, Türkiye.

ÖZ

Giriş: Tiroid hastalığı ve inflamatuar bağırsak hastalığı (İBH) arasında bir ilişki olup olmadığına dair soru henüz cevaplanmamıştır. Bu çalışmada, İBH sı olan bireylerde tiroid hastalığının sıklığını araştırmayı hedefledik.

Yöntem: Otuz beş İBH (23 ülseratif kolit; 12 Crohn hastası) hastası ve 48 sağlıklı kontrol çalışmaya dahil edildi. Hastaların serum serbest T4, serbest T3, tiroid stimulan hormon, anti tiroglobulin, anti tiroid peroksidaz seviyeleri ve tiroid USG leri geriye dönük analiz edildi ve kontrol grubu ile karşılaştırıldı.

Bulgular: İBH hastalarının ortalama yaşı (14 kadın) 40.5±12.6 yıldı. Kontrol grubunda 20 kadın vardı ve ortalama yaşları 39,2±13.4 yıldı ($P > 0.05$). Tiroid hastalığı açısından (otoimmün tiroidit ve guatr dahil olmak üzere), İBH hastaları (% 42.8) ve kontroller (% 37.5) benzerdi ($P = 0.655$). Subklinik hipotiroidi ve guatrı olan iki kontrol vakası dışında hasta ve kontrol grubunda tiroid fonksiyon anormalliği saptanmadı. Tiroid hormon profilleri, tiroid otoantikor pozitiflik sıklıkları ve tiroid volüm ölçümleri açısından hastalar ve kontroller arasında anlamlı fark saptanmadı ($P > 0.05$). İBH hastalarının % 14.2'si ve kontrollerin % 16.7'sinde otoimmün tiroidit vardı ($P=1$).

Sonuç: Tiroid bozuklukları İBH hastalarında daha yüksek prevalans göstermemektedir. İBH hastalarında tiroid bozukluklarına dair standard yaklaşımın ötesinde ek tetkik ve taramaya ihtiyaç görünmemektedir.

Anahtar Kelimeler: otoimmün tiroidit, crohn hastalığı, guatr, inflamatuar bağırsak hastalığı, ülseratif kolit

ABSTRACT

Objective: The question whether there is a link between thyroid disease and inflammatory bowel diseases (IBD) is still to be answered. In this study, we aimed to investigate the frequency of thyroid disease in patients with IBD.

Method: Thirty-five IBD (23 ulcerative colitis; 12 Crohn's disease) patients and 48 healthy control subjects were recruited into the study. Serum free T4, free T3, thyroid stimulating hormone, anti thyroglobulin, anti thyroid peroxidase levels and thyroid USG of the patients were analyzed retrospectively and compared with a control group.

Results: The mean age of IBD patients (14 women) was 40.5±12.6 years. Among the control group 20 were female and their mean age was 39.2±13.4 years ($P > 0.05$). In terms of the frequency of thyroid disorder (including autoimmune thyroiditis and goiter), IBD patients (42.8 %) and controls (37.5 %) were similar ($P = 0.655$). Except for two control cases with subclinical hypothyroidism and goiter, no thyroid function abnormality was determined in patient and control groups. No significant differences were found between the patients and controls with respect to thyroid hormone profiles, the frequency of thyroid antibody positivity and thyroid volume measurements ($P > 0.05$). 14.2 % of IBD patients and 16.7 % of controls had autoimmune thyroiditis ($P=1$).

Conclusion: Thyroid disorders are not more prevalent in patients with IBD. Regarding thyroid disorders in IBD patients, there does not seem to be a need for additional examinations and screenings other than the standard approach.

Keywords: autoimmune thyroiditis, crohn's disease, goiter, inflammatory bowel diseases, ulcerative colitis

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Correspondence: Doç. Dr. Eda Demir Önal, Kocaeli Şehir Hastanesi, Endokrinoloji Bölümü, Kocaeli, Türkiye. **E-mail:** dredademir@gmail.com

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INTRODUCTION

Inflammatory bowel diseases (IBD) are chronic inflammatory conditions of the gastrointestinal tract and include two main types: Crohn's disease (CD) and ulcerative colitis (UC). Etiology is not clear but it is suggested that environmental factors, immunological alterations, intestinal flora and genetic predisposition play role in the pathogenesis (1-3). In patients with IBD, various organ systems other than the gastrointestinal tract may be affected, such as the musculoskeletal, dermatologic, hepatobiliary, ocular, renal, and pulmonary systems (4). There is a relation between these extraintestinal manifestations (EIMs) and immune responses from the intestine during the IBD course and EIMs and IBD may have a common environmental or genetic predisposition (4).

Although above mentioned EIMs are well defined with respect to their frequency, course, association with IBD activity and their management, the question whether there is a link between thyroid disease and IBD is still to be answered because previous studies about the subject provide conflicting results (5-9). In this study, we aimed to investigate the frequency of thyroid disease in patients with IBD.

MATERIALS AND METHODS

The study group included a total of 35 patients with IBD (12 CD, 23 UC) who were recruited in a retrospective manner from april 2023 to october 2023 and age and sex matched 48 controls. IBD was diagnosed after the detection of relevant clinical, laboratory, endoscopic and imaging findings. The following clinical and demographic characteristics were noted: Age, sex, IBD subtype, duration, activity and extent of the disease and medication. The severity of CD was determined by Crohn's disease activity (CDAI) index (10) whereas simple clinical colitis activity index (SCCAI) was used to grade activity in patients with UC (11). CDAI < 150 and SCCAI < 5 were remission criteria for CD and UC respectively. Activity indices (hemogram, C-reactive protein) and thyroid parameters (Serum free T4 (FT4), free T3 (FT3), thyroid stimulating hormone (TSH), thyroid peroxidase (Anti TPO) and thyroglobulin antibodies (Anti TG) levels) were analyzed as the laboratory tests.

Thyroid gland was evaluated by ultrasonography (USG) in supine position with the patient's neck hyper-extended using a linear transducer (Hitachi). All of the sonographic examinations were performed by the same investigator who had more than 10 years of experience in thyroid USG. Measurements of thyroid lobes in three dimensions and thickness of thyroid isthmus, echogenicity (compared tos trap muscles) and vascularization of the thyroid parenchyma and possible lesions including nodules were all noted. A significant reduction of thyroid echogenicity was defined as a hypoechoic pattern of thyroid gland in comparison to submandibular gland and neck muscles. A slight reduction in thyroid echogenicity was defined as hypoechoic thyroid parenchymal pattern in comparison to submandibular gland.

According to laboratory thyroid parameters and thyroid USG, patients and controls were categorized as follows: no thyroid disease, hyperthyroidism, hypothyroidism, subclinical hyperthyroidism, subclinical hypothyroidism, autoimmune thyroiditis and goiter (diffuse or nodular). Autoimmune thyroiditis was diagnosed by the presence of the relevant sonographic findings and positive antibody tests (12, 13). The normal ranges for hormone levels and antibodies were as follows: TSH: 0.27-4.2 mIU/L, fT4: 0.8-1.76 ng/dL, fT3: 2-4.4 pg/mL, Anti TPO: 0 - 34 U/mL and Anti TG: 0-115 U/mL. The patient was noted to have thyroid antibody positivity when at least one of Anti TPO and Anti TG level was elevated more than upper limit of range. Thyroid gland volume was calculated based on sonographic measurements according to the previously defined formula (14). The limits of normal thyroid volume (excluding isthmus, unless its thickness is >3 mm) were 10-15 ml for females and 12-18 ml for males.

Data were analyzed with the Statistical Package for Social Sciences (SPSS; version 27.0; SPSS Inc. Chicago, IL) for Windows software. Continous data were expressed as mean ± SD. Categorical variables were provided as percentages. Means were compared using independent sample t-test in normally distributed data. The comparison of the nonnormally distributed data was done by using the Mann–Whitney U test while chi square and Fisher's exact test were used for categorical variables. A value of $p < 0.05$ was regarded as significant.

The study was carried out in accordance with Helsinki Declaration and approved by Kocaeli City Hospital Ethics Committee (Date 26/10/2023 No 2023-6).

RESULTS

The demographic characteristics were similar between the patients with IBD and controls ($P > 0.05$) (Table 1). IBD related parameters were presented in Table 2. Accordingly, all patients with CD had ileal involvement and most of them (83.3 %) were under immunosuppressive therapy whereas only two patients with UC (8.7 %) had azathioprine. Most of the patients (CD: 75 % and UC: 91.3 %) were in remission. Thyroid hormone profiles, the frequency of thyroid antibody positivity and thyroid volume measurements are demonstrated in Table 3 and no significant differences were found between the patients and controls with respect to these parameters. Except for two control cases with subclinical hypothyroidism and goiter, no thyroid function abnormality was determined in patient and control groups. In terms of the frequency of thyroid disorder (including autoimmune thyroiditis and goiter), patient group (42.8 %) and control group (37.5 %) were similar ($P > 0.05$) (Table 4).

Table 1. Comparison of Demographic Characteristics Between Patient and Control Groups.

Parameter	IBD	CD	UC	Control	P value
n (%)	35	12 (34.2)	23 (65.8)	48	
Age (years) mean±SD	40.5±12.6	40.6±11.5	40.5±13.4	39.2±13.4	0.09
Sex (%)	21 male (60) 14 female (40)	9 male (75) 3 female (25)	12 male (52.2) 11 female (47.8)	28 male (58.3) 20 female (41.7)	0.423

IBD: Inflammatory Bowel Disease, CD: Crohn's Disease, UC: Ulcerative Colitis, P < 0.05 significant

Table 2. The Detailed Characteristics of the Patients with Inflammatory Bowel Disease.

Parameter	Crohn's Disease n (%) n=12	Ulcerative Colitis n (%) n=23
Site of involvement	Ileitis 8 (66.7) Ileocolitis 4 (33.3)	Proctitis 8 (34.8) Left sided colitis 8 (34.8) Extensive colitis 7 (30.4)
Duration (months) mean±SD	76.9±48.5	48.8±56.7
Medication	Mesalamine only 2 (16.7) Mesalamine and Azatihoprine 3 (25) Azathioprine only 4 (33.3) Azathioprine and Anti TNF 1 (8.3) Methotrexate 2 (16.7)	Mesalamine only 21 (91.3) Mesalamine and Azatihoprine 2 (8.7)
Disease activity	Active 3 (25) Remission 9 (75)	Active 2 (8.7) Remission 21 (91.3)

Table 3. Comparison of Thyroid function Tests, Thyroid Antibody Positivity and Thyroid Volume Between the Patients with Inflammatory Bowel Disease and Controls.

Parameter	Free T3 (pg/mL)	Free T4 (ng/dL)	TSH (mIU/L)	Thyroid Antibody Positivity* n (%)	Thyroid Volume (ml)
IBD	3.1±0.7	1.3±0.2	1.4±0.9	4 (11)	13.5±5.7
CD	3.2±0.4	1.3±1.3	1.2±0.7	3 (25)	11.4±10.1
UC	3±0.8	1.2±1.6	1.6±0.9	1 (4.3)	12.7±7.2
Control	2.8±0.4	1±0.3	1.6±0.9	7 (14.6)	14.4±2.8
P	0.103	0.06	0.322	0.212	0.203

*Positivity of anti thyroid peroxidase and/or anti thyroglobulin antibodies
IBD: Inflammatory Bowel Disease, CD: Crohn's Disease, UC: Ulcerative Colitis
All values expressed as mean±SD.P < 0.05 significant

DISCUSSION

This study demonstrated that there was no significantly obvious difference in the prevalence of thyroid disease between IBD patients and general population. According to our findings thyroid disorders cannot be included within the extraintestinal manifestations of IBD or no specific assocation between IBD and thyroid disease can be speculated.

IBD is an immune mediated chronic inflammatory disorder. It is proposed that enteric bacteria trigger an abnormal immune response in genetically susceptible individuals (15). Immune-mediated pathological conditions can occur together, and the presence of one may increase the risk of the other. EIMs are frequently encountered in IBD (30 %) and may cause debilitating symptoms and decrease in quality of life (16). Additionally there has been some evidence that autoimmune diseases may accompany IBD (17). Immunosuppressive IBD medications may trigger autoimmune diseases as in the example of Anti TNF drugs and multiple sclerosis as well as potentially affecting the course of coexisting immune-mediated diseases (18). Autoimmune thyroiditis (AT) is an autoimmune mediated destruction of the thyroid gland. Several studies investigated the prevalence of AT in IBD and reported as 0.07-4.4 % (19,20). A large population-based study including 8072 IBD patients showed that the rate of AT was not significantly different between IBD patients and the controls (21). Although we observed a higher rate of AT in our series when compared to the literature data, patient (14.2 %) and control groups (16.7 %) were similar in this regard (P=1). Additionally we did not observe any thyroid dysfunction in this subgroup of patients. Higher prevalence of AT in our study may have been caused by our relatively small sample size.

Thyroid hormone is an essential mediator for the organism. On the other hand it is subject to tight regulation because its excess or deficiency might result in derangement of homeostasis. In thyroid disease the results of relevant metabolic alterations may be more pronounced in patiens with comorbid conditions e.g. IBD. From this point of view, to answer the question whether there is an association or coexistence between IBD and thyroid disorders becomes important. In IBD patients, the reported rates of hyperthyroidism and hypothyroidism ranged from 0 to 3.7 % and from 0 to 3.8 % respectively and were similar to the rates of general population (5). In parallel with these data, none of our IBD patients had thyroid dysfunction. In our study, almost half of IBD patients (42.8 %) had thyroid disorder. This rate seems to be very high when it is considered that Cesarini et al documented a total rate of 6.6 % (6). The difference may be explained by the geographical variations in goiter prevalence. Endemic goiter is an important public health problem in Turkey and goiter prevalence ranged between 5 and 56% in several cities (22). For this reason the thyroid disorder (37.5 %) and goiter (25 %) rates were also high in our control group and our patient and control groups were similar with respect to these two entities. An advantage of our study is that thyroid USG was performed by a single and experienced operator and thyroid volume was rigorously calculated based on dimensional measurements. Volumetric analysis (Table 3) also supported the fact that thyroid size is similar IBD patients and controls.

Our study has several shortcomings that it is retrospective in nature and sample size is relatively small. Prospective design with a long follow up period and involvement of more patients with immunsuppressive therapy especially Anti TNF drugs could have enabled us to observe the effect of these drugs on thyroid function and autoimmunity.

CONCLUSIONS

Thyroid disorders are not more prevalent in patients with IBD. Regarding thyroid disorders in IBD patients, there does not seem to be a need for additional examinations and screenings other than the standard approach.

Ethics Committee Approval: Kocaeli City Hospital Ethics Committee (Date 26/ 10/ 2023 No 2023-6)

Author Contributions: EDÖ designed the study. EDÖ, Zİ, AEH and GD collected data. EDÖ and Zİ performed the data analysis and interpreted the analyses. AEH and GD reviewed the literature. EDÖ, Zİ, AEH and GD critically reviewed the article and made critical revisions. All authors have read and approved the final version of the article.

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