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Features of Endoscopic Findings In Patients With Hypothyroidism Secondary To Hashimoto Thyroiditis

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ABSTRACT

The most common cause of hypothyroidism is Hashimoto's disease, Hypothyroidism slows down all metabolic events. Therefore, it has a motility-reducing effect on the intestine. In our study, we aimed to examine the differences between hypothyroid patients and the healthy control group who underwent upper-gastrointestinal system endoscopy for dyspeptic complaints.

Demographic data, drug, smoking and alcohol use, endoscopic, histological findings, data on TSH levels were documented. Data were analyzed statistically. Values with $p>0.05$ were considered significant. Endoscopic findings were compared between patients and control group. In addition, the effect of disease severity on mucosa was investigated.

61 hypothyroid patients, 50 non-hypothyroid patients with functional-dyspepsia, were included in the study. Alkaline reflux and gluten enteropathy were found with a significantly higher rate in hypothyroid patients. Alkaline reflux and gluten enteropathy were found with a significantly higher rate in the group with TSH level higher than 10 mIU/L. Atrophic gastritis was observed with a higher rate in the hypothyroid patient group and the group with high TSH, but it was not statistically significant. There was no difference between the groups in terms of other endoscopic findings.

Hashimoto's thyroiditis is a common autoimmune phenomenon. It is closely associated with other autoimmune events. Since hypothyroidism slows down the metabolic rate, the intestinal passage time is prolonged. As a result, alkaline reflux occurs in patients. However, the results we found need to be supported by prospective studies conducted with larger patient groups.

Keywords: Hypothyroidism; endoscopy; motility

Introduction

Although thyroid diseases are common in the community, hypothyroidism is the most common thyroid hormone disorder. Its prevalence in populations without iodine deficiency is reported to be approximately 2-3%, and it is seen 10 times higher in women than in men. The most common cause of hypothyroidism is Hashimoto's thyroiditis, which is chronic lymphocytic thyroiditis (1-3).

Thyroid dysfunctions affect the gastrointestinal system. In hypothyroidism, all metabolic events slow down, as well as intestinal motility, in hyperthyroidism on the contrary intestinal motility accelerates. Therefore, diarrhea and constipation are common symptoms in thyroid dysfunction (4,5). In studies examining the relationship between intestinal motility and thyroid dysfunction, it has been shown that the intestinal passage time is long mostly in patients with hypothyroidism (6,7). It has been reported that there is bacterial overgrowth in the small intestine secondary to slowing motility and symptoms develop accordingly (8,9). Regardless of the effect of thyroid dysfunction on motility, the presence of accompanying autoimmune diseases also affects the gastrointestinal system. In studies conducted, especially gluten enteropathy and atrophic gastritis are frequently seen together with autoimmune thyroiditis (6,7). In addition, it has been reported that many diseases such as inflammatory bowel diseases, primary biliary cirrhosis and sclerosing

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cholangitis are significantly associated with hypothyroidism (8-11).

Although there are many studies in terms of motility disorders and other accompanying autoimmune diseases in patients with hypothyroidism, it is seen that other endoscopic findings except atrophic gastritis and gluten enteropathy have not been adequately examined. Therefore, in our study, we aimed to examine the differences between hypothyroid patients who underwent upper gastrointestinal system (GIS) endoscopy due to dyspeptic complaints and patients diagnosed with functional dyspepsia without hypothyroidism.

Materials and Methods

Study Design: Following a diagnosis of hypothyroidism from our internal diseases outpatient clinic between January 2018 and June 2020, 61 hypothyroid patients who had dyspeptic complaints and were examined by endoscopy for upper GIS and 50 functional dyspepsia patients without hypothyroidism were included as the control group. Our study was designed retrospectively. Pregnant women, patients who underwent organ transplantation (liver, kidney, bone marrow), those with chronic liver disease and chronic kidney disease, and those who had an operation related to GIS were not included in the study. Data on demographic characteristics (age, gender), treatments (non-steroidal anti-inflammatory drugs, steroids, acetylsalicylic acid), smoking and alcohol use were documented. Attention was paid to the equal distribution of factors that could affect the gastrointestinal system, such as cigarette, alcohol, drugs taken and demographic characteristics. Celiac disease was diagnosed as a result of the histopathological examination of the tissue sample (duodenum), which was positive for Tissue Transglutaminase Antibody in case of clinical or laboratory suspicion of celiac disease, and was taken as a result of upper gastrointestinal system endoscopy.

Clinical and Laboratory Measurements: Blood was collected from individuals after 12 hours of fasting. Serum specimens were used to evaluate the minimum detectable concentration and intra- and inter-assay precisions for the three analytes (TSH, FT4, T3), linearity for the TSH assay. The Electro-chemiluminescence immunoassay (ECLIA) method was used for serum TSH, T3 and FT4 measurements.

Endoscopic Evaluation: Endoscopic findings and histopathological data of the patients were documented. The endoscopy of the patients was performed by using the Fujinon EG530WR endoscopy device in the endoscopy unit of our hospital. All patients starved for 6 hours before the endoscopy, and after the local pharyngeal xylocaine anesthesia, the endoscopy procedure was performed. The stomach and duodenum was examined in detail during the endoscopy, and biopsies were taken for helicobacter pylori infection. The difference between endoscopic findings and histopathological findings was evaluated between patients with hypothyroidism and patients without hypothyroidism.

Histopathological Evaluation: Punch biopsy was taken from the antrum of the patients who underwent endoscopic evaluations using biopsy forceps. The biopsy materials taken were sent to the pathology laboratory in 10% formaldehyde. After routine tissue monitoring procedures, tissue samples embedded in paraffin were cut at 5 micron thickness, stained with routine Giemsa and evaluated under a light microscope. Samples without tissue competence for evaluation were excluded from the study. The materials obtained were evaluated by three different experienced pathologists without clinical information. An evaluation was made for the presence of HP in the tissue.

Evaluation Patients With Celiac Disease: Celiac disease was diagnosed as a result of the histopathological examination of the tissue sample (duodenum), which was positive for Tissue Transglutaminase Antibody in case of clinical or laboratory suspicion of celiac disease, and was taken as a result of upper gastrointestinal system endoscopy. Because of its high specificity and sensitivity, only anti- Tissue Transglutaminase Antibody positivity was observed in patients. In patients with antibody positivity endoscopic examination was performed using a video endoscope and biopsies were taken from the second / third part of the duodenum. All biopsies were examined by a specialist pathologist and histopathology was performed according to the Marsh classification (12).

Ethical Statement: Ethical approval for this study was obtained from the Ethics Committee of our hospital (Approval no: 07/01/2021/2021-01). All procedures were in accordance with the ethical standards of our institution's human experiment committee and the Helsinki Declaration. Written informed consent forms were obtained from all participants in the study.

Statistical Analysis: The results of our study were analyzed with the program "The Statistical

Table 1. Comparison of Demographic Characteristics and Drug Use of Patients With and Without Hypothyroidism

Drugs and demographic features	Ptients with Hypothyroidism (n:61)	Patients without Hipothyroidism (n:50)	Total (n:111)	p
Age (Year±SD, range)	45.9±12.5 (21-76)	42.4±11.7 (19-65)	44.4±12.2 (19-76)	0.136
Sex (Female)	42 (68.9)	28 (56.0)	70 (63.1)	0.163
Smoker	19 (31.1)	12 (24.0)	31 (27.9)	0.404
Alcohol user	5 (8.2)	7 (14.0)	12 (10.8)	0.327
NSAID	40 (65.6)	31 (62.0)	71 (64.0)	0.696
Asetil salicylic acid	18 (29.5)	10 (20.0)	28 (25.2)	0.251
Steroids	13 (21.3)	10 (20.0)	23 (20.7)	0.865

SD: Standart deviation. **NSAID:** Non steroidal anti-inflammatory drugs

Package for the Social Sciences 19.0 (SPSS Armonk, NY: IBM Corp.)". Data with continuous values were given as mean ± standard deviation, categorical data as frequency and percentage (n,%). Data were tested for compliance with normal distribution using the Kolmogorov-simirnov test, histogram, and ± standard deviation. Parametric data of the groups were compared using the Student T test and one sample chi-square or Two-Proportions Z test was used to test categorical data. In addition, Fisher's Exact test was used in comparisons with less than 5 observations. The cases with $p < 0.05$ were considered statistically significant.

Results

The study included 61 hypothyroid patients 42 (68.8%) female, 19 (31.2%) male, 50 non-hypothyroid functional dyspepsia patients, 28 (56%) female, 22 (44%) male. There was no significant difference between hypothyroid patients and non-hypothyroid patients in terms of demographic characteristics, drug use, and smoking and alcohol use ($p > 0.05$) (Table 1).

When hypothyroid patients and patients without hypothyroidism were compared in terms of endoscopic findings and presence of HP, among endoscopic findings, alkaline reflux and Celiac disease were statistically significantly higher in the hypothyroid patient group ($p = 0.033$ and $p = 0.003$ respectively). Atrophic gastritis was also seen with a higher rate in hypothyroid patients, but was not statistically significant ($p = 0.065$). Other endoscopic findings were similar in both groups (Table 2).

Hypothyroid patients were divided into two groups according to their TSH values. Patients with TSH ≤ 10 were considered as group 1, and patients with TSH > 10 as group 2. In the comparison between the groups in terms of endoscopic findings and the presence of HP; Alkaline reflux and Celiac disease were significantly higher in the group with high TSH values ($p = 0.003$ and $p = 0.001$ respectively). Similarly, atrophic gastritis was observed with a higher rate in the group with high TSH levels, but was not statistically significant ($p = 0.063$). Other endoscopic findings and presence of HP were similar in both groups ($p > 0.05$) (Table 3).

Discussion

Hypothyroidism is a common endocrine disorder (1-3). Although it is a treatable disorder, almost half of the patients are not under control with treatment. This is mostly due to disruption of treatment or misuse of the drug (3). GIS complaints are quite common in patients who are not treated or cannot be controlled with treatment. Constipation is the leading symptom of GIS (13-15). This is because metabolism slows down in hypothyroidism. In severe hypothyroidism, the metabolism is at the basal level. In the case of myxedema, there is a metabolic rate below the basal metabolic level (1-3,5,14,15).

It is known that Hashimoto's thyroiditis disease (chronic lymphocytic thyroiditis), which is the most common cause of hypothyroidism, is frequently seen together with other autoimmune diseases. Although its association with atrophic gastritis and gluten eneropathy is frequently reported, studies have reported that the frequency of hypothyroidism increases in other autoimmune diseases involving the gastrointestinal system such

Table 2. Comparison of Endoscopic Findings of Patients With and Without Hypothyroidism

Endoscopic findings	Ptients with Hypothyroidism (n:61)	Patients without Hipothyroidism (n:50)	Total (n:111)	p
Antral gastritis (n,%)	18 (28.5)	18 (36.0)	36 (32.4)	0.467
Pangastritis (n,%)	44 (72.1)	32 (64.0)	76 (68.5)	0.359
Esophagitis (n,%)	18 (29.5)	16 (32.0)	34 (30.6)	0.777
Gastric ulser (n,%)	3 (4.9)	4 (8.0)	7 (6.3)	0.506
Duodenal ulser (n,%)	2 (3.3)	4 (8.0)	6 (5.4)	0.274
Bulbitis (n,%)	4 (6.6)	1 (2.0)	5 (4.5)	0.249
Hiatal hernia (n,%)	1 (1.6)	4 (8.0)	5 (4.5)	0.108
LES disfunction (n,%)	9 (14.8)	7 (14.0)	16 (14.4)	0.910
Alkalen reflux (n,%)	8 (13.1)	1 (2.0)	9 (8.1)	0.033
Barret metaplasia (n,%)	1 (1.6)	1 (2.0)	2 (1.8)	0.887
Atrophic gastritis (n,%)	4 (6.6)	0 (0)	4 (3.6)	0.065
Celiac disease (n,%)	10 (16.4)	0 (0)	10 (9.0)	0.003
H.P (n,%)	37 (60.7)	31 (62.0)	68 (61.3)	0.885

LES: Lower Esophageal Sphincter, **HP:** Helicobacter Pylori

Table 3. Comparison of Endoscopic Findings, Demographic Characteristics and Hp Presence By TSH Level

	TSH ≤10 (n:41)	TSH >10 (n:20)	Total (n:61)	p
Antral gastritis (n,%)	13 (31.7)	5 (25.0)	18 (29.5)	0.590
Pangastritis (n,%)	28 (68.3)	16 (80.0)	44 (72.1)	0.338
Esophagitis (n,%)	11 (26.8)	7 (35.0)	18 (29.5)	0.511
Gastric ulser (n,%)	3 (7.3)	0 (0.0)	3 (4.9)	0.215
Duodenal ulser (n,%)	1 (2.4)	1 (5.0)	2 (3.3)	0.598
Bulbitis (n,%)	3 (7.3)	1 (5.0)	4 (6.6)	0.731
Hiatal hernia (n,%)	1 (2.4)	0 (0.0)	1 (1.6)	0.481
LES disfunction (n,%)	4 (9.8)	5 (25.0)	9 (14.8)	0.115
Alkalen reflux (n,%)	2 (4.9)	6 (30.0)	8 (13.1)	0.003
Barret metaplasia (n,%)	0 (0.0)	1 (5.0)	1 (1.6)	0.149
Atrophic gastritis (n,%)	1 (2.4)	3 (15.0)	4 (6.6)	0.063
Celiac disease (n,%)	2 (4.9)	8 (40.0)	10 (16.4)	0.001
H.P (n,%)	24 (58.5)	13 (65.0)	37 (60.7)	0.628

as inflammatory bowel diseases, primary biliary cirrhosis and primary sclerosing cholangitis (10,13). The reason for this is thought to be that existing diseases develop as a result of type 4 hypersensitivity reaction in which cellular mediated (T-lymphocyte) autoimmune mechanisms play a role (1,3,16,17). Because of this association, thyroid function tests should also be performed in the follow-up of patients with atrophic gastritis and gluten enteropathy (7,13,18-20). In terms of the association of celiac disease with hypothyroidism, Kayar et al. found the rate of accompanying hypothyroidism (hashimato thyroiditis) patients to be 17% in their study in which 230 celiac patients were included, and they reported that this rate was significantly higher than the normal population (21). Similarly, in our study, celiac disease is observed with a significantly higher rate in patients with hypothyroidism. In addition, celiac disease is seen with a significantly higher rate in the group with high TSH levels. Examining the association of atrophic gastritis and hypothyroidism, Cellini et al. found that 40% of patients with atrophic gastritis had autoimmune thyroid diseases (22). In our study, although atrophic gastritis was higher in the

hypothyroid group, it was not statistically significant. Similarly, atrophic gastritis was observed with a higher rate in the group with high TSH levels, but it was not statistically significant.

Hypothyroidism lowers the body metabolic rate. For this reason, most of the metabolic events slow down. Similarly, intestinal motility slows down (1,8,23). Yaylalı et al. Examined 30 female patients with hypothyroidism and 10 healthy volunteers with esophagus and stomach scintigraphy and compared the groups in terms of motility; Esophageal transit time was longer in patients with hypothyroidism, and esophageal emptying rate was slower. When gastric emptying time was compared, no significant difference was found between the groups. In addition, groups with and without atrophic gastritis were compared in this study, and no significant difference was found in terms of motility. In the light of these results, it has been reported that the main factor affecting motility is hypothyroidism (8). Lauritano et al. They concluded that hypothyroidism is a risk factor for bacterial overgrowth in the small intestine. The reason for this was thought to be the decrease in the motor functions of the intestines in hypothyroidism and the bacterial emptying of the lumen as a result (9). When the endoscopic findings related to the slowing of motility are examined in the studies; It was observed that there was a significant increase in alkaline reflux rate in patients affected by motility secondary to hypothyroidism (8,9). Similarly, alkaline reflux was found to be significantly higher in the hypothyroid group in our study where we compared the hypothyroid and non-hypothyroid groups. In addition, in the comparison made according to TSH levels in hypothyroid patients, alkaline reflux was found with a higher rate in the group with high TSH levels.

Our study has strengths and weaknesses. The small number of our patients and the retrospective design are the weaknesses of our study. The strengths of our study include performing endoscopic and histopathological examinations on all patients included in the study, and making laboratory comparisons (according to TSH levels) between the groups in remission and those without endoscopic and histological data, along with patients with hypothyroidism and non-hypothyroidism.

In conclusion Hashimoto's thyroiditis is a common autoimmune phenomenon. It is closely associated with other autoimmune events. Since hypothyroidism slows down the metabolic rate, the intestinal passage time is prolonged. As a result, patients develop alkaline reflux. However, the results we found need to be supported by prospective studies conducted with larger patient groups.

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