D J Med Sci 2021;7(2):121-125
doi: 10.5606/fng.btd.2021.25058

Original Article

Evaluation of gastric endoscopic biopsy results in accordance with history of previous thyroidectomy

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ABSTRACT

Objectives: This study aimed to establish a link between total thyroidectomy and *Helicobacter pylori (H. pylori)* infection, which is one of the most implicated risk factors that cause gastric intestinal metaplasia (GIM) and is also a risk factor for gastric adenocarcinoma.

Materials and methods: This retrospective study was conducted at Giresun University. We retrospectively reviewed gastric biopsies from 78 thyroidectomized patients (41 males, 37 females; mean age: 64.5±8.5 years; range, 29 to 79 years) in a single center. A control group of 150 subjects (45 males, 105 females; mean age: 59±7.5 years; range, 32 to 78 years) was selected from age-matched dyspeptic subjects with no history of thyroidectomy.

Results: There were no significant differences in baseline sociodemographic characteristics between groups. Histopathological analysis of gastric biopsy specimens showed that the rate of *H. pylori* infection was found to be significantly lower in the thyroidectomized group (43.3% *vs.* %60.8; p<0.05). Although in multivariate analysis the relationship between atrophic gastritis and thyroidectomy was not statistically significant (p=0.857), there was a stronger correlation between GIM and thyroidectomy compared to the control group (13.3% *vs.* 3.3%; p<0.05).

Conclusion: To our knowledge, this is the first study comparing the gastric and endoscopic findings between thyroidectomized patients and those with non-thyroidectomized gastroesophageal reflux disease patients. Further studies are needed to determine a causal link between thyroidectomy and gastric intestinal metaplasia. Evidence has accumulated suggesting that autoimmune thyroid diseases increase the risk of gastric mucosal damage and adversely affect *H. pylori* status.

Keywords: Gastric mucosa, intestinal metaplasia, thyroidectomy.

A total thyroidectomy is an operation that involves the complete surgical removal of the thyroid gland. Surgeons often perform a thyroidectomy when a patient has thyroid cancer, noncancerous enlargement of the thyroid (goitre), overactive thyroid (hyperthyroidism) or indeterminate or suspicious thyroid nodules.[1] Although thyroidectomy is a common surgical procedure, it has several potential complications: temporary or permanent change in voice, temporary or permanent hypocalcemia, need for lifelong thyroid hormone replacement, bleeding, infection, and the remote possibility of airway obstruction due to bilateral vocal cord paralysis.[2]

Hashimoto's thyroiditis (HT) is characterized by either lymphocytic infiltration or follicular destruction of thyroid tissue which is the result of thyroidal nodules and heterogeneity of the thyroidal parenchyme. Eastern European and Caucasian individuals who live in iodine sufficient areas are at higher risk of developing HT and have had a risk of further development of multinodular goitre which requires a surgical approach.[3]

Received: January 28, 2021 ***Accepted:*** February 07, 2021 **Published online:** September 07, 2021

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Cite this article as:
Vural S, Dülger AC, Ayvaz MA, Aydın İ, Kesicioğlu T, Gülmez M. Evaluation of gastric endoscopic biopsy results in accordance with history of previous thyroidectomy. D J Med Sci 2021;7(2):121-125.

Individuals with a history of thyroidectomy can experience dysphagia or globus hystericus, either of which could require an upper gastrointestinal (UGI) tract endoscopy. Furthermore, previous studies have also shown that patients with a history of thyroidectomy are faced with a wide range of UGI symptoms, but the relationships with endoscopic findings of the UGI system are not described yet.[4] Studies involving the effects of thyroidectomy on both gastric mucosa and other UGI diseases are limited and have not investigated whether these effects are related to thyroidectomy.

MATERIALS AND METHODS

This single-center, retrospective study was conducted at Giresun University Prof. Dr. A. Ilhan Özdemir Training and Research Hospital, Department of General Surgery between January 2015 and January 2020. We retrospectively reviewed gastric biopsies from 78 thyroidectomized patients (41 males, 37 females; mean age: 64.5±8.5 years; range, 29 to 79 years) who were admitted to General Surgery Clinic. A control group of 150 subjects (45 males, 105 females; mean age: 59±7.5 years; range, 32 to 78 years) was selected from age-matched dyspeptic subjects with no history of thyroidectomy.

Study subjects who were priorly treated for *Helicobacter pylori (H. pylori)* infection were excluded from the study. We used the hospital's data to define the endoscopic findings and the results of histopathologic examinations of the gastric biopsy specimens of the 78 patients with a history of total thyroidectomy who had UGI tract endoscopy. Histopathologic examination of gastric mucosa with Giemsa staining is reported to be highly sensitive for the diagnosis of *H. pylori* infection, with reported sensitivities of 90-100%. Therefore, we examined all biopsy specimens of patients in the study. We also examined the laboratory parameters between groups. Data were collected using the hospital database. A written informed consent was obtained from each patient before their involvement in this study. The study protocol was approved by the Ordu University Clinical Research Ethics Committee (date/no: 01.10.2020/2020/197). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 20.0 (IBM Corp., Armonk, NY, USA) software. Normality assumption was checked using the Kolmogorov-Smirnov test. The parameters with a normal distribution

Table 1. Demographic and laboratory characteristics of thyroidectomized and control patients

	Thyroidectomy Group			Control Group			
	n	Mean	95% CI	n	Mean	95% CI	*p*
Age (year)	60	59.4	56.7-62	181	54.9	52.8-56.9	0.008
Hemoglobin (gr/dL)	60	13.4	12.9-13.8	181	13.1	12.8-13.4	0.429
WBC $\times 10^3$ mL	60	7.68	6.72-8.65	181	7.85	7.48-8.21	0.539
Neutrophil $\times 10^3$ mL	60	5.02	3.83-6.21	181	4.69	4.37-5	0.349
Platelet	60	249	228-269	181	279	250-308	0.056
Glucose	60	111	101-122	181	107	100-114	0.149
Urea	60	31	27-34	181	30	28-32	0.561
Creatinine	60	3.1	0.1-6.1	178	0.8	0.76-0.84	0.132
AST	60	24	19-28	181	22	20-25	0.945
ALT	60	21	17-24	177	24	20-27	0.533
Albumin	60	4.4	4.2-4.5	49	4.6	4.4-4.7	0.617
Ferritin	49	69.81	40.01-99.62	38	52.34	38.21-66.47	0.804
TSH	60	3.58	1.85-5.31	137	2.02	1.69-2.34	0.681

WBC: White blood cell; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TSH: Thyroid-stimulating hormone.

Table 2. Comparison of two groups according to the endoscopic biopsy results

	Thyroidectomy group		Control Group		
	n	%	n	%	*p*
Helicobacter pylori					0.024
-	34	56.7	71	39.2	
+	26	43.3	110	60.8	
Intestinal metaplasia					0.008
-	52	86.7	175	96.7	
+	8	13.3	6	3.3	
Atrophy					0.857
-	46	76.7	142	78.5	
+	14	23.3	39	21.5	

were compared between groups by t-test and parameters with nonnormal distribution were compared between groups by non-parametric tests such as the Mann-Whitney U test or the Fisher's exact test.

RESULTS

There were no significant differences in baseline sociodemographic characteristics between groups. All of the patients had benign thyroid nodules due to autoimmune (Hashimoto) thyroiditis. Pantoprazole (80%) was the most commonly used drug for the treatment of dysphagia followed by *H. pylori* drugs (33%), and oral alginic acid preparations (23%). The most common symptoms were proximal dysphagia (88%), pyrosis (67%), pain or discomfort at the proximal esophagus with swallowing (62%), weight gain (46%), and fear of cancer (38%).

There was no statistical difference between the laboratory parameters associated with the two groups (Table 1). From an endoscopic perspective, we did not find any statistical differences between the groups in terms of esophagitis, axial hernia and peptic ulcer (p=0.296, p=0.116 and p=0.351). When we histopathologically analyzed gastric biopsy specimens, we found that the rate of *H. pylori* infection was significantly lower in thyroidectomized group (43.3% *vs.* 60.8%; p<0.05). Although in multivariate analysis the relationship between atrophic gastritis and thyroidectomy was not statistically significant (p=0.857). There was a stronger correlation between gastric intestinal metaplasia and thyroidectomy compared to the control group (13.3% *vs.* 3.3%; p<0.05) (Table 2).

DISCUSSION

To our knowledge, this is the first study comparing the gastric and endoscopic findings between thyroidectomized patients and non-thyroidectomized gastroesophageal reflux disease patients. A recent Italian study involving 152 subjects with HT and non-specific thyroiditis showed that *H. pylori* infection and CagA positive (+) *H. pylori* infection were associated with Graves' disease and HT, possibly due to increased inflammatory activity and molecular mimicry.[5] On the other hand, HT is characterized by autoimmune destruction of thyroid parenchyma with positive anti-thyroid peroxidase antibody (TPO-Ab), and is the most common autoimmune disease which could lead to thyroidal nodules and hypothyroidism. The authors also mentioned that presence of TPO-Ab in serum has been associated with *H. pylori* infection.[6] Furthermore, a recent study revealed that treating *H. pylori* infection could lead to reduced levels of TPO-Ab.[7] Moreover, *H. pylori* infection and autoimmune thyroid diseases are highly interdependent conditions that share several risk factors including atrophic gastritis-related immune thyroid diseases, smoking tobacco-related gastric, and thyroidal damage.[8] Thus, in connection with recent publications regarding the link between *H. pylori* infection and thyroid autoimmunity, we showed an inverse correlation between thyroidectomy and *H. pylori* infection, probably due to reduced autoimmunity caused by the removal of thyroid tissue as well as autoimmunity. Improvement in

the rate of *H. pylori* infection seems influenced by thyroidectomy, as we have shown.

Gastric intestinal metaplasia (GIM) is a premalignant condition of gastric mucosa and is characterized by the exchange of normal gastric mucosa with intestinal mucin-secreting cells due to genetic and environmental factors.[9] The pooled prevalence of GIM has been reported as 4.8% in subjects who underwent gastrointestinal endoscopy regardless of the causative disease in the United States.[10] *H. pylori* infection is one of the most implicated risk factors that cause GIM and could cause gastric adenocarcinoma. However, salt intake and spicy foods in line with low socioeconomic status are the main environmental factors contributing to the development of GIM.[11]

There have been several environmental links between GIM and thyroid nodules related to autoimmune thyroiditis. Primarily, patients that were exposed to *H. pylori* had higher rates of GIM compared to those without.[12] *H. pylori* infection is also capable of thyroid autoimmunity. We postulated that *H. pylori*-induced GIM could have been sharing the same factors responsible for developing thyroid nodules. In the current study, we found that the patients with thyroidectomy were due to nodules associated with Hashimoto thyroiditis. It is important to mention once again that any differences in visualized endoscopic findings including esophagitis, axial hernia and peptic ulcer were not observed, which is an indication of lack of negative effects prior to thyroidectomy on macroscopic endoscopic findings.

It is also possible that high salt diets, poor vegetable, and fruit intake and smoky meats are factors capable of developing both HT and GIM. In addition, deficiencies of iodine, iron, selenium, and vitamin D, which are also responsible for the development of GIM, have been implicated in having HT.[13]

Regulatory T cells, dendritic cells, neutrophils, eosinophils, natural killer (NK) cells, and natural killer T (NKT) cells are key players of the gastric cancer microenvironment.[14] In addition, the percentages of double-negative memory B cells, plasma cells, T follicular helper cells, and Tc17 cells were higher in HT patients than in the healthy controls. The percentages of Tc17 cells and NK cells were higher in the patients with severe HT than in the patients with mild HT.[15] Thus, we postulated that both HT and GIM could share the same immunologic properties through Tc17 cells and NK cells.

There were several limitations in this study. We did not evaluate potential prognostic factors for developing GIM and the extent of GIM, histopathologic subtype, family history of gastric cancer, *H. pylori* virulence factors, other noninvasive biomarkers (e.g. pepsinogen), alcohol consumption, tobacco use, and dietary habits due to the retrospective nature of the study.

Data combined in this study suggests that total thyroidectomy could reduce the rate of *H. pylori* infection, probably by reducing the burden of the immune system with the removal of thyroidal nodules. Further studies are needed to determine a causal link between thyroidectomy and GIM. Evidence has accumulated suggesting that autoimmune thyroid diseases increase the risk of gastric mucosal damage and adversely affect *H. pylori* status.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Patel KN, Yip L, Lubitz CC, Grubbs EG, Miller BS, Shen W, et al. The American association of endocrine surgeons guidelines for the definitive surgical management of thyroid disease in Adults. Ann Surg 2020;271:e21-e93.
2. Park H, Park J, Choi MS, Kim J, Kim H, Shin JH, et al. Preoperative serum calcitonin and Its correlation with extent of lymph node metastasis in medullary thyroid carcinoma. Cancers (Basel) 2020;12:2894.
3. Ragusa F, Fallahi P, Elia G, Gonnella D, Paparo SR, Giusti C, et al. Hashimotos' thyroiditis: Epidemiology, pathogenesis, clinic and therapy. Best Pract Res Clin Endocrinol Metab 2019;33:101367.
4. Gumus T, Makay O, Eyigor S, Ozturk K, Erdogan Cetin Z, Sezgin B, et al. Objective analysis of swallowing and functional voice outcomes after thyroidectomy: A prospective cohort study. Asian J Surg 2020;43:116-23.

5. Figura N, Di Cairano G, Moretti E, Iacoponi F, Santucci A, Bernardini G, et al. Helicobacter pylori infection and autoimmune thyroid diseases: The role of virulent strains. Antibiotics (Basel) 2019;9:12.
6. Choi YM, Kim TY, Kim EY, Jang EK, Jeon MJ, Kim WG, et al. Association between thyroid autoimmunity and Helicobacter pylori infection. Korean J Intern Med 2017;32:309-13.
7. Hou Y, Sun W, Zhang C, Wang T, Guo X, Wu L, et al. Meta-analysis of the correlation between Helicobacter pylori infection and autoimmune thyroid diseases. Oncotarget 2017;8:115691-700.
8. Cuan-Baltazar Y, Soto-Vega E. Microorganisms associated to thyroid autoimmunity. Autoimmun Rev 2020;19:102614.
9. Huang RJ, Choi AY, Truong CD, Yeh MM, Hwang JH. Diagnosis and management of gastric intestinal metaplasia: Current status and future directions. Gut Liver 2019;13:596-603.
10. Altayar O, Davitkov P, Shah SC, Gawron AJ, Morgan DR, Turner K, et al. AGA technical review on gastric intestinal metaplasia-epidemiology and risk factors. Gastroenterology 2020;158:732-44.
11. Gupta S, Li D, El Serag HB, Davitkov P, Altayar O, Sultan S, et al. AGA clinical practice guidelines on management of gastric intestinal metaplasia. Gastroenterology 2020;158:693-702.
12. Kato I, Vivas J, Plummer M, Lopez G, Peraza S, Castro D, et al. Environmental factors in Helicobacter pylori-related gastric precancerous lesions in Venezuela. Cancer Epidemiol Biomarkers Prev 2004;13:468-76.
13. Hu S, Rayman MP. Multiple nutritional factors and the risk of Hashimoto's Thyroiditis. Thyroid 2017;27:597-610.
14. Sammarco G, Varricchi G, Ferraro V, Ammendola M, De Fazio M, Altomare DF, et al. Mast cells, Angiogenesis and Lymphangiogenesis in human gastric cancer. Int J Mol Sci 2019;20:2106.
15. Liu Y, You R, Yu N, Gong Y, Qu C, Zhang Y, et al. Increased proportions of Tc17 cells and NK cells may be risk factors for disease progression in Hashimoto's thyroiditis. Int Immunopharmacol 2016;40:332-8.