

Relationship between H. Pylori Patients and Autoimmune Thyroid Disease

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Abstract

Autoimmune Thyroid Disease (AITD) Autoimmune Thyroid Disease is one of the diseases, more common in women than men, caused by a combination of reasons discussed later. In this study, we have tried to understand how Autoimmune Thyroid Disease is related to H. pylori or Helicobacter Pylori. We have discussed the pathology and the manner in which AITD is developed

This report depicts the relationship between Helicobacter pylori (H. pylori) and Autoimmune Thyroid Disease or Autoimmune Thyroiditis. However, some other reports concerning the relationship between H. pylori infection and Autoimmune Thyroiditis are conflicting. We've discussed how AITD is developed, along with the causes and effects of the disease. In this study, we've also aimed at determining the presence of H. pylori bacteria in AITD patients, particularly in Hashimoto's Thyroiditis and Grave's disease two of the commonly occurring thyroid diseases. The manner in which AITD develops is multi-factorial and H. pylori infection is reported more in AITD patients (adults). H. pylori is said to be involved usually in non-gastrointestinal conditions.

Keywords: *Helicobacter pylori infection, H. pylori, Autoimmune Thyroid Disease, Cag-A, Grave's Disease, Hashimoto's Thyroiditis*

Introduction

Thyroid is a tiny gland located in the front portion of the neck that produces organ-controlling hormones. These can be any organs in the body. When there's deficiency of these hormones in the body, the functioning of the body is affected, which in turn affects your energy level and mood, along with gain in weight. If the thyroid is inflamed, the condition is known as Thyroiditis. In some cases, the antibodies produced in by the body attacks the thyroid accidentally. This condition is known as autoimmune thyroiditis. It is also known as chronic lymphocytic thyroiditis¹.

The commonly occurring Autoimmune Thyroid Disease (AITD) or Autoimmune Thyroiditis are:

- Grave's Disease (GD)
- Hashimoto's Thyroiditis (HT)
- Atrophic Thyroiditis (AT)
- Painless Thyroiditis (PT) or Silent Thyroiditis (ST)
- Subacute Lymphocytic Thyroiditis (SLT) or Postpartum Thyroiditis (PPT)

The presence of autoantibodies against Thyroglobulin (TgAbs), TPO-Abs, and Thyrotropin Receptor (TRAbs) was a typical marker of GD and HT. The pathogenesis of Grave's Disease (GD) and Hashimoto's Thyroiditis (HT) is nearly same, in which the autoantibodies act against Thyroglobulin (TgAbs), Thyroperoxidase (TPO-Abs) and Thyrotropin Receptor (TRAbs)².

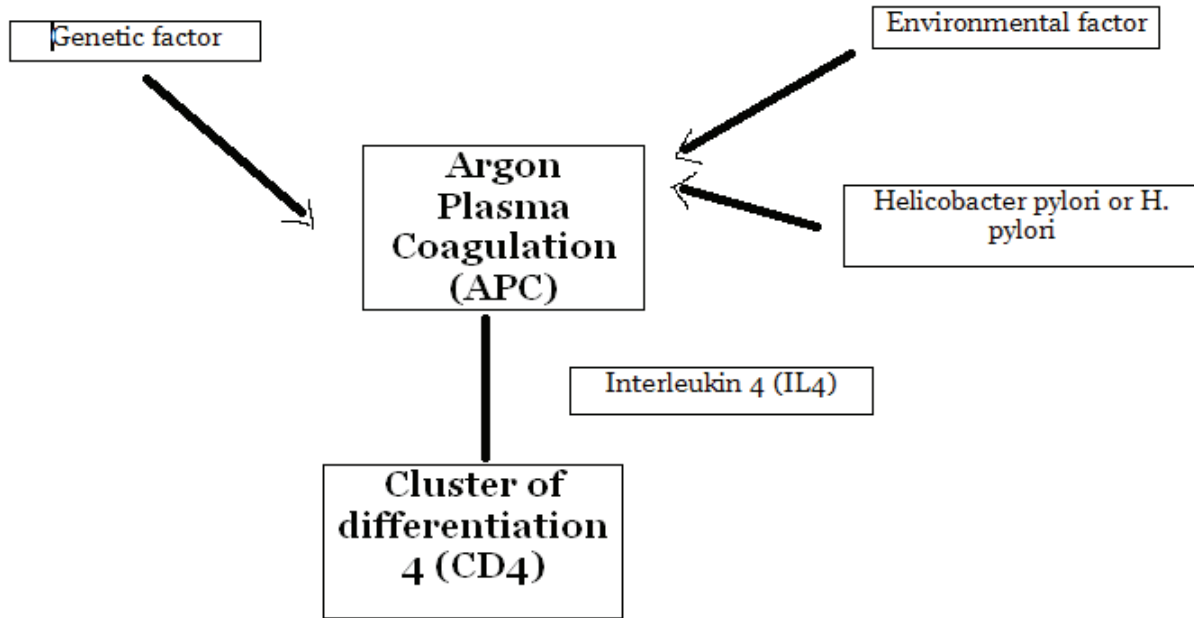


Figure 1. Pathogenesis for Grave's Disease is described in the above diagram. The role of H. pylori is showed for the commencement of Grave's Disease.

Causes of Autoimmune Thyroiditis

The Autoimmune Thyroid Disease is said to be caused by both genetic and environmental factors. The H. pylori bacteria mirror the antigen present in the thyroid cells and play a major role on the onset of AITDs. According to the data captured, the H. pylori bacteria have predominantly affected people in the third world countries. Its presence seemed to be profound in older people. It proliferates with age in some people. Apart from being the causative factor for the commencement of AITDs, these motile bacteria also cause diseases related to abdomen, such as ulcer (gastroduodenal ulcer), gastritis, and carcinoma. An individual has the tendency to get autoimmune thyroiditis for a combination of reasons given below ³:

- If you are a woman
- You are middle-aged
- If you are suffering from any of the other autoimmune disorders such as:
 - Lupus
 - Type 1 diabetes
 - Rheumatoid arthritis

- If a person having autoimmune thyroiditis is related to you
- If you are affected by environmental radiation

Helicobacter pylori (H. pylori or Hp)

Helicobacter pylori is a gram-negative gastric pathogen that causes disorders such as gastritis, gastric & duodenal ulcers, gastric mucosa-related lymphoid tissue lymphoma, and gastric cancer. Moreover, it has been proved that H. pylori infection can bring about autoimmune processes against mucosa, with resulting autoimmune gastritis. Also, H. pylori is believed to be involved in the pathogenesis of non-gastrointestinal condition, including rosacea, ischemic heart disease, and Type 1 diabetes. Finally, H. pylori infection is seen in most of the adult AITD patients ⁴.

H. pylori-specific Antibody Determination

Antibodies to H. pylori was identified during the first diagnosis in patients affected by Autoimmune Thyroid Disease. In patients having Turner Syndrome, serology for H. pylori was assessed in cases without thyroid autoimmunity and well before the emergence of autoantibodies.

Gastric mucosa that contains glands and gastric pits is the primary target of *Helicobacter pylori* that groups and destroys surface epithelium and brings about a chronic inflammatory reaction in lamina propria, a thin layer of loose connective tissue that lies beneath the epithelium. Lamina propria and epithelium collectively constitute mucosa. Gland atrophy and intestinal metaplasia are two of the long-term consequences of this process. The *H. pylori* prompts antibodies that are cross-reacting with epithelial components of gastric mucosa, periglandular T cells, and elevated glandular cell apoptosis that might bring about diffuse, restricted corpus fundus, and atrophic gastritis of autoimmune type. Some of the clinical consequences of *H. pylori* include Achlorhydria with secondary hypergastrinemia, with or without pernicious anemia, and elevated risk for gastric enterochromaffin⁵.

This examination suggested that thyroid gland might be another target for *H. pylori*-invoked immune-inflammatory response and Autoimmune Thyroid Disease might be its consequence. Significantly increased existence of *H. pylori* was identified in patients having Autoimmune Thyroid Disease, with or without Turner Syndrome^[6].

Material & Methods

The current study was carried out on 100 subjects in the age group of 30 to 70 years. The serum levels of Thyroxine (T4), Thyroid Stimulating Hormone (TSH), Thyroid Peroxidase Antibody (TPO-Ab), and *H. pylori* Immunoglobulin G (IgG) antibody were also tested. All the subjects that had a history/family history related to thyroid disease were not considered for the study.

Table.1 The clinical characteristics of the cases considered

Group	n	Sex(Female/male)	Age	Smokers(Yes/No)
Control	100	92/10	49.2 ± 4.7	42/62
GD	56	52/5	48.6 ± 3.8	24/33
HT	66	58/6	50.4 ± 9.8	28/35
AITDs	100	112/10	49.4 ± 6.8	54/64

Laboratory test

The thyroid test was carried out in the lab that included T4 test, TSH test, and TPO-Ab test. The concentration of serum TPO-Ab was fixed using BRAHMS anti-TPO Radioimmunoassay, maintaining the sensitivity of the solution at about 30 U/mL. As a conclusion, the TPO-Ab of over 60 U/mL was calculated as positive.

In the laboratory, the *H. pylori* bacteria were considered, in order to measure the presence of anti-*H. pylori* IgG. This complete test included solid phase, 2-step, and chemiluminescent enzyme immunoassay.

A careful examination is necessary to detect *H. pylori* as it helps in the diagnosis of *H. pylori* bacteria infection. An invasive procedure was carried out since it helps better diagnose a disease. Because *H. pylori*

has a role to play in gastroduodenal ulcer, an invasive procedure was carried out in some cases, especially in people whose age ranges from 32 to 45. The invasive procedure comprised of historical test, culture test, and rapid urease test.

Findings

The thyroid autoimmunity was considered positive regardless of whether there is thyroid dysfunction or not. The presence of IgG antibodies and *Helicobacter pylori* was considered:

- Conclusive for 1.6 U/mL or more
- Ambiguous for 0.8 U/mL to 1.6 U/mL
- Negative for 0.8 U/mL or less

The H. pylori and IgG were ignored for ambiguous cases.

Examination of H. pylori Present in Stool Samples

All the samples were tested in the lab and the diagnosis of the subjects were perplexing. The samples were proved with the help of the same kind of amplified enzyme immunoassay in order to determine the H. pylori antigens. The test value >0.155 was considered positive for H. pylori.

Exposure of Cag-A Antibodies

Cag-A (Cytotoxin-associated gene A) is a H. pylori virulence factor. All the raw samples were taken for ELISA (enzyme-linked immunosorbent assay). Because the value for anti-Cag-A immunoglobulin-G for those samples was over 15 U/mL Cag-A was considered positive.

Results

The H. pylori bacteria were present in the stool samples of the one hundred patients who were diagnosed with Autoimmunity Thyroid Disease. Out of these 100 patients, 89% had Grave’s Disease and 74% of them had Hashimoto’s Thyroiditis and about 54% of them had a p value of < 0.0001.

When immunoassay test was carried out, the results were positive for patients who had H. pylori bacteria infection in gastric mucosa in the past than for cases that didn’t have H. pylori bacteria infection. Also, there was no correlation between smoking and presence of H. pylori bacteria infection.

83% of H. pylori-positive patients who had Grave’s Disease and 89.5% of H. pylori-positive patients who had Hashimoto’s Thyroiditis we’re positive for Cag-A antigens. The result showed significant difference when compared for the presence of Cag-A H. pylori-positive patients.

Table 2. shows HP-positivity and Cag-A-positivity in patients of different groups

Group	n	HP-	HP+	CagA+ CagA+	CagA-	Overall
Control	100	54	46	24	23	24/100
GD Total	56	9	48c	35b	7	46c/58
HT Total	60	31	282	28b	3	28a/62
AITDs Total	100	42	712	64c	10	64c/110

The H. pylori bacteria are present globally, affecting close to 50% of the population, in the developed nation. Cag-A has found to be the most fatal antigen. According to a recent study, a significant correlation was seen for Cag-A carrier for H. pylori strains and for Grave’s Disease. The results were not dependent on the hormone levels of the patients who were examined.

On the other side, many studies have demonstrated the association between microorganisms and Hashimoto’s Thyroiditis (HT), where there were conflicting results and a few other studies have shown a significant correlation.

So, to avoid any discrepancy and correctly analyze the infection caused by the H. pylori bacteria, a number of techniques we’re used. With the serological test for H. pylori, distinguishing between the past and present condition was not possible whereas the 13-C urea breath test or immunoassay test, done with fresh stool samples, helped determine the present condition of the H. pylori bacteria infection. These procedures come under the non-invasive method of examination. Apart from this, if the analogous antigenic sites were present for Cag-A and TPO, the obtained results were false positive.

Apart from this, other thyroid tests were performed in patients with Hashimoto's Thyroiditis, such as Frank Hypothyroidism test. However, this test wasn't found to be a reliable one. On doing the stool antigen test, we were able conclude that there was some Correlation between patients with *H. pylori* and hyperthyroid GD patients. However, such a correlation was not seen been patients with *H. pylori* (HT) and hyperthyroid patients.

In the result, it was noticed that the presence of Cag-A was proportionately present in both the groups – GD and HD. These results were in agreement with the previous observation for TH patients. Other factors such as subclinical or Frank Hypothyroidism may mislead the conclusion of the study. The stool antigen test clearly showed the correlation between. *pylori* and hyperthyroid GD patients.

Discussion

According to recent studies, we learned that there was a significant correlation between Cag-A carrier, *H. pylori* strains, and Grave's Disease and the results did not depend on the hormonal status of the cases considered for study. There may be other studies that show a positive relationship between *H. pylori* and Hashimoto's Thyroiditis. According to some observations, gastroduodenal tract need not necessarily be the only cause of attracting *H. pylori* infection. A number of studies gave a convincing explanation about the correlation between *H. pylori* infection and Autoimmune Thyroid Disease^[7]. One such study declares that people having a history of Atrophic Thyroiditis are at the risk of attracting *H. pylori* infection. In our current study, we looked into the presence of Cag-A antibodies, monoclonal antibodies for Cag-A, having *H. pylori* strains had Thyroid glandular cells, which in turn contain an endogenous peroxidase.

Further, when the infected bacteria were cultured, it was observed that it became more susceptible to thyroid disease. It was observed that patients who possessed thyroid disease had the tendency to have autoantibodies against thyroid cells, such as thyroglobulin and mitochondrial peroxidase^[8].

According to a recent study by Tom et. Al, *H. pylori* can encode genes for an endogenous peroxidase and facilitates the immune system of an individual by

promoting the bacterial enzyme activity, which in turn reacts with the receptors on human tissues. Subsequently, the serum autoantibody titer for peroxidase and thyroglobulin was tested and Thyroid Stimulating Hormone (TSH) receptors were monitored. In the process, the receptors kept decreasing after *H. pylori* bacteria were reacted. In one case, the titer reduced sixteen-fold after *H. pylori*^[9].

A few microorganisms give rise to complicate carbohydrates, which resemble the constituents of Glycoconjugate that can be seen on the superficial surface of human blood cells and CD4 on the cells of other organs.

According to Hein HO et.al, genes have the specificity for *H. pylori* infection as well as duodenal ulcer development. Ultimately, we can conclude that the inflammation brought about by the bacteria *H. pylori* has induces a few pathological changes like increased TLC, neutrophils, and basophilis. The association of *H. pylori* infection, particularly by strains that articulate Cag-A with autoimmune thyroid diseases is not coincidental and further study is necessary^[10].

Conclusion

According to a study, the thyroid gland might be a target for *H. pylori*-invoked immune-inflammatory response and Autoimmune Thyroid Disease might be its consequence. An increased existence of *H. pylori* bacteria was identified in Autoimmune Thyroid Disease. The *H. pylori* bacteria were present in the stool samples of the one hundred patients who were diagnosed with Autoimmunity Thyroid Disease. Out of 100 patients, 89% had Grave's Disease and 74% of them had Hashimoto's Thyroiditis. It was also concluded that there was a correlation between *H. pylori* and Grave Disease and HT. By eliminating *H. pylori* infection, we can reduce thyroid autoantibodies. The existence of TPO-Ab (Thyroid Peroxidase Antibody) was more frequent in cases having *H. pylori* infection.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Community

Health Technologies and all experiments were carried out in accordance with approved guidelines.

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