ORIGINAL RESEARCH

The relationship between helicobacter pylori infection and gastric cancer

Aziz Ari, Kenan Buyukasik

Istanbul Training and Research Hospital Department of General Surgery, Istanbul, Turkey

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Abstract
Immediately after Helicobacter pylori (H. pylori) was discovered in 1983, its relationship with upper gastrointestinal diseases has begun to be investigated. This study was carried out to investigate the relationship between H. pylori and gastric cancer by comparing the frequency of H. pylori infection between gastric cancer patients and controls. Histological results were evaluated in the diagnosis of H. pylori. This study included 60 patients who were diagnosed as gastric cancer at the Endoscopy Unit of Education and Research Hospital and were operated at the General Surgery Department of Istanbul Education and Research Hospital. The patients were questioned about major complaints and duration of these complaints, cigarette smoking and tea drinking habits, family history, and previous gastrointestinal surgery. The localization, macroscopic appearance, histology, and extent of the tumor were determined. Endoscopy, biopsy and tomography examinations were used for the localization, shape and spread of the tumor in other patients. In 40 patients undergoing resection, histological presence of H. pylori in tumor-adjacent tissue was detected in 28 (70%) patients. When all patients (60 patients) were evaluated together, H. pylori infection was detected in 40 (66.7%) patients. 40 patients undergoing resection were included in the evaluation. Although the frequency of H. pylori infection was higher in diffuse-type than in intestinal-type, this was not statistically significant. Both patients with intestinal and diffuse gastric cancers were accompanied by H.pylori infection. The rate of H.pylori infection was higher in patients with diffuse gastric cancer. Although H. pylori is one of the etiologic factors for gastric cancer, there was no significant difference in H. pylori infection between those with and without gastric cancer.

Keywords: Cancer, gastric, helicobacter pylori

Introduction
Immediately after Helicobacter pylori (H. pylori) was discovered in 1983, its relationship with upper gastrointestinal diseases has begun to be investigated. In the first few years, the results in support of this issue could not be obtained in tissue samples taken from gastric cancer patients. However, studies have concentrated again on this issue when it has been understood that H. pylori infection is common in areas at higher risk of cancer. The number of publications in support of this relationship has increased steadily since 1989. At the end of the meeting in which the experienced cancer specialists from 11 countries assessed available data with initiative of the International Agency for Research on Cancer (IARC) in 1994, it has been concluded that H. pylori is carcinogenic to the human stomach.

The first studies investigating the relationship between cancer type and bacteria reported that H. pylori infection was more common in intestinal gastric cancer than in diffuse gastric cancer. For this reason, the first hypothesis on H. pylori and cancer has suggested that chronic gastritis caused by this bacterium play a role in carcinogenesis by causing atrophic gastritis, intestinal metaplasia and dysplasia over time.

A recent study has reported that the prevalence of H. pylori infection is higher in diffuse gastric cancer patients.

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Material and Methods
This study included 60 patients who were diagnosed at the Endoscopy Unit of Istanbul Training and Research Hospital. Education and Research Hospital and were operated at the General Surgery Department of Istanbul Education and Research Hospital. The patients were questioned about major complaints and duration of these complaints, cigarette smoking and tea drinking habits, family history, and previous gastrointestinal surgery. The localization, macroscopic appearance, histology, and extent of the tumor were determined. Endoscopy, biopsy and tomography examinations were used for the localization, shape and spread of the tumor in other patients.

The samples taken from both the tumor and the surrounding mucosa in patients undergoing resection during the operation were first fixed in 10% neutral buffered formalin. The paraffin-embedded blocks were then sectioned on a microtome at thicknesses of 4 to 5um. These sections were stained with the conventional hematoxylin-
When tumor type and localization were compared, only 32 patients (50.3%) had antral involvement. Of the patients with antral involvement, 10 (30.1%) were inoperable, and 22 (69.9%) were able to undergo tumor staging. Of the patients undergoing tumor staging, 12 (54.5%) had intestinal gastric cancer, 6 (27.2%) had diffuse gastric cancer, and 4 (18.3%) had mixed gastric cancer.

Of the 20 (33.3%) patients with antral and corpus involvement, 10 (50%) were inoperable. Of the 10 (50%) patients undergoing tumor staging, 10 (100%) had diffuse gastric cancer. Of the 4 (6.7%) patients with corpus involvement, 2 (50%) had intestinal gastric cancer and 2 (50%) had diffuse gastric cancer. Of the 4 (6.7%) patients with cardia involvement, 4 (100%) had intestinal gastric cancer.

According to the TNM classification system, 24 (40%) patients had stage IV, 16 (26.6%) patients had stage I, 12 (20%) patients had stage III, and 8 (13.4%) patients had stage II (Table 2).

### Results

Of the 60 patients with gastric cancer included in the study, 36 (60%) were male and 24 (40%) were female. Their ages ranged from 26 to 80 years, with a mean of 60.8±14.5 years. The average age of women was 57.5 ± 15.5 years (range 26-77). The average age of men was 62.7 ±10.8 years (range 38-80).

The most obvious symptom of the patients was pain. While 46 (76.7%) patients had pain, 14 (23.3%) patients had no pain. In 28 (40.7%) patients, the duration of pain was 3 months or less. In 10 (16.7%) patients, the duration of pain was 6 months. 36 (60%) patients had significant weight loss. 16 patients lost weight 5 or more kilograms per month. Other patients lost weight 10 or more kilograms in 6 months. 34 (56.7%) patients had dyspeptic complaints.

20 (33.3%) patients smoked cigarettes, and 4 (6.7%) patients drank alcohol. 4 (6.7%) patients had a history of vagotomy operation for duodenal ulcer. 2 (3.3%) patients had a family history of gastric cancer (father).

Tumor localization was the antrum in 32 (53.3%) patients, the antrum-corpus in 20 (33.3%) patients, the corpus in 4 (6.7%) patients and the cardia in 4 (6.7%) patients (Table 1).

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<th>N</th>
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<tr>
<td>Antrum</td>
<td>32</td>
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<td>Antrum-Corpus</td>
<td>20</td>
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<td>Corpus</td>
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<td>Cardia</td>
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<td>Total</td>
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Tumor type was investigated in 40 (66.7%) patients undergoing resection. There were 18 (45%) patients with intestinal-type, 18 (45%) patients with diffuse-type, and 4 (10%) patients with mixed-type.

When tumor type and localization were compared, only 32 patients (50.3%) had antral involvement. Of the patients with antral involvement, 10 (30.1%) were inoperable, and 22 (69.9%) were able to undergo tumor staging. Of the patients undergoing tumor staging, 12 (54.5%) had intestinal gastric cancer, 6 (27.2%) had diffuse gastric cancer, and 4 (18.3%) had mixed gastric cancer.

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### Discussion

A significant association between H. pylori infection and gastric cancer was first demonstrated in epidemiological studies. In 1994,
H. pylori was classified as group 1 carcinogen by the International Agency for Research on Cancer [1]. The risk of developing gastric cancer during life in H. pylori-positive individuals has been reported to be 1-3% [2]. The risk of gastric cancer development following H. pylori infection increases in proportion to the follow-up period and is 9 times higher than normal when the duration exceeds 15 years [3].

H. pylori is responsible for 75% of gastric cancers. However, its role in gastric carcinogenesis is not fully understood because only a small proportion (1-3%) of infected individuals develop gastric cancer [2].

In some studies analyzing gastric tumor localization in relation to H. pylori infection, H. pylori infection was found to be significantly associated with gastric cancer in the fundus, corpus, and antrum, but no relationship was found for gastric cardia cancer [4,5]. 35-89% of distal gastric cancers are directly related to H. pylori. The increase in risk is more pronounced in women and blacks [6]. Although the majority of studies have reported that there is no difference in the seroprevalence of H. pylori between intestinal and diffuse type cancers, there are also studies showing that the seroprevalence rate is higher in intestinal type cancer (80-90%) than in diffuse type cancer (30%) [7].

Various studies using serological, histological and microbiological methods have shown that the prevalence of H. pylori infection in gastric cancer patients is 21-100% [8]. The reason why the prevalence rates vary widely may be related to socioeconomic status, dietary and environmental factors in the societies studied, and the quality of the laboratory methods used is also important.

In a study conducted in Brazil, at least three sections were taken from 4 different gastric regions immediately after the operation in 40 patients with gastric cancer who underwent total gastrectomy. Histological, culture, urease and smear examinations were made. The detection rate of H. pylori in at least one test was found to be 82.5% [9]. However, the individual detection rates of H. pylori infection for each of these methods was much lower. The same researchers retrospectively examined the histological slides of 67 patients with gastric carcinoma and detected H. pylori in only 20 (30%) patients. Widespread areas of intestinal metaplasia and dysplasia are not suitable for H. pylori colonization.

Studies investigating the relationship between H. pylori and gastric cancer can be grouped into three different groups. The first group was epidemiological studies, and the prevalence of H. pylori infection was investigated in different gastric cancer risk regions [10-12].

In the second group, serum samples were obtained years ago and stored. The presence of antibody against H. pylori was investigated using these serum samples. It was compared between those who developed gastric cancer in the following years and those who did not [12,13].

In the third group, H. pylori infection status was investigated at the diagnosis of gastric cancer and compared with the control group [14,15]. Different methods have been used for the diagnosis of H. pylori infection in these studies. In one group, the histological method was used for diagnosis. In these types of studies, very different results were obtained. This is due to the fact that while some samples were taken from the tumor tissue in order to detect H. pylori, other samples were taken from the surrounding gastric mucosa.

Atrophy and intestinal metaplasia in tumor-adjacent tissue are very common changes in gastric cancer patients, especially in intestinal gastric cancer. For this reason, false-negative histology would be high even though it is studied in the surrounding tissue, not only in tumor tissue [16].

Several hypotheses have been proposed for H. pylori and gastric carcinogenesis. Because studies on cancer type and H. pylori infection have found that H. pylori infection and atrophy and intestinal metaplasia in the surrounding tissue are more common in intestinal gastric cancer patients, the most adopted hypothesis among them is the Correa’s biological model of gastric carcinogenesis [13]. According to this model, it can be schematized as follows: chronic superficial gastritis (unless H. pylori is eradicated) → chronic atrophic gastritis → reduced acid secretion → increased intragastric bacterial population → increased concentrations of carcinogenic N-nitroso compounds → intestinal metaplasia, dysplasia and cancer development.

In our study, when the relationship between tumor type and H. pylori was investigated, H. pylori positivity was 55.6% in intestinal gastric cancer and 77.8% in diffuse gastric cancer. In a study conducted in California, H. pylori positivity was found to be 89% in intestinal gastric cancer and 31.8% in diffuse gastric cancer. In addition, the relationship between H. pylori and intestinal gastric cancer was reported to be statistically significant [13]. In another study in the Netherlands, H. pylori positivity was found to be 60% in intestinal gastric cancer and 46% in diffuse gastric cancer. However, this was not statistically significant [17].

In our study, the relationship between tumor localization and H. pylori was investigated, but no significance was established. H. pylori was detected in 4 (two) patients with gastric cardia cancer. In a study of Talley, an association could not be found between gastric cardia cancer and H. pylori [18]. Rudi et al. [19] found that H. pylori positivity in gastric cardia cancer was close to that in tumors localized in the antrum and corpus.

In our study, H. pylori positivity was found lower in gastric cancer patients than in the control group. Accordingly, this study could not establish an association between H. pylori and gastric cancer. When the literature is examined, similar studies investigating the relationship between H. pylori and gastric cancer have found the results in support of this relationship. However, there have been a lot of studies showing that the relationship is not significant [19-21].

The largest epidemiological study supporting the relationship between H. pylori and gastric cancer was conducted in 46 different rural areas of China by Forman. The death from gastric cancer was 20 times higher in areas with high prevalence of H. pylori than in areas with low prevalence of H. Pylori [22]. In Colombia, two cities with low and high prevalence of H. pylori were compared. It was found that the death from gastric cancer was 4 times higher in the city with high prevalence of H. pylori than in the city with low prevalence of H. Pylori [11]. In 1993,
the EUROGAST study group examined the relationship between the prevalence of H. pylori infection and gastric cancer rates in 17 populations from 13 countries. They found an approximate six-fold increase in the incidence of gastric cancer in populations with 100% H. pylori infection compared to a population with no infection [12]. In addition, although the various publications from Africa have reported that the incidence of H. pylori infection is 85% (especially in early childhood), gastric cancer is rarely seen in Africa [18]. Deficiencies in data collection may be responsible for this situation. The same situation is also true for our country. Although H. pylori infection is widespread in our country, the mortality rates of gastric cancer are very low [23].

**Conclusion**

Both patients with intestinal and diffuse gastric cancers were accompanied by H. pylori infection. The rate of H. pylori infection was higher in patients with diffuse gastric cancer. Although H. pylori is one of the etiologic factors for gastric cancer, there was no significant difference in H. pylori infection between those with and without gastric cancer.

**Competing interests**

The authors declare that they have no competing interest.

**Financial Disclosure**

The authors declare that they have no competing interest.

**Ethical approval**

Before the study, permissions were obtained from local ethical committee.

**References**