

HELICOBACTER PYLORI INFECTION IN GASTRIC CANCER: A STUDY OF 84 CASES FROM ASIR REGION

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Gastric cancer can be divided into three histologic types: intestinal and diffuse adenocarcinoma, and malignant lymphoma. To determine whether *Helicobacter pylori* was associated with either cancer type, we reviewed histologic sections from stomachs of 84 patients with the diagnosis of gastric cancer. Of 63 patients with histologic evidence of intestinal adenocarcinoma, 53 (84%) contained *H. pylori* in noncancerous tissue compared with six (66.7%) of nine patients with diffuse adenocarcinoma (odds ratio = 2.65; $Z=1.048$; $P>0.05$) and with eight (66.7%) of 12 patients with non-Hodgkin malignant lymphoma of the stomach (odds ratio = 2.65; $Z=0.826$; $P>0.05$). Our findings are compared with reported data from other countries and we are not aware of similar reports from the Kingdom of Saudi Arabia. *Ann Saudi Med* 1994;14(4):286-289.

Gastric cancer is a leading cause of death worldwide. Although its incidence has steadily decreased over the last five decades in the United States, Western Europe, in countries in Latin America, Asia and South Africa, gastric cancer remains among the most common malignancies.^{1,2} Several studies from Saudi Arabia reported intermediate frequencies of gastric cancer compared to Western and developing countries with frequencies ranging from 6% to 10% of all cancer cases.³⁻⁶ Gastric cancer is the fifth leading type of all cancer cases in the Asir area, Southern Saudi Arabia, representing 6.7% of the cases.⁷

There are many ways to classify gastric adenocarcinoma histologically. From an epidemiologic standpoint, one helpful classification is the Lauren classification; the latter divides gastric carcinoma into two histologic types, intestinal and diffuse.⁸ The intestinal type of adenocarcinoma has been linked to chronic superficial gastritis and atrophic gastritis. The intestinal type of gastric adenocarcinoma predominates in developing countries,⁹ and when gastric cancer incidence declines in Western countries, it has been predominantly the intestinal type that has diminished in frequency.¹⁰

In the evolution of intestinal type gastric carcinoma, the mucosa progresses through the steps of superficial gastritis, chronic atrophic gastritis and intestinal metaplasia before malignancy appears.^{11,12} Chronic superficial gastritis has been strongly linked with *Helicobacter pylori* (HP) infection¹³⁻¹⁵ and HP has been suggested as an environ-

mental factor in the evolution of gastric carcinoma. Recently, studies from Western countries have reported high incidences of HP infection in association with intestinal type gastric carcinoma, using serological methods to identify HP infection.¹⁶⁻¹⁸ Very few studies have used histologic identification of HP as evidence of infection¹⁹⁻²¹ and we are not aware of similar reports from the Kingdom of Saudi Arabia. The current study explored the possible association of HP infection among patients with primary gastric cancer from the Asir region, Southern Saudi Arabia.

Patients and Methods

The current study included all patients with histopathologic diagnosis of gastric cancer between 1987 and 1991 at Asir Central Hospital, Abha, Saudi Arabia. The age, sex and tumor location of patients were recorded and available slides and tissue blocks obtained. Thirty-four patients had undergone gastrectomy and in the remaining 50 cases, the diagnosis was made in endoscopic biopsies only.

Hematoxylin and eosin (H&E) stained sections from gastrectomy specimens were separated into two groups; sections of malignant gastric tissue and sections of nonmalignant gastric tissue. Malignant tissue was evaluated only for tumor type and histologic classification of gastric carcinoma into intestinal and diffuse types conforming to criteria set forth by Lauren,⁸ and based on architectural structures, cytologic features and stromal response. H&E stained sections from nonmalignant tissue (mostly from resected margins as far from the tumor as possible) were evaluated for *H. pylori* infection and histology of associated gastritis. If *H. pylori* was negative, a Giemsa stain was done and the tissue sections were re-examined.

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TABLE 1. *Helicobacter pylori* (HP) infection in 84 gastric cancer cases distributed according to site and histologic type of tumor.

*Site	Adenocarcinoma (intestinal type)		Adenocarcinoma (diffuse type)		Malignant lymphoma		Total	
	No. of Cases	**No. Positive	No. of Cases	No. Positive	No. of Cases	No. Positive	No. of Cases	No. Positive
Antrum	24	22	3	2	4	3	31	27 (87.1)
Fundus	10	7	2	1	1	1	13	9 (69.2)
Cardia	11	8	1	1	-	-	12	9 (75.0)
Body	18	16	3	2	7	4	28	22 (78.6)
Total	63	53 (84)	9	6 (66.7)	12	8 (66.7)	84	67 (79.8)

*=site of the tumor:where the major portion of the tumor was present as assessed during endoscopy and/or examination of gastrectomy specimens;
 **=no. positive:number of cases positive for HP infection in sections from non-neoplastic gastric tissue; ()=number in parentheses are percentages of total number of cases.

In the remaining 50 cases without gastrectomy, the tissue was similarly processed except that all tissue fragments (malignant and nonmalignant) were sectioned in one block. All endoscopic biopsies included in this study (50 cases) contained at least two pieces of nonmalignant gastric tissue, ranging from two to five pieces with an average of 3.1 pieces of non-neoplastic gastric tissue. In each case, non-neoplastic gastric tissue biopsies were obtained from the gastric area surrounding the tumor in order to estimate the extent of gastric involvement by the tumor preoperatively. The tumor location was judged by endoscopic evaluation and/or gastrectomy specimens when available and tumor site was identified as the gastric area containing the major bulk (portion) of the tumor. All statistical comparisons were made using Z-test and P values were calculated. The data were tabulated and expressed in absolute numbers and/or crude (relative frequency) percentages.

Results

The current study included all patients with gastric cancer diagnosed at Asir Central Hospital during a five year period (1987 to 1991). The mean age of the cases was 60 years with a range of 22 to 85 years. Seventy-two patients (86%) were Saudis and 12 patients (14%) were non-Saudis. Sixty-nine patients were males (82%) and 15 patients were females (18%).

Table 1 shows the distribution of *Helicobacter pylori* (HP) infection according to the histology of the tumors and their gastric locations. A total of 79.8% of all gastric cancer cases were HP positive and the frequencies of HP infection for intestinal type adenocarcinoma, diffuse type adenocarcinoma and non-Hodgkin malignant lymphoma (NHL) were 84%, 66.7% and 66.7% respectively. When the frequency of HP infection in diffuse adenocarcinoma and NHL was compared to that of intestinal adenocarcinoma, the Z values were 1.048 and 0.826, P>0.05 and odds ratios were 2.65 respectively. Also, when the Z-test was used to compare the frequency of HP infection of antral tumors to tumors of cardia, fundus and body, all P values were >0.05 with Z values = 1.147, 0.79, and 1.155 respectively.

TABLE 2. Frequency of *Helicobacter pylori* (HP) in 84 cases of primary gastric cancer according to the type of gastric tissue available for histopathologic diagnosis.

Type of gastric tissue for dx	*No. of HP positive cases	Total no. of cases
Gastrectomy	28 (82.4)	34 (40)
Endoscopy bx	39 (79.0)	50 (60)
Total	67 (79.8)	84 (100)

dx=diagnosis; bx=biopsy; ()=numbers in parentheses are percentages of HP (+ve) cases to total number of cases; *=the difference of HP positivity in gastrectomy and endoscopic biopsies is not significant (P>0.05).

Table 2 compares the frequency of HP infection in gastrectomy and endoscopic biopsy specimens. Although the frequency of HP infection was slightly higher in gastrectomy than endoscopic biopsy specimens (82.4% and 79% respectively), the difference is statistically insignificant (Z=1.123 and P>0.05). In order to evaluate the confidence of histologic typing of tumors in endoscopic biopsies, the endoscopic biopsies done before gastrectomy in our 34 cases were revised. All intestinal type adenocarcinoma and NHL cases were correctly classified in endoscopic biopsies. Only one case diagnosed endoscopically as intestinal type turned out to be of diffuse nature in gastrectomy specimen.

The histologic types of associated gastritis were studied in non-neoplastic tissue sections from the 34 cases of gastrectomy. Histologic evidence of gastritis was seen in all 34 cases. Histologic types of gastritis were as follows: 21 cases of chronic diffuse superficial gastritis, nine cases of chronic superficial gastritis with focal atrophic changes and four cases of diffuse atrophic gastritis. Intestinal metaplasia was seen in 14 of the 34 gastrectomy specimens.

Discussion

General pattern of cancer and pattern of primary gastrointestinal tract cancer in Asir Province, Southern Saudi Arabia, have been recently reported.^{7,9} Gastric cancer represented 6% of all cancer cases and 27% of patients with primary gastrointestinal cancer. The ratio of gastric cancer: colorectal cancer in Asir area is 1.3:1 compared to a reverse ratio of 1:4 in Western populations.

The first study to demonstrate a direct histopathologic association between *H. pylori* infection and gastric cancer in a Western population was published in mid 1990,²¹ and subsequently, two similar studies were reported from the United States¹⁹ and Singapore.²⁰ We are not aware of similar studies from the Kingdom of Saudi Arabia. Several studies in Western countries have demonstrated HP infection association with gastric cancer using serological tests for identification of HP infection with or without correlation to gastric cancer type and/or location.¹⁶⁻¹⁸

The current study demonstrated that prevalence of *H. pylori* infection in our patients with gastric cancer is 79.8% (67 of 84 cases). *H. pylori* infection was seen in 84% (53 of 63) of patients with intestinal type gastric adenocarcinoma and 66.7% of patients with diffuse adenocarcinoma and primary gastric lymphoma. The difference between HP infection frequency of 79.8% and 66.7% is not statistically significant ($Z=1.048$ and 0.826 , $P>0.05$).

Our results concur with those from Europe²¹ and Singapore,²⁰ which found no difference in the occurrence of *H. pylori* between intestinal and diffuse type gastric carcinoma. In a similar study from the United States,¹⁹ the frequency of *H. pylori* infection in intestinal type gastric adenocarcinoma was 89.2% (33 of 37 cases) compared with 31.8% (7 of 22 cases) in diffuse type gastric adenocarcinoma (odds ratio=17.7; $P<0.001$). No comment on the association of *H. pylori* infection and primary gastric lymphoma was reported. In our study, intestinal type adenocarcinoma was sevenfold more than diffuse adenocarcinoma (63:9) and malignant lymphoma presented 14% of all gastric cancer cases (12 of 84 cases). In a Western population,¹⁹ intestinal type gastric adenocarcinoma was only 1.7 fold higher than diffuse adenocarcinoma and malignant lymphoma was seen in 2% to 5% of all gastric cancer cases. The frequency of *H. pylori* infection in intestinal type gastric adenocarcinoma in our study and the report from the United States¹⁹ are comparable (84% and 89.2%); however, in the diffuse type of adenocarcinoma, the frequency of *H. pylori* infection in our patients was twice the frequency in the American population (67% and 31.8% respectively). The 89.2% frequency of infection in the U.S. population of patients with intestinal type gastric tumors greatly exceeded both the rate of infection in patients with diffuse type gastric adenocarcinoma and the 35% to 50% prevalence rate of HP in the normal U.S. population. In our patients, this association was not statistically significant where the frequency of *H. pylori* infection in diffuse type gastric adenocarcinoma and in normal Saudi population living in the Riyadh area²² were 67% and 70% respectively ($Z=1.048$ and 0.984 , $P>0.05$ in both cases). Also, in our study, prevalence of *H. pylori* in gastric malignant lymphoma was comparable to that of diffuse type gastric

adenocarcinoma. Similar findings were also noted in studies from Southeast Asia.²⁰ The high incidence of HP infection in gastric lymphoma in our study and other studies from Southeast Asia is not clear. One possibility is that these findings are related to the high incidence of HP infection in developing countries. HP might be a contributing causal factor in gastric lymphoma. This issue will need further investigation in large series studies of HP infection in gastric lymphoma patients.

In our study, the location of tumors did not influence the frequency of HP infection. Similar findings were seen in other reports.¹⁹⁻²¹ However, in the latter reports, HP infection in gastric cardia tumors was considerably less when compared to antral and body tumors. In our study, gastric cardia tumors were associated with HP infection as frequent as in antral and body tumors, mostly at the distal resected margins in body type mucosa.

In summary, our study has shown strong association of HP infection with intestinal type gastric adenocarcinoma comparable to findings from other countries. However, tumor histology and tumor location did not affect the frequency of associated HP infection in our patients. The role of HP as a possible causal factor in gastric cancer has to be further evaluated.

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