Bangladesh Med Res Counc Bull 2009; 35: 7-10
DOI: 10.3329/bmrcb.v35i1.2315

Association of *Helicobacter pylori* infection with gastric carcinoma

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Abstract

This is a cross-sectional study on 140 gastric neoplasm subjects diagnosed by upper gastrointestinal endoscopy. The commonest site of cancer was the antrum of stomach (52.86%), followed by the antrum and body (32.86%) and only body region (12.14%). Histology revealed adenocarcinoma in all patients. The associations of *Helicobacter pylori* with gastric cancer were studied by rapid urease test, serology and histology by Giemsa stain. The positivity of *H. pylori* determined by serology in 70 patients (50%) was significantly higher than those determined by histology 22 patients (15.71%). No significant association between *H. pylori* infection and gastric cancer was observed.

Introduction

Gastric cancer is one of the most common malignancies worldwide[1]. It tops the list of cancer related death in many countries of the world including countries in Asia. Gastric carcinogenesis is a multifactorial process[2].

Gastric cancer is important historically and has been the subject of extensive research. Hippocrates first described a patient with black vomiting and a "karkinoma" of the stomach in 400 BC[3]. Napoleon Bonaparte was found, at autopsy, to have a large gastric cancer that had perforated and, in fact, several members of the Bonaparte family were reported to have died from gastric cancer[4]. More recently, Marshall and Warren[5] were awarded the 2005 Nobel Prize in Medicine and Physiology, in part for their discovery of *Helicobacter pylori* and its causative role in gastric cancer.

Recently it has been found that a casual relation may exist between *H. pylori* infection and gastric cancer. *H. pylori* cause chronic gastritis, gastric atrophy and intestinal metaplasia ultimately leading to gastric malignancy[6]. But the issue of carcinogenesis is yet unresolved because of discrepancy in epidemiological studies[7]. Most of the studies implicating *H. pylori* infection in the development of gastric cancer have been carried out in the developed countries in the west. The etio-pathological background may be different among the people of this region[8]. The present study is likely to answer this question of co-relation between *H. pylori* and gastric carcinogenesis in Bangladesh.

Materials and Methods

This study was carried out from July 2006 to June 2007. One hundred forty endoscopically and histologically proven cases (male 105, femal 35) of gastric cancer were included. Patients with chronic disease, immunosuppressed, using non-steroid anti-inflammatory, previous radiotheraphy/ chemotherapy and H_2 blockers were excluded. All patients were operated for gastric cancer (partial or total gastrectomy). After resection, the greater curvature of the stomach was opened and three to five mucosal biopsies samples were collected from non-necrosed region of cancer and the adjacent macroscopically non-tumorous mucosa within 4 cm distance from the tumor margin. Two paired biopsies from non-cancerous part preferably antrum, body or body and fundus were taken.

The *H. pylori* infection status was assessed by the urease rapid test, observed during 30 min (Gastroteste kit). *H. pylori* IgG antibody in plasma was measured by an enzyme-linked immunosorbent assay (ELISA), using commercially available kit Cobas Core II (Roche). A cut off value of >7.5 U was taken to categorize positive samples, as recommended by the manufacturer. For histopathological evaluation of the *H. pylori* colonization, the specimens from tumor tissue and adjacent mucosa were loaded into 1% formalin and

routinely screened with microscope (Giemsa staining).

One piece of each paired specimen was placed in the urea-agar media for rapid-urease test for detection of *H. pylori*. Other two mucosa biopsy specimens placed in alcohol and send to microbiology department for direct detection of *H. pylori* after Giemsa stain in addition to H & E staining.

Blood samples were taken from all the selected patients and the serum was assayed for anti *H. pylori* IgG by quantitative measurement with ELISA method.

Statistical analysis: Statistical analysis was done by Chi-square (χ^2). Proportion (z) and correlation co-efficient (r) tests were done when and where applicable. A p value of <0.05 was taken as statistically significant. It is done by using software SPSS 16.0.

Table I: The result of different methods of detecting *H. pylori* in stomach cancer

	Giemsa		Rapid urease		Serology (IgG)	
Age	Negative	Positive	Negative	Positive	Negative	Positive
20-29	8	2	7	3	5	5
30-39	16	2	16	2	8	10
40-49	29	5	26	8	21	13
50-59	23	2	19	6	12	13
60-69	25	6	23	8	15	16
70-79	15	3	13	5	8	10
80+	2	2	2	2	1	3
Total	118	22	106	34	70	70

Results

The mean ages of cancer patients were 51.48 years (range 20-85 years). Peak incidence (24.29%) occurs in the age group 40 years to 49 years.

The *H. pylori* were detected in three methods (Giemsa, Rapid urease and serology). Using serology, there were 70 positive cases of *H. pylori* infection whereas only 34 and 22 cases were identified using rapid urease and Giemsa staining respectively (Table I).

The blood sample of all 140 patient of carcinoma stomach was analyzed for the detection of anti *H. pylori* IgG using the commercially available ELISA kits. The assay had a sensitivity of >95.9% and a specificity of 98%. Total 70 (50%) patient of stomach cancer were *H. pylori* sero-positive, of which 15 female and 55 were male.

As per the site distribution (Table II) of gastric cancer, antral lesion comprised 52.86% with antrum and body 32.86% and only body 12.14%. *H. pylori* were positive in 54.05% (40/74) cases of lesion in antrum; 63.4% (29/46) in antrum and body and 64.7% (11/17) in only body lesion. Only one (0.71%) malignancy found in fundus area of stomach.

Table II: Distribution of gastric cancer

Site	Number of patients	Percentage
Antrum	74	52.86
Antrum and body	46	32.86
Body	17	12.14
Body and fundus	2	1.43
Fundus	1	0.71

Table I shows the age wise distribution of *H. pylori* presence by different methods of detection in carcinoma stomach. If we combine all methods then total number of 82 positive found. It indicates that around 58.57% of stomach cancers were infected with *H. pylori.*

Discussion

Once clinical manifestations appear, gastric cancer has an extremely poor prognosis since a 5-year survival rate using currently available treatments, surgery and radio-chemotherapy, is less than 20%. Therefore, the challenge in gastric cancer, as in many other cancers, is to prevent its development by detection and treatment of pre-cancerous lesions and elimination of known risk factors. In order to achieve this goal, it is necessary to understand the patho-mechanisms of gastric carcinogenesis. Although stomach cancer is an ancient disease, probably affecting man for several millennia, its pathogenesis remains obscure. Epidemiological studies of migrant populations suggest that gastric cancer is associated with exposure to some environmental factor early in life[9].

The association between *H. pylori* and gastric cancer was proven by numerous case control studies nested in large cohorts which could prospectively examine the *H. pylori* status of gastric cancer patients[9-11]. This association was considered sufficient by the Working Group of the International Agency for Research on

Cancer/World Health Organization to recognize *H. pylori* as a Group I carcinogen for humans in 1994[12].

Since then, data from several epidemiological, interventional and experimental studies have been gathered, confirming the causal link between *H. pylori* and gastric cancer. Ecological studies mostly confirm the geographical association between the prevalence of *H. pylori* and prevalence of gastric cancer, showing a declining incidence of gastric cancer in countries with falling rates of *H. pylori* infection. The results obtained with an animal model, the Mongolian gerbil, mimicking the gastric carcinogenesis steps after *H. pylori* infection, is another strong argument[13].

In our study only 15.71% of gastric carcinoma patient were histologically positive for *H pylori.* Though the prevalence of *H. pylori* infection in the apparently healthy young adults is reported to be 92%[14] in Bangladesh, which was much higher.

Lee et al[15] in 1998 shows *H. pylori* infection rates were 78.9% in gastric cancer patients and 41.6% in normal control subjects (OR=7.03; $p<0.0005$), which is not matching with our study.

A study in Korea[16] reported that the infection rates showed only a slight difference between gastric cancer patients (60%) and control subjects (51.9%).

In this preliminary study, we found that among specimens of 140 stomach cancer patients 15.71% were infected with *H. pylori* by Giemsa stain in either the tumor or tissues adjacent to the tumor. Interestingly, however, only 8.57% (12/140) was Giemsa test-positive among tumor specimens, while 14.28% (20/140) was positive among tissues adjacent to the tumor. The tissues adjacent to the tumor may be more suitable for *H. pylori* detection than the tumor itself, presumably reflecting the preferred habitat of *H. pylori*.

In our study *H. pylori* positive carcinoma stomach found different in different methods like Giemsa= 15.71%, rapid urease = 24.285%, serology= 50%. It indicates that carcinoma itself decrease the *H pylori* infection rate. Serology (IgG) indicates old infection. So carcinoma itself may create a hostile environment for *H. pylori* growth.

These results suggested that *H. pylori* infection may not play a certain role in the early stage of carcinogenesis of gastric mucosa epithelia.

Acknowledgments

We acknowledge research and training monitoring cell of Bangladesh College of Physicians and Surgeons for providing fund for the study and Dr. Abdul Mazid Millon for collecting data from the patient.

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