Role of *Helicobacter pylori* in gastric carcinoma

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**ABSTRACT**

Background. *Helicobacter pylori* infection has recently been incriminated in the pathogenesis of gastric carcinoma and chronic atrophic gastritis and intestinal metaplasia are considered to be precursors of this condition. Although the incidence of *Helicobacter pylori* infection in India is high that of gastric carcinoma is low. We, therefore, decided to examine the association between *Helicobacter pylori*, intestinal metaplasia and gastric carcinoma in a prospective study.

Methods. Fifty patients with carcinoma of the stomach and 50 with non-ulcer dyspepsia underwent upper gastro-intestinal endoscopy and had biopsies from the antrum, body and carcinomatous tissue.

In 12 cases of gastric carcinoma, tissue was obtained from resected specimens at operation. The types of gastritis, intestinal metaplasia and presence of *Helicobacter pylori* were assessed by staining with haematoxylin and eosin, periodic acid-Schiff reagent with alcian blue and Warthin-Starry stains.

Results. The incidence of chronic atrophic gastritis, intestinal metaplasia and *Helicobacter pylori* were 82%, 36% and 38% in patients with carcinoma and 86%, 4% and 68% in those with non-ulcer dyspepsia. *Helicobacter pylori* positivity was significantly higher (p<0.05) and intestinal metaplasia significantly lower (p<0.001) in patients with non-ulcer dyspepsia than in those with carcinoma.

Of the 50 cases with carcinoma, 28 were of the intestinal and 22 of the diffuse type. The incidence of chronic atrophic gastritis, intestinal metaplasia and *Helicobacter pylori* in the intestinal type of carcinoma was 71%, 46% and 39% while in the diffuse type it was 32%, 23% and 36%. The incidence of *Helicobacter pylori* infection did not differ significantly in the two types of carcinoma.

Conclusions. We have found that although *Helicobacter pylori* infection and chronic atrophic gastritis are common in Indians, the incidence of intestinal metaplasia is low. *Helicobacter pylori* infection was equally common in both the intestinal and diffuse type of gastric carcinomas. Our findings, therefore, cast doubt on the role of *Helicobacter pylori* infection in gastric carcinogenesis.

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INTRODUCTION

Since the discovery of *Helicobacter pylori* (*H. pylori*)\(^1\) in the gastric mucosa, various studies have demonstrated the role of *H. pylori* in gastroduodenal disorders.\(^2\)-\(^7\) *H. pylori* is considered to be a causative agent of chronic gastritis and chronic gastritis is considered to be a risk factor for carcinoma of the stomach.\(^8\)-\(^9\) It has, therefore, been proposed that *H. pylori* infection may be involved in gastric carcinogenesis.\(^10\)-\(^13\) Serological studies, from areas where there is a low prevalence of *H. pylori*, have shown that this infection is related to gastric carcinoma.\(^14\)-\(^18\) However, if *H. pylori* is responsible for gastric carcinoma, the incidence of this tumour should be proportional to the prevalence of *H. pylori* in the community. Yet in countries which have a high prevalence of *H. pylori* infection (India, Yemen, Nigeria and Taiwan) there is a low incidence of gastric carcinoma.\(^19\)-\(^25\) In India, by the age of 30 years, the seropositivity rate of the population for *H. pylori* infection is nearly 90%.\(^19\) Hence, a seroprevalence study comparing *H. pylori* infection in controls and patients with gastric carcinoma above the age of 30 years is unlikely to yield any difference unless long-term studies are carried out in a high-risk population with sequential biopsies and serological tests. We, therefore, decided to examine the association between chronic atrophic gastritis (CAG), *H. pylori*, intestinal metaplasia (IM) and gastric carcinoma.

PATIENTS AND METHODS

Fifty patients with gastric carcinoma and 50 with non-ulcer dyspepsia (NUD; controls) were investigated. Twelve of the patients' surgically resected specimens were available and 38 endoscopic biopsies from the tumour along with its adjacent tissue were evaluated. The specimens were fixed in 10% formalin and paraffin embedded histological sections were stained with haematoxylin-eosin, periodic acid-Schiff reagent with alcian blue and Warthin-Starry stain for the identification of *H. pylori*.

All the cases were assessed for the histological type of carcinoma, gastritis, IM, lymphoid aggregates or follicles and the presence of *H. pylori*. Gastric carcinomas were classified using Lauren's\(^26\) classification as being of the intestinal and diffuse type. Chronic gastritis was classified according to Whitehead's\(^27\) system as

1. Chronic superficial gastritis—Infiltration of the upper one-third of the lamina propria with plasma cells and lymphocytes.
2. Atrophic gastritis—Extensive inflammation with a varying degree of mucosal atrophy. Atrophic gastritis was subdivided into mild, moderate and severe according to the degree of atrophy.
3. Gastric atrophy—severe damage of glands without infiltration.

Intestinal metaplasia was judged to be either present (complete or incomplete) or absent. Presence of lymphoid aggregates or follicles was also noted in both groups. The extent of *H. pylori* infection was scored as follows:

Grade 0: No characteristic bacteria
Grade 1: Occasional spiral bacteria found after searching
Grade 2: Scattered bacteria in most high power fields or occasional groups of numerous bacteria
Grade 3: Numerous bacteria in most high power fields

The statistical methods used for analysis of the data were Student's unpaired t-test and the Chi-squared test.

**RESULTS**

The demographic profile of the study population shows that the patients with gastric carcinoma were older than those with NUD by 7 to 8 years and this age difference was statistically significant.

Although the incidence of CAG was similar in both the groups, that of Im was higher and of *H. pylori* positivity was lower in the patients with carcinoma (Table I). Only 2 patients with NUD had complete Im while 16 patients with carcinoma had complete and 2 had incomplete Im.

In 28 (56%) patients the carcinoma was of the intestinal type and in 22 (44%) it was of the diffuse type. The positivity rates of CAG, Im, *H. pylori* in the intestinal and diffuse types of carcinoma are shown in Table II. CAG was seen in all patients with intestinal carcinoma and in 13 (59%) with diffuse carcinoma. There was, however, no difference in the incidence of *H. pylori* positivity in the two groups.

Lymphoid aggregates and follicles were seen in 40% and 38% patients in the carcinoma and NUD groups respectively and there was no correlation between the presence of lymphoid aggregates and *H. pylori*.

**DISCUSSION**

CAG and Im are considered to be precursors of carcinoma of the stomach and *H. pylori* is known to cause CAG.9,28 Hence this organism has been implicated as one of the major aetiological factors in gastric carcinoma.10-13

We found the incidence of CAG to be similar in patients with gastric carcinoma and with NUD. We have previously reported that about 50% of asymptomatic Indians above the age of 30 years have CAG.29 This is considerably higher compared to a western population.30 In spite of having a high incidence of CAG, the incidence of gastric carcinoma is much lower in India.21

Seroepidemiological and biopsy studies from our country revealed gastric *H. pylori* infection in more than 90% of the adult population.19 In contrast to these studies, we found that the incidence of *H. pylori* infection in biopsies of gastric carcinoma patients was significantly lower than in the NUD group (Table I).

The natural history of *H. pylori* infection suggests that it causes chronic superficial gastritis which progresses to CAG with Im.28 *H. pylori* may not be detected in the areas with Im presumably due to the hypoacidity prevalent in severe atrophic gastritis with which Im is associated. Our observations are in agreement with the above mentioned sequence as the incidence of Im is significantly higher and of *H. pylori* lower in gastric carcinoma patients compared to controls.

Though *H. pylori* infection is common in our country, the incidence of Im is low.31 Similar observations have been reported from other developing countries.22-25,32,33 As the correlation between CAG, Im and the intestinal type of gastric carcinoma is well established in gastric carcinogenesis, the low incidence of Im in our control population explains the low incidence of gastric carcinoma. Thus, factors other than *H. pylori* infection may be responsible for development of Im and subsequent gastric carcinoma.34

**REFERENCES**


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—Editor