Clinicopathological Study of Gastric Carcinoma with Special Reference to *Helicobacter pylori*

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**Abstract**

Gastric cancer (GC) is one of the most common malignancies. Although *Helicobacter pylori* (*H. pylori*) is being recognized as a Type I carcinogen for GC and primary gastric lymphoma (PGL), yet many studies especially from the Indian subcontinent do not show any such association. The aim of the study was to evaluate the clinicopathological characteristics of gastric adenocarcinoma and to determine the association of *H. pylori* infection. This prospective study included 50 cases of histologically proven gastric adenocarcinoma. A detailed clinical history, physical examination and upper gastrointestinal endoscopy were done in all the cases and mucosal biopsies were taken from the growth and the surrounding mucosa. Rapid urease test (RUT) was done to diagnose *H. pylori* infection. 50 patients of functional dyspepsia were taken as controls. GC was more common in males (70%). The maximum cases were recorded in elderly persons, mostly from 5\(^{th}\) to 6\(^{th}\) decades. Anorexia (60%), dyspepsia (54%) and weight loss (24%) were the commonest clinical presentation. Most of the patients presented within 3-12 month of onset of symptom. In majority of cases, the lesion was confined to the antrum (62%) and body (26%) of the stomach. *H. pylori* infection was more commonly isolated from the antrum. *H. pylori* infection was not significantly associated with GC as compared to patients with functional dyspepsia. No association was found between *H. pylori* infection and gastric carcinoma. Probably gastric cancer is multifactorial disease where dietary, genetic and environmental factors play contributing roles.

**Keywords:** Gastric Neoplasm, India, *Helicobacter pylori*.

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INTRODUCTION

Gastric cancer (GC) is one of the most common malignancies, not only in Asia but also worldwide. It ranks second among males and third among females as the commonest malignancy in the world. Most of the gastric cancer patients present in advanced stages and the five-year survival are less than 20% in developing countries like India. International Agency for Research on Cancer has recognized Helicobacter Pylori (H pylori) as a Type I carcinogen for gastric cancer (GC) and primary gastric lymphoma (PGL), way back in 1994. Meta-Analyses and various epidemiological studies have revealed a strong relationship between H pylori and GC and PGL.

H. pylori infection colonizes the mucosal lining of the gastrointestinal tract, mainly the stomach and duodenum. It causes chronic active gastritis in almost all cases. As the infection is rarely self-limiting, it initiates a sequence of inflammatory-mediated changes, within the gastric epithelium. It is seen that over a period of decades, there occur degenerative changes which later evolves into the well-established precancerous conditions such as atrophic gastritis, metaplasia, and dysplasia.

There has been a paradoxical observation of high prevalence of H. pylori infection and low GC rates, in some geographical region like Africa and India. The authors have used terms like “African Enigma” and “Indian Enigma” of H. pylori infection and GCs. It has been observed that etiological factors, other than H. pylori infection, are also involved in gastric carcinogenesis, such as dietary and host genetic factors.

The aim of the study was to study the clinicopathological types of gastric malignancies with special reference to H. pylori infection.

MATERIAL AND METHODS

The present study was conducted in the department of pathology and gastroenterology of S.C.B. Medical College, Cuttack, Odisha from January 2004 to January 2005. A total number of 50 consecutive cases of gastric adenocarcinoma, which were suspected on endoscopy and later proven histologically, were included in this study. A detailed clinical history was taken and physical examination was done in all the cases. The mucosal biopsies were taken from the growth and the normal surrounding region. At endoscopy, the site, extent, appearance and mucosal friability of the suspected lesions were noted. Additional biopsy bits were taken from the growth and also the normal surrounding areas to test for H. pylori. Rapid urease test (RUT) was done to look for H pylori infection. All the tissue samples were processed and stained with routine haematoxyline and eosin (HE) stain and special stain, i.e the giemsa stain. Another 50 patients of functional dyspepsia who had apparently normal mucosal studies were tested for H. pylori using RUT. All values are presented in mean and percentage, chi square test was used to test association using SPSS software. P value < 0.05 was considered to be statistically significant.

Observation

In this study, all the patients were in the age range of 20-80 years. The maximum number of cases were found within the age range of 5th & 6th decades (54%). Males (70%) were seen more commonly affected than females (30%) and Gender (Male to Female) ratio was found to be 2.3:1 [Table1].

Table 1. Age and Sex Distribution of Cases studied

| Age gr. | Male | Female | Total |
|---------|------|--------|-------|
| In years | No. | % | No. | % | No. | % |
| 21-30   | 1   | 2      | 4     | 8  |
| 31-40   | 3   | 6      | 6     | 12 |
| 41-50   | 7   | 14     | 6     | 12 |
| 51-60   | 13  | 26     | 1     | 2  |
| 61-70   | 6   | 12     | 3     | 6  |
| 71-80   | 5   | 10     | 0     | 0  |
| Total   | 35  | 70     | 15    | 30 |

In this study, the most common symptoms of GC patients were anorexia (60%) and dyspepsia (54%) [Table 2]. The other symptoms were vomiting (34%), abdominal pain (32%), melena (30%), nausea (26%), weight loss (26%) and haematemesis (16%). The maximum number of cases were reported within 3-12 months of onset of symptoms.

Endoscopic observation showed antrum (62%) to be the most common site of involvement, followed by body or corpus (26%), fundus (6%) and G.E. Junction (6%). Only the malignant growths at the pyloric antrum and body showed positive results for H. pylori inflammation. The growth at
other sites did not reveal any *H. pylori* in the tissue section [Table 3].

Endoscopically ulcerated lesion (66%) was found to be most common type followed by fungating (16%), nodular (14%) and ulcer infiltrative type (4%). Histological examination showed that diffuse patterns (68%) were predominant over intestinal type (32%) of adenocarcinoma. Out of all cases, only 12 (24%) cases were *H. pylori* positive and the rest did not show any evidence of organisms. The incidence of *H. pylori* in intestinal type adenocarcinoma (31.25%) was slightly higher than diffuse type (20.5%) [Table 4]. Only 9 cases out of 35 males (25.7%) and 3 cases out of 15 females (20%) were *H. pylori* positive. However, RUT was positive in 56% of controls, which was statistically higher than the malignant cases [Table 5].

**Table 2. Clinical Presentation of Gastric Carcinoma**

| Presenting Symptoms | Number (n) | Percentage (%) |
|---------------------|------------|----------------|
| Anorexia            | 30         | 60             |
| Dyspepsia           | 27         | 54             |
| Vomiting            | 17         | 34             |
| Abdominal pain      | 16         | 32             |
| Weight Loss         | 13         | 26             |
| Melena              | 15         | 30             |
| Hematemesis         | 8          | 16             |

**DISCUSSION**

The result of the study as regards to age incidence of patients was compatible with a study performed in southern India, where it was observed that the maximum number of cases were beyond the age of 50 years. In this study, significant male predisposition was seen with male to female ratio 2.3:1. This was similar to the studies by Parkin *et al.* and Sumathi *et al.*, in which it was noted that the cancer was twice as common in males as compared to females.

In this present series, the most common symptoms were anorexia, weight loss and gastrointestinal bleed which is similar to other studies done from India. The most common site of involvement of GC was antrum (62%), followed by body (26%) fundus (6%) and gastro esophageal junction (6%). The study by Marson *et al.* also found that distal (antral) carcinoma was more common in comparison to cardia. However, there has been a trend in the increase of proximal gastric carcinomas especially those involving the cardia in recent years as compared to distal sites. Majority (> 95 %) of GCs are adenocarcinoma. They are further divided into intestinal and diffuse types. It is seen that the intestinal pattern is more common than diffuse pattern and mixed pattern. However, the present study shows that the diffuse type (68%) is more common than the intestinal (32%) type. Some authors have postulated that intestinal type of adenocarcinoma was prominent in high risk geographical regions and it was less commonly found in low risk region. As India belongs to the low prevalence region of gastric carcinoma, this might be the cause of low incidence of intestinal type of gastric adenocarcinoma in the present study.
In this present study, the incidence of \(H.\ pylori\) positivity in GC patients was only 24%, which was significantly less than the control group. Although \(H.\ pylori\) is being recognized as a causative agent for GC, yet the few case control studies published from India unexpectedly fail to show an association between \(H.\ pylori\) infection and GC. Kate \textit{et al}. performed a case control study where 50 patients with gastric neoplasms and 50 controls with non-ulcer dyspepsia (NUD) were enrolled. They found that \(H.\ pylori\) infection was detected less commonly in GC (38%) than those with NUD (68%)\textsuperscript{17}. Another study from South India showed that 64.7% of patients with gastric adenocarcinoma and 74.4% of patients with NUD tested positive for \(H.\ pylori\)\textsuperscript{18}. Another case control study from Lucknow had taken a better sample size of 279 cases with gastric neoplasms (263 GCs and 16 GLs) and 456 healthy controls. This study also failed to demonstrate that \(H.\ pylori\) infection was more common in patients with gastric neoplasm as compared to the controls\textsuperscript{19}. The authors have postulated a few reasons for such a low prevalence of \(H.\ pylori\) in GC patients in India. All these studies have used gastroscopy based rapid urease tests (RUT) to diagnose \(H.\ pylori\) infection. The problem with these endoscopy-based tests is that in patients with GC due to the presence of underlying gastric atrophy and intestinal metaplasia, the tests can be false negative. A combination of methods (RUT and serology) improved the detection of \(H.\ pylori\) infection in comparison to a single method. It is postulated that in a country like India, etiological factors (such as diet, addictions, host genetic factors) other than \(H.\ pylori\) infection might be the cause of gastric carcinoma\textsuperscript{10,14}.

The landmark paper by Parsonet \textit{et al}. on the \(H.\ pylori\) association with GC has shown that distal GC had higher incidence of \(H.\ pylori\) infection as compared to proximal GC (especially of gastric cardia and GE junction). The present paper also showed a similar observation. Another interesting finding was that the prevalence of \(H.\ pylori\) in the intestinal type was slightly higher than the diffuse type, although the study by Parsonet \textit{et al}. observed that both diffuse and intestinal type have an almost equal association with \(H.\ pylori\) infection.

**Limitation of the study**

There are a few limitations of the study. RUT only was used to diagnose \(H.\ pylori\) infection, which can be false negative in a few cases of gastric atrophy. Serology would have been better. The other risk factors such as diet and genetic factors were not studied in the present paper.

**CONCLUSION**

Gastric carcinoma was more common in males. The maximum cases were recorded in elderly persons, mostly in 5\textsuperscript{th} to 6\textsuperscript{th} decades. Anorexia, dyspepsia and weight loss were the dominant clinical presentation and most of the patients presented within 3-12 months of onset of symptoms. In majority of cases, malignant lesion was confined to the antrum and body of the stomach and \(H.\ pylori\) was more commonly isolated from the antrum. The diffuse pattern of adeno carcinoma is more common than the intestinal type of adenocarcinoma in the stomach. \(H.\ pylori\) infection was not significantly associated with GC as compared to patients with functional dyspepsia. GC is probably a multi factorial disease where genetic, dietary and environmental factors and \(H.\ pylori\) together play an important role in the pathogenesis.

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**CONFLICT OF INTEREST**

The authors declares that there is no conflict of interest.

**AUTHORS’ CONTRIBUTIONS**

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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None.

**DATA AVAILABILITY**

All datasets generated or analyzed during this study are included in the manuscript and/or the Supplementary Files.
ETHICS STATEMENT

This article does not contain any studies with human participants or animals performed by any of the authors.

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