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Original Research Article

Association of *Helicobacter pylori* infection and stomach cancer: our experience

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ABSTRACT

Background: Infection with *Helicobacter pylori* (H. pylori) has been linked with chronic atrophic gastritis, an inflammatory precursor of gastric adenocarcinoma. There are data on the epidemiology, pathophysiology, and histology of this disease that show that *Helicobacter pylori* gastritis has an important role in gastric carcinogenesis. However, it has to be considered that only very few of those infected with *Helicobacter pylori* will develop gastric cancer. Hence, it will be a major target of future research to identify individuals who carry a greater risk for developing gastric cancer, and therefore may benefit from eradication of *Helicobacter pylori* in terms of gastric cancer prevention. Various studies revealed that approximately more than 50% of the world's human population is infected by *Helicobacter pylori*. In underdeveloped countries, this association is shown to be much higher according to different studies.
Methods: This study was conducted over a period of 36 months from 1st January 2014 till December 31st, 2016. All patients who underwent Gastrectomy during this period were taken. All specimens were investigated to see presence of helicobacter pylori by histological examination. A total of 50 Gastrectomy was performed by one surgical team over 36-month period.
Results: Out of 50 patients, *Helicobacter pylori* positivity was seen in 33 (66%) cases by histopathological examination (HPE). Gastric cancer is more prevalent among males 31 (62%) as compared to 19 (38%) in females. It is more common among the older age group.
Conclusions: *Helicobacter pylori* infection is higher in prevalence in cases of stomach cancer. Present study also showed that there is significant association of *Helicobacter pylori* infection with gastric carcinoma. *Helicobacter pylori* infection could be one of the etiological factors for gastric carcinoma.

Keywords: *Helicobacter pylori*, *Helicobacter pylori* IARC, Histopathological examination MALT lymphomas, International agency for research on cancer HPE, Mucosa associated lymphoid tissue lymphomas, Stomach carcinoma

INTRODUCTION

Over the past years *Helicobacter pylori* (H. pylori) has been confirmed as causative agent in the pathogenesis of chronic active gastritis of the stomach, on which severe diseases such as duodenal and gastric ulcer may develop.[1,2] There is strong evidence to show that *Helicobacter pylori* infection may also be associated with gastric neoplasms, i.e. carcinoma of the stomach and primary low-grade B cell gastric lymphoma of mucosa-associated lymphoid tissue, known as MALT lymphoma.[2]

Gastric cancer is the second most common cause of cancer related deaths in the world.[3] The incidence of

gastric cancer is dramatically declining in USA and Western Europe over the past 50 years but it incidence remains still very high in most regions of Latin America and Asia especially in Japan and China.[4,5] It is also becoming a major problem in India.[6] It is hypothesized that incidence of gastric cancer is determined by environmental factor rather than genetic factors because of its dramatic change in incidence from place to place and from one generation to the next.[7] The International Agency for Research on Cancer (IRAC) in 1994 has categorized Helicobacter pylori infection as a class 1 carcinogen and a definite cause of human gastric cancer.[2]

The global burden of gastric cancer and non-Hodgkin's lymphoma due to chronic *Helicobacter pylori* infection was reassessed based on new cancers registered in 2002.[8] In that year almost 20% of cancers were considered to be attributable to infectious diseases, with *Helicobacter pylori* being the leading cause (5.5% of all cancers) followed by human papilloma viruses, hepatitis B and C viruses, Epstein–Barr virus, Human immunodeficiency virus (HIV), and human herpesvirus.[8] *Helicobacter pylori* was estimated to be responsible for about 75% of noncardia gastric cancers and gastric non- Hodgkin's lymphomas, and 65% of all stomach cancers worldwide.

Various studies revealed that approximately more than 50% of the world's human population is infected by *Helicobacter pylori*.[9] However, such studies are still lacking in underdeveloped world, where the incidence of *Helicobacter pylori* is thought to be still on the rise. Authors knowledge of the pathogenesis of gastric neoplasms is increasing day by day, and new approaches to the prevention of gastric cancer by antibiotic treatment of a precursor of this disease, namely *Helicobacter pylori* gastritis, can be considered.

METHODS

This study was carried out in the department of General Surgery, JNIMS, Porompat from January 2014 to December 2016. Fifty histologically proven cases of gastric carcinoma were included in this study. The approval of Medical Ethics was taken from Medical Ethics committee of JNIMS. Informed consent was taken from patients for this study.

Data were collected from the study patients regarding age and sex. At endoscopy, site of the lesion was Identified and recorded. These patients underwent Subtotal/total Gastrectomy depending on the site of the lesion. Histological slides were made from formalin preserved specimens. All specimen sections were stained with Hematoxylin-eosin and Giemsa for assessment of *Helicobacter pylori* infection.

Inclusion criteria

- All the patients who have undergone either subtotal or total Gastrectomy.

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made, Assumptions: 1) Dependent variables should be normally distributed, 2) Samples drawn from the population should be random, Cases of the samples should be independent. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis.

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)
* Moderately significant (P value: $0.01<P\leq0.05$)
** Strongly significant (P value: $P\leq0.01$)

Statistical software

The Statistical software namely SPSS 18.0, and R environment ver. 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate, Tables etc.

RESULTS

A total of 50 patients were included in the study. Of them 31 (62%) patients were male and 19(38%) patients were female. In this study males were more affected compared to females (Table 1).

Table 1: Sex distribution.

Gender	Total no. of patients	Percentage
Male	31	62
Female	19	38
Total	50	100

The age distribution is as shown in Table 2. Maximum number of cases in present study comes in between the age group of 41-60 followed by 61-80. In this study we have 28 patients (56%) in the age group of 41-60 and 15 patients (30%) in the age group of 61-80 years.

Table 2: Age distribution of patients with gastric cancer.

Age (Years)	Numbers of patients	Percentage
0-20	0	0
21-40	5	10
41-60	28	56
61-80	15	30
>80	1	2

A total of 50 patients histologically proven cases of Gastric cancer were taken for this study. Out of 50 cases, a total of 33(66%), were positive for *Helicobacter pylori*. All these were proven histopathologically. This Table also shows the association of *Helicobacter pylori* infection associated with Gastric cancer.

Table 3: *Helicobacter pylori* infection in Gastric cancer.

	Helicobacter pylori	Percentage
Positive	33	66
Negative	17	34

90% of gastric carcinoma in present study was seen in antral region. The most common site of gastric cancer found in this study is mainly in antrum of the stomach.

Table 4: Site of Gastric lesion.

Site of Gastric lesion	Percentage
Antrum	45 (90%)
Proximal stomach	05 (10%)

The association of *Helicobacter pylori* infection was 64.5% in males and 73.68% in female respectively.

Table 5: Sex distribution in relation to *Helicobacter pylori* infection.

Sex	No.	*Helicobacter pylori* positive	*Helicobacter pylori* negative
Male	31	20 (64.5%)	11 (36.66)
Female	19	14 (73.68)	5 (26.31)

DISCUSSION

Gastric cancer is the second and four most common cause of cancer-related death in male and female respectively in the world.[3] Since Warren and Marshall first isolated *Helicobacter pylori* from human gastric mucosa in 1983, a large volume of literature on the association of *Helicobacter pylori* infection and gastric cancer has been published.[2,10] The first definite evidence linking *Helicobacter pylori* infection to gastric cancer was obtained from seroepidemiologic studies in the United States and Britain.[11] Despite the overwhelming evidence that *Helicobacter pylori* infection is a risk factor for noncardia gastric cancer, accumulating evidence indicates that although *Helicobacter pylori* eradication is relatively simple to achieve, impacting the global burden of gastric cancer will be a much more difficult challenge.

Since the time of discovery of *Helicobacter pylori*, much has been studied about this gram negative spiral bacterium and its associated disease status. In 1994, the National Institute of Health (NIH) recognized *Helicobacter pylori* as a cause of gastric and duodenal ulcers. Later that year, the International Agency for Research on Cancer (IARC) declared *Helicobacter pylori* as group 1 human carcinogen for gastric adenocarcinoma.[2] There is also evidence that *Helicobacter pylori* infection is a risk factor for gastric mucosa associated lymphomas (MALT lymphomas). Infection with *Helicobacter pylori* leads to acute gastritis, which becomes chronic and progresses to atrophic gastritis, intestinal metaplasia (IM), and dysplasia, which have been Identified as important steps in the pathogenesis of gastric cancer.[12]

The presence of the *Helicobacter pylori* infection can be diagnosed by various invasive (like upper gastrointestinal endoscopy and biopsy, culture and rapid urease test) and non-invasive methods (like *Helicobacter pylori* antibody assay, polymerase chain reaction, *Helicobacter pylori* antigen test, ELISA and the urea breath test).[13] Demonstration of bacilli on histopathology of gastric biopsy specimen after staining with appropriate stains is the most sensitive (98%) and specific (98%) test.[14] In present study also, *Helicobacter pylori* was identified on histopathological specimens.

In the United States, the majority of patients with gastric cancer present between the ages of 65 and 74 years, with a median age at diagnosis of 70 years in men and 74 years in women.[15] In Japan, a country with high incidence of gastric cancer, the mean age of diagnosis is roughly a decade earlier.[16]

Afridi et al showed that the mean age of carcinoma stomach in Pakistan was 48.6±4.47 years, ranging from 26 to 65 years and male to female ratio was 1.5:17.[17] Satti et al showed the mean age in Saudi Arabia was 57 years with age range 21-102 and male to female ratio was 2.2:18.[18] Cherian et al in there study, done in Tamil Nadu, a southern state of India, reported the mean age for gastric carcinoma was 54.13±12.53 years.[19] Qurieshi et al showed the male to female ratio of carcinoma stomach in Kashmir, a northern state in India of 3.3:1 and the average age of male patients was 61 years but in females it was 63 years, slightly higher than that of males.[20] In present study the highest incidence (56%) was seen in between the ages of 41 to 60 with male to female ratio of 1.42:1.

There is a steady increase in the incidence of gastric cancer in cardia and proximal stomach and a decline in the incidence of cancers in the distal stomach in the West.[21] Reports from Asian countries like Japan, Korea and Iran have been conflicting. The Japanese and the Korean populations have a predominance of noncardiac gastric cancers while the Iranians have reported a trend similar to that in the west.[22-24] Qurieshi et al showed the site of growth among the Kashmiri patients at proximal stomach in 42%, distal stomach in 45.7%, at mid stomach and diffuse throughout the stomach in 6.2% each.[20] Afridi et al reported in the study conducted in Pakistan that growth was found at the cardiac end in 33%, at pylorus and antrum in 40%, linitus plastica in 13.3% patients,

only body and body and pylorus were involved in 6.7% each.[17] Satti et al also showed that majority of carcinoma occurred in the antrum (60%).[18] In present study, antrum (90%) was the most common site of the lesion and the proximal stomach (10%) was less involved by stomach cancer.

Investigators have reported different prevalence rates of *Helicobacter pylori* infections in gastric carcinoma specimens. The prevalence in Japan, where gastric carcinoma is the most common cancer, is 90%, a group of investigators in Holland has found a lower prevalence (58.5%).[25,26] Demirel et al in their study conducted at Ankara, Turkey, a developing country, had showed a prevalence (25%) of *Helicobacter pylori* that is lower than that reported in a developed country like the United States (30%).[27,28]The prevalence of *Helicobacter pylori* infection (66%) in present study is similar with those of other studies (41% - 70%) done in and outside India.[29]

Wang et al, had done a study on 2719 subjects, in their finding, 1671 (61.5 %) subjects were *Helicobacter pylori* positive; 1, 048 (38.5 %) were *Helicobacter pylori* negative.[30] Results from a large prospective interventional study contrast with many of the observational studies that appeared to indicate a much greater benefit of *Helicobacter pylori* eradication. An example is the study by Takenaka et al, who observed gastric cancer in six of 1519 (0.4%) subjects who were treated with *Helicobacter pylori* eradication therapy after having an endoscopy in Japan versus five of 288 (1.7%) subjects who failed *Helicobacter pylori* eradication therapy.[31] The association between *Helicobacter pylori* and gastric lymphoma has been proven by the complete regression of the tumor when the patients are treated with antimicrobials effective against *Helicobacter pylori*.[32] The gastric carcinoma is significantly related to *Helicobacter pylori* infection in the antral region.[33] Association of *Helicobacter pylori* infection is more with intestinal type and distally located tumour.[34]

The present study has showed a higher association of helicobacter pylori infection with stomach cancer, but to know the accurate incidence we need to find out and employ other possible investigation with higher sensitivity and specificity in a very large volume of patients.

CONCLUSION

Carcinoma stomach is a common malignancy and one of the leading causes of death throughout the world. Its association with *Helicobacter pylori* infection is higher in developing country, early detection of infection and eradication therapy will probably reduce the incidence of stomach cancer and its health-related burden to the country. Present study also showed that there is significant association of *Helicobacter pylori* infection with gastric carcinoma. So, the recognition of transmission routes and successful eradication therapy will be the cornerstones of future prevention of gastric carcinogenesis cause by *Helicobacter pylori*.

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