Association of Helicobacter Pylori Infection and Gastric Cancer


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ABSTRACT

INTRODUCTION: Gastric cancer remains one of the most common cancers worldwide and the second leading cause of cancer mortality in the world. Helicobacter Pylori is a major risk factor. Early detection of infection and eradication therapy will probably reduce the incidence of stomach cancer. This study is carried out to see the association of the H. pylori infection in gastric cancer patients in our population.

METHODS: This is a prospective cross sectional descriptive study done in Gastroenterology unit, Department of medicine, National Academy of Medical Sciences, Bir Hospital. Patients who were suspected of cancer of stomach clinically as well as endoscopically, their thorough history was taken and demographic profiles like age, sex and geographic location were recorded. Similarly, symptoms, risk factors and endoscopic finding were recorded. Likewise, result of rapid urease test and histopathology results were documented.

RESULTS: Male patients were seen to be more frequently affected than females with stomach cancer which is 22 (59.46%) with male: female ratio being 1.47:1. The mean age of the subject was 61.14 years with SD of ±13.82 years and the highest number of patients were from 61 to 70 years age group amounting to 27.03%.

Cancer of antropyloric region was seen highest. Out of the 25 cases 16 (64%) were H. pylori positive with OR: 2.86, 95% C. I.: 0.24-34.67. Among the studied 37 patients with Histopathology confirmed adenocarcinoma of stomach, 21(56.75% with 95% C I: 39.48% - 72.90%) patients had H. pylori positive. H. pylori infection could be the etiological factor.

CONCLUSION: Males were seen to be affected more than female in case of stomach cancer and the incidence and relative risk of H. pylori infection was significantly higher in distal cancers of stomach.

KEY WORDS: Gastric cancer, H. Pylori, Risk factors, Rapid Urease Test, Histopathology

INTRODUCTION

Gastric cancer remains one of the most common cancers worldwide and the second leading cause of cancer mortality in the world. It is one of the most fatal malignancies especially in developing countries. Adenocarcinoma of the stomach accounts for 10% of cancers worldwide. Despite a steady decline in the incidence rate over the last few decades, the absolute incidence has risen due to the aging of the worldwide population.

H. pylori infection is considered as a major risk factor in the development of gastric cancer and classified in 1994 by the World Health Organization as a type I carcinogen. Several risk factors have been identified for non-cardia gastric cancer: Helicobacter pylori infection, low socioeconomic status, smoking, salty and smoked food intake and low consumption of fruits and vegetables and familiarity for gastric cancer.

We are in high prevalence zone for H pylori infection and our socio-economic status favor its transmission. Gastric cancer is a relatively common malignancy in...
developing countries. We have limited data regarding H. pylori prevalence and its association with various gastric pathologies. Here, it was hypothesized that there is a link between H. pylori infection and gastric cancer. So, in this study, H. pylori infection and its associations with gastric cancer was investigated.

**METHODS**

This is a prospective cross sectional descriptive study done in Gastroenterology unit, Department of medicine, National Academy of Medical Sciences, Bir Hospital from November 2012 to October 2013. Study patients were taken from outpatients, inpatient department of Gastroenterology unit as well as referred patients from other departments. All enrolled patients were explained about the nature of study and their rights to refuse. All patients gave informed consent and the study protocol was approved by the institutional review board (IRB), National Academy of Medical Sciences. Suspected patient aged 18 years and above and with biopsy proven gastric cancer were included in this study. Those patients who were unfit for upper gastro-intestinal endoscopy and patients under H. Pylori regime were excluded. Among the patients who were suspected of cancer of stomach thorough history was taken and demographic profiles like age, sex and geographic location were recorded. Similarly, symptoms and risk factors for gastric cancer were recorded according to Performa. Thorough clinical examination was done in every patient and findings were recorded and all relevant laboratory investigations were done as per clinical requirement. Those patients with symptoms consistent with gastric cancer were planned for upper gastro-intestinal endoscopy and subsequently endoscopy was done in clinically indicated patients. Endoscopy findings were recorded and endoscopically suspected lesion was biopsied. At least six to eight biopsy specimens from the edge and base of the ulcer were taken. The biopsy specimen was kept in formalin vial and submitted to histopathology to confirm Gastric cancer. For Helicobacter Pylori detection biopsy specimen was taken from the prepyloric region, but an additional biopsy specimen was obtained from the fundic mucosa to increase the test’s sensitivity, especially in those patients who were treated with a proton-pump inhibitor recently. Detection of H pylori was done by two separate methods. One test was done immediately in endoscopy room by Rapid Urease Kit (Urease based test). Next test was done by Giemsa Staining for H. pylori detection and Hematoxylin and eosin for tissue diagnosis in Pathology Department

Only those patients with biopsy proven gastric cancer were enrolled in the data analysis of this study. Those patients who were negative for gastric cancer in histopathology were excluded from the study. All the data was analyzed using the statistical software STATA 9.0

**RESULTS**

A total of forty five patients with clinical as well as endoscopic features suggestive of cancer of stomach were enrolled in this study. Among them, eight were excluded from data analysis. Patient with endoscopic features suggestive of cancer of stomach were biopsied, sent for histopathogical examination and result were followed up. Initially, the eight patients tested negative for malignancy in histopathology reports and so were subjected for repeat upper gastrointestinal endoscopy and biopsy. Out of these eight patients, five patients did not come for repeat upper gastrointestinal endoscopy and three patients proved negative for malignancy in repeat biopsy too. Of the remaining thirty seven patients who had histopathologically documented cancers of stomach were taken for subsequent data analysis. In this study, there were thirty seven patients with 22 (59.46%) males and 15 (40.54%) females. Male: female ratio was 1.47: 1. Age and sex distributions of these patients are given in table 1.

<table>
<thead>
<tr>
<th>Ages (Yrs.)</th>
<th>Gender</th>
<th>Total</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>Female</td>
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<tr>
<td>31-40</td>
<td>2</td>
<td>1</td>
<td>3</td>
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<td>41-50</td>
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<td>3</td>
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<td>51-60</td>
<td>4</td>
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<tr>
<td>61-70</td>
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<td>4</td>
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<tr>
<td>71-80</td>
<td>5</td>
<td>3</td>
<td>8</td>
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</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>15</td>
<td>37</td>
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Among the presenting features, upper abdominal discomfort (70.3%) was the most common symptom followed by weight loss (67.6%), upper abdominal pain (62.2%), anorexia (59.5%) and nausea (56.8%). Similarly, malena was in 24.3 %, & haematemesis in
16.2% while none of the patients had dysphagia as the presenting features. These presenting features of patients are given in bar diagram in figure 1.

Among the studied thirty seven patients, thirteen patients proved H. Pylori positive by rapid urease test (RUT) while histopathology showed twenty–one patients positive for H. Pylori. Thus eight patients were negative for H. pylori by rapid urease test and regarded as false negative. These values are expressed in table 2.

Similarly, H. pylori status was recorded according to age of the patients. The highest number of patients with H. pylori positive was seen from 61 – 70 yrs age (42.85 %) followed by patients in 51-60 yrs age (28.57%). This is given in figure 2.

Site of lesion noted in endoscopic finding showed that antropyloric region (67.56%) was highest followed by body (24.32%) and cardia region (8.10%). Distal gastric cancer which includes body and antrum of stomach had a higher positivity for H pylori. The odds of having H. pylori positive in distal stomach causing gastric cancer is found to be almost three times higher ( OR : 2.86, 95% CI: 0.24 – 34.67) as compared with other sites though it was not statically significant.. The site of lesion is shown in bar diagram figure 3.

Among the risk factors, more patients were seen smokers 22 (59.45%) than non smokers 15 (40.55%). H. pylori infection was seen higher in smokers 14 (63.63%) as compare to non-smokers 8 (36.36%). Most of these patients were from low social economical status.

In this study, 37 patients had histopathological confirmed adenocarcinoma of stomach. According to cellular differentiation, poorly differentiated adenocarcinoma was 19 (51.35%) which was the highest number followed by moderately differentiated 14 (37.83%) and the lowest was well differentiated4 (10.81%). Among 37 patients with histopathological confirmed adenocarcinoma of stomach, 21 (56.75% with 95% CI: 39.48% - 72.90%) patients proved H. pylori positive in histopathology which can be considered significant.
DISCUSSIONS

Gastric cancer remains one of the most common cancers worldwide and the second leading cause of cancer mortality in the world. Helicobacter Pylori is a gram negative spiral shaped bacterium found in mucous layer of the stomach. It was first successfully cultured by Marshall and Warren in 1984. This discovery dramatically revolutionized the understanding of gastro duodenal diseases and this work eventually made Marshall and Warren to earn Nobel Prize in Medicine or Physiology in 2005.

In this study, Males were predominantly affected than females in case of stomach cancer which is 22 (59.46%). Male: female ratio was 1.47: 1. The mean age of the subject was 61.14 years with SD of ±13.82years. The highest number of patients belongs to 61 to 70 years which is similar to other studies where gastric cancer has found predilection to elderly patients, with incidence peaks in the seventh decade. Men are commonly affected than women, with the incidence rate double those for female. Similarly, Wanebo HJ et al in their study of 18,365 patients, 63% were males. The median ages were 68.4 years in males and 71.9 years in females which is quite similar to our finding.

Among the presenting features, upper abdominal discomfort (70.3%) was the most common followed by weight loss (67.6%), upper abdominal pain (62.2%), anorexia (59.5%) and nausea (56.8%). Similarly, melena was seen in 24.3% and haematemesis 16.2% of patients. In a study of 18,365 patients, Wanebo EJ et al reported symptoms of weight loss in 61.6%, abdominal pain in 51.6%, nausea in 34.3%, anorexia in 32%, melena in 20% and early satiety in 17.5% of patients. This shows that our patients were more symptomatic than the reported by Wanebo HJ et al. This may be our patients’ usually present later stages of diseases. This may be due to our social, economical and literacy factors which causes delay in presentation of diseases in health care facilities.

In this study, site of lesion noted in endoscopic finding showed that antropyloric region (67.56%) was highest followed by body (24.32%) and lowest was cardia (8.10%). Distal gastric cancer which includes body and antrum of stomach was seen higher H. pylori positivity than in other site. The odds of having H. pylori positive in distal stomach causing gastric cancer is found to be almost three times higher (OR : 2.86, 95% CI: 0.24 – 34.67) as compared with other site though it could not be statically significant which is almost similar finding reported by Bhasin et al. Similar finding is reported by Siman JH et al and Helicobacter and cancer collaborative group. In this study, site of lesion noted in endoscopic finding showed that antropyloric region (67.56%) was highest followed by body (24.32%) and lowest was cardia (8.10%). Distal gastric cancer which includes body and antrum of stomach was seen higher H. pylori positivity than in other site. The odds of having H. pylori positive in distal stomach causing gastric cancer is found to be almost three times higher (OR : 2.86, 95% CI: 0.24 – 34.67) as compared with other site though it could not be statically significant which is almost similar finding reported by Bhasin et al. Similar finding is reported by Siman JH et al and Helicobacter and cancer collaborative group.

In this study, thirteen patients had positive for H. Pylori by rapid urease test (RUT) and twenty–one patients had H. Pylori positive in histopathological examination. So, Histopathological examination is seen more sensitive test to detect H. pylori. Histology of gastric biopsy samples is considered to be the gold standard for diagnosing H. pylori infections. Special staining enhances the identification of organisms in the biopsy specimen and a variety of staining options exist.

Rapid urease test takes advantage of the fact that H. pylori are a urease-producing organism. This test has the advantages of being inexpensive, fast, and widely available. Rapid urease test is considered highly accurate with sensitivity and specificity over 90%, the rapid urease test is able to offer a sensitivity of 80-99% and a specificity of 92-100% in untreated patients when compared with histology as the gold standard in the diagnosis of H. pylori.

In this present study, histopathology showed more sensitive than rapid urease test. The reason for low sensitivity of rapid urease test in our study may be due to proton pump inhibitors that patients were taking. Patients those who had taken recently or taking H. pylori regime were excluded from this study. Still patients may be taking proton pump inhibitors. These drugs were available as over the counter drug in our country and patients may take it as needed (SOS) medication. This is considered a strong factor for negative test for rapid urease test. Though this factor is taken in mind and biopsy from more proximal site of stomach was taken when considered appropriate.

In this study most of the cases of gastric cancers were found to be adenocarcinoma which is similar to other study where adenocarcinoma were reported about 90%. Now-a-days, gastric cancer is reported on the basis of WHO classification and our Hospital follow the same. In this study, 37 patients had histopathological confirmed adenocarcinoma of stomach. According to cellular differentiation, poorly differentiated adenocarcinoma was 19 (51.35%) case which was the highest number followed by moderately differentiated 14 (37.83%) and the lowest number...
was 4 (10.81%) with well differentiated. According to Lauren classification it was classified into two histological types: intestinal type and diffuse type. Intestinal type was found to be more associated with H. pylori infection.

Correa P described the sequential steps with phenotypic changes in the gastric mucosa and hypothesized as a model for carcinogenesis of intestinal type adenocarcinoma: superficial gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia, and finally carcinoma. Furthermore, a number of studies have demonstrated a clear association between H. pylori infection and gastric adenocarcinoma. The link has been demonstrated in both the intestinal and diffuse subtypes of gastric cancer.

In this study, among the risk factors, smoking was seen higher 22 (59.45%) than non smoking 15 (40.55%) patients. H. pylori positive was seen higher in smoker 14 (63.63%) patients as compare to non-smokers 8(36.36%) patients. Similar findings were described by Ladeiras-Lopes R et al and Rajashekar V et al.

In this study, 37 patients with histopathological confirmed adenocarcinoma of stomach, 21 (56.75% with CI: 39.48% - 72.90%) patients had H. pylori positive in histopathology which can be considered significant which is nearly similar to results’ other studies. To be more precise, need more study with larger number of patients.

CONCLUSIONS

Gastric cancer remains one of the most common cancers and fatal malignancies especially in developing countries. Helicobacter Pylori is considered as a major risk factor in the development of gastric cancer. H. pylori infection is higher in developing country, early detection of infection and eradication therapy will probably reduce the incidence of cancer of stomach and its health related burden to the country.

In this study, Male was seen predominantly affected than female in case of stomach cancer.

The incidence and relative risk of H. pylori infection was significantly higher in distal cancers of stomach. Among the studied 37 patients with histopathology confirmed adenocarcinoma of stomach, 21(56.75% with 95% C I: 39.48% - 72.90%) patients had H. pylori positive. H. pylori infection could be the etiological factor.

This study is a small size to conclude it. So to know the accurate incidence we need to find out and employ other possible investigation with higher sensitivity and specificity in a large volume of patients.

REFERENCES

15. Helicobacter and cancer collaborative group. Gastric cancer and Helicobacter pylori: a combined analysis
of 12 case control studies nested within prospective cohorts. Gut, 2001 Sep;49(3):347-53


