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"A Comparative Study Of Helicobacter Pylori In Patients Undergoing Upper Gastrointestine Endoscopy In Benign And Malignant Conditions Of Upper Gastrointestine Tract In Karpaga Vinayaga Medical College And Hospital, Madhuranthagam"

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Abstract: *AIMS & OBJECTIVES: To study the prevalence of Helicobacter pylori in patients with dyspepsia undergoing upper Gastrointestinal endoscopy(UGIE) in KARPAGA VINAYAGA MEDICAL COLLEGE AND HOSPITAL, MADHURANTHAGAM and to study the association of Helicobacter pylori with Acid peptic diseases & Malignant conditions of upper Gastro intestinal tract. MATERIALS & METHODS: 389 cases of dyspepsia, studied clinically, were subjected to UGIE, during which 4 biopsies, two each from the antrum and the pathological areas were taken. One of the antral area and the other of the pathological finding were immediately subjected to Rapid urease test. Positive test for Helicobacter pylori was indicated by change in colour of the medium from yellow to pink or red. The other two biopsy specimens were sent for routine histopathology and special staining with Giemsa stain. The case was taken as Helicobacter pylori positive when the rapid urease test and/or histopathological examination was positive. RESULTS: Out of 389 patients, with mean age of 41.8 years, 172 patients were diagnosed to have been infected with Helicobacter pylori (44.21%). Out of 49 patients with gastric & duodenal ulcers, 37 patients were infected with Helicobacter pylori (75.51%). In which 22 out of 25 patients(88%) with duodenal ulcers and 10 out of 14 patients(71.4%) with gastric ulcers were positive for H. pylori while only 8 out of 10 patients(80%) with gastric cancer were positive for H. pylori. CONCLUSION: In this study, we found that Helicobacter pylori were consistently associated with peptic ulcer disease and malignant conditions of upper GI tract, which is in broad agreement with the studies done earlier. Thus we conclude that, Helicobacter pylori infection may have a major role in the etiopathogenesis of peptic ulcer disease and malignant conditions of upper GI tract appear to be no significant association between Helicobacter pylori infection and unexplained dyspepsia.*

I. Introduction

Acid peptic disease comprises of a wide spectrum of diseases, which cause considerable morbidity. Helicobacter pylori, a curved rod shaped bacterium, has been consistently associated with patients suffering from acid peptic diseases, more in ulcer disease than in non-ulcer disease. Due to this high association, it is now believed that Helicobacter pylori play an important role in the etio pathogenesis of acid peptic disease[1]. Several studies have revealed the association of Helicobacter pylori in 70-75 percent of patients with dyspepsia. Endoscopic studies have shown that, Helicobacter pylori is found in 80-100 per cent of patients with duodenal ulcers and 60-75 per cent of patients with gastric ulcers[2-4]. Amidst these profound variations proposed by many workers in the previous studies, we have attempted to study the prevalence of Helicobacter pylori in patients undergoing upper gastro-intestinal endoscopy at our hospital and its association with acid-peptic disease.

AIMS OF THE STUDY

1. To study the prevalence of Helicobacter pylori in patients with dyspepsia undergoing upper gastrointestinal endoscopy.
2. To study the association of Helicobacter pylori with acid peptic diseases and malignant conditions of upper GASTROINTESTINE

II. Methodology

389 cases of dyspepsia were studied clinically. The inclusion and exclusion criteria were as follows;

Inclusion Criteria

1. Patients above 20 years of age.
2. Patients having chronic upper abdominal pain.
3. Patients diagnosed as having chronic gastritis, gastric/duodenal ulcers on gastro-duodenoscopy
4. Patients who are known cases of chronic pancreatitis.
5. Patients on NSAID's for more than one month duration.
6. Patients who have received Anti-Helicobacter pylori treatment.

Exclusion Criteria

1. Patients below 20 years of age.
2. Pregnant and Lactating women.
3. Patients with oesophageal growths on endoscopy
4. Unwilling or unfit patients for upper gastrointestinal endoscopy
5. Patient having acute abdominal pain

In this study, there were cases of oesophageal carcinoma which were excluded from the study. There were 62 cases which had features of both gastritis and duodenitis. There were 11 cases of duodenal ulcer which additionally showed features of gastritis or duodenitis or both.

Procedure

All the patients in this study group, both in-patient as well as outpatient underwent upper gastro-intestinal endoscopy under topical anesthesia. The patients were asked to fast for 12 hours prior to the procedure. The cases admitted with gastric outlet obstruction were given stomach wash the night before and the morning of the day on which the procedure was scheduled. Lignocaine viscous or oral lignocaine sprays were given to the patient 5-10 minutes before the procedure for the local anesthetic effect. The upper gastro-intestinal endoscopy was conducted with flexible, fibrooptic endoscope with patients in left lateral positions[5].

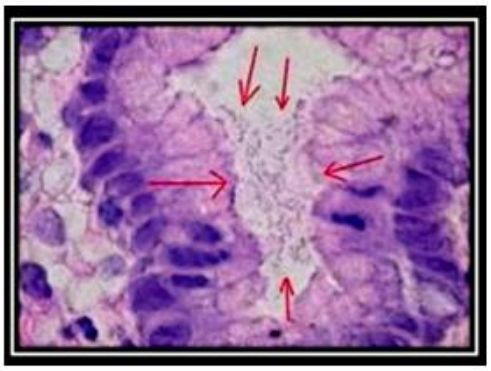
Four endoscopic biopsies were taken; 2 each from the gastric antrum and the body of stomach in the area of severe gastritis (maximum redness) or the edge of the ulcer crater depending on the findings. The biopsies from the body and the antrum were randomly taken in cases whereas the endoscopic findings were normal. Two biopsy specimens, one of the antral area and the other of the pathological finding were immediately inoculated into freshly prepared urea broth containing phenol red as the indicator. Positive test for Helicobacter pylori was indicated by change in colour of the medium from yellow to pink or red. The test was read as strongly positive when the change in colour occurred within 5-15 minutes following inoculation and weakly positive when the colour change occurred in first 6 hours. Any colour change in between was read as intermediate.

Figure – 1:

The other two biopsy specimens were sent in formalin solution for histopathology and special staining. Each of the biopsy specimens were fixed in 10% buffered formalin, routinely processed to paraffin and 3 μm sections cut. One section of each biopsy specimen was routinely stained with Haematoxylin & eosin stain and examined microscopically for presence of Helico bacter pylori organisms. The other sections of the biopsy specimen were dewaxed and taken to water and then incubated in 2% Giemsa solution in D-water for 30 minutes at room temperature. After rinsing in tap water, the sections are quickly dehydrated through ethanol solution before being cleared with xylene and examined for the presence of Helicobacter pylori. Histopathology test was given as positive when Helicobacter pylori were detected by routine Haematoxylin & eosin stain and/or Giemsa stain.

Figure - 1: Rapid urease test showing change in colour to pink

Figure - 2: Antral gland of the stomach with Giemsa stained colony of H. pylori.



III. Results

Out of 389 patients, there were 247 male patients and 142 female patients, age ranging from 15 years to 60 years (Mean-41.8). Out of 389 patients, 172 patients were diagnosed to have been infected with Helicobacter pylori (44.21%). All these patients presented to our hospital with upper abdominal pain or discomfort. 99 patients presented with nausea or vomiting out of which 37 had Helicobacter pylori infection. 25 patients had haematemesis, out of which 10 patients were positive for Helicobacter pylori infection. 19 patients had malena out of which 13 turned out to be Helicobacter pylori positive.

19 patients also had loss or weight or appetite on presentation. Of them, 7 patients were positive for Helicobacter pylori. On examination of these patients, 59 patients were anaemic out of whom 30 patients were positive for Helicobacter pylori. Of these 389 patients, 300 patients had epigastric tenderness on palpation and 4 patients had an epigastric mass palpable. Of these 300 patients, 151 patients were tested positive for Helicobacter pylori and of those 4 patients, who had an epigastric mass, only 3 patient was positive for Helicobacter pylori.

Table – 1: Percentage of H. pylori positivity in various clinical presentations

Table – 1:

Clinical Presentation	Number Of Cases	H.pylori Positive	Percentage
Abdominal pain / discomfort	389	171	44.07
Nausea/ Vomiting	99	37	37.37
Haematemesis	25	10	40.00
Malena	19	13	68.42
Loss of Weight/Appetite	19	7	36.84
Anaemia	59	30	50.84
Epigastric mass	4	3	75.00
Epigastric tenderness	300	151	50.33

Table – 2: Percentage of H. pylori positivity in Ulcer and nonulcer Dyspepsia.

Cases	Total Number	H.pylori Positive	Percentage
Ulcer Dyspepsia	49	37	75.51
Non-Ulcer Dyspepsia	340	135	39.7

A]. Ulcer Dyspepsia:

In this group there were 49 patients, out of which there were 30 males and 19 females. The age range was from 15 years to 60 years (Mean- 49.57) [Graph-3]. 37 out of these 49 patients were infected with Helicobacter pylori (75.51%). This group was further divided into 3 subgroups: [Graph-4].

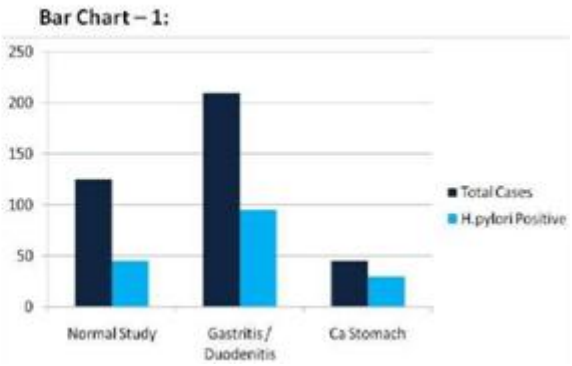
1. Duodenal Ulcer
2. Gastric Ulcer
3. Carcinoma Stomach

Out of 25 patients, 16 males and 9 females who had duodenal ulcer, there were 22 patients were infected with Helicobacter pylori (88.00%). There were 15 male patients and 7 female patients in this group. The age range was from 15 years to 60 years (Mean- 47.12). On Chi-square test, $\chi 2 = 25.01$, $p<0.01$, hence there is a significant association of Helicobacter pylori with duodenal ulcers.

Table – 3: Sex preponderance of Ulcer and nonulcer Dyspepsia

Cases	Male : Female	Age Range	Mean age
Ulcer Dyspepsia	30 : 19	15-60 yrs	49.57
Non-Ulcer Dyspepsia	214 : 126	15-60 yrs	40.56

Table – 3: Sex preponderance of Ulcer and nonulcer Dyspepsia



Gastric Ulcer

There were 14 patients, 9 males and 5 females who had gastric ulcer, of which 10 patients were infected with Helicobacter pylori (71.42%). In this group there were 6 males and 4 female patients. Their age range was from 15 years to 60 years (Mean- 50.36). On applying Chi-square test, $\chi 2 = 7.59$, $p<0.01$, thus we found a significant association of Helicobacter pylori with gastric ulcers in our study.

Carcinoma Stomach

Out of 20 cases of carcinoma stomach that were diagnosed, there were 16 males and 4 females out of which 13 males and 2 females were positive for Helicobacter pylori (50%). The age range was >15 Years (Mean- 54.6).On Chi-square test, $\chi 2 = 3.81$, $p<0.05$, hence significant association was found between Helicobacter pylori and gastric cancer in our study.

Non-Ulcer Dyspepsia

In this group, there were 340 patients out of which 138 patients were infected with Helicobacter pylori (40.58%). There were 214 male patients and 126 female patients in this group. The age range was > 15 years (Mean- 40.56).

This group was further divided into:

1. Normal Study
2. Gastritis/Duodenitis/ Ca Stomach

Normal Study

These patients presented symptoms of dyspepsia, but the upper G.I endoscopy was normal. There were 127 patients in this group out of which 43 were found to be positive for Helicobacter pylori infection (33.85%). Out of 127 patients, 72 were males and 55 were females. The age range was from 15 years to 60 years (Mean- 42.45).

Gastritis / Duodenitis/ Ca Stomach

In this subgroup there were 213 patients, of which 92 were infected with Helicobacter pylori (43.19%). There were 145 males and 68 females. The age range was > 15 years (Mean- 39.44). On Chi-square test, $\chi 2 = 1.06$, $p>0.01$, hence there was no significant association between Helicobacter pylori and gastritis/duodenitis in our study. Out of the 172 patients with Helicobacter pylori infection, 37 had Ulcer Dyspepsia (21.14%). Remaining 135 patients (78.48%) even though having Helicobacter pylori infection did not have ulcer diseases. Out of the 172 patients who were H. pylori positive, 14 patients were negative for Rapid urease test but positive for the histopathological examination and Giemsa staining (False negative). There were also 6 cases which were positive for the Rapid Urease test but negative on histopathological examination (False positive). Thus in our study, Rapid urease test had a sensitivity of 96.34% and specificity of 93.78% when compared with histopathology. In the histopathological tests, out of 166 positive cases, 157 cases were positive for both H&E and Giemsa staining. 9 cases were negative on H&E staining but positive on Giemsa staining whereas all positive cases of Giemsa staining were also positive for H&E staining. Thus H&E and Giemsa stains were in accordance with each other in 94% cases.

Table – 4: Percentage of H. pylori positivity in various pathologies

Table – 4:

CASES	TOTAL NUMBER	H.PYLORI POSITIVE	PERCENTAGE
Normal Study	127	43	33.85
Gastritis/ Duodenitis	203	92	45.32
Duodenal Ulcer	25	22	88.00
Gastric Ulcer	14	10	71.42
Carcinoma Of the Stomach	20	15	75.00

IV. Discussion

After the discovery of Helicobacter pylori by Marshall and Warren in 1983, many studies were conducted to confirm the association of Helicobacter pylori with various acid-peptic diseases and carcinoma stomach.

The following observations were made:

1. The treatment of Helicobacter pylori led to the reversal of gastritis in patients with chronic non-specific gastritis.
2. The eradication of Helicobacter pylori decreases the relapse of peptic ulcer to 1%-3% when compared to 80% relapses in patients with persistent Helicobacter pylori infections after medical management.

In spite of the above findings, the cause-and- effect relationship between Helicobacter pylori and peptic ulcer disease is not proved and furthermore many people infected with Helicobacter pylori did not develop peptic ulceration. The association of Helicobacter pylori with non-ulcer dyspepsia is controversial. Therapeutic trials in non-ulcer dyspepsia patients with Helicobacter pylori infection produced conflicting results. Thus, at this stage in the history of acid–peptic disease and its association with Helicobacter pylori, the causation or association between the two is still unclear. In case of non-ulcer dyspepsia this is still more augmented by the conflicting results produced by the workers world-wide.

Thus we at the "Department of Surgery, KARPAGA VINAYAGA MEDICAL COLLEGE AND HOSPITAL, MADHURANTHAGAM have made a sincere attempt to explore the possibility of proving this association between Helicobacter pylori and ulcer dyspepsia and its contribution to non-ulcer dyspepsia and Malignant conditions.

In the present study, the overall positivity for H.pylori was 190 out of 399 patients (47.6 %). This result is slightly lower than the results of the other studies. However it is comparable to the results of the study by

Tytgat G N 56 in which, the prevalence of Helicobacter pylori is decreasing worldwide, probably due to improved hygiene, increased awareness regarding H. pylori and increase in consumption of anti-microbials. The incidence of H.pylori is higher in patients with ulcer dyspepsia (75.51%) when compared to patients with non-ulcer dyspepsia (39.7%). In our study, we also found 20 cases of carcinoma stomach out of which 15 cases (75%), proved to be H. pylori positive. This association wasn't significant as per the Chi-square test. In patients with peptic ulcer disease, patients with duodenal ulcer have higher incidence of Helicobacter pylori (88%), when compared to patients with gastric ulcer (71.42%), similar to other studies.

But, why Helicobacter pylori which colonizes the gastric antrum is associated more with duodenal ulcers is not clearly explained till now. It may be because of the hyperacidity that usually is seen associated with duodenal ulcers, which offers a favorable environment for the Helicobacter pylori to thrive. In 172 patients who were positive for Helicobacter pylori only 37 patients developed peptic ulcer disease (21.51%). The remaining 78.48% patients even though harboring Helicobacter pylori did not have peptic ulcer disease.

The development of peptic ulcer may be because of infection with virulent strains of Helicobacter pylori. A vacuolizing cytotoxin is more commonly present in Helicobacter pylori isolated from duodenal ulcer patients. This is proposed to be the cause of duodenal ulcer disease. But, till now, no toxin or virulent strains of Helicobacter pylori is proved to be the cause of peptic ulcer disease. In non-ulcer dyspepsia group, the patients with gastritis/duodenitis had high incidence of H.pylori positivity (43.19%) when compared to patients with normal upper G.I endoscopy. In our study, the rapid urease test had a sensitivity of 96.34% and specificity of 93.78% when compared with histopathology. This is comparable with the results of the study done by Tokunaga et al.

All our observations in the present study are comparable to other studies except for the overall prevalence of Helicobacter pylori and the percentage of gastritis/duodenitis patients with H.pylori positivity which was less when compared to the other studies

V. Conclusion

This was a prospective study conducted to determine the role of Helicobacter pylori in acid-peptic diseases.This study design was based on clinical study and endoscopic biopsy from gastric mucosa and duodenal mucosa(whenever necessary) in 389 patients with a history of dyspepsia.

Endoscopy confirmed the diagnosis. Rapid urease test and Giemsa staining were conducted on endoscopy biopsy specimens and Helicobacter pylori positivity was based on either Rapid urease test and histopathological examination was positive.

From the present study it is evident that, There was no specific symptom attributable to H. pylori infection. Helicobacter pylori is consistently associated with peptic ulcer disease than non-ulcer dyspepsia, which is in broad agreement with the studies done earlier. Thus we conclude that, Helicobacter pylori infection may have a role in the etio pathogenesis of peptic ulcer disease. Helicobacter pylori have a role in the etio pathogenesis of Carcinoma Stomach. There appears to be no significant association between Helicobacter pylori infection and unexplained dyspepsia. This finding does not exclude the possibility that a small undefined subset of infected individuals will have symptoms induced by the infection, but only large randomized trials will be able to establish this.

Hence, we recommend eradication of the bacteria only in patients positive for the bacterium, who have peptic ulceration.

We believe in, Peter C Robin's dictum:

"If a person with peptic ulcer disease is shown to have Helicobacter pylori, then eradication is indicated".

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