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## Association of helicobacter pylori infection in carcinoma stomach and peptic ulcer disease: A cross sectional analytical study

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### Abstract

**Background and Aims:** The Helicobacter pylori (H. pylori) prevalence in Asian countries is highly variable. We aimed to determine the current H. pylori prevalence, correlate with gastroduodenal diseases and study gastric cancer incidence in western Odisha.

**Methods:** Out of 3289 patients referred for endoscopy, 2820 eligible patients underwent upper gastrointestinal endoscopy with biopsy and included in the study; H. pylori was considered positive when either of Rapid Urease Test (RUT) or histopathology showed positive result.

**Results:** The H. pylori prevalence was 29.2% in overall distribution, 41.1% in gastritis and or duodenitis, 65.1% in gastric ulcer, 83.3% in duodenal ulcer, 19.2% in gastric polyp and 11.1% in gastric cancer. The H. pylori infection was significantly associated with gastritis and or duodenitis [P<0.001; Odds Ratio (OR) 1.53, 95% Confidence Interval (CI) 1.47-1.59], gastric ulcer (P<0.001; OR 18.62, 95% CI 12.40-27.81), duodenal ulcer (P<0.001; OR 48.89, 95% CI 25.2394.75), gastric polyp (P=0.001; OR 7.66, 95% CI 3.18-18.44) and gastric cancer (P=0.005; OR 3.78, 95% CI 1.82-7.86).

**Conclusions:** The H. pylori prevalence in Western Odisha was lower than that shown in the previous studies of developing Asian countries, but was significantly high in gastritis and or duodenitis, and peptic ulcers. Similarly, the gastric cancer incidence was also low in Western parts of Odisha and was significantly associated with H. pylori. Further study is needed to establish the association of H. pylori with gastric cancer in Western Odisha.

**Keywords:** helicobacter pylori, peptic ulcer disease, carcinoma stomach

### Introduction

Gastritis is one of the most common problem in day to day medical practice and incidence of gastric cancer is in an increasing trend. Helicobacter pylori is found in association with 90-95% of duodenal ulcer and in 60-75% of patients with gastric ulcer <sup>[1]</sup>.

Though a wide range of etiological factors play a role, the exact cause of peptic ulcer disease is inconclusive. Helicobacter pylori is associated with chronic active gastritis in virtually 100% of patients <sup>[2]</sup>. It is also associated with 88% of intestinal type and 55% of gastric type of gastric cancer. Recently, warren and Marshall received Nobel prize for their outstanding work on Helicobacter pylori in the year 2005.

Recent works like eradication of Helicobacter pylori leading to healing of peptic ulcer diseases and reduction of ulcer recurrence rate have given encouraging results and proved beyond doubt an association between Helicobacter pylori infection and acid peptic diseases <sup>[3]</sup>. H. pylori infection also has been associated with the development of gastric non-Hodgkin's lymphoma and with another lymphoproliferative disorder, gastric mucosa associated lymphoid tissue (MALT) lymphoma (MALToma) <sup>[4, 5, 6]</sup>. Importantly, gastric MALToma patients with antibiotics that eradicate H. pylori often leads to regression of the tumor <sup>[7, 12]</sup>.

The prevalence of association of H. pylori is more in low socioeconomic status group than middle and high socioeconomic status group. Also the association of H. pylori is high in smokers and NSAIDS users but in alcoholics the association of H. pylori varies in different studies.

Though many bacterial organisms were indeed found earlier in gastric mucosa associated with gastroduodenal diseases, it was Warren and Marshall (1984) who isolated these Gm-ve organisms from these cases and found a relation to its causation. The role of H. pylori in the

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pathogenesis of acid peptic diseases and carcinoma stomach is unclear. Evidence to support a role of this organism is reviewed here in and includes:

The major structural, functional and pathophysiological changes occurring in the mucosa of infected individuals and higher prevalence of *H. pylori* in subjects with acid peptic diseases and carcinoma stomach [13, 17].

Eradication of the bacteria leading to clinical improvement and corresponding mucosal restoration in subjects [18].

The new concept of infective role of *Helicobacter pylori* for gastritis and carcinoma stomach has got the respectable attention by over-whelming reports from Marshall (2005) and the ongoing research in this field generated our interest in carrying out the project on "Association of *Helicobacter pylori* infection in carcinoma stomach and peptic ulcer disease" to prove that *H. pylori*, despite its normally innocent habitat can be alarmingly dangerous as either the primary agent or agent which is responsible for recurrence and recrudescence.

The present study was under taken to evaluate the role of *H. pylori* in carcinoma stomach and peptic ulcer disease.

### Background and aim of the study

Asian countries shows is highly variable *H. pylori* prevalence. We aimed to determine the current *H. pylori* epidemiology, correlate with gastroduodenal diseases and study of gastric cancer in patients coming to V.S.S. Institute of medical science and research, Burla, Sambalpur.

### Rational of the study

Epidemiological studies point to a role for *H. pylori*, although its importance is disputed.

This study will helpful in finding out the prevalence and distribution of *H. pylori* in carcinoma stomach and peptic ulcer diseases and gastritis which will make a humble addition to the past works.

### Objective

**Primary Objective:** To find out the prevalence of *H. pylori* infection in carcinoma stomach and peptic ulcer disease.

**Secondary Objective:** To compare the association of *H. pylori* with carcinoma stomach and peptic ulcer disease.

### Materials and Methods

The present study titled "Association of *Helicobacter pylori* infection in carcinoma stomach and peptic ulcer disease: A cross sectional analytical study" was conducted in the Department of General surgery of V.S.S. Institute Medical Science and Research, Burla during the period of 2017 to 2019.

A total of 2820 patients were eligible for study out of 3289 patients undergone upper gastrointestinal (GI) endoscopy. The exclusion criteria for the study were: 1) patients who had received proton pump inhibitors or histamine 2-receptor antagonists for a minimum of 2 weeks and antibiotics for 4 weeks prior to the study; patients who had Antacid, Bismuth, Non-steroidal anti-inflammatory drugs or had *H. pylori* eradication therapy in the past, 2) patients with a diagnosis of portal hypertensive gastropathy and esophageal varices 3) patients with an abnormal coagulation profile, 4) patients with severe medical co-morbidities like COPD, heart failure, kidney failure, etc. and 5) patients not giving an informed consent for the study.

Detail history, physical examination and relevant investigations were done as per the proforma.

All eligible 2820 subjects underwent upper GI endoscopy at V.S.S. Institute of medical science and research, Burla, Sambalpur district of Odisha during the period of November 2017 to October 2018.

The informed consent was taken from all study subjects and the study protocol was approved by the ethics committees of VIREC.

Upper GI endoscopy was performed in each patient and Two gastric antral biopsy specimens were taken. One specimen from each patient was subjected to Rapid Urease Test (H-P test Commercial Kit) and the other one was 10% formalin fixed for histopathological examination. Hematoxylin and Eosin stain was used for histopathological examination and *H. pylori* was studied using Warthin Starry stain.

### Details of Endoscopy and Procedure

Patient was kept nil per oral the night before. The details of endoscopic procedure and its risks were explained to the patients in their own language and a written consent was obtained from the patients Lignocaine 2% spray was used as local anesthesia for anaesthetizing pharynx.

The endoscopic findings were recorded and with biopsy forceps; two pieces of antral tissues taken. Rapid urease test is performed in one chunk of tissue and other bit of tissue was preserved in 10% formalin for histological examination

### Details of Rapid Urease Test (RUT):

It is done with H-P test kit, a commercially available kit, product of Lenus Medicare & Research (OPC) Private Limited, Kolkata, India.

### Principle

High concentration of urea is present in gastric mucosa. Urease produced by *H. pylori* reacts with urea in the presence of water molecules and  $H^+$  ions producing ammonia and bicarbonate. Ammonia in turn raises the pH of the medium immediately. This change of pH can be readily detected by pH indicator e.g. phenol red.

### Composition

H-P test kit contains (1) urea, (2) pH indicator, (3) Stabilizing agent, (4) Bacteriostatic agent (does not react on *H. pylori*)

### Procedure of Test

It was done with H-P test rapid urease test kit. After taking out of the fridge, H-P test kit, having yellow color was checked and allowed to attain room temperature in order to enhance chemical reaction.

Biopsy was taken from pyloric antrum adjacent to the opening avoiding the areas of erosion and ulceration.

Urease enzyme of *H. pylori* reacts with urea of gel media changes the color from yellow to red or pink elevating pH.

### Interpretation

Examination of the color change from yellow to red or pink at 30-minute intervals for 4 hours was observed. Most of the positive cases showed the result within 4 hours. The observation was continued up to 24 hours.

If the color changed from yellow to red or pink, the result was positive i.e. presence of *H. pylori* is confirmed in the biopsy. If the color did not change, the result was negative.



**Fig 1:** Freshly opened Rapid Urease Test Kit.



**Fig 2:** H. pylori positive in Gastric biopsy specimen.



**Fig 3:** H. pylori positive in Antral biopsy specimen.



**Fig 4:** H. pylori negative in Gastric biopsy specimen.

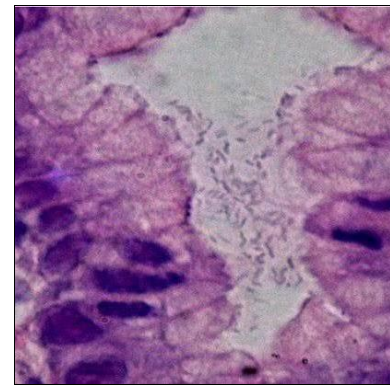
### Histopathology & Tissue Processing

In each patient, two endoscopic biopsies taken from the stomach were sent in 10% formalin for histopathology. The tissue biopsies were routinely processed. All the tissue had been studied with Hematoxylin-eosin and Giemsa for histopathological examination and warthin Starry stain for H. pylori study.

### Methods of Staining

#### Haematoxylin and Eosin (Alan Stevens And Bancroft, 1982)

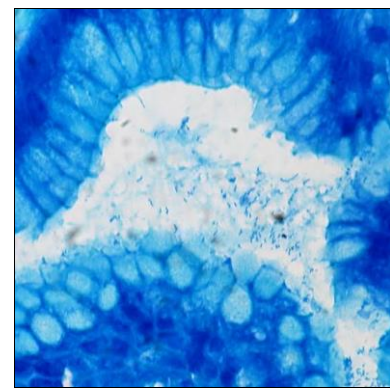
- Nuclei - Blue black
- Cytoplasm – Pink
- H. pylori – Pink rods



**Fig 5:** Demonstration of H. pylori by H&E stain (High power view)

#### 2. Giemsa Stain (Alan Stevens and Bancroft, 1982)

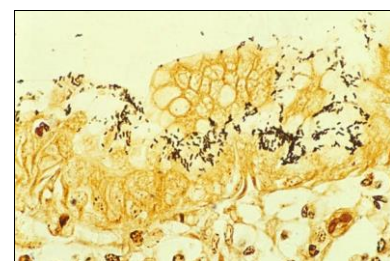
- Nuclei –Blue
- Cytoplasm – Pale blue
- H. pylori – Dark blue rods



**Fig 6:** Demonstration of H. pylori in Gastric biopsy specimen by Giemsa staining

#### 3. Warthin–Starry Stain (Manual of histologic & special staining techniques AFIP, 2<sup>nd</sup> Edn. 1960)

- Bacteria – Black
- Background – Pale yellow to light brown.



**Fig 7:** Demonstration of H. pylori by Warthin–Starry stain. (High power view)

Prospectively all data of endoscopy and the H. pylori reports were recorded in a personal computer and the results of H. pylori were categorized according to the age group, gender and different diagnosis. All the data were analysed using SPSS 16.0 software. All data were analyzed statistically by using Chi-square test or Fisher exact test, Odds Ratio (OR) and 95% Confidence Interval (CI), as appropriate. The patients with normal endoscopic findings were taken as the control group. The P value less than 0.05 was considered to be statistically significant.

Out of 2820 eligible patients, males were 54% and females were 46% with the mean age of 44.6 years  $\pm$ 17.6 ranging from 13 to

88 years. The distribution of the endoscopic findings were as follows: normal 20.6%, esophagitis 10.1%, gastritis and or duodenitis 59.5%, peptic ulcer 5.10% (gastric ulcer 3%, duodenal ulcer 2.1%), gastric polyp 0.9%, duodenal polyp 0.2%, esophageal cancer 1%, gastric cancer 1.9%, duodenal cancer 0.1%, achalasia cardia 0.1%, hiatus hernia 0.2%, duodenal diverticulum 0.1% and esophageal stricture 0.1%. Table 1 shows distribution of different diagnosis according to the gender and mean age. The distribution of different diagnosis according to age group is shown in table 2.

The overall prevalence of H. pylori infection was 29.2%; the males had 29.1% and females had 29.3% of H. pylori, showing the similar distribution of H. pylori among the gender (table 3).

The prevalence of H. pylori in ≥20 years age group (20-29 years)

24.3%, 30-39 years 24.3%, 40-49 years 32.4%, 50-59 years 34%, 60-69 years 27.2% and ≥70 years 31%) was greater than that in <20 years age group (15.3%), which was statistically

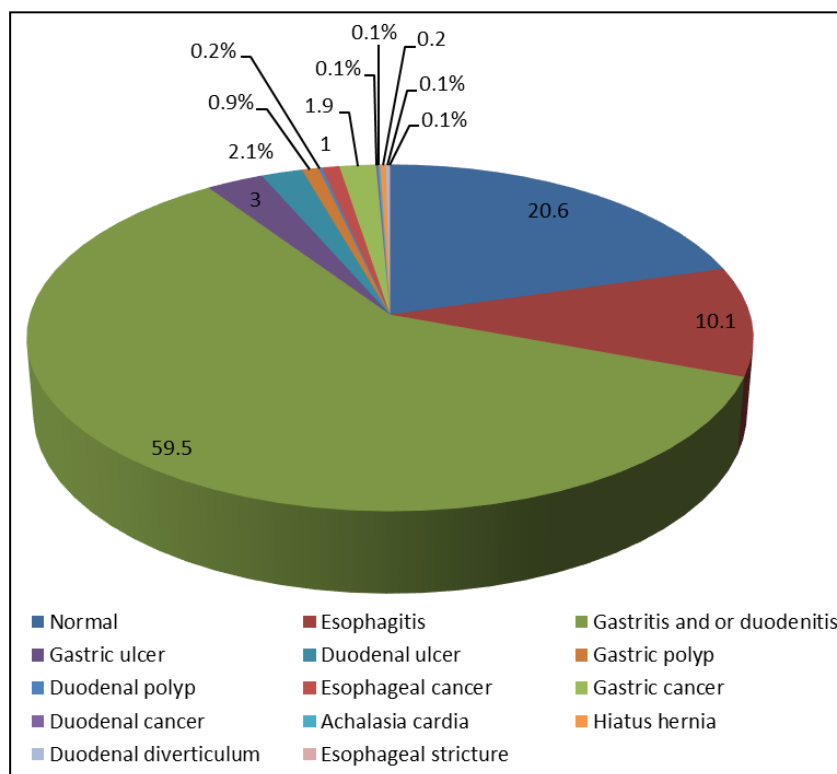
significant (P=0.001) [table 4].

The H. pylori infection was significantly associated with gastritis and or duodenitis [P<0.001; Odds Ratio (OR) 1.53, 95% Confidence Interval (CI) 1.47-1.59], gastric ulcer (P<0.001; OR 18.62, 95% CI 12.40-27.81), duodenal ulcer (P<0.001; OR 48.89, 95% CI 25.23-94.75), gastric polyp (P=0.001; OR 7.66, 95% CI 3.18-18.44) and gastric cancer (P=0.005; OR 3.78, 95% CI 1.82-7.86), but there is inverse relationship of H. pylori association with esophagitis (P=0.058; OR 0.35, 95% CI 0.09-1.29).

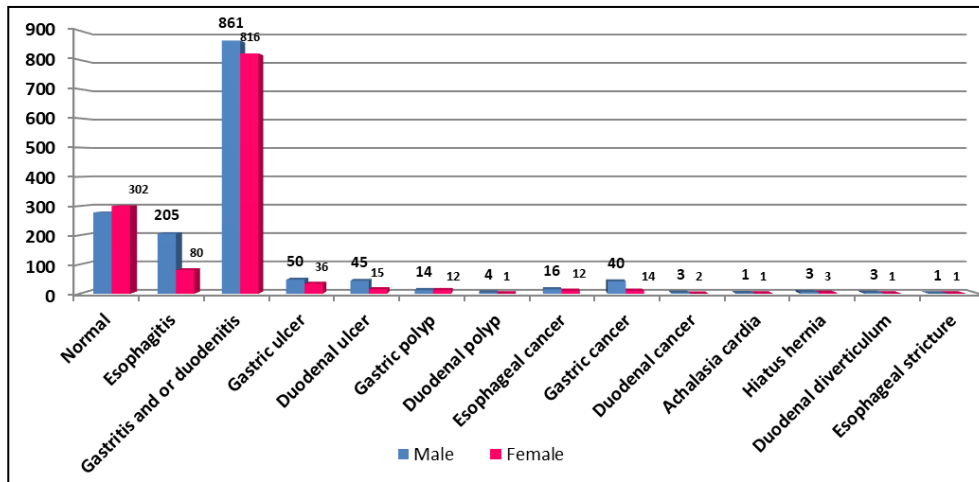
The distribution of H. pylori infection among different diagnosis was as follows: normal 2.4%, esophagitis 0.7%, gastritis and or duodenitis 41.1%, gastric ulcer 65.1%, duodenal ulcer 83.3%, gastric polyp 19.2%, duodenal polyp 0%, esophageal cancer 0%, gastric cancer 11.1%, duodenal cancer 0%, achalasia cardia 0%, hiatus hernia 0%, duodenal diverticulum 0% and esophageal stricture 0% as shown in table 5.

**Table 1:** Distribution of different diagnosis according to the gender and mean age

Total (N=2820)	%	Male (n=1524)	%	Female (n=1296)	%	Mean age in years (SD)
Normal (n=582)	20.6	280	48.1	302	51.9	38.6 (+/-15.8)
Esophagitis (n=285)	10.1	205	71.9	80	28.1	51.7 (+/-16.9)
Gastritis and or duodenitis (n=1677)	59.5	861	51.3	816	48.7	46.5 (+/-17)
Gastric ulcer (n=86)	3	50	58.1	36	41.9	55.1 (+/-17.6)
Duodenal ulcer (n=60)	2.1	45	75	15	25	46.3 (+/-18.7)
Gastric polyp (n=26)	0.9	14	53.8	12	46.2	49.0 (+/-18.0)
Duodenal polyp (n=5)	0.2	4	80	1	20	55.4 (+/-5.3)
Esophageal cancer (n=28)	1	16	57.1	12	42.9	65.7 (+/-9.5) [median age:68]
Gastric cancer (n=54)	1.9	40	74.1	14	25.9	66.7 (+/-12.5) [median age:68]
Duodenal cancer (n=4)	0.1	2	50	2	50	45.7 (+/-23.6) [median age:44]
Achalasia cardia (n=2)	0.1	1	50	1	50	62.0 (+/-10.4)
Hiatus hernia (n=6)	0.2	3	50	3	50	45.9 (+/-19.2)
Duodenal diverticulum (n=3)	0.1	2	66.7	1	33.3	50.5 (+/-19.3)
Esophageal stricture (n=2)	0.1	1	50	1	50	66.5 (+/-7.8)



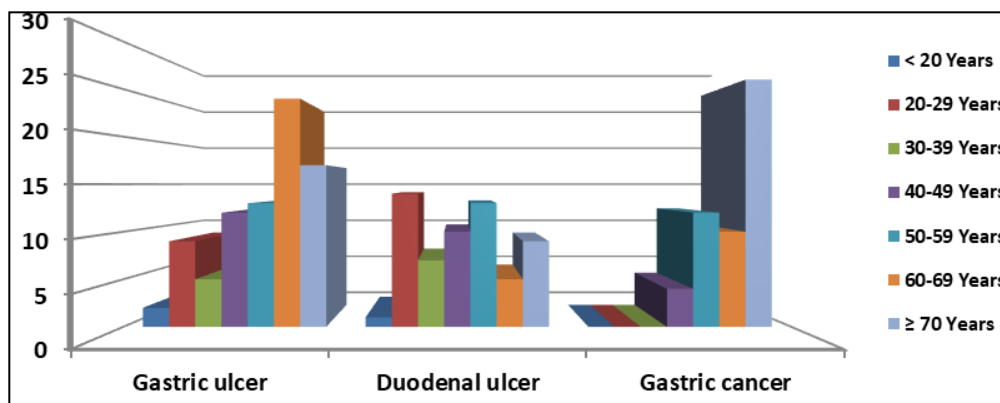
**Chart 1:** Percentage of different diagnosis



**Chart 2:** Distribution of different diagnosis according to the gender

**Table 2:** Distribution of different diagnosis according to age group

Total (N=2820)	<20 years	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	≥70 years
Normal (n=582); (20.6%)	38 (38.8%)	176 (35.6%)	120 (24.6%)	97 (18.7%)	69 (14.7%)	54 (13.3%)	28 (8%)
Esophagitis (n=285); (10.1%)	10 (10.2%)	24 (4.8%)	24 (4.9%)	64 (12.3%)	56 (11.9%)	66 (16.3%)	41 (11.8%)
Gastritis and/or duodenitis(n=1677); (59.6%)	46 (46.9%)	270 (54.6%)	320 (65.7%)	320 (61.8%)	288 (61.2%)	225 (55.5%)	210 (60.3%)
Gastric ulcer (n=86); (3%)	1(1%)	8 (1.6%)	7 (1.4%)	14 (2.7%)	15 (3.2%)	25 (6.1%)	16 (4.6%)
Duodenal ulcer (n=60); (2.1%)	1 (1%)	14 (2.8%)	7 (1.4%)	10 (1.9%)	14 (3%)	5 (1.2%)	9 (2.6%)
Gastric polyp (n=26); (0.9%)	2 (2%)	1 (0.2%)	6 (1.2%)	2 (0.4%)	5 (1%)	6 (1.5%)	4 (1.1%)
Duodenal polyp (n=5); (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	2 (0.5%)	0 (0%)
Esophageal cancer (n=28); (1%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	4 (0.8%)	11 (2.7%)	11 (3.1%)
Gastric cancer (n=54); (1.9%)	0 (0%)	0 (0%)	0 (0%)	4 (0.8%)	14 (3%)	10 (2.5%)	26 (7.5%)
Duodenal cancer (n=4); (0.1%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	1 (0.3%)
Achalasia cardia (n=2); (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)
Hiatus hernia (n=6); (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.6%)
Duodenal diverticulum (n=3); (0.1%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Esophageal stricture (n=2); (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.3%)



**Chart 3:** Distribution of carcinoma stomach and peptic ulcer disease in different age group

**Table 3:** Distribution of H. pylori according to the gender

	H. pylori positive	H. pylori negative	P value
Male (n=1524)	444 (29.1%)	1080 (70.9%)	0.8
Female (n=1296)	380 (29.3%)	916 (70.7%)	

**Table 4:** Distribution of H. pylori according to the age group

	Total (N=2820)	H. pylori positive (n=824) [29.2%]	H. pylori negative (n=1996) [70.8%]	P value - 0.001
<20 (n=98)		15 [15.3%]	83 [84.7%]	
20-29 (n=494)		120 [24.3%]	374 [75.7%]	
30-39 (n=487)		143 [24.3%]	344 [75.7%]	
40-49 (n=518)		168 [32.4%]	350 [67.6%]	
50-59 (n=470)		160 [34%]	310 [66%]	
60-69 (n=405)		110 [27.2%]	295 [72.8%]	
≥70 (n=348)		108 [31%]	240 [69%]	

**Table 5:** Distribution of H. pylori according to different diagnosis

Total (N=2820)	H. pylori positive	H. pylori negative	P value*	Odds ratio (**95% CI)
Normal (n=582)	14 (2.4%)	568 (97.6%)		
Esophagitis (n=285)	2 (0.7%)	283 (99.3%)	0.058	0.35 (0.09-1.29)
Gastritis &/OR Duodenitis (n=1677)	690 (41.1%)	987 (58.9%)	<0.001	1.53 (1.47-1.59)
Gastric ulcer (n=86)	56 (65.1%)	30 (34.9%)	<0.001	18.62 (12.40-27.81)
Duodenal ulcer (n=60)	50 (83.3%)	10 (16.7%)	<0.001	48.89 (25.23-94.75)
Gastric polyp (n=26)	5 (19.2%)	21 (80.8%)	0.001	
Duodenal polyp (n=5)	0 (0%)	5 (100%)	1.0	
Esophageal cancer (n=28)	0 (0%)	28 (100%)	1.0	
Gastric cancer(n=54)	6 (11.1%)	48 (88.9%)	0.005	3.78 (1.82-7.86)
Duodenal cancer (n=4)	0 (0%)	4 (100%)	1.0	
Achalasia cardia (n=2)	0 (0%)	2 (100%)	1.0	
Hiatus hernia (n=6)	0 (0%)	6 (100%)	1.0	
Duodenal diverticulum (n=3)	0 (0%)	3 (100%)	1.0	
Esophageal stricture (n=2)	0 (0%)	2 (100%)	1.0	

§ Patients with normal endoscopic findings were taken as the control group.

\*P value obtained using Chi square test or Fischer exact test as appropriate

\*\* 95% confidence interval

## Discussion

More than half of patients referred for endoscopy had gastritis and or duodenitis, although one fifth patients had normal findings and one tenth patients had esophagitis; the prevalence of peptic ulcer disease was 5.1 %, gastric cancer 1.9% and esophageal cancer 1% showing that there is no wide difference of prevalence between peptic ulcer disease and malignancy.

There is higher prevalence of H. pylori in developing countries than the developed countries, which may be due to poor socioeconomic status and hygiene practices.

Our current study demonstrated that H. pylori prevalence of 29.2%. This is in contrary to the age-old data of high prevalence of H. pylori in developing Asian countries. This could be attributed to change in lifestyles, Westernization and rampant use of proton pump inhibitors and antibiotics.

However, our study didn't show any significant difference of H. pylori prevalence among the male and female population under study.

In our study, the age group <20 years had lower prevalence (15.3%) of H. pylori than that of ≥20 years group, which showed the highest prevalence (34%) being seen in the age group of 50-59 years followed by 32.4% in 40-49 years group. This difference in H. pylori prevalence among different age group was statistically significant and it shows increasing trend of H. pylori prevalence with aging

Our study showed that there is significant association of H. pylori with Gastric polyp along with gastritis and duodenitis.

Our study showed that prevalence of gastric cancer is 1.9% and overall H. pylori positivity is 29.2%. The gastric cancer was associated with H. pylori positivity in 11.1% which was statistically significant when compared to 2.4% of H. pylori positivity in normal subjects taken as the controls, giving an OR of 3.78 (95% CI 1.82-7.86).

There were certain limitations in our study. Our study did not include the demographic data which might have some bearing on prevalence of H. pylori. Some subjects might have taken antacids, proton pump inhibitors and antibiotics but missed and included in study group which may be due to sampling error. Despite the above shortcomings this meager work, we trust has proved beyond doubt that an association does prevail in the peptic ulcer disease and carcinoma stomach.

## Conclusion

The present study suggests that H. pylori infection is the causative factor of gastroduodenal diseases in majority of cases.

H. pylori detection by endoscopic antral biopsy RUT and histology along with other diagnostic tests would increase the prevalence rate and facilitate early and specific treatment of H. pylori infection. However, long term follow up studies are necessary to accurately evaluate the outcome of H. pylori positive gastro duodenal diseases. Our study suggested the following salient features:

- H. pylori have a definite role as the causative agent for carcinoma stomach and different forms of gastritis.
- H. pylori are more prevalent in low socio-economic status.
- Early detection of H. pylori and its eradication and regular follow up will decrease the incidence of carcinoma stomach and different forms of gastritis.
- The H. pylori prevalence in Western Odisha was lower than that shown in the previous studies of developing Asian countries, but was significantly high in gastritis and to establish the potential association of H. pylori with gastritis or duodenitis, and peptic ulcers.

I firmly believe that this work is a humble addition to the past studies and may infuse future works to undertake more keen studies in this field.

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