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Helicobacter Pylori Related Gastritis in Adults, a Clinical, Endoscopic, Histopathological and Rapid Urease Test Study

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Abstract: ***H. Pylori is major etiological factor in the development of Peptic ulcer disease. Objectives: The Aim and objective of this study find out the association of H.pylori with gastric lesions in endoscopic biopsy specimen in semi-urban regions and to study the specificity and sensitivity of Rapid Urease test,to evaluate the usefulness of Giemsa stain in addition to histopathological examination for identification of H.pylori. Study design: A prospective study of 50 adult patients presenting with upper abdominal pain,[20] dyspepsia, vomiting, haematemesis is undertaken to evaluate the relationship of this symptomcomplex to inflammatory gastroduodenal lesions with special reference to H.pylori infection. The clinical endoscopic findings, rapid urease test and histopathological evaluation of gastric antral specimen with special stains to demonstrate the organism are presented and analysed.***

Keywords: Gastritis, H.Pylori, Upper gastro intestinal endoscopy, Rapid urease test

1. Introduction

The understanding of etiopathogenesis of peptic ulcer, expressed as gastritis, gastric ulcer, duodenitis, duodenal ulcer has been revolutionised during last decade with the discovery in 1983, of a new pathogen categorized as Helicobacter Pylori by Warren and Marshall.[1,2] Several reports have subsequently supported the association of H.pylori as a major etiological factor in the development of peptic ulcer disease [3] and recent reports also suggest its association with gastric carcinoma and lymphoma.[4] Bacterium has been classified as class I definite gastric carcinogen to human. A prospective study of adult presenting with upper abdominal pain, dyspepsia, vomiting, haematemesis is undertaken to evaluate the relationship of this symptomcomplex to inflammatory gastroduodenal lesions with special reference to H.pylori infection. The clinical endoscopic findings, rapid urease test and histopathological evaluation of gastric antral specimen with special stains to demonstrate the organism are presented and analysed**.**

In addition to more common inflammatory cell infiltration it is only recently the histopathologic effect of H.pylori on gastric epithelium at light microscopic level has been stressed and this has been studied systematically, describing striking changes in surface epthelium and attributing them as specific for H.pylori colonization and correlating them with type of cytotoxin,,production and risk of peptic ulcer.[3] H.pylori infection can be diagnosed by invasive [5] (requiring endoscopy) and non invasive technique.[6]

In this study the various methods of identification of H.pylori and histopathological features associated H.pylori in gastric mucosa in patients, presenting with dyspepsia are discussed and described in detail paying particular attention to histopathological effects of H.pylori on epithelial cells

2. Materials and Methods

In the present study, endoscopic biopsies were taken from 50 patients, who attended gastro enterology department with complaints of nausea, vomiting, dyspepsia, flatulence and fullness were screened with detailed clinical history regarding socio-economics status, housing conditions, water supply etc. After thorough clinical evaluation, patients suspected to have gastric lesions were subjected to endoscopic biopsy procedure.

3. Methodology

Endoscopy: Upper gastro – intestinal endoscopy was performed with flexible fiber optic endoscope manufactured by Pentax model number 29P.

- Informed consent was obtained from patients. Relevant history and clinical details were recorded.
- After overnight fasting, endoscopy was done on the following morning, endoscopic changes were noted in esophagus, stomach, duodenum were recorded.
- Three gastric biopsy specimens were taken from antrum and corpus and one was immediately used for Rapid Urease test (Annexure I) and the other was immediately fixed in 10% buffered neutral formalin for histopathological evaluation.

Histopathologic study of biopsy Specimens

The biopsy specimens that were fixed in 10% buffered neutral formalin were processed in automatic tissue processor for paraffin embedding, then 3-5 µ sections were cut.. The sections were stained with Haematoxylin & Eosin (Annexure II) for evaluation of histopathological features and special stains like Giemsa and Alcian Blue / PAS stain (Annexure III) used to detect H.pylori organisms.

Gastritis was defined and classified according to established histological criteria with revised updated Sydney system.

The density of H.pylori, chronic inflammation, neutrophil polymorphic activity, glandular atrophy and intestinal metaplasia were recorded in all cases of gastritis and graded as mild, moderate and marked scale according to the guidelines provided by the updated revised Sydney system, using the visual analogue scale. The most prevalent appearance on each slide was matched with the graded panel that resembles it most closely. Lesion being active was signified by presence of neutrophils within glandular and surface epithelial layer. Glandular atrophy was identified, when gastric glands were correspondingly decreased in amount and widely separated. An increase in lymphocytes and plasma cells in lamina propria categorizes the gastritis as chronic. Infiltration involving upto 1/3 of gastric pits and surface are designated as mild between ½ to 2/3 as moderate and more than this as severe gastritis.

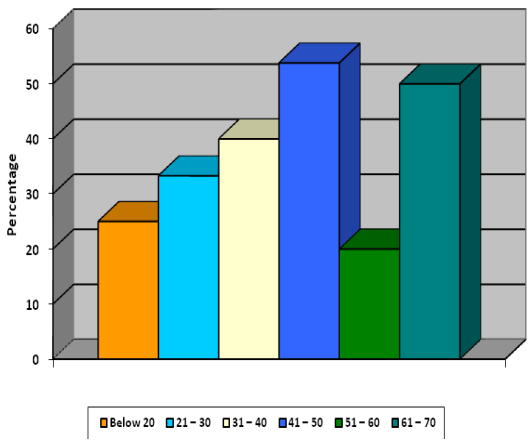
Apart from graded variables described in the updated revised Sydney system, special attention has been thrown on non-graded variables like surface epithelial changes, mucin depletion, erosions, lymphoid follicles, cells drop out, foveolar hyperplasia, pseudopyloric metaplasia and endocrine hyperplasia

4. Observations and Results

This study covered 50 patients clinically suspected to have gastritis and undergone upper-gastro intestinal endoscopy. In the 50 cases, 35 were males with age ranging from 20 years to 70 years (mean age 45 years) 15 were females with age ranging from 20 years to 60 years (mean age 40 years).

When the patients were divided into 6 groups according to their age (< 20, 21 – 30, 31 – 40, 41 – 50, 51 – 60, 61 – 70) there was significant increase in the Helicobacter pylori (H.pylori) positivity in the age group of 41 – 50 years (53.8%) followed by 31 – 40 years (50.0%). Table – 1

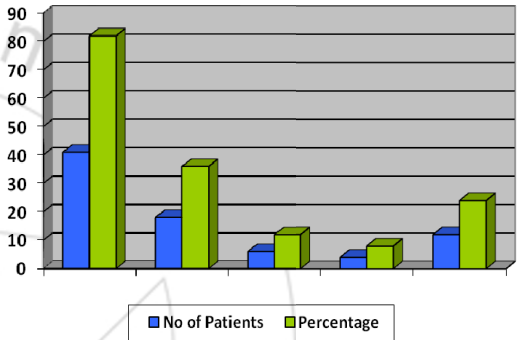
S.No	Age (in Years)	Total no. of cases	H.pylori Positive Cases	Percentage
1	Below 20	4	1	25.0%
2	21 – 30	6	2	33.3 %
3	31 – 40	20	10	50.0 %
4	41 – 50	13	7	53.8 %
5	51 – 60	5	1	20.0 %
6	61 – 70	2	1	50.0 %
	Total	50	22	44.0 %



Abdominal pain with dyspepsia more than 3 months is the commonest clinical presentation followed by abdominal discomfort with vomiting and nausea. Abdominal discomfort with anemia was noticed in some cases. The clinical presentations of the patients are summarized in the following table.2.

Table 2

S. No	*Clinical Presentation*	*No.of Patients*	*Percentage*
1.	Upper abdominal pain, Bloating sensation, Belching (dyspepsia) more than 3 months	41	82 %
2.	Abdominal discomfort with Vomiting, Nausea	18	36 %
3.	Epigastric Pain + Malena + Heart burn	6	12 %
4.	Epigastric Pain + Haematomesis	4	8 %
5.	Post cibal abdominal distension + Loss of appetite + Iron deficiency anemia	12	24 %



Endoscopic Examination

Upper gastro-intestinal endoscopy revealed **12** ases showed gastric ulcer ranging from 0.5 cm to 2 cm with erosion and edema; **12** cases antral gastritis with duodenal ulcer; **5** cases showed nodularity of gastric mucosa; **6** cases with patchy erythematous gastric mucosa; **5** cases were with duodenal erosion and edema with ulceration ranging from 0.25 cm x 1 cm to 1.5 cm to 3 cm and **10** patients did not show any endoscopically detected lesion.

Detailed endoscopic findings in all the 50 cases are listed in Table-3.

Table 3

S.No	Endoscopic diagnosis	No. of Patients	Percentage
1	Gastric ulcer < 2cm with erosion and edema	12	24 %
2	Antral gastritis with duodenal ulcer	12	24 %
3	Nodularity of gastric mucosa	5	10 %
4	Patchy erythematous gastric mucosa	6	12 %
5	Duodenal erosion with edema	5	10 %
6	Unremarkable mucosa	10	20 %

Endoscopic findings and corresponding histopathologic diagnosis of **50** endoscopic biopsies are listed in the following table (Table-4).

In 10 cases, where endoscopy was normal, there was histological evidence of chronic active gastritis in one case and mild gastritis in one case and eight cases shows normal gastric mucosa. These shows an apparent lack of correlation between endoscopic and Histopathalogical diagnosis of gastritis in dyspeptic patients.

Table 4

S.No	*Endoscopic Feature*	*Histopathological Feature*
1.	Gastric Ulcer with erosion – 12	Chronic Active antral gastritis –10 with surface epithelilalchanges Normal mucosa – 2
2.	Antral gastritis with duodenal ulcer – 12	Chronic mild gastritis– 8Atrophic gastritis - 2Chronic active gastriti– 2
3.	Nodularity of gastric mucosa– 5	Chronic active antral gastritis – 3Chronic gastritis with Intestinal Metaplasia - 2
4.	Patchy erythematous changes –6	Chronic mild gastritis– 1 Chronic active antral gastritis – 5
5.	Gastric Ulcer Duodenitis – 5	Chronic mild gastritis-2 Chronic gastritis with Intestinal Metaplasia - 3
6.	Unremarkable mucosa – 10	Normal mucosa –8Chronic mild gastritis –1Chronic active antral gastritis – 1

Rapid Urease Test (RUT):

RUT for detection of H.pylori from endoscopic specimen.The biopsy specimen was subjected to Urease testing in 50 cases, of which there were 24 positive cases. Among the 24 Urease positive cases, 22 cases were detected Histopathologically for H.pylori.

In the 26 Urease negative gastritis biopsy, Giemsa staining also did not detect H.pylori.

RUT is a simple, cheap test, performed at endoscopy room itself using Helicheck test device. It contains urea solution with indicator that detects alkalinity resulting from formation of ammonia in most infected patients (70%) and gives positive result within 2 Hours. In cases of positive result, it shows a change in colour from yellow/orange to pink/ red. Whereas, in cases of negative result, the colour remains as yellow colour itself. Urease test detects upto 0.3 unit of urease present in sample

Limitations of this test

1) The test is pH sensitive and therefore, any contamination in the reaction wells will change the reaction.
2) Biopsy specimen collected in preservatives with acidic or basic pH such as formalin etc should not be used for Heli-Check RUT test device.

Demonstration of H.pylori by Giemsa stain:

Though the H.pylori organisms were visible in the H&E stain, demonstration by Giemsa stain is considered as the gold standard for H.pylori detection. It facilitates the identification of H.pylori by darkening the organism.

Using Giemsa stain, the spiral shaped bacteria of H.pylori is attached to brush borders of gastric foveolar cells and inside the gastric pits (Luminal side of gastric mucosa). The distribution was mostly patchy and single. Lying close to surface epithelium and more densely distributed within lumen of gastric pits. It also extends less into the deeper portion of the mucosa. The organisms are absent in the areas of intestinal metaplasia.

In this present study, H.pylori was demonstrated by using Giemsa stain in 22 out of 50 biopsies.

Association between Gastritis & presence of H.pylori:

Most of the biopsy specimen, which were positive for H.pylori showed histological evidence of Gastritis

Twenty-four cases showed chronic active antral gastritis and activity implying the presence of high number of Neutrophilic polymorphs in the lamina propria and within epithelium.

Relationship between H.pylori density and severity of Gastritis:

There was no correlation between the degree of inflammation, noted in the histolopathologic study and density of H.pylori organisms.

Histopathology of gastric antral biopsies:

The following table (Table 6) shows details of histopathological findings of all the **50** gastric biopsies. Out of the **50** cases, only **22** cases show gastritis with H.pylori positive.

The presence or absence of H.pylori with varying degree of chronic inflammation, Neutrophilic polymorphic activity, glandular atrophy, intestinal metaplasia and gastric surface epithelial changes were recorded in **50** cases.

Table 6

S. No	Histopathology	No. of cases	Percentage	H.pylori Status	H.pylori %
1.	Normal gastric mucosa	10	20 %	2 positive 11 negative	20 %
2.	H.pylori associated chronic active antral gastritis (CAAG)	24	48%	16 positive 8 negative	66.6%
3.	H.pylori associated chronic non active gastritis (mild)	9	18%	4 positive 17 negative	44.3%
4.	Chronic gastritis with atrophy	2	4%	All Negative	0%
5.	Chronic gastritis with intestinal metaplasia	5	10%	All Negative	0%
6.	H.pylori Negative chronic non active gastritis	28	76%	All Negative	0%

5. Discussion

Chronic gastritis is defined as the presence of chronic mucosal inflammatory changes eventually leading to mucosal atrophy [7] & epithelial metaplasia. By far the most important etiological association is chronic infection by the

bacillius H.pylori.[8] The organism is a world wide Pathogen that has the highest infection rates in developing countries.

Sex distribution

Age and sex related possibility of H.pylori was studied. In the present study, out of 35 male cases 16 cases (45%) are positive for H.pylori and out of 15 female 6 cases (40%) are positive for H.pylori. The male to female ratio is 2:1 which is in contrast to the study literature and study conducted by Abdur Rauf Khan [2]

Age distribution:

The higher prevalence of H.pylori is in the age group of 41-50 years, which had highest percentage (53.8%) and followed by the age group 31-40 years (50.0%) This is in consonance with Richard,Freferick J[14] who states that prevalence of H.pylori increased with advanced age. Anderson states that the prevalence of H.pylori in adults approximates 100% in many developing tropical countries.

The prevalence of H.Pylori in the present study is 44%. It does not coincide with study of Abdul Rahman E, Fakhro[15] et al.,, In their study the prevalence rates are 79.4%.

This high percentage may be due to low socio economic status of the patient and lack of education about hygiene in most of those people. This accordance with James Fox at la Dube C :N F Tanih at al stated that H.pylori spreads from person to person and via a route that depends on hygiene proved by several studies.

In the present study, 45 cases out of 50 shows dyspepsia, abdominal pain, iron deficiency anemia. These are the most common symptoms encounter in other studies also.

Perusal of literature shows epigastric pain, which is the most common symptom (**92%)** followed by vomiting (**51**%) and hematemesis (**17**%) in H.pylori associated chronic gastritis.

As per study done by Graham Gill Desai etal who revealed that geographic and social patterns play a role in transmission of H.pylori. According to Anderson, East Asian countries where wide spread sanitation has been introduced, prevalence of H.pylori has shown downward trend.

Transmission from patient to patient after endoscopy has also been described.

As per study the high percentage of H.pylori positive individuals having gastric lesions were found to have history of intake of spicy and non-vegetarian food. H.Pylori infection highly frequent in dyspeptic patients, and it is cardinal risk factor for chronic gastritis.[16]

Endoscopic features

The advent of the fiber optic gastroscope with biopsy facilities has provided the means of obtaining biopsy specimens under direct vision from any part of stomach.

In this present study, there were 12 cases gastric ulcer with erosion, out of which 8 cases (66%) were positive for H.Pylori and 12 cases of duodenal ulcer in which 9 cases were positive (70%) and small proportion of cases showing patchy erythematous changes, nodularity of gastric mucosa and of unremarkable mucosa were also found in endoscopy examination.

Normal looking gastric mucosa is commonest single endoscopic finding, accounting for 20% cases. Though the results of endoscopic examination may show normal mucosa, [7] histopathological examination may show positive for H.pylori. In these cases, risk of re-infection is always there

The positivity rate for duodenal ulcer is 70% and gastric ulcer is 66% in our study. It is comparable to study by Tytget (1988) who found that 15 patients of duodenal ulcer and 9 out of 11 (81.8%) patients with gastric ulcers have the organism. And in 2002 Sengupta et al[17] studied antral biopsy specimens from 25 patients with symptoms and diagnosis of duodenal ulcer, amongst whom the positivity rate is 84%. In a study by Zhang C, Yamada N et al [18] the prevalence of H.pylori in gastric ulcer is 80.8%. Duodenal ulcer is usually associated with H.pylori infection. Treatment of duodenal ulcer must, therefore include acid reduction and H.pylori eradication all the time.

The most convincing data implicating H.pylori as a cause of cancer are furnished in the case-control studies from Hawaii, California, Great Britain, Taiwa[19] . In the first three studies (mean follow – up years 13, 14, 6 years respectively), serologic evidence of H.pylori infection associated with increased risk of developing gastric cancer, is 2.8 to 6 fold. The fourth nested case control study also identified an elevated risk of cancer (odds ratio = 1.6) but the finding was not statistically significant. This last study was hampered, however by a small number of cases, and short follow-up period. Overall the association between H.pylori and cancer appeared to be restricted to tumors distal to gastric cardia.

One line of research currently favours H.pylori infection as a causal factor in both MALT and non-MALT gastric lymphomas.[19]

When the density of H.pylori is low, application of endoscopic brush cytology helps in rapid detection.

Good evidence exists in the literature that H.pylori can cause chronic active gastritis. Most compelling and direct evidence are studies by Dr. Marshall et. al and subsequently by Moris and Nicholson. In these studies Moris and Marshall infected themselves with H.pylori and this led to the development of clinical and microscopic gastritis in these subjects and Koch's postulates of the etiology of the disease seemed to be fulfilled.

As further evidence of pathogenicity, secretory IgA directed against H.pylori has been isolated, and phagocytosis of the organism has been shown by intra gastric neutrophil. Others have successfully eradicated the organism with antibiotics, with resultant improvement of histologic gastritis.

In the present study, it is found that, more or less the antral biopsies colonized by H.pylori, showed evidence of gastritis, It confirms the previously reported high prevalence of H.pylori infection in association with antral gastritis further

supporting the contention that H.pylori is the etiologic agent of this lesion in most cases.

Helicobacter Pylori is now accepted cause of gastritis and peptic ulcer disease in adult.[3]

Table No 7 shows comparative analysis of various studies in children, reporting relationship between H.pylori infection and histological evidence of gastritis percentage in adults. This shows 50% of cases of gastritis show H.pylori positivity in contrast to the pediatric cases. Probably environmental factors, socio economic status, alcohol and smoking modified the development of gastritis with typical symptoms in adults.

According to Dixon degree of chronic inflammatory cell infiltration is correlated to the extent and density of H.pylori colonization. But we couldn't find significant correlation between these two factors and the differences can be explained [20]as follows:-

1) Difference immunological as well as histological responses in various age groups, could be due to genetic, social cultural economical, psychological factors.[90]
2) Some patients may have chronic inflammation (gastritis due to other causes and H.pylori, infection) simultaneously.
3) Partially treated patient may show lower degrees of inflammation.

Table 7

No	Name of the author and year	H.pylori – infection (No. of cases)	Histo pathological gastritis (No. of cases)	% of H.pylori – infection associated with gastric inflammation
1.	Musgrove et al[9] 1988	54	61	88%
2.	Hartley Cohen et al [10]1989	22	22	100%
3.	Grace W Elta et al[11] 1989	16	16	100%
4.	Siobhan M Gormally et al[12]1995	19	19	100%
5.	C.K. yeung et al 1990	64	64	100%
6.	Present study	22	45	50%

6. Conclusion

Helicobacter pylori is now widely recognised as the most common cause of primary or unexplained gastritis in adults as well as children. RUT is a simple, cheap test, performed at endoscopy room itself using Helicheck test device. A "test and treat" strategy is recommended for most patients with undifferentiated dyspepsia. With this approach, patients undergo a noninvasive test for H.pylori infection and if positive, are treated with eradication therapy. This strategy reduces the need for antisecretory medications as well as the number of endoscopies.

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