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Original Article

Helicobacter pylori and Gastric Metaplasia: Their Status after Eradication Therapy

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Abstract

This study was carried out with an aim to investigate the relationship between gastric metaplasia with *H. pylori* and the effect of eradication therapy. A total of 210 patients with history of dyspepsia were included in the study of which 50 were enrolled in the eradication therapy. After the eradication therapy 35 patients came for follow-up endoscopy. Paired endoscopic biopsies were taken from antrum and duodenal ulcer margin and were examined for *H. pylori* and for duodenitis and gastric metaplasia. Gastric metaplasia was significantly associated with *H. pylori*. After eradication *H. pylori* showed further extension of gastric metaplasia. It can be recommended that these patients can be further followed up to see the course of gastric metaplasia and what impact it has on ulcer recurrence and re-infection.

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Introduction

Since the demonstration of *H. pylori* in inflamed gastric mucosa by Marshall and Warren in 1983[1], this bacterium has been blamed to play a crucial role in the pathogenesis of gastritis and peptic ulcer diseases. Gastric metaplasia has been viewed as a protective response for the duodenum to exposure of high acidity. Gastric metaplasia infected by *H. pylori* is associated with active duodenitis[2] and duodenal ulceration[3, 4]. In *H. pylori* associated duodenal ulcer, gastric metaplasia and duodenal inflammation are frequently found[5]. Gastric metaplasia is most often seen on the top of the duodenal villi. Gastric metaplasia was defined by the presence of periodic acid Schiff positive neutral mucin in the lining epithelial cells, together with the absence of brush border[5] and it is most often seen on the top of the duodenal villi. Chronic duodenitis was characterized by definite increase in chronic inflammatory cells together with flattening of villi and evidence of epithelial cell damage. Neutrophils infiltrate the lamina propria in addition to the above changes in active duodenitis. Wyatt et al proposed that *H. pylori* infection spread from stomach to the site of gastric metaplasia in duodenum and causes inflammation and ulceration. *H. pylori* induces increased gastric secretion leading to increased gastric acidity and may cause gastric metaolasia6. Khulushi et al in 1995 further revealed eradication of H. pylori is accompanied by reduction in extent of gastric metaplasia[7]. Contradicting this, Urakami in 1997 showed that with successful eradication of *H. pylori* gastric metaplasia becomes well developed with abundant mucin and this prevents ulcer recurrence for a significant period but does not

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prevent re-infection. He also took into consideration the factors other than *H. pylori* for ulcerogenesis[8].

Aims and objectives

In this study, in a developing country like Bangladesh with high prevalence of *H. pylori*[9] we investigated the relationship between gastric metaplasia and *H. pylori* and the change in severity of gastric metaplasia after eradication of *H. pylori*.

Materials and Methods

Patients

Patients attending the Department of Gastroenterology with complaints of dyspepsia and undergoing endoscopic examination for suspected benign lesions were selected for the study. The subjects in this study were 210 patients (137 male and 73 female) who on endoscopy were diagnosed as gastric ulcer, duodenal ulcer or gastritis. Patients who had taken prior antibiotics, acid suppression treatment or corticosteroid in the past month were excluded. Patients who had undergone gastric surgery or diagnosed as malignant lesion on histopathology or in whom endoscopic biopsy was contraindicated were also excluded. Of these, 50 patients were assigned to an eradication therapy with one-week regime of pantoprazole, amoxycillin and furazolidine. Of the 50 patients 35 patients underwent a follow-up endoscopy at the end of six weeks.

Clinical procedure and histological methods

At the initial visit, all patients underwent endoscopy and two-paired biopsies were taken from the gastric antrum and two from the body. Of each pair one was used for Rapid Urease Test and the other was placed in 10% buffered formalin for histological examination to confirm *H. pylori* infection with Giemsa stain. The histological changes on haematoxylin-eosin and combined alcian-blue and periodic acid-Schiff stained slides were also noted. Two duodenal biopsies were taken from non-specific sites of first part of duodenum in absence of ulcer or from the margin of the ulcer on endoscopy. The biopsies were placed in buffered formalin and processed similarly and stained. Among eradication group who came for follow-up visit, biopsies were repeated and this time duodenal biopsies were taken from the center of the scar. Gastric metaplasia was seen on combined alcian blue periodic acid-Schiff and duodenitis on haematoxylin-eosin stained sliders.

Duodenitis was scored according to Mc. Callam et al. 1979 (cited by Fitzgibbons, 1988)[10]

Grade I: Slight thickening of villi, mild increase in cellularity of lamina propria including lymphocytes, plasma cells but without significant number of neutrophils.

Grade II: Moderate thickening and blunting of villi, moderate increase in cellularity of lamina propria and infiltration of the mucosa by neutrophils.

Grade III: Severe distortion of villous architecture with increase in inflammatory cells and erosion of the surface.

Gastric metaplasia was scored according to Gormall et al.[11]

Grade I: When eight consecutive cells of duodenum show gastric metaplasia.

Grade II: Island of gastric metaplasia scattered between areas of duodenal epithelium.

Grade III: All the duodenal biopsy show gastric metaplasia.

By the above methods, the possible relationship of H. pylori with duodenitis and gastric metaplasia was assessed and after the eradication the extent and progression of gastric metaplasia was evaluated.

Statistical analysis

The Chi-square test was used to analyze the data. The difference was considered statistically significant when $p<0.05$.

Results

In the present study a total of 210 patients were selected with a mean age of 39.06 years (SD± 14.57 years). Of the study population 137 are male and 73 are female with male: female ratio

1.88:1. The presence of *H. pylori* as detected by Rapid Urease Test (RUT) and Giemsa staining of the biopsy material was 76.66% (161 out of 210). Gastric metaplasia was seen in 38 patients (23 male, 15 female) out of all 210 patients of different age group (Table-I). Giemsa yielded *H. pylori* at this metaplastic site in duodenum, in only five of these patients. Of the 38 patients with gastric metaplasia 30 were *H. pylori* positive and were *H. pylori* negative (Table-II). Gastric metaplasia was significantly higher in *H. pylori* positive patients (Chi-square, X^2=3.967, p<0.05.

Table-I: *H. pylori* infection and gastric metaplasia in different age group

Age group In years	No. of patients	H. pylori Positive	Gastric metaplasia Positive
<20	27	23	06
21-30	44	41	06
31-40	57	40	12
41-50	41	37	05
51-60	31	16	06
61-70	06	02	02
>70	04	02	01

Table-II: Relationship of *H. pylori* infection and gastric metaplasia

H. pylori status	Gastric metaplasia	
	Present	Absent
Positive, 161 patients	30	131
Negative, 49 patients	08	41
Total, 210 patients	38	172

Table-III: Grading of gastric metaplasia and their *H. pylori* status.

H. pylori	Grading of gastric metaplasia			Total
Status	1	2	3	
H. pylori positive	22	08	0	30
H. pylori negative	07	01	0	08
Total	29	09	0	38

Of the 35 patients who came for follow-up, eradication was successful in 32 patients, the eradication rate being 91.42. Of these 32 patients 12 had gastric metaplasia and 23 had duodenitis before eradication (Table-IV).

Table-IV: Patients in different grades of gastric metaplasia and duodenitis before and after eradication *H. pylori*. (32 patients)

	Gastric metaplasia			
	Absent	Present in grade		
		1	2	3
Pretreated Condition	20	09	03	00
Post-treated Condition	18	02	11	01

	Duodenitis			
	Absent	Present in grade		
		1	2	3
Pretreated Condition	09	04	16	03
Post-treated Condition	27	03	02	00

Duodenitis decreased after eradication of *H. pylori* but gastric metaplasia extended. Two new cases of gastric metaplasia were detected after eradication. The extent of gastric metaplasia was significantly greater after eradication of *H. pylori* (chi-square, X2 = 21.94, p<0.005).

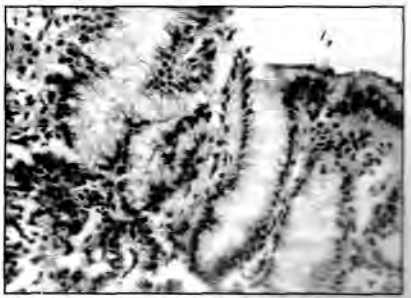

Fig. 1: Photomicrograph of the histological section of antral region, showing *H. pylori* in the gastric pit (Case no. 41, H&E X 650).

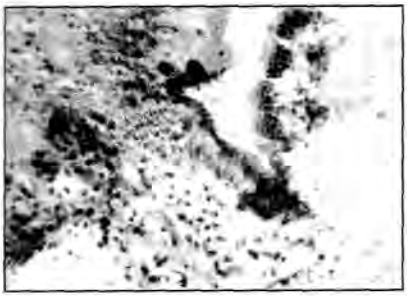

Fig. 2: High power view of the histological section of duodenal mucosa, showing gastric metaplasia (arrow indicating presence of neutral mucin in the absorptive cells) (Case no. 101; Alcian blue-PAS stain X 160).

Fig. 3: Photomicrograph of the histological section of duodenal mucosa, showing gastric metaplasia with duodenitis (Case no. 45; Alcian blue-PAS stain X 650).

Discussion

Several investigators have suggested that a close link exist between *H. pylori*, high acid output gastric metaplasia and causation of duodenal ulcer[12]. In the present series *H. pylori* positivity was 76.66%, which is close to previous investigators[13, 14]. In Bangladesh peptic ulcer disease and *H. pylori* infection are very common but frequency of gastric metaplasia is lower than other countries as revealed by previous investigators[14, 8]. In the present series similar lower rate was found. Also the yield of H. pylori t the metaplasia site was much lower as detected by Giemsa stain in the present series and so as found by other investigator in Bangladesh14. The fewer number of duodenal biopsies taken and the patchy distribution of *H. pylori* and gastric metaplasia can explain this. Two new cases of gastric metaplasia detected after eradication may be explained that they have been missed due to their patchy distribution. A better yield can be suggested by increasing the number of duodenal biopsies and using dual stain. Dual stain such as periodic acid-Schiff and modified Steiner silver impregnation method can detect gastric metaplasia and *H. pylori*, on the same slide[15]. Information on gastric metaplasia in developing country is scanty, In Peru though there is high prevalence of *H. pylori*, duodenal ulcer rate is low. This has been explained by their low incidence of gastric metaplasia, which may be constitutional[16]. In the present series, gastric metaplasia showed significant association with H. pylori. In other studies it was already shown that *H. pylori* infection causes increased gastric acidity and so metaplasia may be the protective response[17]. Earlier investigator of Bangladesh Nasim et al did not find significant association though the extent of gastric metaplasia was higher in *H. pylori* positive patients[14]. The possible causes may be small number of patients in their series and less number of duodenal biopsies taken. The other contributory factor may be the high prevalence of H. pylori in Bangladesh. For this it is difficult to assess the prevalence of gastric metaplasia excluding the influence of this infection. Examining serologically *H. pylori* negative patients for gastric metaplasia and comparing this group with *H. pylori* positive patients will give a better idea if the lower rate of gastric metaplasia is constitutional. It is yet to be investigated at what extent duodenal ulcer occurs in *H. pylori* positive patients without prior gastric metaplasia formation and harboring of the metaplastic site in duodenum by *H. pylori*. In the present series male showed increased incidence of gastric metaplasia, which was similar to the earlier investigators [14,8]. The high level of acid output in male can explain this16. In the present series it was observed that with eradication, gastric metaplasia extended though duodenitis decreased.

Previous investigators also revealed similar results[8]. They further showed that this extension of gastric metaplasia prevented ulcer recurrence.

Conclusion

It can be concluded that by eradication of *H. pylori*, gastric metaplasia can be extended with abundant intracellular mucin, resulting in adequate defensive mechanism against ulcer recurrence. These patients can be further followed up for longer period to see the course of gastric metaplasia. Comparing these groups it may be possible to evaluate the modalities to prevent re-infection and recurrence of *H. pylori* infection in a country like Bangladesh with high prevalence of *H. pylori*[9,12].

References

1. Warren J R, Marshall B J. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet 1983; 1:1273-5.
2. Wyatt J I, Rathbone B J, Dixon M F, et al *Campylobacter pyloridis* and acid-induced gastric metaplasia in the pathogenesis of duodenitis. J Clin Pathol 1987; 40:841-8.
3. Steer H W. Surface morphology of the gastro duodenal mucosa in duodenal ulceration. Gut 1984; 25:1203-10.
4. Satoh K, Kimura K, Yoshida Y, et al. *Helicobacter pylori* status in the duodenal mucosa and the course of duodenal ulcer disease. Gastroenterol Hepatol 1992; 4(suppl 1): 75-8.
5. Wyatt J I, Rathbone B J, Sobela G M et al Gastric epithelium in the Duodenum: Its association with Helicobacter pylori and inflammation. J Clin Pathol 1990; 43:981-986.
6. Michael F Dixon. Histological responses to *Helicobacter pylori* infection: gastritis, atrophy and preneoplasia. Bailliere's Clinical Gastroenterology 1995; 9(3): 467-486.
7. Khulushi S, Mendall M A, *Badve* S et al. Effect of *Helicobacter pylori* eradication on gastric metaplasia of the duodenum. Gut 1995; 36:193-197.
8. Yoshihito U, Masuo K, Hiromu S. Gastric metaplasia. American Journal of Gastroenterology 1997; 92:5: 795-799.
9. Khan A K A, Hassan M, Roy P K et al. Peptic ulcer in Bangladesh. Bang Med Res Coun Bull 1987; 8:29-42.
10. Fitzgibbons P L, Dooley C P, Cohen H, Appleman M D. Prevalence of gastric metaplasia, inflammation and *Campylobacter pylori* in the duodenum of number of normal population. Am J Clin Pathol 1988; 80:711-14.
11. Gormally S M, Kierce B M, Daly L E. Gastric metaplasia and duodenal ulcer disease in children infected by *H. pylori*. Gut 1996; 38:513-17.
12. Goodwin C S. Duodenal Ulcer: *Campylobacter Pylori* And The 'Leaking Roof' Concept. Lancet 1988; 24:1467-69.
13. Talukder S I. Association Of *Helicobacter Pylori* With Gastric Cancer And Other Gastroduodenal Lesions. M. Phil. (Pathology) Thesis; 1995; University of Dhaka.
14. Ahmed N, Arfin M S, Rahman A J E N et al. Gastric metaplasia in the duodenum and its association with *H. pylori*. Bang Med Col J. 2003; 11:16-18.
15. Hala M T, El-Zimaity Jain W et al. A reliable method for the simultaneous identification of *H. pylori* and gastric metaplasia in Duodenum. J Clin Pathol 1990; 52:914-16.
16. Gastrointestinal Physiology Working Group of the Cayentano Heredia and The Johns Hopkins University. Ecology Of Helicobacter Pylori In Peru: Infection Rates In Coastal, High Altitude, And Jungle Communities. Gut 1992; 33:604-6.
17. Sack R B, Gyr K. *Helicobacter* infection in developing world. Lancet 1993;341:1274-75.

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