



Original Article

Prevalence of subtypes of gastric intestinal metaplasia and its relationship with Helicobacter pylori infection

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ABSTRACT

Background: Gastric intestinal metaplasia is seen chronic gastritis associated with Helicobacter pylori. The objective of this study was to determine the prevalence of subtypes of intestinal metaplasia and presence of Helicobacter pylori infection.

Materials and Methods: This was a cross sectional study done at Kathmandu Medical College teaching Hospital in Pathology department from December 2018 to August 2019. The endoscopic biopsies were evaluated for intestinal metaplasia and Helicobacter pylori with the help of Hematoxylin and Eosin stains as well as Giemsa stain. Subtypes of intestinal metaplasia were classified with the help of periodic acid- Schiff/Alcian Blue stain combination and High Iron Diamine- Alcian Blue stain at pH 2.5. The relationship between Helicobacter pylori and subtypes of intestinal metaplasia were compared. Fisher's exact test was used for statistical evaluation. A p value of <0.05 was considered as statistically significant.

Results: The prevalence of intestinal metaplasia was found in 57 (12.2%) biopsies. Type I intestinal metaplasia was found in 23 (40.4%) biopsies, type II in 10 (17.5%) biopsies and type III in 24 (42.1%) biopsies. Helicobacter pylori was positive in 28(49.1%) and it was negative in 29(50.9%) biopsies. No statistical significant correlation was seen in the subtypes of intestinal metaplasia with Helicobacter pylori status (p>0.05).

Conclusion: Intestinal metaplasia is frequently observed in endoscopic biopsies, most common being type III subtype.

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INTRODUCTION

Gastric intestinal metaplasia (IM) is a replacement of gastric mucosal epithelium by mucosal cells with intestinal morphology and is considered as a precursor lesion for gastric cancer.¹ Prevalence of gastric IM worldwide is unknown, however the study done by Sonnenberg and colleagues found 7% prevalence.²

Based on the histomorphology and mucin-histochemistry, the gastric IM are classified as complete (type I) and incomplete (types II and III). It has been suggested that, chronic gastritis induced mainly by Helicobacter pylori (H. pylori) infection is usually associated with IM.³ Several

studies have shown the relation between gastric carcinoma and the subtype of IM, the incidence of cancer being highest among patients with IM subtype III.⁴⁻⁶

The aim of the present study was to evaluate the prevalence of IM and its subtypes in gastric biopsy specimen. We also compared the relationship between *H. pylori* infection and subtypes of intestinal metaplasia.

MATERIALS AND METHODS

This was a prospective cross-sectional study conducted among patient visiting Kathmandu Medical College Public Limited, Sinamangal, Nepal from December 2018 to August 2019. The ethical approval for the study was taken from Institutional Review Committee of Kathmandu Medical College Teaching Hospital, Sinamangal. The written informed consent was obtained from each participant. The inclusion criteria include history of abdominal pain, dyspeptic symptoms, and reflux. The exclusion criteria include patient with acute upper gastrointestinal bleeding and patient with the history of gastric surgery.

All the patients who meet the above criteria and undergoing upper gastrointestinal endoscopy during the study period were included. The biopsy was taken and fixed immediately in 10 % formalin solution. These were then processed in the tissue processor and embedded in paraffin wax. Serial sections were cut at 3-5 μ . The biopsies were stained with hematoxylin and eosin (H&E) stain to evaluate for the presence of intestinal metaplasia. In addition Giemsa staining were carried out to determine for the presence or absence of *H. pylori*. These biopsies were then stained with periodic acid- Schiff/Alcian Blue (PAS/AB) at pH 2.5 stain combination and High Iron Diamine- Alcian Blue (HID/AB) at pH 2.5 stain to identify neutral mucin, sialomucin and sulphomucin. These mucin stains (PAS/AB and HID/AB) are not routinely used in histopathology for gastric biopsy samples. We used these stains to separate the types of IM. Additional cost was not charged to the patient for these stains. Subtypes of IM are determined according to Filipe et al classification.⁷

Type I IM is characterized by the presence of mature absorptive and goblet cells, the latter secreting acid sialomucin.

Type II IM is characterized by few or absent absorptive cells; presence of columnar intermediate cells in various stages of differentiation, secreting neutral and acid sialomucin; goblet cells secreting sialomucin and/or occasionally sulphomucin.

Type III IM cell dedifferentiation is more marked than in type II; intermediate cells secrete predominantly sulphomucin; goblet cells secrete sialo- and/or sulphomucin. A variable degree of disorganised glandular architecture is often present.

The relationship between *Helicobacter pylori* and subtypes of intestinal metaplasia were compared. Fisher's exact test was used for statistical evaluation. A p value of <0.05 was considered as statistically significant.

RESULTS

We found 57 (12.2% of 467 gastric biopsies) gastric IM. Mean age was 46.6 (range 26-72) years.

Type I gastric IM was 23 (40.4%), type II was 10 (17.5%) and type III was 24 (42.1%) (Table 1). Among type III gastric IM, 4(7%) had associated dysplasia and 8(14.03%) had associated adenocarcinoma.

H. pylori was seen in 28(49.1%) biopsies. No statistical significant difference was found in the prevalence of types of gastric IM with *H. pylori* status (p>0.05) (Table 2).

On mucin histochemistry, type I IM reveals acid sialomucin in goblet cells (Figure 1A & 1B) while acid sialomucin in goblet cells as well as mixture of neutral and acid mucin in intermediate cells was detected in type II IM (Figure 2A & 2B). Acid sialo and sulpho mucin in goblet cells as well as sulpho mucin in intermediate cells was detected in type III IM (Fig. 3A & 3B).

Table 1: Prevalance of subtypes of intestinal metaplasia

Types of gastric intestinal metaplasia	Frequency	Percent
Type I	23	40.4
Type II	10	17.5
Type III	24	42.1
Total	57	100

Table 2: Relationship between *Helicobacter pylori* and subtypes of intestinal metaplasia

Types of gastric intestinal metaplasia	Frequency Percent			Total	Fisher's exact test p value
	Type I	Type II	Type II		
Positive	13 (56.5%)	6 (60.0%)	9 (37.5%)	28 (49.1%)	0.305
Negative	10 (43.5%)	4 (40.0%)	15 (62.5%)	29 (50.9%)	
Total	23 (100%)	10 (100%)	24 (100%)	57 (100%)	

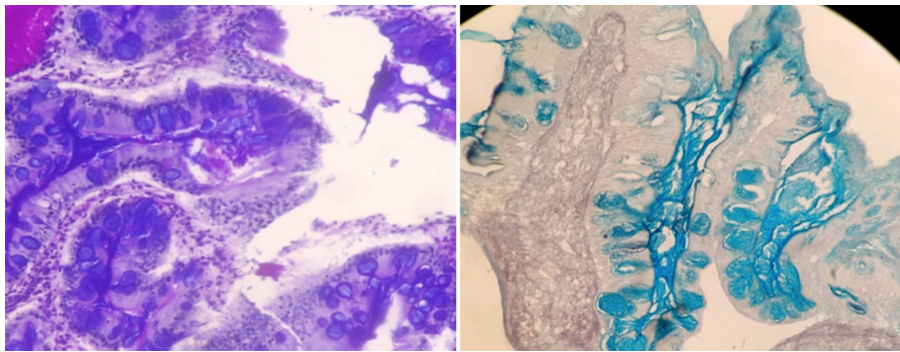


Figure 1: Intestinal metaplasia Type I: (A) PAS/AB stain, goblet cells secreting acid mucin. (B)HID-AB stain, absorptive cells mucin is predominantly neutral mucin (unstained) and goblet cells secreting sialomucin. (Magnification, X400)

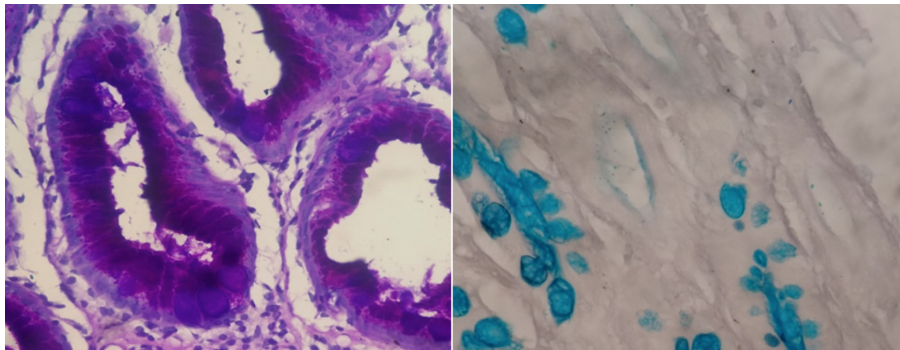


Figure 2: Intestinal metaplasia Type II: (A) PAS/AB stain, goblet cells secreting acid mucin and intermediate cells in between contain a mixture of neutral and acid mucins. (B)HID-AB stain, intermediate cells mucin is predominantly neutral mucin (unstained). (Magnification, X400)

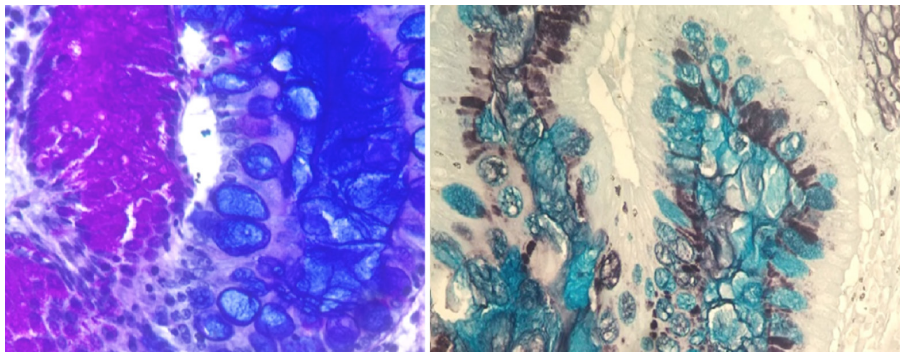


Figure 3: Intestinal metaplasia Type III: (A) PAS/AB stain, goblet cells secreting acid mucin (B)HID-AB stain, intermediate cells mucin is predominantly sulphomucin (brown) and goblet cell secreting sialo (blue) and sulpho (brown) mucin. (Magnification, X400)

DISCUSSION

The prevalence of gastric IM was found to be 12.2% in our study which is similar to the reported prevalence.^{1,8} However in contrast to our study low prevalence of IM was observed in other studies, the possible cause for this might be less prevalence of H. pylori infection in their countries.^{2,9}

In a research of prevalence of gastric IM done in Turkey, the commonest IM found was type III (38%), followed by type II (32%) and type I (8.2%).¹ We also found type

III as a commonest gastric IM. However in other studies done in Finland and Netherland higher prevalence of type I IM was reported.^{6,10} This might be because we had higher prevalence of H. pylori infection and also the H. pylori eradication program was not active in our country.

It has been emphasized that sulphomucin secreting IM, that is type III is found significantly more often in surrounding dysplasia and gastric adenocarcinoma.¹¹ In our study we also found type III IM associated with dysplasia and adenocarcinoma in 4(7%) and 8(14.03%) cases respectively.

The cause for this late diagnosis in our country is because patients were reluctant to do endoscopy and biopsy as per protocol for the early detection of precancerous lesions. Several studies suggested that routine endoscopic evaluation and histopathological follow up could be cost effective in patient with IM as this could detect gastric cancer at an early stage.¹²⁻¹³ Recently published updated guidelines 2019 for the management of epithelial precancerous conditions and lesions in the stomach (MAPSII) recommend that patients with IM at a single location but with a family history of gastric cancer, incomplete IM, or persistent *H. pylori* gastritis, endoscopic surveillance with chromoendoscopy and guided biopsies may be considered in 3 years.¹⁴

This study showed *H. pylori* was positive in 28 (49.1%) cases with gastric IM. Significant difference was not found between types of IM with *H. pylori* infection ($p > 0.05$). We found type III subtype was lower in *H. pylori* positive case than in *H. pylori* negative which suggest that gastric environment is not suitable for *H. pylori* in type III IM positive patient. Similar type of result was found in other studies.^{1,10} It has been postulated that *H. pylori* causes chronic gastritis and may progress over years to atrophic gastritis. IM, which is considered as a premalignant lesion arising in the background of atrophic gastritis finally leads to dysplasia and carcinoma.¹⁵

CONCLUSIONS

Gastric IM is a common finding in endoscopic biopsies. Type III subtype is more commonly observed than other subtypes. *H. pylori* can be absent in type III IM because of alteration in gastric environment. The practice of using PAS/AB and HID/AB stain is essential in routine histopathological examination to differentiate subtypes of IM.

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Conflict of Interest: None

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