

# Histopathological Study of Gastric Lesions and its Correlation with Mucin Histochemistry and Helicobacter Pylori Infection

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## ABSTRACT

**Background:** Gastric disorders are responsible for a great deal of mortality and morbidity and are one of the most common encountered problems in clinical practice. H. Pylori infection is responsible for majority of acid peptic disease and is also a known carcinogen. Intestinal metaplasia is considered a precancerous lesion. We studied the incidence of H. pylori infection and mucin histochemistry of different gastric lesions.

**Methods:** This study was conducted for a period of 1 year, in 50 gastric specimens received for histopathological study in the Department of Pathology, AMCH. Slides were stained with routine H&E and Giemsa for H. pylori detection. PAS/AB stain (at pH 2.5 & pH 1.0) was done to study mucin histochemistry.

**Results:** Out of 50 cases, 58% cases were malignant and 42% cases were benign. H. Pylori was seen in 42% cases. IM was observed in 40% of gastric lesions. IM was more common in malignant lesions. On subclassification, Type 1 and 2 IM were seen almost equally in both benign and malignant gastric lesions, but Type 3 IM was more common in malignant lesion. Incidence of IM was higher in intestinal than diffuse adenocarcinoma. A statistically significant association was seen between H. Pylori infection and IM.

**Conclusion:** Routine detection of H. pylori by special stains and mucin study in all gastric biopsy specimens helps in early detection of precancerous gastric lesions.

**Keywords:** Gastric Lesions, Helicobacter Pylori Infection, Mucin Staining, Intestinal Metaplasia

## Introduction

Stomach is a common site for inflammatory and neoplastic lesions. <sup>[1]</sup> H. pylori infection is an important step of gastric carcinogenesis cascade <sup>[2]</sup>, resulting changes from chronic gastritis, atrophic change and intestinal metaplasia to gastric cancer. Study of mucin histochemistry has been used to characterize the transformations of normal gastric epithelium leading to intestinal metaplasia and to carcinoma. <sup>[3]</sup> Objective of this study is to detect incidence of H-pylori infection, study mucin histochemistry and the histopathology of gastric lesions.

## Materials and Methods

The study was conducted in the department of Pathology, AMCH for a period of 1 year from June 2017 to May 2018. 50 gastric tissue including both endoscopic biopsy and gastrectomy specimens of both benign and malignant gastric disease were included. Tissue sent for histopathology was processed and routinely stained with H&E. Giemsa staining was done to detect H. pylori. AB/PAS staining was done at pH 2.5 to differentiate neutral mucin from acidic mucin & pH 1.0 to differentiate sialomucin from sulphomucin.

## Result

Out of 50 cases, 44 were endoscopic biopsies and 6 were gastrectomy specimens. Majority of patients were from 41 to 70 years. Male to female ratio was 1.5:1. 42% (21) cases were benign and 58% (29) cases were malignant. Most common benign lesion was chronic gastritis 33.33% and most common gastric carcinoma was MDADC 50%. Distribution of gastric lesion based on histopathology shown in table 1.

H. Pylori was detected by Giemsa staining in 21 (42%) cases out of 50. Of which 08 (38.09%) were malignant and 13 (61.91%) were benign. Table 2 shows incidence of H. Pylori positive cases in different gastric lesions. IM was seen in 20 (40%) cases out of 50 by AB/PAS staining. 12 (60%) were malignant and 08 (40%) were benign lesions. Table 3 shows distribution of IM in different gastric lesions. Type 1 and 2 IM was equally seen in both benign and malignant gastric lesions, but sulphomucin positive Type 3 intestinal metaplasia was seen in only 25% benign lesion and 75% malignant lesion.

Out of 20 IM positive cases, 14 (70%) cases showed H. pylori infection. Statistically significant association was seen between IM and H. Pylori infection (p value 0.001 by Fischer exact test).

## Discussion

Although incidence of gastric carcinoma is on decline but still it remains the fourth most commonly diagnosed cancer

**Table 1: Distribution of gastric lesions based on histopathological diagnosis.**

Category	Histopathological diagnosis	Frequency	Percentage
Benign lesions	Chronic gastritis	07	14%
	Gastric ulcer	05	10%
	Hyperplastic polyp	03	6%
	Dysplasia	06	12%
Malignant lesions	Well differentiated ADC	07	14%
	Moderately differentiated ADC	12	24%
	Poorly differentiated ADC	05	10%
	Mucinous adenocarcinoma	02	4%
	Signet ring cell carcinoma	02	4%
	Squamous Cell carcinoma	01	2%
	<b>TOTAL</b>	<b>50</b>	<b>100%</b>

**Table 2: Incidence of H. Pylori positive cases by Giemsa staining in different gastric lesions.**

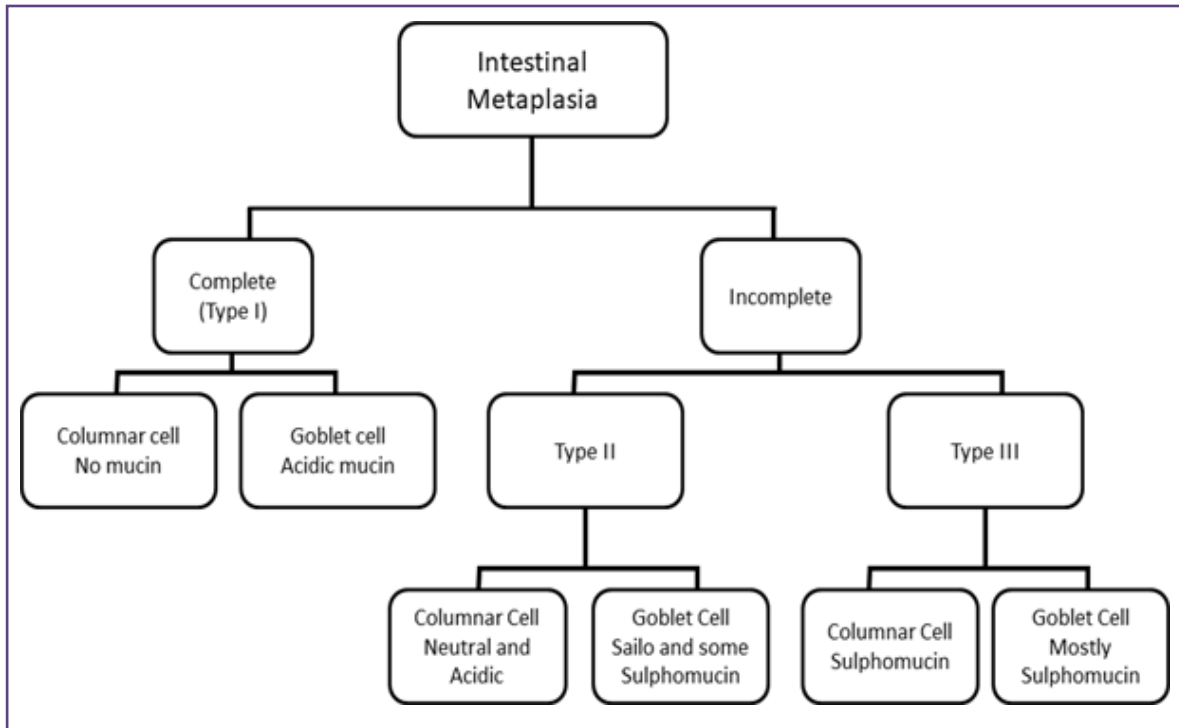
Histology diagnosis	H. Pylori positive	Percentage
Chronic gastritis	03	14.29%
Gastric ulcer	05	23.81%
Hyperplastic polyp	02	9.52%
Dysplasia	03	14.29%
WD ADC	03	14.29%
MD ADC	04	19.05%
PD ADC	01	4.76%
Mucinous ADC	00	0%
Signet ring cell ca	00	0%
SCC	00	0%
<b>TOTAL</b>	<b>21</b>	<b>100%</b>

**Table 3: Distribution of Intestinal Metaplasia in gastric lesions based on Alcian blue/PAS staining at pH 2.5 and pH 1.0.**

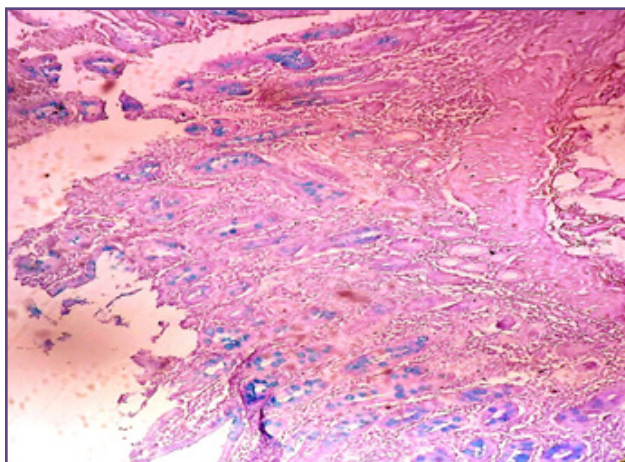
Histopathological diagnosis	No. of specimen		Sub types of IM		
	All	IM %	Type 1	Type 2	Type 3
Chronic gastritis	07	2 (28.57%)	1 (50%)	1 (50%)	-
Gastric ulcer	05	3 (60%)	1 (33.3%)	1 (33.3%)	1 (33.3%)
Hyperplastic polyp	03	1 (33.3%)	-	1 (100%)	-
Dysplasia	06	2 (33.33%)	1 (50%)	1 (50%)	-
WD ADC	07	3 (42.85%)	-	2 (66.67%)	1 (33.33%)
MD ADC	12	4(33.33%)	1 (25%)	2(50%)	1 (25%)
PD ADC	05	2 (40%)	-	1 (50%)	1 (50%)
Mucinous ADC	02	1 (50%)	-	1 (100%)	-
Signet ring cell ca	02	2 (100%)	1 (50%)	1 (50%)	-
SCC	01	-	-	-	-
<b>Total</b>	<b>50</b>	<b>20 (35%)</b>	<b>05 (25%)</b>	<b>11 (55%)</b>	<b>04 (20%)</b>

**Table 4: Distribution of sub types of IM in intestinal & diffuse type of gastric carcinoma.**

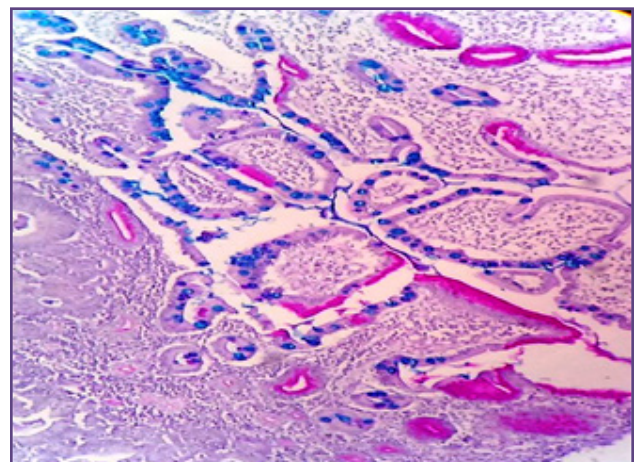
Study	Intestinal type			Diffuse		
	No. cases	Type 1 & 2 IM%	Type 3 IM %	No. cases	Type 1 & 2 IM%	Type 3 IM %
Jass et al. <sup>[23]</sup>	23	26.1	73.9	7	100	0
Jass Filipe et al. <sup>[24]</sup>	24	25	75	6	100	0
Segura DI Montero C et al. <sup>[25]</sup>	19	11	89	14	65	35
Rehman et al. (2016) <sup>[26]</sup>	13	-	-	3	-	-
Present	21	75	25	8	100	0



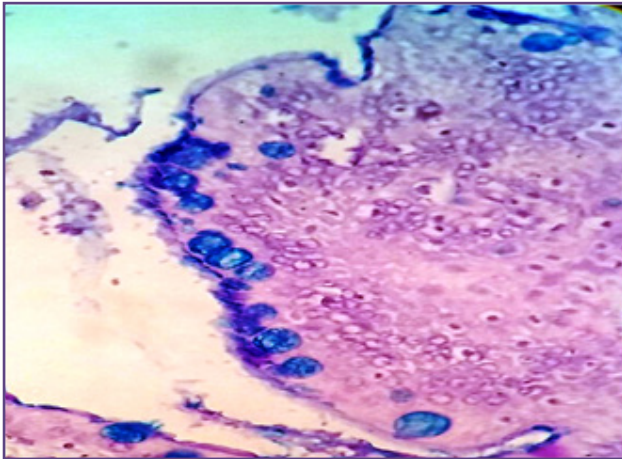
**Fig. 1:** Based on the mucin detection gastric intestinal metaplasia can be divided into 3 subtypes [18, 22, 23].



**Fig. 2 :** Photomicrograph of Type 1 IM, showing sialomucin in the goblet cells (Alcian blue/PAS at pH 2.5 40X).



**Fig. 3 :** Photomicrograph of Type 2 IM, showing mostly sialomucin in goblet cells, along with neutral mucin in columnar cells (Alcian blue/PAS at pH 2.5,10X)



**Fig. 4: Photomicrograph of Type 3 IM, showing sulphomucin secreting columnar cells Alcian blue/PAS at pH 1.0.**

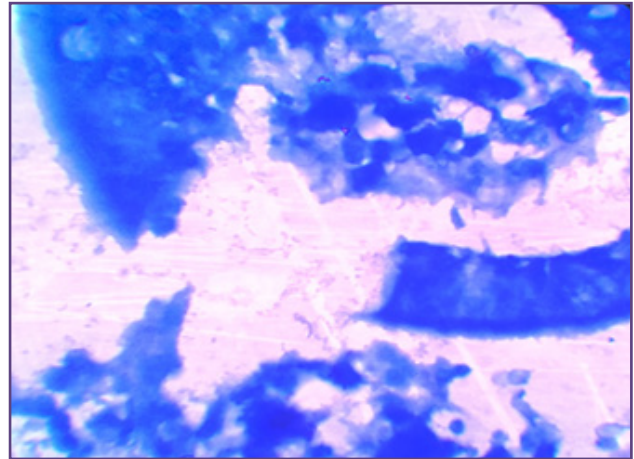
<sup>[4]</sup> and second most common cause of cancer related death in the world <sup>[5]</sup>. The rates for gastric cancer in North-eastern registries are higher than that of rest of the country <sup>[6]</sup>.

*Helicobacter Pylori* has been implicated as an important etiological factor in gastric carcinoma through its role in the development of chronic gastritis. *H. Pylori* infection is an important initiating and promoting step of this gastric carcinogenesis cascade <sup>[2]</sup>. Hence, it is necessary to detect *H. Pylori* routinely in all gastric lesions.

*H. Pylori* is a gram negative, microaerophilic, urease positive, curved, motile bacterium that resides in the gastric pits and the overlying mucus blanket <sup>[7]</sup>. There are number of methods of detecting *H. pylori*, but the histological detection in a gastric biopsy is the commonest and among the most sensitive <sup>[8]</sup>. Effective antimicrobial treatment depends on sensitive and accurate diagnostic approaches <sup>[9]</sup>. Therefore, there is great interest in the detection and eradication of this bacterium for good prognostic outcome.

The distribution and number of mucins varies in different regions of the GIT. The mucosa of the stomach has been found to have some qualitative as well as quantitative changes in the non-neoplastic and neoplastic lesions compared to normal mucosa by mucin histochemistry <sup>[10]</sup>. Neutral mucins present in normal mucosa gradually decrease during the initial development of IM, while sialomucins appear and become predominant. In more advanced stages, sulfomucins appear and may become predominant <sup>[11]</sup>.

Based on the mucin secretion & cell differentiation, three types of intestinal metaplasia can be recognized in the stomach i.e., Type I (complete), Type II (incomplete) and type III (incomplete) <sup>[12]</sup>. Intestinal metaplasia (IM) has been observed in various gastric lesions like gastric cancer,



**Fig. 5: Photomicrograph showing *H. pylori* in Giemsa stain (100X).**

gastric ulcer and atrophic gastritis. Studies have indicated a close relation between sulphomucin secreting Intestinal Metaplasia type III and intestinal type of gastric carcinoma <sup>[3]</sup>. It is considered to be a precancerous lesion before development of dysplasia in the evolution of Intestinal type of gastric carcinoma.

Thus, simultaneous assessment of histopathology and mucin histology at the time of initial diagnosis can provide a beneficial role in early diagnosis and individual therapeutic strategies.

Maximum cases were in 41 to 70 years (68%) comparable to Monika Bansal et al. <sup>[8]</sup> study. In our present study, 58% cases were malignant lesions and 42% cases were benign lesions. Thapa R et al. (2013) <sup>[13]</sup> in their study noted that 32.5% cases were neoplastic lesions and 67.5% cases were non-neoplastic lesions. Malignant lesions were more comparable to the other studies this could be supported by the fact that in our study both endoscopy biopsies and gastrectomy specimens were taken. In our study the most common site of gastric lesion was antrum (58%) its less compared to study conducted by UDOH M O et al. (2012) <sup>[14]</sup> where 63.2% gastric lesions were from antrum. Most common clinical feature in our study was dyspepsia (70%) comparable to study conducted by Shanmugasamy K et al. (2016) <sup>[15]</sup> where most common presenting feature was also dyspepsia.

Similar to our study most common non neoplastic lesion was chronic gastritis 44% in Shanmugasamy K et al. <sup>[15]</sup> study. Most common gastric carcinoma were MDADC in Thapa R et al. <sup>[13]</sup> study which is in accordance with our study. Incidence of *H. Pylori* positivity in our study (42%) was in accordance to Dandin AS et al. <sup>[16]</sup> study (43%). In our study, percentage of *H. Pylori* infection in gastric

carcinoma (27.59%) was comparable to study conducted by Sultana A et al. (2011)<sup>[9]</sup>(27.0%) but lower than Bansal M et al.<sup>[8]</sup> study (33.3%). Percentage of H. Pylori infection in chronic gastritis (42.86%) was lower in our study compared to A. Sultana et al.<sup>[9]</sup> (60%) and Bansal M et al.<sup>[8]</sup> (56.7%). Percentage of H. Pylori infection in gastric ulcer (100%) was equivalent to study conducted by Bansal M et al. (2017)<sup>[8]</sup> (100%) but lower than A. Sultana et al.<sup>[9]</sup> study (50%).

Our study shows statistically significant association between H. Pylori infection and gastric ulcer (p value 0.009) and gastric carcinoma (p value 0.021) [p value <0.005 was considered statistically significant]. But no statistically significant association was seen between H. Pylori infection and chronic gastritis in our study.

IM was seen in 40% cases comparable to 35% in Einstein D et al.<sup>[17]</sup> study. In our present study incidence of intestinal metaplasia in malignant lesion was seen in 12(41.38%) cases and in benign lesions was seen in 8(38.09%) cases. It is comparable to Einstein D et al.<sup>[17]</sup> study 30.1% & 64.7% respectively. In our study type I and II intestinal metaplasia in malignant lesion was seen in 75% cases and type III IM was seen in 25% cases which is in accordance with Mandal et al. 2013<sup>[18]</sup> study (78.3% and 17.4% respectively). And in benign lesion type I and type II IM is seen in 87.5% and type III in 12.5% which is in accordance with Rothery, Day et al.<sup>[19]</sup> 84.7% and 15.3%.

Distribution of sub types of IM in intestinal & diffuse type of gastric carcinoma is shown in table 5. It is evident that the incidence of type 3 IM is more common in intestinal type of gastric adenocarcinoma than in diffuse type of gastric adenocarcinoma and is in accordance with our study.

In our study out of 50 cases, 20 cases showed IM out of which 70 % cases were associated with H. pylori infection and 30% cases showed no H. pylori infectivity.

Statistically significant association (p value 0.001) has been found between H. Pylori infection and IM in our study (p value < 0.05 is considered significant). Compared to study conducted by M E Craanen et al. (1992)<sup>[20]</sup> where 33.9% cases of IM were associated with H. Pylori and 15.2% cases of IM was not associated with H. Pylori, p<0.001. In study conducted by Sheng Quan et al. (2017)<sup>[21]</sup>; significant statistical correlation has been found between H. Pylori infection and IM, p value 0.038 (<0.05 is significant).

## Conclusion

H. Pylori infection is seen to be associated with varieties of gastric lesions. It is a known carcinogen. Hence, early detection can halt the cascade and improve prognosis. And

use of special stain like Giemsa significantly improves the diagnosis of H. Pylori.

Presence of type 3 intestinal metaplasia in benign gastric lesions needs to be closely followed up endoscopically because they possess more risk of developing intestinal type of gastric adenocarcinoma.

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Nil

## Competing Interests

The authors declare that there is no conflict of interest

## Abbreviations

ADC : Adenocarcinoma; WDADC : Well differentiated adenocarcinoma ; MDADC : Moderately differentiated adenocarcinoma ; PDADC : Poorly differentiated adenocarcinoma ; H. pylori : Helicobacter pylori ; PAS: Periodic acid Schiff ; AB : Alcian blue ; IM : Intestinal Metaplasia ; H&E: Haematoxylin & Eosin.

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