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Prevalence of Intestinal Metaplasia and its Relation to *Helicobacter Pylori* Infection in Iraq

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Abstract

Objectives The aim of this study was to investigate the prevalence of intestinal metaplasia and its relation to *H. pylori* infection, gastric atrophy, ulcer, age and gender in patients underwent esophagogastroduodenoscopy (EGD) and gastric biopsy for upper gastrointestinal symptoms.

Method 200 gastric biopsy blocks examined for patients underwent esophagogastroduodenoscopy (EGD) and gastric biopsy, between January 2019 October 2020 at Gastroenterology and hepatology Hospital / Medical city / Baghdad / Iraq.

Result (67.5%) of patients examined in the study had *H. pylori* infection, while (20.5%) of the total number patients in the study had gastric intestinal metaplasia. There was significant association between Intestinal metaplasia with both active chronic inflammation and intestinal atrophy but there was no significant association between Intestinal metaplasia with both ulcer and *H. pylori* infection.

Conclusion Gastric intestinal metaplasia encountered more in old age male patients with gastric atrophy and it is not solely related to *H. pylori*, other risk factors could be responsible for it.

Keywords Prevalence, intestinal metaplasia, *Helicobacter pylori* infection.

Introduction

Intestinal metaplasia defined as replacement of the gastric mucosa by epithelium that simulate the mucosa of small bowel as seen in (Figure 1). Intestinal metaplasia results from the diversion of gastric stem cells from proliferation into cells specific to the stomach towards those of the small intestine, like absorptive cells, goblet cells and Paneth cells. This process triggered by repetitive irritation to the gastric mucosa.[1] Intestinal metaplasia classified into two entities: complete and incomplete. The complete type (type I), is defined by the presence of absorptive cells, Paneth cells and goblet cells which secretes sialomucins ssimilar to the small intestine counterpart. The incomplete type, which sub classified into (types II and III), is characterized by the presence of goblet cells and columnar cells. Type II secretes neutral in addition to acidic sialomucins while type III produces sulphomucins. Sulphomucins can be differentiated from sialomucins using specific stains such as high iron diamine/Alcian blue staining.[1] IM is frequently identified in the distal gastric biopsies,[2] also might affect the body and fundic mucosa, with partial replacement by metaplastic goblet cells of intestinal morphology, absorptive cells and Paneth cells; it is considered extensive if involves 25% of biopsy tissue.[3] Gastric intestinal metaplasia is considered a precancerous change of the gastric mucosa with intestinal epithelium, and is associated with an increased risk of dysplasia and cancer.[4] Gastric cancer (GC) considered one of the leading causes of cancer related death in the world, especially in East Asia. According to the Corneas cancer cascade, non-cardia GC developed through a series of mucosal changes starting from non-atrophic gastritis to atrophic gastritis, intestinal metaplasia, dysplasia and then adenocarcinoma.[5] Atrophic gastritis and intestinal metaplasia therefore considered as pre-neoplastic gastric lesions. *Helicobacter pylori* (*H. pylori*) infection as seen in figure 2 is an important promoting step of the gastric carcinogenesis cascade.[5] Researches showed that infection with *H. pylori* confers a 23-fold increase in the risk of gastric cancer development.[6,7] Emerging long-term data showed that eradication of *H. pylori* decreases the risk of subsequent development of cancer. However, it remains confusing whether eradication of the bacterium in patients with preneoplastic gastric lesions could regress these changes as well as in preventing cancer.[5] Whilst *H. pylori* eradication could regress atrophic gastritis, the presence of intestinal metaplasia may be irreversible in this cascade.[5] Gastric cancer passed through a steady decline since the 1930s, which may be partially due to the use of food refrigeration that has replaced smoking meat as a means of preservation. The smoking process has considered promoting carcinogens.[8] However, despite food refrigeration, gastric cancer represent the 7th malignancy causing death in Iraq for the 2019 according to the annual cancer registry of Iraq, ministry of health and environment,[9] and the fifth most common malignancy and third leading cause of cancer death worldwide with 723,000 deaths in 2012, according to the World Health Organization (WHO).[10] The International Agency for Research on Cancer cconsidered *H. pylori* as a "group 1 (definite carcinogen)" in 1994.[11] The infection induces a chronic inflammatory process in the gastric mucosa. Over time, atrophy and IM may develop.[12] The inclusion of IM in a gastric biopsy pathology report often creates uncertainty among the clinical gastroenterologist about the appropriate next step of management. Although the risk of gastric cancer increased in the presence of IM, the overall risk of gastric cancer in a patient with IM is extremely low if compared with the risk of adenocarcinoma in a patient with Barretts esophagus.[13] The aim of this study was to investigate the prevalence of intestinal metaplasia and its relation to *H. pylori* infection, gastric atrophy, ulcer, age and gender in patients underwent esophagogastroduodenoscopy and gastric biopsy for upper gastrointestinal symptoms.

Method

This cross sectional study conducted with 200 patients were undergoing esophagogastroduodenoscopy (EGD) and gastric biopsy, between January 2019 October 2020 at Gastroenterology and hepatology Hospital / medical city / Baghdad / Iraq. Data including age, gender, presence of intestinal metaplasia, associated active or chronic gastritis, atrophy of the gastric mucosa, *H. pylori* bacilli and ulcer obtained from electronic medical records. All the biopsied materials fixed in 10% formalin solution, undergone routine tissue processes, were embedded into paraffin blocks and stained with haematoxylin and eosin stains and assessed by Giemsa stain for *H. pylori* organism identification. Statistical analysis performed with SPSS 22 (Statistical package for social sciences) and Excel 2010 programs. Data analysis done using chi-square test and Fisher's exact test for categorical, also calculate frequencies, percentages, ranges, means standard deviation and standard errors of mean. Values considered statistically significant when *P*-value is equal to or less than 0.05.

Results

Cross sectional study involved 200 patients, mean and SD of age (41 ± 19) years old. According to gender distribution, 43% of them were males and 57% of patients are females as shown in figure (1). The highest proportion according to age group was (49.5%) represented by patients in age group ≥ 40 year-old as seen in figure (2).

Statistics revealed that (67.5%) of biopsies showed *H. pylori* bacilli.While (20.5%) of the total number of biopsies examined were positive for intestinal metaplasia, and patients who had ulcer represented only (0.5%), as shown in figure (3, 4 and 5) respectively.

Gastric biopsies that showed active chronic inflammation recorded (63%) and finally (2%) of patients had intestinal atrophy. As show in figure (6 and 7) respectively.

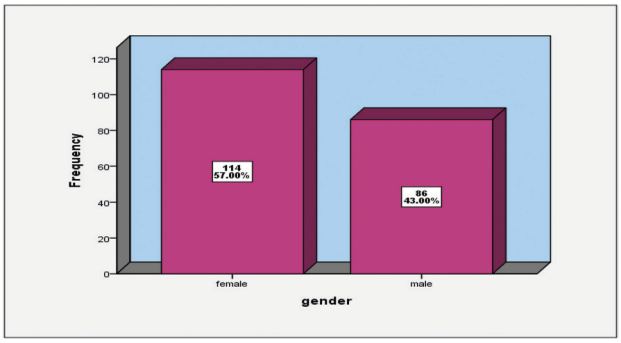

Fig. 1 **Gender distribution.**

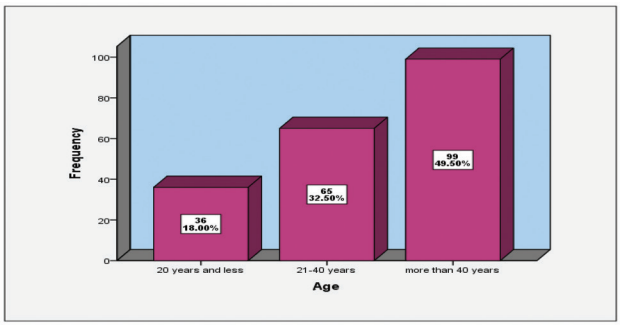

Fig. 2 **Age distribution.**

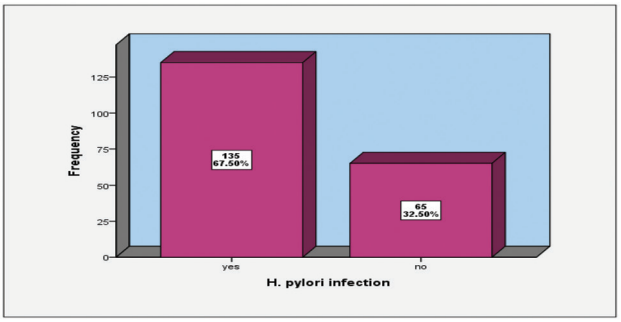

Fig. 3 **Distribution of *H. pylori* infection.**

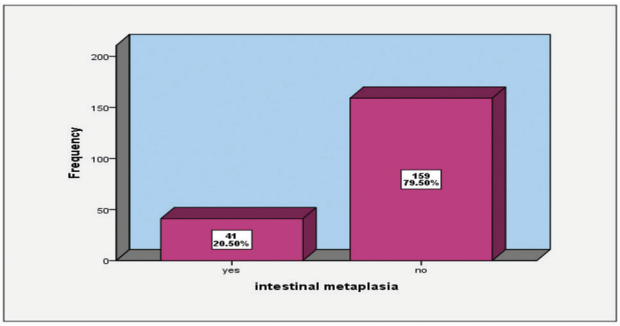

Fig. 4 **Distribution of intestinal metaplasia.**

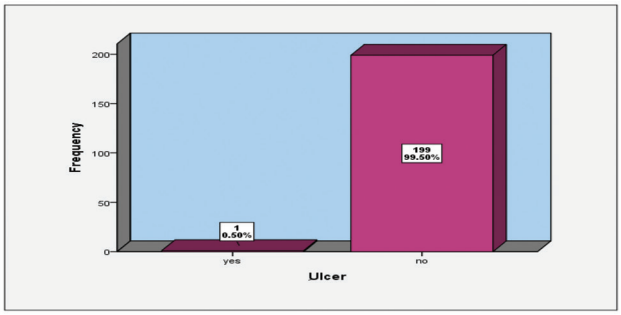

Fig. 5 **Distribution of ulcer in patients.**

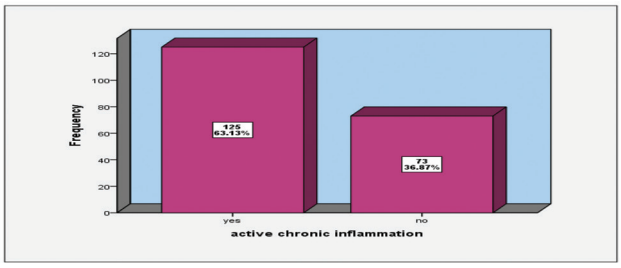

Fig. 6 **Distribution of active chronic inflammation.**

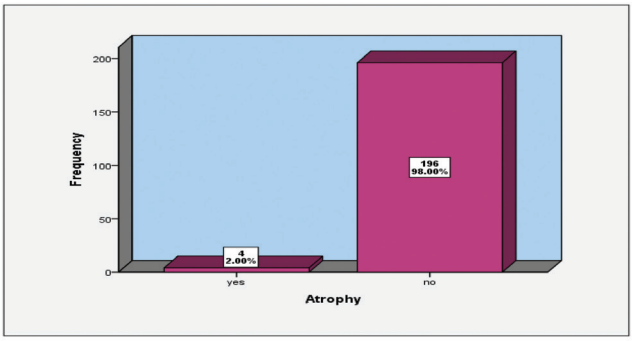

Fig. 7 **Distribution of gastric atrophy.**

According to table 1; there was significant association between *H. pylori* infection and active chronic inflammation, (83%) of patients with *H. pylori* infection had active chronic inflammation (i.e 83% sensitivity) and (80%) of patients had neither *H. pylori* infection nor active chronic inflammation (i.e 80% specificity).

According to table 2; The study showed that there was significant association between intestinal metaplasia and gender, (61%) of intestinal metaplasia patients were male and (39%) were female. As well as significant association between intestinal metaplasia and age group as (75.6%) of intestinal metaplasia, patients were >40 year-old. There was significant association between intestinal metaplasia and active chronic inflammation, as (80.5%) of intestinal metaplasia patients had active chronic inflammation. In addition, there was significant association between intestinal metaplasia and gastric atrophy since all patients who had gastric atrophy had intestinal metaplasia.

There was no significant association between intestinal metaplasia with both ulcer and *H. pylori* infection.

Table 1. **Association between *H. pylori* infection and active chronic inflammation**

		***H. pylori* infection**		***P*-value**
		Yes	No	
Active chronic inflammation	Yes	112 (83%)	13 (20%)	
	No	23 (17%)	52 (80%)	0.0001
	Total	135 (100%)	65 (100%)	

P-value ≤0.05 (significant).

Discussion

The prevalence of intestinal metaplasia of gastric mucosa in the general population considered difficult to ascertain owing to the asymptomatic nature of the lesion.[14,15] This study showed that the prevalence of gastric IM was 20.5%, which was higher than a study done in Al-Sulaymaniyah GIT-Centre in 2010 when a total number of 476 antral gastric biopsies were collected and examined histologically, the frequency of intestinal metaplasia in the antral gastric mucosa of dyspeptic patients was 8.19%.[16] In addition, an approximate number (7.4%) obtained in another study held in 2018 in three medical centers in Karbala/Iraq.[17] Sonnenberg and his colleagues reported a large retrospective study of 78,985 patients underwent EGD and biopsy throughout the United States and found that the gastric intestinal metaplasia prevalence was 7%.[18] While a report represented by Almouradi et al. in 2013 in USA, stated that among the 437 patients whom gastric biopsies performed for them, 66 found to have gastric intestinal metaplasia and thus the overall percentage reached 15%.[19] This difference in

Table 2. **Association between intestinal metaplasia and (gender, age of patients, *H. pylori* infection, ulcer, active chronic inflammation and atrophy)**

Variables		**Intestinal metaplasia**		***P*-value**
		Yes	No	
Gender	Female	16 (39%)	98 (61.6)	
	Male	25 (61%)	61 (38.4%)	
	Total	41 (100%)	159 (100%)	
Age	≤20 years	2 (4.9%)	34 (21.4%)	
	21–40 years	8 (19.5%)	57 (35.8%)	
	>40 years	31 (75.6%)	68 (42.8%)	
	Total	41 (100%)	159 (100%)	
H. pylori infection	Yes	29 (70.7%)	106 (66.7%)	
	No	12 (29.3%)	53 (33.3%)	0.38
	Total	41 (100%)	159 (100%)	
Ulcer	Yes	0 (0%)	1 (0.6%)	
	No	41 (100%)	158 (99.4%)	0.8
	Total	41 (100%)	159 (100%)	
Active chronic inflammation	Yes	33 (80.5%)	92 (57.9%)	
	No	8 (19.5%)	67 (42.1%)	0.005
	Total	41 (100%)	159 (100%)	
	%	100.0%	100.0%	
Gastric atrophy	Yes	4 (9.8%)	0 (0%)	
	No	37 (90.2%)	159 (100%)	0.002
	Total	41 (100%)	159 (100%)	

P-value ≤0.05 (significant).

prevalence of IM may be due to the inadequate number and different localization of biopsies in the stomach. This study showed significant association between intestinal metaplasia and gender, as (61%) of intestinal metaplasia patients were males and (39%) were female. Also a significant association was found between intestinal metaplasia and age group as (75.6%) of Intestinal metaplasia patients were in age >40 years. That goes well with a research done in U.S in 2020, 423 biopsies with gastric intestinal metaplasia and 1,796 controls free of intestinal metaplasia found that patients of older age, male gender, of non-white ethnicity, and positive current smoking status were independently associated with gastric intestinal metaplasia.[20] In this study (67.5%) of the total number of patients had *H. pylori* infection, a proportion that represents approximate result of a study held in 2018 in Karbala/Iraq, when *H. pylori* infection demonstrated (71%).[17] Comparing to a report done in Turkey when Özden and colleagues found that the positivity of *H. pylori* recorded 81% in the general population.[21] The above difference might be due to: firstly, the biopsies might not have been obtained in sufficient number or from corresponding areas of the stomach. Secondly, results of such studies (i.e *H. pylori* infection) could be affected by medical treatment such as antibiotic usage in some patients.[22]

Additionally, a significant association found between intestinal metaplasia and active chronic inflammation in this study, i.e (80.5%) of patients with intestinal metaplasia had active chronic inflammation. As was the case in intestinal metaplasia and gastric atrophy. This could be attributed to the Correa's cancer cascade, which states that non-cardia gastric cancer usually developed through a series of events including mucosal changes starting from non-atrophic gastritis to atrophic gastritis and reaching to intestinal metaplasia.[5] There was no significant association between intestinal metaplasia and both ulcer and *H. pylori* infection in this study, this result almost agree with Karbala/Iraq study when there was a significant negative relation between *H. pylori* infection and the existence of intestinal metaplasia, which could be attributed to multiple risk factors that have been associated with the development of gastric intestinal metaplasia interplay, including factors related to host genomics, environmental milieu, rheumatologic disorders, intestinal microbiota and diet.[4] A five year prospective randomized control research wad done in Shandong, a Chinese province in which gastric cancer incidence is considered among the highest there.[23,24] In this study, randomized *H. pylori* infected subjects received either anti-Helicobacter therapy or placebo. The conclusion stated that there was an obvious response and improvement in acute and chronic gastritis for patients who received therapy. Five years later, on one hand, after *H. pylori* eradication, the progression of gastric intestinal metaplasia declined in the treated group. On the other hand, a considerable percentage of patients in either treatment strategies continued having morphological progression of intestinal metaplasia. It is thus clear that this progression may be affected by and related to other parameters in addition to *H. pylori* eradication. In fact, many previous studies stated that factors contributed to progression of intestinal metaplasia such as current smoking,[25] the patients age,[23] and pattern or severity of gastritis,[26,27] may affect the development and progression of gastric cancer precursors including the intestinal metaplasia.

Conclusion

Gastric intestinal metaplasia encountered more in old age male patients with gastric atrophy and it is not solely related to *H. pylori*, other risk factors could be responsible for it. ■

References

1. Leung, W. K., & Sung, J. J. Y. (2002). Intestinal metaplasia and gastric carcinogenesis. Alimentary Pharmacology & Therapeutics, 16(7), 1209-1216.
2. Espey DK, Wu XC, Swan J, et al. Annual report to the nation on the status of cancer, 1975-2004, featuring cancer in American Indians and Alaska Natives. Cancer. 2007;110:2119,52.
3. Glickman, J. N., Wang, H., Das, K. M., Goyal, R. K., Spechler, S. J., Antonioli, D., & Odze, R. D. (2001). Phenotype of Barrett's esophagus and intestinal metaplasia of the distal esophagus and gastroesophageal junction: an immunohistochemical study of cytokeratins 7 and 20, Das-1 and 45 MI. The American Journal of Surgical Pathology, 25(1), 87-94.
4. Jencks, D. S., Adam, J. D., Borum, M. L., Koh, J. M., Stephen, S., & Doman, D. B. (2018). Overview of current concepts in gastric intestinal metaplasia and gastric cancer. Gastroenterology & Hepatology, 14(2), 92.
5. Liu, K. S. H., Wong, I. O. L., & Leung, W. K. (2016). Helicobacter pylori associated gastric intestinal metaplasia: Treatment and surveillance. World Journal of Gastroenterology, 22(3), 1311.
6. Huang JQ, Sridhar S, Chen Y, et al. Meta-analysis of the relationship between Helicobacter pylori seropositivity and gastric cancer. Gastroenterol 1998;114:116979.
7. Helicobacter and Cancer Collaborative Group. Gastric cancer and Helicobacter pylori: a combined analysis of 12 case control studies nested within prospective cohorts. Gut 2001;49:34753.
8. La Vecchia C, Negri E, D'Avanzo B, Franceschi S. Electric refrigerator use and gastric cancer risk. Br J Cancer. 1990;62(1):136-137.
9. The annual cancer registry of Iraq, ministry of health and environment for 2019.
10. International Agency for Research on Cancer, World Health Organization. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. [Accessed January 23, 2018].
11. Lin, D., & Koskella, B. (2015). Friend and foe: factors influencing the movement of the bacterium Helicobacter pylori along the parasitism–mutualism continuum. Evolutionary Applications, 8(1), 9-22.
12. Correa P, Haenszel W, Cuello C, et al. A model for gastric cancer epidemiology. Lancet. 1975;2:58-60.
13. Fennerty MB. Gastric intestinal metaplasia on routine endoscopic biopsy. Gastroenterology. 2003;125:58690.
14. A. C. de Vries, J. Haringsma, and E. J. Kuipers, "The detection, surveillance and treatment of premalignant gastric lesions related to Helicobacter pylori infection," Helicobacter, vol. 12, no. 1, pp. 1–15, 2007.
15. A. Zullo, C. Hassan, A. Romiti et al., "Follow-up of intestinal metaplasia in the stomach: when, how and why," World Journal of Gastrointestinal Oncology, vol. 4, no. 3, pp. 30-36, 2012.
16. Al-Esawi, A. A., Al-Koubaisi, H. N., & Tafash, M. (2010). Frequency of Intestinal Metaplasia in Dyspeptic Patients in Northern Iraq. Al-Anbar Medical Journal, 8(1).
17. AlSafi, R. A. A. N., Alqanbar, M. F., & Al-Sabbagh, W. R. M. (2019). Premalignant changes associated chronic gastritis in Karbala Province: multi institutional study. Journal of Contemporary Medical Sciences, 5(5).
18. A. Sonnenberg, R. H. Lash, and R. M. Genta, "A national study of Helicobactor pylori infection in gastric biopsy specimens," Gastroenterology, vol. 139, no. 6, pp. 1894.e2–1901.e2, 2010.
19. T. Almouradi, T. Hiatt, and B. Attar, "Gastric intestinal metaplasia in an underserved population in the USA: prevalence, epidemiologic and clinical features," Gastroenterology Research and Practice, vol. 2013, Article ID 856256, 4 pages, 2013.
20. Tan, M. C., Mallepally, N., Liu, Y., El-Serag, H. B., & Thrift, A. P. (2020). Demographic and lifestyle risk factors for gastric intestinal metaplasia

among US veterans. American Journal of Gastroenterology, 115(3), 381-387.
21. A. Özden, Ş. Dumlu, and Ö. Dönderici, Helicobacter pylori infeksiyonunun ülkemizde seroepidemiyolojisi, Gastroenteroloji, vol. 3, pp. 664-668, 1992.
22. Tacheci I, Edakkanambeth Varayil J, Zelinkova Z, Kopacova M, Zavoral M. Advanced Studies in Clinical and Experimental Research in Gastroenterology. Gastroenterol Res Pract. 2016;2016:4253143.
23. Sung JJY, Lin SR, Ching JYL, et al. Atrophy and intestinal metaplasia one year after cure of H. pylori infection: a prospective, randomized study, Gastroenterology, 2000;119:7-14.
24. Zhou LY, Sung JJY, Lin SR, et al. A five-year follow-up study on the pathological changes of gastric mucosa after H. pylori eradication. Chin Med J 2003;116:11-14.
25. Russo A, Maconi G, Spinelli P, et al. Effect of lifestyle, smoking, and diet on development of intestinal metaplasia in H. pylori-positive subjects. Am J Gastroenterol 2001;96:14028.
26. Uemura N, Okamoto S, Yamamoto S, et al. Helicobacter pylori infection and the development of gastric cancer. N Engl J Med 2001;345:7849.
27. You WC, Lee JY, Blot WJ, et al. Evolution of precancerous lesions in rural Chinese population at high risk of gastric cancer. Int J Cancer 1999;83:615-19.