Original paper

Assessment of Gastric Glandular Atrophy, Intestinal Metaplasia, and Dysplasia among Patients Underwent Upper GIT endoscopy in Karbala

Rasha A Neama^*

^Department of pathology, College of Medicine, Karbala University, Karbala, Iraq.

Abstract

Background: The current study is reflecting the commonness of gastric precancerous lesions in patients underwent upper GIT endoscopy.
Aim of the study to assess the prevalence of *H. pylori* related precancerous changes in gastric biopsies and theie clincopathological correlations.
Methods: The data was gathered from patients attending Al Hussein teaching hospital and private laboratories. It includes (414) patients who were subjected to esophagogastroduodenoscopy in this period. From all patients endoscopic mucosal biopsies were obtained and stained with hematoxylin-eosin. Giemsa stain was used to detect *H. pylori* organisms.
Results: All patients have gastritis and H. Pylori infection was detected in 301 (72.7%) patients. glandular atrophy, intestinal metaplasia and dysplastic changes were detected in 95 (22.9%), 36 (8.7%) and 6 (1.4%) patients respectively. There was a significant statistical relation between each of glandular atrophy and gastric intestinal metaplasia with age. There was a significant statistical relation between glandular atrophy and H. Pylori. A significant negative relation between H. Pylori infection and the presence of intestinal metaplasia was observed meanwhile there was a significant correlation between the intestinal metaplasia and dysplastic changes.
Conclusion: The current study spots a light on how common the gastric changes can be detected in patients with chronic gastritis**.** There was a significant relation between the age and gastric glandular atrophy and intestinal metaplasia, a negative significant relation between *H.Pylori* infection and intestinal metaplastic changes. There was a significant relation between intestinal metaplasia and gastric dysplasia.
Keywords: *H.Pylori* infection, chronic atrophic gastritis, intestinal metaplasia.

Introduction

Stomach cancer is looked at as an important leader cause of death worldwide with a statistical remarkable decrement in the incidence rate over the last years. [1,2] A set of precancerous lesions may predate the intestinal variant of gastric carcinoma like chronic atrophic gastritis, intestinal metaplasia (IM), and dysplasia.[3] However, the evolution of the diffuse type is not perceived yet.[4]

The infection with H.pylori may coexist with lesions that may appear orderly or sequentially such as severe gastritis, chronic atrophic gastritis, IM and gastric cancer [5,6]. An extreme degree of atrophic gastric mucosa that was detected side by side with intestinal metaplastic alterations may be resulted from infection with a high risk strain of H. pylori. [7, 8] The infection with *H. pylori* during early childhood is an essential point for attention that increases the likelihood for the development of gastric cancer later since it paves the way

*for correspondence email: rasha.alsafi@uokerbala.edu.iq

for the premalignant condition of pangastritis in adulthood. [9, 10] The consumption of high salt, smoking, being alcoholic and chronic bile reflux all are additional risk factors for the development of IM. [11]

Many Middle Eastern countries like Iraq, Iran, Turkey, Libya, Egypt, Israel, Bahrain, Oman, Saudi Arabia, and the United Arab Emirates make records to evaluate and assess the prevalence of *H. pylori infection*. It has been seen that the prevalence of infection with *H.Pylori* is almost comparable in these nations with some range of variations in that the prevalence of infection may peak in Iran while it is seldom and infrequent in Iraq and Egypt. [12]. In Iraq, a study claimed that the "The mild pathology and antral-predominant gastritis may help to explain the low cancer rate in Iraq". [13]

The **aim** of the study is to assess the prevalence of *H. pylori* infection, atrophy, intestinal metaplasia, and dysplasia in patients with gastric biopsy and to highlight the correlation of each of the age of the patients and the *H. pylori* infection with precancerous histopathological parameters. Finally to investigate the association between metaplastic and dysplastic changes in the examined biopsies.

Material and methods

This is a cross-sectional study. The data was gathered from patients attending Al Hussein teaching hospital and several private laboratories from January to September 2019. It includes (414) patients who were subjected to esophagogastroduodenoscopy (EGD) in this period. From all patients endoscopic mucosal biopsies were obtained. Every biopsy has minimally two mucosal segments that subjected to a standard histological processing and stained with hematoxylin-eosin stain to diagnose the gastric mucosal changes. Giemsa stain was used to detect *H. pylori* organisms in all biopsies. The parameters like age, sex, and histopathological findings (gastritis, *H.Pylori* infection, atrophic changes, intestinal metaplasia and dysplastic changes) were included in the study. Informed written consent was obtained from all patient prior to inclusion.

Statistical analysis: Chi-square test was used to measure the association between different parameters and *P* values of <0.05 was considered significant.

Results

Four hundred fourteen (414) patients were subjected to esophagogastroduodenoscopy, involved in the current study from January to September 2019. The mean age was (39.97 +/- 14.5 years Standard Deviation). There were 195 (47.1%) males and 219 (52.9%) females.

All findings of the 414 patients detected by the endoscopy were displayed as frequencies and percentages of gastritis, *H. Pylori* infection, glandular atrophy, intestinal metaplasia and dysplastic changes in Table 1. All patients have gastritis 414 (100%) and *H. Pylori* infection was detected in 301 (72.7%) patients.

From all patients; 95 (22.9%) were presented with glandular atrophy; thirty six patients (8.7%) had intestinal metaplasia and only 6 (1.4%) patients had dysplastic changes.

The relationship of the microscopical findings with age was demonstrated in table (2).

The table shows that a valuable number of patients infected with H. Pylori were divided out between 20-49 age groups; but this relation not reach a statistical significant level, P value (0.2).

Gastric glandular atrophy, table 2 shows that the frequencies of patients presented with glandular atrophy in the

background of chronic gastritis were increasing with age starting from 20-59 years forming about 74 (77.8%) out of total 95 cases and this relation was significant statistically with a P value of (0.01).

Regarding intestinal metaplastic changes, table 2 shows a successive rise in the number of patients who have metaplastic changes starting from age of 20 years forward. The relationship was statistically significant level, P value (0.011).

The results of the current study demonstrate that the whole cases presented with dysplastic changes were six (1.4%) out of 414 cases as shown in table (2). These were dispersed irregularly through age groups from 30-69 years. Statistically the relationship was insignificant, p value (0.7).

From 301 infected patients with *H. Pylori*, there were 86 (28.5%) cases show atrophied gastric glands on examination in contrast to nine (7.9%) out of 113 cases who lack infection with *H. Pylori* and diagnosed to have an atrophied gastric mucosa and this figure was significant from the statistical point, p value (0.001) as shown in table (3).

Table (4) presents the association between H.Pylori infection and the development of intestinal metaplasia in the included endoscopic biopsies. There was a negative statistically significant association between H Pylori infection and IM. Seventeen patients (5.64%) out of 301 with H.Pylori infection were diagnosed with intestinal metaplasia compared to 19 patients (16.8%) without H.Pylori infection show intestinal metaplastic changes.

Concerning the relation between gastric metaplastic changes and the evolution of dysplasia in the examined specimens, it was illustrated in table (5) which shows that three cases (8.4%) from total 36 cases with intestinal metaplastic changes present with dysplasia in comparison with only (0.8%) of those who lack the metaplastic changes and present with dysplasia. Accordingly, there was a significant statistical association between the occurrence intestinal metaplasia and the existence of dysplastic changes, P value (0.001).

Discussion

In the prototype of gastric carcinogenesis, H. pylori has a vital task in provoking chronic active gastritis. Gastritis can be induced or initiated after prolonged H. pylori infection and may proceed and be advanced over years to a sequence of atrophic gastritis, IM, and dysplasia to gastric adenocarcinoma. (14,15)

Table 1. the microscopical findings of patients with upper GIT endoscopy.

Microscopical findings	Number	Percentage %
Gastritis	414	100%
H. Pylori infection		
Positive	**301**	72.71**%***
Negative	**113**	**27.29%***
Glandular atrophy		
Positive	**95**	22.95 **% ***
Negative	**319**	**77.05%***
Intestinal metaplasia		
Positive	**36**	8.7**%***
Negative	**378**	**91.30%***
Dysplastic changes		
Positive	**6**	**1.4%***
Negative	**408**	**98.6%***

*: percentage from total sample size (414).

Table 2. the relation of microscopical changes with age.

microscopical changes (p-values)	Age groups (years)								To-tal
	10-19	**20-29**	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**>=80**	
H. Pylori (0.2)									
- Positive	24	63	75	62	40	27	10	0	**301**
- Negative	5	19	27	30	21	7	3	1	**113**
Glandular atrophy (0.01)									
- Positive	9	15	18	20	21	5	7	0	**95**
- Negative	20	67	84	72	40	29	6	1	**319**
Intestinal- metaplasia (0.011)									
- Positive	0	4	10	7	8	5	1	1	**36**
- Negative	29	78	92	85	53	29	12	0	**378**
Dysplastic –changes (0.7)									
- Positive	0	0	2	1	2	1	0	0	**6**
- Negative	29	82	100	91	59	33	13	1	**408**

Table 3. the correlation between *H.Pylori* infection and atrophied gastric glands.

	Gastric glandular atrophy		Total	P value
	Negative	Positive		
H.Pylori infection				**0.001**
- Positive	215 (71.5%)*	86 (28.5%)*	301	
- Negative	104 (92.1%)**	9 (7.9%)**	113	

*: percentage out of total positive cases infected with H.Pylori.
**: percentage out of total cases not infected with H.Pylori.

Table 4. the correlation of *H. Pylori* infection and Intestinal metaplasia.

	Intestinal metaplasia		Total	P value
	Negative	Positive		
H.Pylori infection				
- Positive	284 (94.36%)*	17 (5.64%)*	301	**0.0001**
- Negative	94 (83.2%)**	19 (16.8%)**	113	

*: percentage out of total positive cases infected with H.Pylori.
**: percentage out of total cases not infected with H.Pylori.

Table 5. the correlation between gastric dysplasia and intestinal metaplastic changes.

intestinal metaplasia	Dysplasia		Total	P value
	Negative (%)	Positive (%)		
				0.001
-Negative	375 (99.2%)*	3 (0.8%)*	378	
- Positive	33 (91.6%) **	3 (8.4%)**	36	
Total	408	6	414	

*: the percentage is out of total negative cases.
**: the percentage is out of total positive cases.

In this study, *H. Pylori* infection was diagnosed in 301 (72.71%) patients and this agree with a previous studies which gave similar figures. [16,17] From latest studies the prevalence in North Europe and North America was lower than 40%, while it was more than 70% in East Asia, Africa, and Middle East region. [18,19] which comes in consistency with the results of this study; at the same time it is situated at a great distance from the result of a Turkish study in which *H. pylori* diagnosed in 82% of cases. [20] the divergence in the results may be attributed to the fact that multiple factors may influence the incidence of *H. pylori* infection in different communities like environment, occupation, geographic distribution and a wide range of detection methods that can be used.

In the current study, 95 (22.95 %) patients were diagnosed to have glandular atrophy; this result may be a little

higher than that recorded in Dohuk with smaller sample size which stated that gastric atrophy was found in 3% of the reported cases [21]. it was claimed that regardless the age of acquiring *H. pylori* as an infection, the prevalence of gastric glandular atrophy associated with chronic gastritis is somewhat rare in Iraq. [22] According to the site of involvement to be an antral predominant and to some extent the lower pathogenic type gastritis can predispose to low gastric cancer rate in Iraq. [21] In Al-Kuwait, a study show a result that pass side by side with that of the current study in that 28.3% of patients had atrophic gastritis that differ from those recorded in Jordan and Egypt, which stated that 65% and 54% of patients presented with atrophied gastric glands respectively. [23, 24,25] additional Turkish study demonstrated that atrophy was detected in 75% of the enrolled patients. [26] In the UAE, gastric atrophy in a study was detected in 54% of cases. [27] In Iran, where the prevalence rate of gastric cancer is exceed and out way that of Turkey, a study point to that mucosal atrophy was found in 39% and 22% of antral and corpus biopsies, respectively. [28]

In the current study, thirty six (8.7%) out of the total number of patients had intestinal metaplasia, this picture comes in congruent with those detected in United States and Netherlands where the prevalence of intestinal metaplasia in the examined samples were 7% and 8% respectively. [29,30]

This low prevalence of IM may deduced from the inappropriate number of cases enrolled in the study and imprecise allocation of biopsies during sampling. Al mouradi et al. reported in a study that the prevalence rate of gastric IM in the sample of his study was 66 (15%). [31] 13.8% was the prevalence of intestinal metaplastic changes documented by a further Turkish study. [32]

The currency of gastric intestinal metaplasia in the community keeps hard to be assessed precisely because most cases stay silent and symptomless for long time and the patients seek medical advice too late beside the use of different modalities in the diagnosis in the studies. Addionally, the important influencer is the multifocality and the small size of the lesion that may increase the chance that the lesion can be missed during sampling. Consequently, inaccuracy during sampling may be inevitable. [32] From 414 cases six (1.4%) patients presented with dysplastic lesion. This result comes near to that reported by a Turkish study in which dysplastic changes was (2%) only [20] but it differ from figure reported in in Iran, China and Columbia where the dysplastic changes may rank much higher and reach to 71% according to several studies. [28, 33, 34,35]

A substantial and significant factor that may participate gastric carcinogenesis is the existence of lesions which are premalignant in the gastric mucosa, like intestinal metaplasia, atrophied gastric mucosa, and dysplastic changes.[36,37] The occurrence and spread of these changes in communities differ globally being conditioned and may rely on the status and prevalence of H. pylori infection. [38] Whether eradications of *H. pylori* can inhibit or hold the carcinogenic process in premalignant gastric lesions stays a matter of debate. Depending on some studies, the eradications of *H. pylori* can ameliorate the gastric lesions provoked by infection and surprisingly may suppress the propagation of gastric dysplasia to cancer. [39-43]

In this study (28.5%) cases of those infected with H.Pylori were presented with glandular atrophy. The sequential lack of the glandular tissue of the stomach due to prolonged mucosal damage is termed as atrophic gastritis. [44]

In atrophic gastritis the specialized cells within the lining of the stomach will be

lost with time in a sequential manner; these cells include the parietal cells, chief cells and mucus producing glandular cells. After shrinkage of all these cell types, the stomach will lose its protective layer of mucus and acid secretion will terminate. [45] These pathological alterations may raise the likelihood of gastric ulceration and the evolution of gastric cancer. [46] In two Turkish studies the prevalence of mucosal atrophy in Helicobacter associated gastritis was different recording 43% and 75% respectively, [46, 47] while in UAE it was seen in 54% of cases. [48]

In Iran, where the rate of gastric cancer was exceeding that of Turkey, in a single study it was found that mucosal atrophy was detected in 39% and 22% of antral and corpus biopsies, respectively. [28] In Kuwait, atrophic gastritis was detected in 28.3% of those infected with H. pylori. [49]In Jordan and Egypt the figure was 65% and 54% of examined patients were diagnosed to have atrophic gastritis respectively. [50, 51]

The current study shows that there is a significant negative relationship between H.Pylori infection and gastric intestinal metaplasia. This picture comes in line with that recorded by other studies. [52, 53,54] the intestinal metaplasia may mask the field and minimize the diagnostic accuracy of *H. pylori* infection [55] . This can be clarified as *H. pylori* is a highly selective and can live in the mucosa of the stomach in an acidic media. Hence, the failure of colonization of these organisms in gastric foci presenting intestinal metaplastic changes is highly expected. [56] In the meantime, lining mucosa of the stomach that pass through the intestinal metaplstic changes still preserve with some of its gastric character depending on the degree of metaplasia. Consequently, *H. pylori* still can be detected on examination in specimens involved with intestinal metaplasia. [20]

The results of this study demonstrates that there was a strong significant correlation between intestinal metaplasia and the presence of gastric dysplasia. This result coincides with many studies conducted recently. [57, 58,43] this can be interpreted since chronic active gastritis may pass through a sequences of carcinogenic events outset with atrophic gastritis, intestinal metaplasia and dysplasia that may end with gastric adenocarcinoma.[59]

Conclusion

The current study spots a light on the prevalence of *H. pylori* infection and clarify how common the gastric changes (atrophy, metaplasia and dysplasia) can be detected in patients attending the health institute with chronic gastritis and subjected to esophagogastroduodenoscopies. In this study (72.71%) of the patients were H. Pylori positive on histopathology. Glandular atrophy was diagnosed in (22.95 %) of total cases, while intestinal metaplasia and dysplastic changes were seen in (8.7%) and 1.4% respectively.

According to the current results it was observed that gastric glandular atrophy and intestinal metaplasia were related significantly to the age of the patients in contrast to the dysplastic changes which show no relation to the age.

Gastric glandular atrophy was statistically related to the infection with *H. pylori*, p value were (0.001) while intestinal metaplastic changes detected to have a significant negative relation with *H. pylori*, p value (0.0001). Finally, there was a significant relation between gastric intestinal metaplasia and dysplastic changes.

References

1. J. Ferlay, H.-R. Shin, F. Bray, D. Forman, C. Mathers, and D. M. Parkin, "Estimates of worldwide burden of cancer in 2008:

GLOBOCAN2008," International Journal of Cancer, vol. 127, no. 12, pp. 2893–2917, 2010.
2. A. Ferro, B. Peleteiro, M. Malvezzi et al., "Worldwide trends in gastric cancer mortality (1980–2011), with predictions to 2015, and incidence by subtype," European Journal of Cancer, vol. 50, no. 7, pp. 1330–1344, 2014.
3. Sehmus Olmez, Mehmet Aslan, Remzi Erten, Suleyman Sayar and Irfan Bayram., The Prevalence of Gastric Intestinal Metaplasia and Distribution of *Helicobacter pylori* Infection, Atrophy, Dysplasia, and Cancer in Its Subtypes. Gastroenterology Research and Practice Volume 2015, Article ID 434039, 6 pages.
4. D. Y. Park, A. Srivastava, G. H. Kim et al., "CDX2 expression in the intestinal-type gastric epithelial neoplasia: frequency and significance," Modern Pathology, vol. 23, no. 1, pp. 54–61, 2010.
5. J. Houghton and T. C. Wang, "Helicobacter pylori and gastric cancer: a new paradigm for inflammation-associated epithelial cancers," Gastroenterology, vol. 128, no. 6, pp. 1567–1578, 2005.
6. V. Catalano, R. Labianca, G. D. Beretta, G. Gatta, F. de Braud, and E. Van Cutsem, "Gastric cancer," Critical Reviews in Oncology/Hematology, vol. 71, no. 2, pp. 127–164, 2009.
7. N. Uemura, S. Okamoto, S. Yamamoto et al., "Helicobacter pylori infection and the development of gastric cancer,"the new England Journal of Medicine, vol. 345, no. 11, pp. 784–789, 2001.
8. Y.-C. Lee, T. H.-H. Chen,H.-M. Chiu et al., "The benefit of mass eradication of helicobacter pylori infection: a community-based study of gastric cancer prevention," Gut, vol. 62, no. 5, pp. 676– 682, 2013.
9. Blaser MJ, Nomura A, Lee J, Stemmerman GN, Perez-Perez GI. Early-life family structure and microbially induced cancer risk. PLoS Med 2007; 4: e7.
10. M. Dinis-Ribeiro, M. Areia, A. C. de Vries et al., "Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED)," *Virchows Archiv*, vol. 460, no. 1, pp. 19–46, 2012.
11. P. Correa,M.B.Piazuelo, and K. T.Wilson, "Pathology of gastric intestinal metaplasia: clinical implications," American Journal of Gastroenterology, vol. 105, no. 3, pp. 493–498, 2010.
12. GLOBOCAN IARC. Cancer Map: Male Stomach Cancer, Age-Standardized Incidence Rate per 100,000 in 2002. Available from: URL: http://www-dep.iarc.fr/. Accessed on May 30, 2007.
13. Nawfal R. Hussein, Sarbar M. Napaki, John C. Atherton. A Study of Helicobacter Pylori-associated Gastritis Patterns in Iraq and Their Association with Strain Virulence. The Saudi Journal of Gastroenterology 2009 15(2): 125-7.
14. L. Fuccio, R. M. Zagari,M. E.Minardi, and F. Bazzoli, "Systematic review: Helicobacter pylori eradication for the prevention of gastric cancer," Alimentary Pharmacology and Therapeutics, vol. 25, no. 2, pp. 133–141, 2007.
15. P. Correa, "Human gastric carcinogenesis: a multistep and multifactorial process—first American Cancer Society Award lecture on cancer epidemiology and prevention," Cancer Research, vol. 52, no. 24, pp. 6735–6740, 1992.
16. Essmaa H. Gutef. PREVALENCE OF HELICOBACTER PYLORI INFECTION WITH PEPTIC ULCER DISEASES IN IRAQI PATIENTS. EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH, 2016,3(4), 479-482.
17. Yasir S, Moin F and Akhtar S M. Frequency of Helicobacter Pylori Infection on Histopathology in Patients with Dyspepsia. American Journal of Clinical Medicine Research, 2014; 2(3): 53-56.
18. Ahn HJ and Lee DS. Helicobacter pylori in gastric carcinogenesis. World J Gastrointest Oncol 2015; 7: 455-465.
19. Eusebi LH, Zagari RM and Bazzoli F. Epidemiology of helicobacter pylori infection. Helicobacter 2014; 19 Suppl 1: 1-5.
20. Abdul kerim Ozakay, Erdem Kınacı, Savas Bayrak, Esra Pasaoğlu, Mert Mahsuni Sevinc, Nevra Dursun. Helicobacter pylori, intestinal metaplasia, and the accuracy of biopsies in metaplastic gastric mucosa. Int J Clin Exp Med 2017;10(3):5332-5337.
21. Nawfal R. Hussein, Sarbar M. Napaki, John C. Atherton. A Study of Helicobacter Pylori-associated Gastritis Patterns in Iraq and Their Association with Strain Virulence. The Saudi Journal of Gastroenterology 2009 15(2): 125-7.
22. Hussein NR, Robinson K, Atherton JC. A study of age-specific Helicobacter pylori seropositivity rates in Iraq. Helicobacter 2008;13:306-7.

23. Sarkar C, Anim JT, Ibrahim BH. Atrophic Gastritis and Intestinal etaplasia in Helicobacter pylori-Associated Antral Gastritis. Medical Principles Practice 1994; 4: 197-203.
24. Mahmoud RAK, Morcos HH, Hegazi AA, Abo Seif MA, El- Hadidy KS. The serological gastric biopsy: a non-endoscopical/ histopathologic diagnostic approach in management of the dyspeptic patients. Am J Immunol 2006; 2: 88-96
25. Matalka II, Al-Omari FA, Al-Jarrah MA, Obeidat FN, Kanaan FM. Image-based discriminating morphological features for gastric atrophy assessment: a step to go further. Pathol Res Pract 2008; 204: 235-240.
26. Kaklikkaya N, Cubukcu K, Aydin F, Bakir T, Erkul S, Tosun I, Topbas M, Yazici Y, Buruk CK, Erturk M. Significance of cagA status and vacA subtypes of Helicobacter pylori in determining gastric histopathology: virulence markers of H. pylori and histopathology. J Gastroenterol Hepatol 2006; 21: 1042-1047.
27. Zaitoun AM. Histological study of chronic gastritis from the United Arab Emirates using the Sydney system of classification. J Clin Pathol 1994; 47: 810-815.
28. Malekzadeh R, Sotoudeh M, Derakhshan MH, Mikaeli J, Yazdanbod A, Merat S, Yoonessi A, Tavangar M, Abedi BA, Sotoudehmanesh R, Pourshams A, Asgari AA, Doulatshahi S, Alizadeh BZ, Arshi S, Madjidpoor A, Mir Moomen S, Fleischer DE. Prevalence of gastric precancerous lesions in Ardabil, a high incidence province for gastric adenocarcinoma in the northwest of Iran. J Clin Pathol 2004; 57: 37-42.
29. 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.
30. A. C. de Vries, N. C. T. van Grieken, C. W. N. Looman et al., "Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands," Gastroenterology, vol. 134, no. 4, pp. 945–952, 2008.
31. 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.
32. Sehmus Olmez, Mehmet Aslan, Remzi Erten, Suleyman Sayar, and Irfan Bayram. The Prevalence of Gastric Intestinal Metaplasia and Distribution of Helicobacter pylori Infection, Atrophy, Dysplasia, and Cancer in Its Subtypes. Gastroenterology Research and Practice. Volume 2015, Article ID 434039, 6 pages.
33. You WC, Blot WJ, Li JY, et al. Precancerous gastric lesions in a population at high risk of stomach cancer. Cancer Res 1993;53:1317–21.
34. Wei-ChengYoui, Ji-You LI, William J Blot, et al. Evolution of precancerous lesion in a rural Chinese population at high risk of gastric cancer. Int J Cancer 1999;83:615–19.
35. Correa P, Haenszel W, Cuello C, et al. Gastric precancerous process in a high risk population: cross-sectional studies. Cancer Res 1990;50:4731–6.
36. M. Dinis-Ribeiro, M. Areia, A. C. de Vries et al., "Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED),"Virchows Archiv, vol. 460, no. 1, pp. 19–46, 2012.
37. A. C. de Vries, N. C. T. van Grieken, C. W. N. Looman et al., "Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands," Gastroenterology, vol. 134, no. 4, pp. 945–952, 2008.
38. 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.
39. Saito K, Arai K, Mori M, Kobayashi R, Ohki I. Effect of Helicobacter pylori eradication on malignant transformation of gastric adenoma. Gastrointest Endosc 2000;52:27-32.
40. Correa P, Fontham ET, Bravo JC, et al. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-Helicobacter pylori therapy. J Natl Cancer Inst 2000;92:1881-1888.
41. You WC, Brown LM, Zhang L, et al. Randomized double-blind factorial trial of three treatments to reduce the prevalence of precancerous gastric lesions. J Natl Cancer Inst 2006;98:974-983.
42. Mera R, Fontham ET, Bravo LE, et al. Long term follow up of patients treated for Helicobacter pylori infection. Gut 2005;54:1536-1540.
43. Ilyoung Chon, Chiun Choi, Cheol Min Shin, Young Su Park, Nayoung Kim and Dong Ho Lee. Effect of Helicobacter pylori

Eradication on Subsequent Dysplasia Development after Endoscopic Resection of Gastric Dysplasia. Korean J Gastroenterol 2013;61:307-312.
44. Asaka M, Kato M, Kudo M, Katagiri M, Nishikawa K, Koshiyama H, Takeda H, Yoshida J, Graham DY. Atrophic changes of gastric mucosa are caused by Helicobacter pylori infection rather than aging: studies in asymptomatic Japanese adults. Helicobacter 1996; 1: 52-56.
45. Atherton JC. The pathogenesis of Helicobacter pylori induced gastro-duodenal diseases. Annu Rev Pathol 2006; 1: 63-96.
46. Fikret D, Kaya Ö, Suna E, Vahap O, Mustafa A, ªebnem A. Relationship between atrophic gastritis, intestinal metaplasia, dysplasia and Helicobacter pylori infection. Turkish J Gastro 2001; 12: 169-170.
47. Kaklikkaya N, Cubukcu K, Aydin F, Bakir T, Erkul S, Tosun I, Topbas M, Yazici Y, Buruk CK, Erturk M. Significance of cagA status and vacA subtypes of Helicobacter pylori in determining gastric histopathology: virulence markers of H. pylori and histopathology. J Gastroenterol Hepatol 2006; 21: 1042-1047.
48. Zaitoun AM. Histological study of chronic gastritis from the United Arab Emirates using the Sydney system of classification. J Clin Pathol 1994; 47: 810-815.
49. Sarkar C, Anim JT, Ibrahim BH. Atrophic Gastritis and Intestinal Metaplasia in Helicobacter pylori-Associated Antral Gastritis. Medical Principles Practice 1994; 4: 197-203.
50. Mahmoud RAK, Morcos HH, Hegazi AA, Abo Seif MA, El- Hadidy KS. The serological gastric biopsy: a non-endoscopical/ histopathologic diagnostic approach in management of the dyspeptic patients. Am J Immunol 2006; 2: 88-96.
51. Matalka II, Al-Omari FA, Al-Jarrah MA, Obeidat FN, KanaanFM. Image-based discriminating morphological features for gastric atrophy assessment: a step to go further. Pathol Res Pract 2008; 204: 235-240.
52. Galiatsatos P, Wyse J and Szilagyi A. Accuracy of biopsies for helicobacter pylori in the presence of intestinal metaplasia of the stomach. Turk J Gastroenterol 2014; 25: 19-23.
53. Tarek Almouradi, Tadd Hiatt, and Bashar Attar. Gastric Intestinal Metaplasia in an Underserved Population in the USA: Prevalence, Epidemiologic and Clinical Features. Gastroenterology Research and Practice. Volume 2013, Article ID 856256, 4 pages.
54. Y.-C. Lee, T. H.-H. Chen,H.-M. Chiu et al., "The benefit of mass eradication of helicobacter pylori infection: a community-based study of gastric cancer prevention," Gut, vol. 62, no. 5, pp. 676– 682, 2013.
55. P. Correa,M.B.Piazuelo, andK. T.Wilson, "Pathologyof gastric intestinal metaplasia: clinical implications,"American Journal of Gastroenterology, vol. 105, no. 3, pp. 493–498, 2010.
56. Ahn HJ and Lee DS. Helicobacter pylori in gastric carcinogenesis. World J Gastrointest Oncol 2015; 7: 455-465.
57. Justin M Gomez, James T Patrie, Wissam Bleibel, Jeanetta W Frye, Bryan G Sauer, Vanessa M Shami, Edward B Stelow, Christopher A Moskaluk, Andrew Y Wang. Gastric intestinal metaplasia is associated with gastric dysplasia but is inversely correlated with esophageal dysplasia. World J Gastrointest Endosc 2017 16; 9(2): 61-69.
58. Mohammad Amin Bozorgnia, Seyed Mohammad Hossein Kashfi, Mehdi Ariana, Foroozan Ghalkhani, Shahrokh Iravani, Mohammad Hossein Lashkari, Hasan Jalaeikhoo, Pedram Azimzadeh, Amir Shabdini Pashaki, Nastaran Saeedi, Mohsen Azizi. Prevalence and correlation of chronic atrophic gastritis, intestinal metaplasia and other precancerous lesions of stomach in Iran: a historical cohort study. Transl Gastrointest Cancer 2015;4(6):413-422.
59. Correa P. Human gastric carcinogenesis: a multistep and multifactorial process--First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. Cancer Res 1992;52: 6735-6740.