Clinics in Surgery

Review Article
Published: 31 Aug, 2016

Value of Additional Corpus Biopsy for Diagnosis of Helicobacter Pylori in Atrophic Gastritis

AbdEl-Latif M[1], HafrEl-Batin E[2], Shahin R[3], Shawqy A[4], Arafa M[5], Ghafar Saleh AA[6] and Husien AM[7]*

[1]Department of Surgery, Mansoura University Hospital, Egypt

[2]Department of Pathology, Mansoura University Hospital, Egypt

[3]Department of Clinical Pathology, Benha University Hospital, Egypt

[4]Department Of Internal Medicine, Gastroenterology unit, Mansoura University Hospital, Egypt

[5]Department of Pathology, Mansoura University Hospital, Egypt

[6]Department of Internal Medicine, Gastroenterology Unit, Mansoura University Hospital, Egypt

[7]Department of Internal Medicine, Benha University Hospital, Egypt

Abstract

Background: There is still debate on the best sites for biopsy- based tests of Helicobacter pylori infection in patients with gastritis. This study was designed to determine if it is important to add corpus biopsies to the routine antral ones for identification of H. pylori, especially in case of gastric atrophy and/or intestinal metaplasia.

Methods: This is a prospective multicenter study (Mansura University Hospital-Egypt, Benha University hospital–Egypt, Hafer Al Batin Central Hospital, KSA), including three hundred and twenty eight patients with gastritis from June 2014 through Dec. 2015. Endoscopic mucosal biopsies from the gastric antrum and corpus were submitted to histological examination according to updated Sydney system for detection of H. pylori and to evaluate the degree of gastritis with or without atrophy and intestinal metaplasia using both routine H&E and modified Giemsa stained tissue sections.

Results: In the study period, a total 328 consecutive patients underwent upper gastrointestinal endoscopy for different reasons. The mean age of the patients was 39+12 years; 183 (55.7%) were women. H pylori was found positive in 193 (58.8%) of the patients. Combined antral and corpus biopsies increased the result by 20.8% compared to antral biopsies alone and 4.5% compared to corpus biopsies alone. 20.8% of patients infected with H pylori would have been misdiagnosed if testing from antrum alone and not combined with corpus. Atrophy and intestinal metaplasia were found in 101(30.8%) and 17(5.2%) of our patients, respectively. Atrophic gastritis was significantly more often in the antrum than the corpus (29.2 vs. 11.9%, respectively, $p< 0.05$). Patients with only positive corpus biopsies showed more incidences of both atrophy and intestinal metaplasia. Detection rates of H pylori decreased as more as atrophy increased regardless of biopsy site. Sensitivity of antrum biopsies alone, 65% compared to 92.5% in corpus alone or 100% if combination of both.

Conclusion: This study clarified that additional gastric corpus biopsy to the antral one increases the sensitivity to detect H pylori infection especially if associated with gastric atrophy.

Keywords: Gastric atrophy; Sydneysystem; H pylori and Gastritis

OPEN ACCESS

Correspondence:
AbdEl-latif M, Department of Surgery, Mansoura University Hospital, Egypt, E-mail: surg_latif@hotmail.com

Received Date: *24 Jun 2016*
Accepted Date: *27 Jul 2016*
Published Date: *31 Aug 2016*

Citation:
AbdEl-Latif M, HafrEl-Batin E, Shahin R, Shawqy A, Arafa M, Ghafar Saleh AA, et al. Value of Additional Corpus Biopsy for Diagnosis of Helicobacter Pylori in Atrophic Gastritis. Clin Surg. 2016; 1: 1093.

Introduction

Helicobacter pylori (H. pylori) affect nearly half of the population among the world. It is one of the most frequent and persistent bacterial infections worldwide [1]. It is responsible for many of the upper gastrointestinal tract diseases; chronic gastritis, gastrointestinal ulcers, mucosa associated lymphoid tissue lymphoma (MALT) and gastric cancer as well [2]. Thus it has been known as "definitive biological carcinogen" by WHO in 1994 [3]. It is already documented that *H. pylori* plays an important role in the promotion of atrophic gastritis. Severe degree of *H. pylori* associated atrophic gastritis is suggested to be an important risk factor in development of gastric carcinoma. Therefore, it is presumed that eradication of *H. pylori* from the stomach is linked to decrease the incidence of gastric cancer development [4]. There are various diagnostic tools to detect *H. pylori* whether

invasive (rapid urease test, histology or culture) or non invasive (urea breath test, serology or stool antigen) [5,6]. Histological examination despite is invasive, is considered one of the most important diagnostic tests for *H. pylori* infection because it also provides critical information related to the mucosa and presence of associated pathology [7,8]. *H. pylori can be seen in hematoxylin and eosin (H&E) stain as gram negative spiral bacteria with sensitivity and specificity as 69-93% and 87-90%, respectively [9]. Accuracy can be increased up to 90-100% by using special stains such as modified Giemsa stain, Warthin-Starry silver stain, Genta stain and immunehistochemical* stain [10]. H&E stain evaluate the degree of inflammation, atrophy and/or intestinal metaplasia (IM). It can also identify the *H. pylori* in a high magnification field; however, it becomes difficult to see the *H. pylori* when a low density of the organism and atrophic mucosal change are combined. As Giemsa stain is easy to use, inexpensive, and provides good results; it is the slandered method in many laboratories for *H. pylori* detection [11]. Also, Uemura et al. [12] reported that eradication of *H. pylori* decreases the incidence of recurrent gastric cancer in patients underwent endoscopic mucosal resection for early cancer stomach. It is widely recommended by many authors that eradication of *H. pylori* is mandatory in case of atrophic gastritis since the atrophy may reverse after successful eradication therapy [13,14]. But, it's difficult and challenging the detection of *H. pylori* in case of atrophic gastritis [15]. This study was designed to determine if it is important to add corpus biopsies to the routine antral ones for identification of *H. pylori*, especially in case of gastric atrophy and/or intestinal metaplasia.

Methods

Patients

Three hundred and twenty eight consecutive patients of uninvestigated dyspepsia, who underwent upper endoscopy were enrolled, (Mansura university hospital-Egypt, Benha University hospital–Egypt, Hafer Al Bat in Central Hospital, KSA) from June 2014 through Dec. 2015. Patients who received antibiotic or proton pump inhibitor treatment one month beforehand were excluded. All procedures in the study were performed in accordance with the institutional research board (IRB) committee in our institute.

Study protocol

All patients underwent upper gastrointestinal endoscopy and two standard gastric biopsies were taken from both antrum (2-3 cm from the pylorus both lesser and greater curvature) and corpus (8-10 cm from the cardia both lesser and greater curvature) for the histological examination [16].

Histological examination

Endoscopic biopsies were processed as formalin fixed paraffin embedded tissues, cut into 3-µm thick sections, and then stained with H&E and modified Giemsa stain. These were scored semi-quantitatively according to the updated Sydney classification (Figure 1) [16]. The following features were evaluated on each slide, inflammatory activity, glandular atrophy and intestinal metaplasia. According to these histological criteria, there were four grades of atrophy; 0, none; 1, mild; 2, moderate and 3, severe. Presence of polymorphonuclear cell (PNC) infiltration in the specimen refers to activity of the *H. pylori* infection. It is scored based on the density of inflammatory cells in both lamina propria and glandular epithelium (Figure 2). When gastric mucosa is replaced by intestinal epithelium (with goblet cells), it is diagnosed as gastric intestinal metaplasia that is also graded as showed above in Sydney system

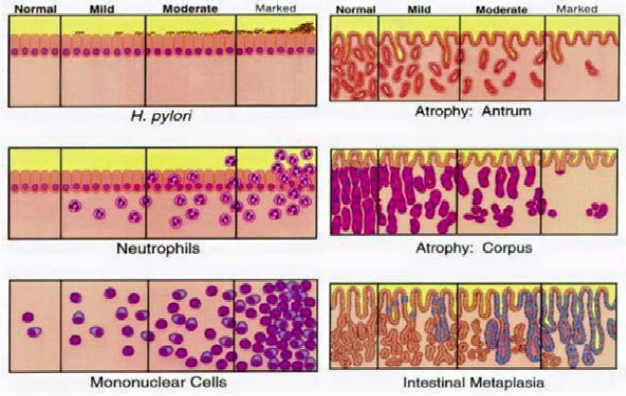

Figure 1: Sydney classification for gastric biopsy [16].

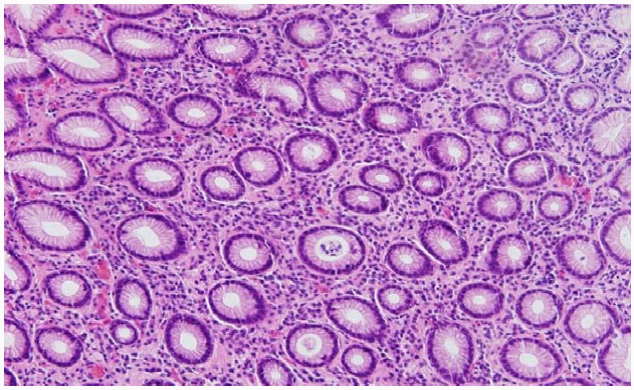

Figure 2: Antrum biopsy showed moderate activity (H&E X200).

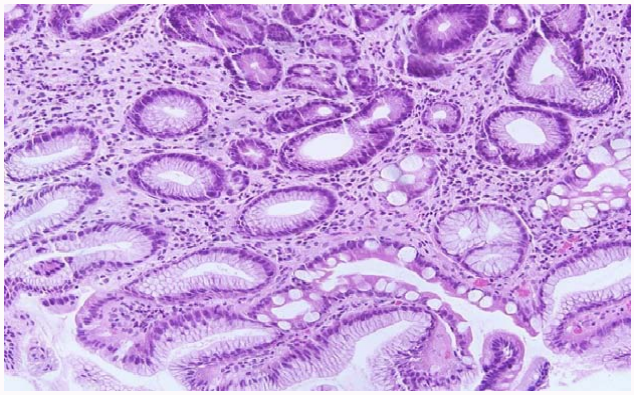

Figure 3: Gastric biopsy showed intestinal metaplasia (H&E X200).

(Figure 3). Lymphocytes and plasma cell infiltration indicate chronic inflammation associated with *H. pylori* infection (Figure 4). Glandular atrophy is defined as loss of gastric glands that fail to regenerate; the stromal space they previously occupied within the lamina propria is replaced by fibroblasts and extracellular matrix (Figure 5). Criteria for positivity and negativity of *H. pylori* were set: Patients were defined positive for *H. pylori* if either one or both was positive with Giemsa stained slides. Patients were considered negative if all specimens were negative. The histological evidence of atrophy was identified when the gastric glands were found decreased in amount and/or widely separated [17].

Statistics

All data were collected prospectively in an excel file for statistic

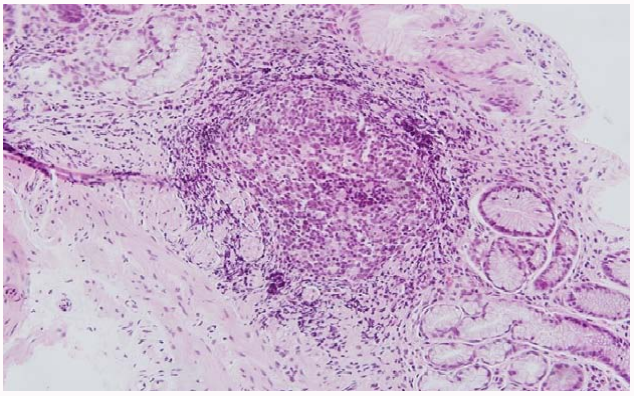

Figure 4: Gastric biopsy showed severe mononuclear inflammation with lymphocytes follicle formation (H&Ex200).

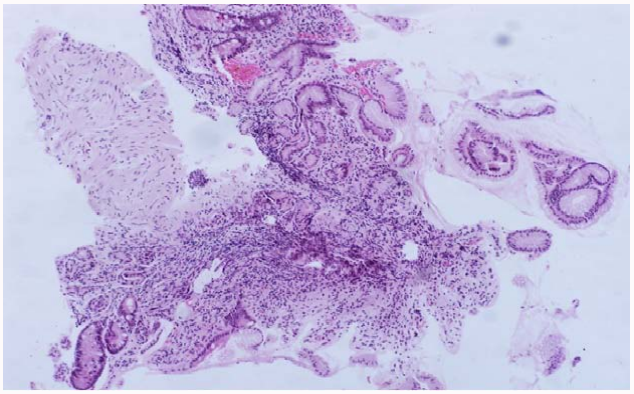

Figure 5: Gastric biopsy showed marked gastric atrophy (H&E x100).

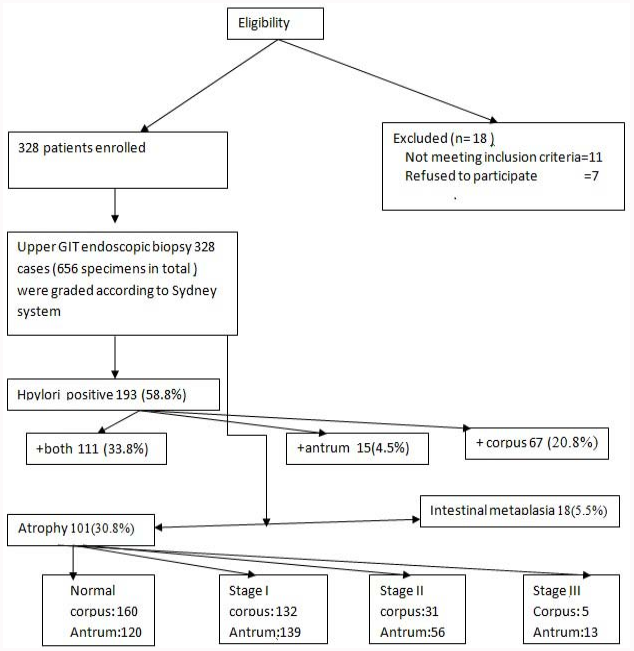

Figure 6: The patients' flowchart.

purposes. We used a Mann-Whitney test to compare continuous or non parametric variables. While, categorical or parametric variables were compared using Chi-square test. P value less than 0.05 was considered statistically significant. We used the SPSS version 11.5 for statistical analysis (SPSS version 11.5) for windows; SPSS Inc, Chicago, IL, USA).

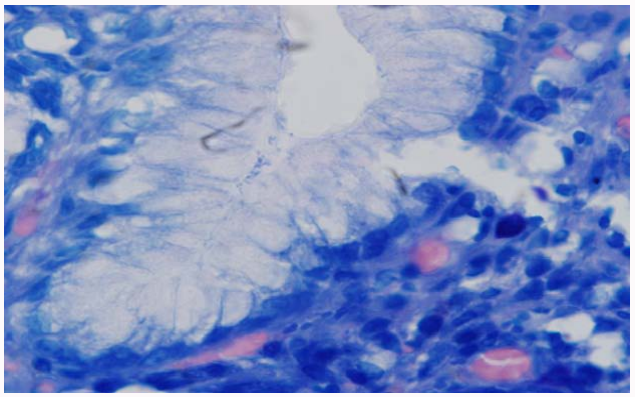

Figure 7: Gastric biopsy showed H pylori bacterai within lumen of glands (Giemsa stain with oil).

Results

Figure 6 shows the study flow chart for the whole study population. A total of 328 consecutive patients underwent an upper endoscopy procedure during the study period. The mean age of our patients was 39+12 years; 145(44.3%) were men. Upper gastrointestinal endoscopy was indicated for functional dyspepsia in 113(34.5%), epigastric pain in118 (35.9%) or heart burn in 97(29.6%) patients. Endoscopic diagnosis was peptic ulcer disease in 52 (15.9%), gastritis or duodenitis in 173(52.7%), or reflux esophagitis in 103(31.4%) patients. None of our patients were diagnosed with gastric carcinoma. Regardless of the biopsy site, a total of 656 biopsy specimens were received for histological evaluation (Table 1). *H. pylori* was found positive in 193 (58.8%) of the patients, (Figure 7). In 111 (33.8%) patients, both antral and corpus biopsies were identified positive for *H. pylori*. Combined antral and corpus biopsies increased the result by 20.8% compared to antral biopsies alone and 4.5% compared to corpus biopsies alone. In all patients with positive *H. pylori*, antral biopsies alone were positive in 15 out of 193 (7.7%) patients compared to corpus biopsies which were positive in 67 out of 193 (34.7%). In endoscopic diagnosis, atrophy was found in 101(30.8%) of our patients. Atrophic gastritis was significantly more often in the antrum than the corpus (29.2 vs. 11.9%, respectively, p< 0.05). Intestinal metaplasia was identified in 17(5.2%) of the patients and antrum was more often than the corpus (4 vs. 2% of all patients, respectively). Patients with only positive corpus biopsies showed more incidences of both atrophy and intestinal metaplasia compared with the other possible outcomes, 55 vs. 24.5% for atrophy and 10 vs. 4.6% for metaplasia (Table 1,2). In biopsies with atrophic gastritis, detection of *H. pylori* in the antrum specimens was inversely correlated with the degree of atrophy. The *H. pylori* positivity in antrum biopsies decreased from 40% within score (0-1) to 18.5% within score [2-3] compared to corpus biopsies (54.6 to 37.5%, respectively). Positivity of *H. pylori* was found significantly more often in the corpus biopsies than in the antrum regardless the degree of atrophy or metaplasia (Table 3). Our results showed that, regardless the gastric biopsy location, as the degree of atrophy increased the prevalence of *H. pylori* infection decreased. Sensitivity of corpus biopsies alone to diagnose *H. pylori* was found significantly higher than the antrum biopsies alone within the same Sydney's score of atrophy (sensitivity of antrum biopsies alone, 65% compared to 92.5% in corpus alone or 100% if combination of both). Prevalence rate of *H. pylori* infection between normal and mild atrophy and moderate or severe atrophy was also evaluated (Table 3).

Table 1: Histology outcomes by patients' characteristics.

Variables	N=328	Both+	Both -	C+only	A+only
Gender					
-Male	215	63%	58%	62%	47%
-Female	113	37%	42%	38%	53%
Age in years	31±9	32±8	27±6	33±7	34±9.5
Endoscopic diagnosis					
-Peptic ulcer	87	33%	24%	26%	29%
-Gastritis/duodenitis	101	27%	29%	22%	16%
-GERD	63	29%	18%	31%	24%
-Normal	11%	13%	21%	31%	31%
Microscopic findings					
-Atrophy	101(30.8%)	43(38.7%)	19(14%)	2(13%)	37 (**55%**)
Corpus and antrum	34	19	-	-	13
Antrum only	62	24	15	-	23
Corpus only	5	-	4	-	1
-Intestinal metaplasia	18(5.5%)	6(5.4%)	5(3.7%)	-	7(**10%**)
Corpus and antrum	3	-	1	-	2
Antrum only	11	5	4	-	2
Corpus only	4	1	-		3

+: Positive; -: Negative; A: Antrum; C: Corpus

Table 2: Histopathological classification of submitted biopsies according to Sydney system.

Sites –based biopsy	Score Variables	Activity	Mononuclear inflammation	Metaplasia	Atrophy
Corpus	Normal(0)	128	170	321	289
	Mild (1)	104	74	7	31
	Moderate (2)	64	54	0	7
	Severe (3)	32	30	0	1
Total		**328**	**328**	**328**	**328**
Antrum	Normal(0)	150	182	315	232
	Mild (1)	86	84	7	69
	Moderate (2)	66	44	6	27
	Severe (3)	26	38	0	5
Total		**328**	**328**	**328**	**328**

Table 3: The sensitivity of biopsy-based test (histology Giemsa stain) according to grade of mucosal atrophy.

Positive H pylori			
	Total	0-1 atrophy	2-3 atrophy
Antrum	126 (38.5%)	121/301 (40%)	5/27 (18.5%) p<0.05
Corpus	178 (54%)	175/320 (54.6%)	3/8 (37.5%) p<0.05
	P<0.05	P<0.05	P<0.05
Atrophy			
-Antral biopsies	126/193 (65%)	121/193 (62.6%)	5/193 (2.6%)
-Corpus biopsies	178/193 (92.2%)	175/193 (90.6%)	3/193 (1.5%)
-Combined	193/193 (100%)	189/193 (97.9%)	4/193 (2%)
	P<0.05	P<0.05	

Discussion

In the clinical setting, it is desirable to find a rapid and cost-effective method for detection of *H. pylori*. There are many methods for detection of *H. pylori* infection [18]. Endoscopic mucosal biopsy and histopathology are considered a valuable diagnostic tool for *H. pylori* detection. As well as, it provides a proper evaluation of gastric mucosal changes that have been attributed to chronic *H. pylori* infection i.e. glandular atrophy and/or intestinal metaplasia. It is still widely used as a main diagnostic method in suspicious patients with upper gastrointestinal symptoms or in highly prevalent areas [7]. We reported in our study that 193 (58.8%) have been detected to have *H. pylori*. 111(38.8%) patients, both antral and corpus biopsies were identified positive for *H. pylori*. 30.8% of our patients had atrophy in the antrum and/ or corpus or both. Intestinal metaplasia was identified in17 (5.2%) patients.

There is always a debate about the best location of gastric mucosal biopsy that can yield more sensitive detection of *H. pylori* especially in presence of atrophic gastritis [18]. In our work; we found that the frequency of *H. pylori* detection in case of gastritis without atrophy or metaplasia was higher with additional corpus biopsy compared with only antrum-based biopsy. According to Zhang et al. [3] and Arimendi-Marillo et al. [19]. *H. pylori* detection rates were significantly varying depending on the site of the gastric biopsy taken, ranging from 30 % at the antrum lesser curvature to 100% at the corpus greater curvature. Their results were almost comparable to ours in showing that the sensitivity of *H. pylori* detection was 92.2% at corpus while it was 65% at antrum, suggesting that corpus biopsy should be evaluated to detect *H. pylori* infection. Hazell et al. [20] also found that it is necessary to evaluate combined biopsies from antrum and corpus. However, other authors reported that antrum biopsy is sufficient to diagnose *H. pylori* gastritis without and morphological

changes [21,22]. Our results showed that, regardless the gastric biopsy location, as the degree of atrophy increased the prevalence of *H. pylori* infection decreased. Sensitivity of corpus biopsies alone to diagnose *H. pylori* was found significantly higher than the antrum biopsies alone within the same Sydney's score of atrophy (sensitivity of antrum biopsies alone, 65% compared to 92.5% in corpus alone or 100% if combination of both). Prevalence rate of *H. pylori* infection between normal and mild atrophy and moderate or severe atrophy were also evaluated. In this study, we found up to 20% of patients with *H. pylori* would be misdiagnosed if *H. pylori* status was based on only antral biopsies. We noticed in our study that patients with only positive corpus biopsies showed more incidences of atrophy and intestinal metaplasia compared with the other possible outcomes. This is explained by the fact that detection of H pylri inversely correlate with the presence of atrophy and as shown from our results that the antrum was the predominant site for atrophy. Therefore, antrum based biopsy only in case of atrophic gastritis yields to more false negative results [23]. This finding was in concordance with Kang HY et al. [24] Satoh K et al. [25] Yoo et al. [26,27] And Kokkola A et al. [15]. This study clarified that the sensitivity of *H. pylori* detection is decreased in cases of antral atrophic gastritis more than corpus one in the same time as inversely correlated with degree of atrophy.

Our study is not without limitations, the overall number of patients enrolled in the study is not that large number. We did not use urease CLO test or culture test to confirm the diagnosis because these tests are not available in our institutions where the histological examination for *H. pylori* is the routine. Our study was not designed to study the incidence of *H. pylori* infection; it was merely designed to determine the benefit of testing *H. pylori* from two separate gastric sites. Another study is recommended to be done over large number. We are currently working on those patients with atrophy and/or intestinal metaplasia to find if their atrophy is reversible after giving the eradication therapy.

Conclusion

H. pylori associated atrophic gastritis decreases sensitivity of detection rates of *H. pylori*. Atrophic changes are predominantly affect antrum first. Adding corpus biopsy to the routine antrum biopsy during endoscopy is recommended for proper evaluation of *H. pylori* infection case of gastric atrophy and to avoid false negative diagnosis.

References

1. Testerman TL, MorisJ. Beyond the stomach: An updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. World J Gastroenterol. 2014, 28; 20: 12781–12808.
2. Kuipers EJ. Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. Aliment Pharmacol, Ther. 1997; 11: 71-88.
3. Zhang C, Yamada N, Wu YL, Wen M. MatsuhisaT, Matsukura N. Comparison of Helicobacter pylori infection and gastric mucosal histological features of gastric ulcer patients with chronic gastritis patients. World J Gastroenterol. 2005; 11: 976-981.
4. Ito M, Haruma K, Kamada T. Helicobacter pylori eradication therapy improves atrophic gastritis and intestinal metaplasia: a 5-year prospective study of patients with atrophic gastritis. Aliment Pharmacol Ther. 2002; 16: 1449–1456.
5. Chey WD, Wong BC. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol. 2007; 102: 1808–1825.
6. Gisbert JP, Pajares JM. Stool antigen test for the diagnosis of Helicobacter pylori infection: a systematic review. Helicobacter. 2004; 9: 347–368.
7. Elvira Garza-González, Guillermo Ignacio Perez-Perez, HéctorJesús Maldonado-Garza, Francisco Javier Bosques-Padilla. A review of Helicobacter pylori diagnosis, treatment, and methods to detect eradication. World J Gastroenterol. 2014; 20: 1438-1449.
8. Aydin O, Egilmez R, Karabacak T, Kanik A. Interobserver variation in histopathological assessment of Helicobacter pylori gastritis. World J Gastroenterol. 2003; 9: 2232-2235.
9. Kuipers EJ. Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. Aliment Pharmacol Ther .1997; 11: 71-88.
10. Fallone CA, Loo VG, Lough J, Barkun AN. Hematoxylin and eosin staining of gastric tissue for the detection of Helicobacter pylori. Helicobacter. 1997; 2: 32-35.
11. Laine L, Lewin DN, Naritoku W, Cohen H. Prospective comparison of H&E, Giemsa, and Genta stains for the diagnosis of Helicobacter pylori. Gastrointest Endosc. 1997; 45: 463-467.
12. Uemura N, Mukai T, Okamoto S, Yamaguchi S, Mashiba H, Taniyama K, et al. Effect of Helicobacter pylori eradication on subsequent development of cancer after endoscopic resection of early gastric cancer. Cancer Epidemiol Biomarkers Prev. 1997; 6: 639–642.
13. Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, et al. Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. 2007; 56: 772-781.
14. Ley C, Mohar A, Guarner J, Herrera-Goepfert R, Figueroa LS, Halperin D, et al. Helicobacter pylori eradication and gastric preneoplastic conditions: a randomized, double-blind, placebo-controlled trial. Cancer Epi demiol Biomarkers Prev. 2004; 13: 4-10.
15. Kokkola A, Kosunen TU, Puolakkainen P, Sipponen P, Harkonen M, Laxen F, et al. Spontaneous disappearance of Helicobacter pylori antibodies in patients with advanced atrophic corpus gastritis. APMIS 2003; 111: 619-624.
16. DixonMF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney system. International workshop on the histopathology of gastritis, Houston 194. Am J Surg Pathol. 1996.
17. Sudraba A, Daugule I, Rudzite D, Funka K, Tolmanis I, Engstrand L, et al. Performance of Routine Helicobacter pylori Tests in Patients with Atrophic Gastritis. J Gastrointestin Liver Dis. 2011; 20349-20354.
18. Tonkic A, Tonkic M, Lehours P, MégraudF. Epidemiology and diagnosis of Helicobacter pylori infection. Helicobacter. 2012; 17: 1-8.
19. Arismendi-Morillo G, Hernández I, Mengual E, Abreu N, Molero N, Fuenmayor A, et al. Gastric cancer risk estimate in patients with chronic gastritis associated with Helicobacter pylori infection in a clinical setting. Rev Gastroenterol Mex. 2013; 78: 135-143.
20. Hazell SL, Hennessy WB, Borody TJ, Carrick J, Ralston M, Brady L, et al. Campylobacter pyloridis gastritis II: Distribution of bacteria and associated inflammation in the gastroduodenal environment. Am J Gastroenterol. 1987; 82: 297-301.
21. Dursun M, Yilmaz S, Yükselen V, Kilinç N, Canoruç F, TuzcuA. Evaluation of optimal gastric biopsy site and numbers for *H. pylori*, gastric atrophy. Hepatogastro-enterology. 2004; 51: 1732-1735.
22. Genta RM, Graham DY. Comparison of biopsy sites for the histopathologic diagnosis of Helicobacter pylori: a topographic study of *H. pylori* density and distribution. Gastrointest Endosc. 1994; 40: 342-345.
23. Kim CG, Choi IJ, Lee JY, Cho SJ, Nam BH, Kook MC, et al. Biopsy site for detecting Helicobacter pylori infection in patients with gastric cancer. J Gastroenterol Hepatol. 2009; 24: 469-474.
24. Kang HY, Kim N, Park YS, Hwang JH, Kim JW, Jeong SH, et al. Progression

of atrophic gastritis and intestinal metaplasia drives Helicobacter pylori out of the gastric mucosa. Dig Dis Sci. 2006; 51: 2310-15.

25. Satoh K, Kimura K, Takimoto T, Kihira K. A follow up study of atrophic gastritis and intestinal metaplasia after eradication of Helicobacter pylori. Helicobacter. 1998; 3: 236–240.

26. Yoo JY, Kim N, Park YS, Hwang JH, Kim JW, Jeong SH, et al. Detection rate of Helicobacter pylori against a background of atrophic gastritis and/or intestinal metaplasia. J Clin Gastroenterol. 2007; 41: 751-755.

27. Lan HC, Chen TS, Li AF, Chang FY, Lin HC. Additional corpus biopsy enhances the detection of Helicobacter pylori infection in a background of gastritis with atrophy. BMC Gastroenterol. 2012; 12: 182.