Role of endoscopy in suspicion of atrophic gastritis with and without intestinal metaplasia in comparison to histopathology

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Abstract

Background and study aims : Atrophic gastritis (AG) and intestinal metaplasia (IM) are established premalignant gastric lesions. Many studies documented a poor correlation between esophagogastroduodenoscopy (EGD) and histopathological (HP) findings of precancerous gastric lesions. The aim was to bridge the gap between endoscopy and HP in detection of chronic gastritis, AG and IM.

Patients and methods : a prospective single-center study involved 150 patients with endoscopic criteria of gastric lesions with upper gastrointestinal symptoms referred for upper GI endoscopy met the endoscopic criteria and classified according to HP of biopsies from targeted gastric lesions into chronic gastritis (GI), AG(GII) or IM(GIII). We correlated the endoscopic criteria of the 3 groups with the HP results.

Results : (73males & 75 females) with ages ranged17-75 years and mean± SD was 41.96 ± 15.95. GI, GII &GIII were [42 patients (28%),82 patients (54.7%) and 26 patients (17.3%)], respectively. Diffuse gastric mottling was more common in GI (74.3%, P<0.001), visible submucosal vessels, gastric atrophy predominated in GII (75.6, 82.3 & 73.1% (P 0.005,0.4 & <0.01)), respectively. Whitish raised lesions were more specific in GIII (85.7%) (P<0.001). The sensitivity and specificity of endoscopic suspicion of chronic gastritis were (86&88% in GI), (87&85% in GII) and (54% &100% in GIII) (p-0.001). The logistic regression model for risk factors was $\chi 2$= 25.74 and 49.32, p < 0.001.

Conclusion : Conventional endoscopy has high sensitivity and specificity for suspicion of chronic gastritis and AG, but low sensitivity and very high specificity for IM. Targeted biopsies may be valuable with image enhanced techniques. (Acta gastroenterol. belg., **2021**, 84, 9-17).

Keywords : endoscopy, atrophic gastritis, histopathology, intestinal metaplasia.

Introduction

Atrophic gastritis (AG) and intestinal metaplasia (IM) are established premalignant gastric lesions (1). Incidence of gastric cancer (GC) is the 5th among cancers worldwide with more than 95% are adenocarcinomas (2) and the 3rd cause of cancer-related deaths worldwide (3). Recently, *H. pylori* infects more than half of the population in developing countries leading to a sequelae of chronic gastritis, AG, IM, and finally invasive gastric carcinoma in untreated patients (4,5).

However, recent studies suggest that eradication of *H. pylori* infection reduces the incidence of its complications especially GC to about 33-47%, other trials documented the development of AG, IM, and GC in previously eradicated patients (5).

Clinically, AG and IM are difficult to be detected as they have no specific symptoms or signs with most cases discovered endoscopically and or by histopathological assessment (3).

AG is a chronic inflammatory condition that results from a decrease or loss of appropriate gastric glands ; however, IM is the replacement of normal gastric glands by small intestinal phenotype metaplastic ones ; the pathogenesis of which remains unclear. A systematic review reported recently a range of 0.53-15.24/1000 person/year with AG and 0.38-17.08/1000 person with IM lead to GC annually (6). A large study done on 61707 patients with gastric IM, revealed annual progression to GC by 0.25% (3). Moreover, IM increases the risk of GC by 6-folds (2).

Pathologically, IM can be identified by simple columnar epithelium containing paneth, absorptive, and goblet cells (3).

Recent European and international Kyoto guidelines highly recommend endoscopic surveillance of patients with extensive AG and IM at a 3-years interval (6).

Endoscopic detection of AG and IM had been missed for long periods until the revolutionary development of methylene blue staining ; a type of chromo endoscopy by Ida et al., (1975) passing through Indigo carmine dye which allowed good visualization of mucosal irregularities and atypical vascular pattern characteristic of IM. However, recently, the great advance in endoscopic technology with the detection of image enhanced endoscopy (IEE) as Narrow Band Imaging (NBI) has increased the detection rate of mucosal abnormalities. Practically, most endoscopists still use the conventional white-light endoscopy (CWLE) and High-definition (HD-WLE) in daily practice for endoscopic diagnosis of chronic gastritis, AG, and IM due to insufficient experience and /or shortage of resources (6).

Moreover, chronic gastritis and AG have been diagnosed by histopathological analysis for long periods with poor correlation with the endoscopic findings.

Recent advance in endoscopic technologies yields endoscopists to largely divert the diagnosis to the endoscopic rather than histological patterns. Endoscopic features that correlate well with histopathology become more evident with many studies done on this aspect (7). Additionally, this will decrease the biopsy costs and post-biopsy complications (8).

Successful eradication of *H. pylori* has been studied with a dramatic reduction in *H. pylori*-induced gastritis, atrophy, metaplasia, and finally GC. However, there is still a debate on post-eradication follow up.

The work aimed to explore endoscopic-histopathological correlation based mainly on white light endoscopy used in routine practice in tertiary centers in Egypt. Additionally, we need to evaluate the effect of treatment or eradication of *H.pylori* on the development of AG and IM.

Patients and methods

Patients

This was a prospective single-center study involved 150 patients with endoscopic criteria of chronic gastritis, AG or IM selected from 300 patients with upper gastrointestinal symptoms who were referred to GI endoscopy units, Tropical Medicine Department, Menoufia university tertiary hospitals for upper GI endoscopy in the period between August 2017 to August 2018. They were 73males (48.7%) and 77 females (51.3%) and their ages ranged between 17 and 75 years with mean value (41.96 ± 15.95 years).

All patients enrolled in this project were complaining of upper gastrointestinal symptoms including dyspepsia, nausea, vomiting, upper gastrointestinal bleeding (UGIB), reflux symptoms, and anemia who were in need of esophagogastroduodenoscopy (EGD) evaluation.

Patients with previous gastric surgery, on proton-pump inhibitor treatment, already diagnosed with GC or lymphoma, or had either a contraindication to undergo EGD or to have gastric biopsies or had esophageal or duodenal lesions as the main cause of their symptoms were excluded from the study (Figure 1). All related laboratory measures were done 24 hours prior to the endoscopic procedures.

Endoscopic evaluation

All patients were assessed with qualified endoscopists with more than 10 years of experience and performing more than 30 EGDs (diagnostic and therapeutic) per month and well-trained on basic and advanced endoscopic features suggesting chronic atrophic and non-atrophic gastritis, IM and early gastric cancer using CWLE, HD-WLE, IEE.

Only Olympus scopes (Tokyo, Japan) models170, 240, and 260 with conventional white light models (C-WLE) were used with fewer patients were examined using
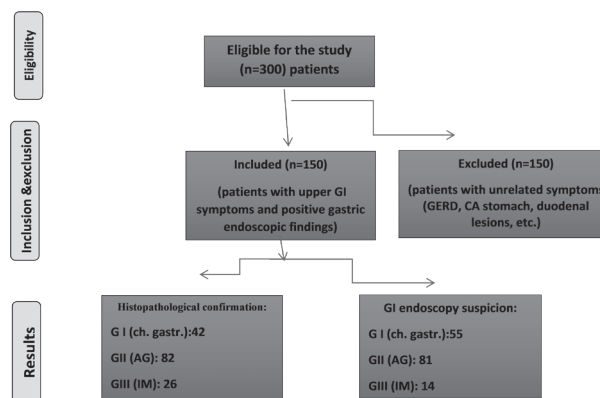

Figure 1. — Flow chart of the studied patients.

higher versions with a high -definition (HD-WLE) and image-enhanced techniques 260,170 &190 with narrow-band imaging (NBI).

The studied patients were prepared for EGD with overnight fasting. EGD was done down to the 2nd part of the duodenum with a complete exploration of the whole stomach including the blind areas. According to a recent European society of gastrointestinal endoscopy guidelines for performance measures of upper gastrointestinal endoscopy, we stressed on complete visualization of the whole gastric mucosa through the absence of any food particles, debris, or mucus and using water jet system. The average endoscopic examination was 10 minutes (9). Endoscopic findings were reported and standardized.

Gastric mucosal atrophy was diagnosed endoscopically by the visibility of vascular pattern and gastric rugae atrophy. While IM was detected as greyish-whitish slightly opaque patches using CWLE or as a light blue crest (LBC), or white opaque substance (WOS) using NBI (7).

Endoscopic features that can characterize *H. pylori* infection were erythema, mucosal swelling, nodularity, streaks, diffuse or localized erythemas or spotty areas. Mucosal swelling is a soft thick edematous mucosa. A normal gastric mucosal fold is about 5mm, smooth and straight. Enlarged fold was considered if more than 5mm in thickness and tortuous. Biopsies were taken from suspicious gastric lesions under CWLE. In order to diagnose chronic *H.pylori* active gastritis and in case of a diffuse gastric pathology as diffuse or spotty redness, nodularity or mottling, biopsies had been taken according to updated Sydney system with 2 biopsies from antrum, one from incisura, one from lesser curvature and the 5th from greater curvature each in a separate tube (9).

All the obtained biopsies were collected for histopathology (HP), fixed in 10% neutral formalin, and sent for preparation of formalin-fixed, paraffin-embedded tissue blocks. 4um thick sections were cut. One set of tissue sections was stained with hematoxylin and eosin for routine analysis and another set with Giemsa stain for detection of *H. pylori* infection in the gastric mucosa (10).
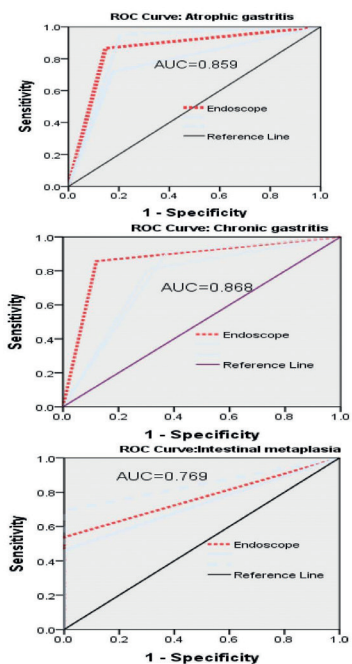
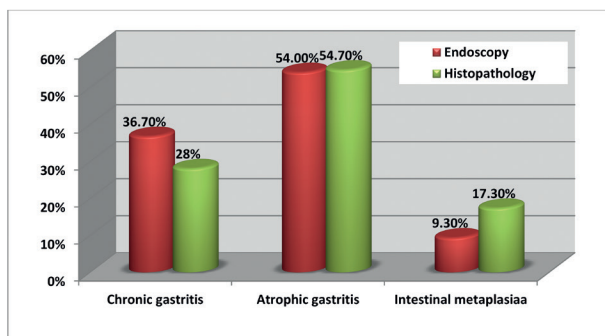Figure 2. — Roc curve for endoscopic findings in relation to histopathology.

Figure 3. — Endoscopy and histopathology findings in the studied groups.

H pylori appear as a bluish-purple rod-shaped, curvilinear and/or dot-like granular organisms along the luminal surfaces of the epithelium (10). All biopsies were evaluated for the intensity of chronic inflammation (mononuclear inflammatory cellular infiltrates), inflammatory activity (neutrophilic infiltrations), glandular atrophy, metaplasia, reparative atypia, and dysplasia according to updated Sydney classification (10) (Figure 5).

EGD findings were standardized before starting the research using the most documented features for each group. Diffuse redness & mottling, antral granularity, ulcers, or enlarged gastric folds suggested chronic inflammation and gastritis, while atrophic gastric mucosa or folds and visible submucosal vessels predicted the AG arm and whitish raised lesions and plaques were suggestive more for IM (Figure 4).

Then, we correlated the endoscopic findings with the histopathological results in all groups.

Patch redness (HD)   Diffuse redness (HD)   Mucosal nodularity(HD)

A) Endoscopic findings commonly detected in H.pylori related chronic gastritis CWLE

Thin atrophic mucosa and rugae of the antrum   CWLE image of the gastric fundus showing thin mucosa, visible submucosal vessels and   NBI:the gastric antrum showing surface structure papillary or villiform and light blue(IM)

B) Endoscopic findings of AG using CWLE & HD-WLE and NBI(IM).

WLE image of IM of the antrum   CWLE image of the gastric antrum showing elevated white plaques of IM.   HD-WLE Fundus showing slightly elevated greyish opalescent patches (IM)

C) Endoscopic findings of IM using CWLE and HD-WLE
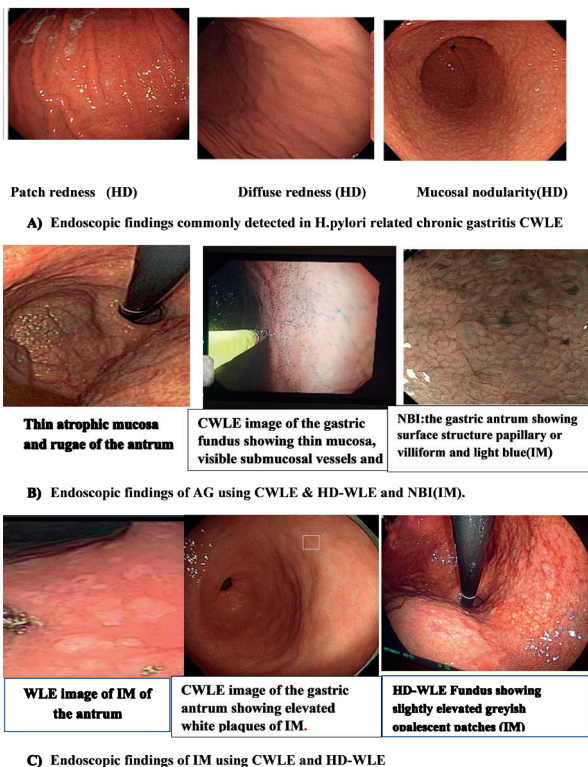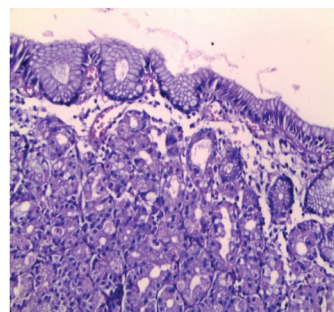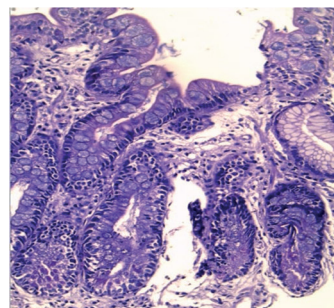
Figure 4. — Endoscopic views of IM and AG using CWLE and NBI.

A case of H pylori associated chronic gastritis showing intestinal metaplasia with evident goblet cells in mucosal glands (H&Ex200).

Another case of H pylori associated chronic gastritis showing marked atrophy of mucosal glands(H&Ex100).

Figure 5. — Histopathological findings in two cases with IM and AG.

Patients were classified into three groups

G I : patients with histopathological confirmation of chronic non-atrophic gastritis (No=42).

G II : patients with histopathological confirmation of chronic AG (No=82).

G III : patients with histopathological confirmation of IM (No=26).

Frequency data were summarized as percentages. continuous variables were summarized as median and range of distribution. A two-sided P <0.05 means the null hypothesis rejection character. 95% CI methods for OR was based on mid P-method. Logistic regression is a statistical technique used to predict the probability of binary response based on one or more independent variables. The SPSS 20.0 (SPSS Inc, IBM Corporation, Armonk, NY, USA) software was used for statistical analysis. This project was approved by Menoufia university ethical board.

Results

In a total, 300 patients were referred for EGD evaluation due to their upper gastrointestinal symptoms,150 patients met the endoscopic criteria of chronic gastritis, AG or, IM. All other patients were excluded .73 were males and 77 were females with ages ranged from 17-75 years ; mean± SD (41.96 ± 15.95). Chronic gastritis (GI), AG (GII) & IM (GIII) were (42 patients (28%), 82 patients (54.7%) and 26 patients17.3%), respectively (Figure 1). Smokers constitutes 67 patients (44.7%), while diabetics were 69(46%). Patients with a history of previous *H. pylori* infection were 95 patients (63.6%), 55% of them had a history of anti-*H. pylori* therapy with the family history of *H. pylori* infection was 55(36.6%) (Table 1).

There was a statistically significant difference between GI and GIII regarding smoking, current and family history of *H.pylori* infection (P<0.001), GI and GII regarding chronic NSAIDs use, smoking and DM (P<0.001) and between GII and GIII regarding family history of *H.pylori* infection with a higher incidence of IM in patients who had a positive family history of *H.pylori* infection(p <0.001) (Table 4).

A logistic regression was performed to ascertain the effects of smoking, DM, *H.pylori*, HB, WBCs, and platelets on the likelihood that participants have AG or IM. The logistic regression model was statistically significant, $\chi2$= 25.74 and 49.32 respectively, p < 0.001. The model explained 61.0 and 70% (Nagelkerke R^2) of the variance in AG or IM and correctly classified 86.3,

Table 1. — **Clinical characteristics of the studied patients**

Clinical characteristics	Studied patients (n=150)	
Age (Y) • Mean ±SD • Range	41.96±15.95 17-75	
Sex	No	%
• Male • Female	73 77	48.7 51.3
Smoking	67	44.7
DM	69	46.0
H. Pylori infection: • Current H.Pylori infection • Previous H.Pylori therapy and it's timing(no=55): <60 > 60 • Family history of H.Pylori infection	95 24 31 55	63.6 43.6 56.4 36.6
Family history of cancer stomach	10	6.7
History of chronic use of NSAIDs	26	17.3
General examination: • Pallor	29	19.3
Indications for EGD: • Abdominal pain (persistent or recurrent) • Dyspepsia • Vomiting • Unexplained anemia • Heartburn • Dysphagia • GI bleeding (melena & hematemesis)	122 75 30 28 24 12 12	81.3 50.0 20.0 18.7 16.0 8.0 8.0
Site of gastric biopsy • Antrum • Fundus • Corpus	92 35 23	61.3 23.3 15.3
Laboratory investigations	Mean ±SD	Range
• Hb (g/dl) • WBCs (….. x 10³) • Platelets (….. x 10³)	10.57±1.63 6.37±1.96 221.92±122.24	7.90-14.0 3-11.0 49-498.0

Table 2. — **Distribution of endoscopic findings among the studied groups**

Endoscopic Findings	Endoscopic evidence						χ^2	P
	Chronic gastritis (N=42)		Atrophic gastritis (N= 82)		Metaplasia (N= 26)			
	No.	%	No.	%	No.	%		
Diffuse redness	42	43.7	44	45.8	10	10.4	34.79	<0.001*
Diffuse mottling	29	74.3	7	17.9	3	7.6	45.28	<0.001*
Antral granularity	20	57.1	10	28.5	5	14.2	19.78	<0.001*
Enlarged gastric folds	18	40.6	11	43.3	3	9.3	16.14	<0.001*
Antral erosions	37	61.6	18	30.0	5	8.3	56.28	<0.001*
Fundal erosions	5	55.5	2	22.2	2	22.2	4.57	0.101
Antral ulcer	10	47.6	4	19.4	7	33.3	12.63	0.001*
Visible submucosal vessels	5	12.2	31	75.6	5	12.2	10.42	0.005*
Atrophic mucosa Atrophic gastric folds	1	5.8	14	82.3	2	11.7	6.38	0.041*
Whitish raised lesions	5	12.1	30	73.1	6	14.6	8.80	0.012*
Bile reflux	2	14.2	0	0.0	12	85.7	51.13	<0.001*
	20	86.9	2	8.6	1	4.3	46.87	<0.001*
H.Pylori intensity								
Mild	13	30.0	49	59.0	5	19.0	**31.53**	**<0.001***
Moderate	27	64.0	17	20.0	17	65.0		
Severe	2	4.0	16	19.0	4	15.0		

Table 3. — **Sensitivity and specificity of CWLE in comparison to histopathology in the studied groups (A):**

Groups	Sensitivity	Specificity	Accuracy	PPV	NPV	Kappa	P value
Chronic gastritis	86.0	88.0	87.0	73.0	94.0	0.70	<0.001*
Atrophic gastritis	87.0	85.0	86.0	88.0	84.0	0.71	<0.001*
Intestinal metaplasia	54.0	100.0	92.0	100.0	91.0	0.65	<0.001*

(B): Sensitivity and specificity of HD-WLE with NBI in comparison to histopathology in the studied groups

Groups	Sensitivity	Specificity	Accuracy	PPV	NPV	Kappa	P value
Chronic gastritis	86.0	88.0	95	58.17	77.22	0.77	<0.01
Atrophic gastritis	87.0	93	88	71.5	71.3	0.8	<0.01
Intestinal metaplasia	100	96	96	70	96.8	0.9	<0.05

Table 4. — **Clinical characteristics of the studied groups**

	Groups						Test of sig	P-value
	Chronic gastritis (N=42)		Atrophic gastritis (N=82)		Intestinal metaplasia (N=26)			
	No	%	No	%	No	%		
Hb Mean ± SD	10.41± 1.28		10.17 ± 1.30		9.30 ± 0.90		Kruskal-Wallis =11.55 P=0.001	P2,P3 <0.001*
WBCs Mean ± SD	6.67± 1.19		6.55 ± 2.04		6.16 ± 1.90		Kruskal-Wallis =17.26 P<0.001*	P2,P3 <0.05*
Platelets Mean ± SD	210.0± 103.32		222.26 ± 120.31		155.38 ± 39.64		Kruskal-Wallis =4.08 P=0.043	P2,P3 <0.05*
Smoking Yes No	3 39	7.1 92.9	47 35	57.3 42.7	17 9	65.4 34.6	χ^2=29.06 χ^2=26.24 χ^2=0.53	P1, P2<0.001* P3= 0.465
DM Yes No	24 18	57.1 42.9	30 52	36.6 63.4	15 11	57.7 4.3	χ^2=4.78 χ^2=0.0 χ^2=3.62	P1=0.028* P2=0.964 P3= 0.057
Chronic use of NSAIDs Yes No	14 28	33.3 66.7	8 74	9.8 90.2	4 22	15.4 84.6	χ^2=10.58 χ^2=2.66 χ^2=0.63	P1<0.001* P2=0.103 P3= 0.426
Current H. Pylori infection Yes No	20 22	47.6 52.4	52 30	63.4 36.6	23 3	88.5 11.5	χ^2=2.85 χ^2=11.52 χ^2=5.84	P1=0.091 P2<0.001* P3= 0.015*
Previous H. Pylori therapy Yes No	15 27	75.0 25.0	30 52	57.7 42.3	10 16	43.5 56.5	χ^2=0.01 χ^2=0.05 χ^2=0.03	P1=0.923 P2=0.819 P3= 0.862
Family history of H. Pylori infection Yes No	8 34	19.0 81.0	27 55	32.9 67.1	20 6	76.9 23.1	χ^2=2.64 χ^2=22.21 χ^2=15.55	P1=0.104 P2<0.001* P3<0.001*

Table 5. — **Multivariate regression analysis of the studied groups**

	Atrophic gastritis			
	Wald	**Sig**	**OR**	**CI 95%**
Smoking	18.30	<0.001*	36.72	7.04-191.37
Diabetes mellitus	2.68	0.101	0. 369	0.11-1.21
H. Pylori	6.60	0.010*	4.498	1.4-14.16
Chronic use of NSAIDs	**7.11**	0.008	0.10	0.01-0.54
Hb	1.46	0.26	0.778	0.51-1.16
WBCS	11.50	0.001	0.548	0.38-0.77
Platelets	0.18	0.669	0.999	0.99-1.0
	Intestinal metaplasia			
Smoking	6.41	0.011*	23.73	2.04-275.42
Diabetes mellitus	0.93	0.335	2.94	0.32-26.53
H pylori	2.74	0.098	4.61	0.75-28.23
Chronic use of NSAIDs	0.02	0.876	1.15	0.18-7.38
Hb	2.41	0.120	0.53	0.23-1.18
WBCS	5.32	0.021	0.50	0.28-0.90
Platelets	0.69	0.403	1.0	0.99-1.01

A logistic regression was performed to ascertain the effects of smoking, DM, H.pylori, Hb, WBCs and platelets on the likelihood that participants have atrophic gastritis or intestinal metaplasia. The logistic regression model was statistically significant, $\chi^2 = 25.74$ and 49.32 respectively, $p < 0.001$. The model explained 61.0 and 70% (Nagelkerke $R2$) of the variance in atrophic gastritis or intestinal metaplasia and correctly classified 86.3, 85.3% of cases respectively. Smokers were 36.72 and 23.73 times more likely to exhibit atrophic gastritis or intestinal metaplasia. Previous H. Pylori was associated with an increased likelihood of exhibiting atrophic gastritis. Also increasing WBCs was associated with an increased likelihood of exhibiting atrophic gastritis or intestinal metaplasia.

85.3% of cases, respectively. Smokers were 36.72 and 23.73 times more likely to exhibit atrophic gastritis or intestinal metaplasia. Previous *H. Pylori* was associated with an increased likelihood of exhibiting atrophic gastritis. Also increasing WBCs was associated with an increased likelihood of exhibiting AG or IM. However, age, sex, and hypertension haven't shown any statistical significance (Table 5).

Etiologically, *H. pylori* infection prior to endoscopy was tested using *H. pylori*-Ag in stool by ELISA ; chronic gastritis, AG, and IM were statistically significant among patients who were positive than negative for *H. pylori* infection. Additionally, when we compared the 3 groups regarding previous therapy for *H. pylori*, we found no statistically significant difference between the groups. Surprisingly, a portion of patients who had completed their anti-*H. pylori* therapy was complicated by chronic gastritis, AG or IM raising the question of progression of gastric inflammatory process post-treatment or there was unsuccessful eradication (Table 4).

On general examination of the total sample, Pallor was the most noticeable sign in 29 patients (19.3%) of the total sample with HB mean± SD was (10.57±1.63) (Table 1 & 4). As regards blood indices, HB, WBCs, and Platelets were significant between GI and GII, p-values (0.001, 0.05, 0.05), respectively and IM showed the lowest HB level mean ±SD (9.30 ± 0.90) (Table 4). Persistent abdominal pain and dyspepsia were the most common indications for EGD 122 patients (81.3%) & 75(50%), respectively. Other manifestations include vomiting, heartburn, unexplained anemia, GI bleeding, and dysphagia (Table 1).

According to the sites where biopsies were taken from the stomach, antral biopsies were the commonest (92, 61.3%), fundal (35,23.3%), and finally corpus (23,15.3%). Glandular atrophy and IM were not significant statistically between antral, corpus, or fundus biopsies (p-value 0.37 & 0.19) (Table 1).

We correlated the standardized endoscopic findings in each group, diffuse redness was more common in GII 45.8%, mottling in GI (74.3%), visible submucosal vessels, atrophic mucosa and/or gastric folds predominated in GII (75.6,82.3&73.1), respectively. Whitish raised lesions were more specific in GIII (85.7%) with a highly statistically significant difference between the groups. *H. pylori* –induced pathology revealed the most common etiology in all groups 132/150 patients (88%) (p-0.001). Bile reflux-induced gastritis was an additional cofactor in 21cases (14%) with no identifiable cause in 18 cases (12%) (Table 2 & Figure 4).

Histopathological distribution according to the updated Sydney system revealed *H. pylori* intensity was a statistically significant difference between the 3 groups (p-value 0.001) with moderate intensity in GI &GIII and mild intensity in GII (Table 2).

According to the above criteria for each group, the sensitivity and specificity of standard EGD regarding the diagnosis of chronic gastritis and AG were high ranging from 85-88% with a good degree of agreement (0.7-0.71) (P<0.001). In contrast, the sensitivity yield of diagnosing IM was very low 54% and specificity was 100% giving the satisfaction that EGD can be a good positive tool regarding the diagnosis of IM (Table 3).

In comparing the ability of CWLE to suspect chronic gastritis, AG and IM with the proven-biopsy, results were 55(36.7), 81(54%), 14(9.3%) and the HP results were 42(28%), 82(54.7%),26(17.3%), respectively. In other words, the standard EGD could truly diagnose 36 out

of 42 patients diagnosed by HP in GI, 71/82 in GII, and 14/26 in GIII. In 42 cases proved by HP to have chronic gastritis, 36 were endoscopically suspected as chronic gastritis, 8 cases were AG with no cases were suspected with IM. Among the 82 cases with AG ; 71 patients from AG and 11 only were chronic gastritis. IM was detected in 26 patients (4 with suspected chronic gastritis, 8 suspected to have AG and 14 were highly predicted to have IM endoscopically). Cases done with endoscopies that have NBI were statistically significant difference than cases done with standard scopes (p-value<0.001) (Figure 3).

Discussion

The aging process nowadays has increased the incidence of GC despite early detection of AG, IM, and successful eradication of *H. pylori* which constitutes the most common etiology of chronic gastric inflammation, which if not treated will develop AG and metaplastic changes and finally GC (11). In Egypt, there is a paucity of data documenting the incidence of AG and IM among patients either actively or previously infected with *H. pylori*. Additionally, due to limited resources in many centers, we still rely on HP diagnosis of AG and IM which may not be accurate due to poor endoscopic resources and consequently ill-defined biopsy mapping.

In the current study, the incidence of previous *H. pylori* infection was increased with AG (P 0.01, OR 4.5) on multivariate analysis and a trend towards increased abdominal pain (122,81.3%) and dyspepsia (75,50%) in all groups. Additionally, there was a statistically significant difference among the groups with aa higher incidence of AG and IM in patients who had a positive family history of *H. pylori* infection (p-value <0.001). However, among risk factors for IM in Gomez et al., there was a statistically significant difference between weight loss and IM (P -0.01 OR 0.07) (3).

Among the most common indications for EGD in the current project patients' with gastric IM were abdominal pain and weight loss (41.7% & 13.5%) on univariate analysis, P values for abdominal pain and weight loss were (P - 0.005 & 0.01), respectively with a trend towards increased the frequency of gastric IM(GIM) [OR 1.81 (0.95, 3.66) P = 0.073].

Anemia deemed to be significant in GIII (P-0.001) probably due to vomiting, dyspepsia, *H. pylori* infection and gastric erosions and/or ulcers that may cause chronic blood loss.

In our research, there was a trend on multivariate analysis towards increased frequency of smoking (P <0.01, OR 23.73) and increasing WBCs (P <0.02, OR 0.5) among patients with IM. Gomez et al. proved a statistically significant difference between 468 patients with GIM and 118 without GIM as regards age, a smoking lifetime without difference regarding positive family history of cancer stomach and gender. Patients with GIM had older ages and a longer duration of

smoking than a group without GIM on univariate analysis (P<0.001&0.007), respectively. Moreover, multivariate analysis for tobacco use had an odds ratio (OR) 1.73(CI 1.18,2.55) p=0.073 (3).

In Gomez et al., there was no statistically significant difference between positive family history of GC and the development of IM (P-0.5, OR-1.38) (3) ; our study consisted with these results with the family history of GC in the total sample was 10/150(6.7%) patients, but not related to the development of AG and IM(p>0.05). This result was proved in a meta-analysis that described (OR) of 1.982 for the presence of GIM in first-degree relatives of GC patients (13).

Most of the studies estimated the incidence of IM in patients underwent EGD and had biopsies to be less than 10% (3). In our study, the incidence of IM reported 17.3% may be due to late detection and lack of routine cancer screening programs.

Sydney system recommends taking five gastric specimens to diagnose *H. pylori* infection and gastric mucosal abnormalities, albeit in daily practice it seems to be impractical to have five biopsies with higher costs and overload for histopathologists especially with a revolutionary advance in magnifying endoscopies (11). A recent study from Thailand in 2015 done on 500 patients complaining of dyspeptic symptoms, EGD has done with a site-specific biopsy technique to detect *H.pylori* infection and premalignant conditions, it yielded a good efficacy than a standard biopsy with sensitivity, specificity, positive and negative predictive values using standard endoscopies to detect *H.pylori* infection were (95.4%,97.3%,98.8%,90%), respectively with P<0.01(11).

Many hypotheses reported a strong correlation between *H. pylori* and the development of AG and IM. After eradication of *H. pylori*, the regression of these lesions occurs. Several meta-analyses reported the decreased occurrence in GC by 33% in *H. pylori*-successfully eradicated cases. However, eradication after developing gastric atrophy and IM remains unclear (12). Gomez et al. showed a potent significant correlation between *H. pylori* and IM (p=0.007 OR 3.07) (3). In our study, *H. Pylori* infection was associated with an increased likelihood of exhibiting AG (p=0.01 & OR 4.49) and IM p=0.09& OR 4.6. However, a large meta-analysis by Wang and his colleagues involved 12 studies with more than 2500 patients having AG and IM, concluded that antral AG could regress with treatment while corpus AG and gastric IM failed to regress despite eradication therapy, augmenting the theory that, IM is a breakpoint for cancer stomach (10).

AG is generally underestimated especially mild AG using standard CWLE by the visibility of submucosal vessels and increasing gastric mucosal whitish areas. However, by using magnifying endoscopy (ME) techniques, mild cases may be easily determined (12).

In a previous study comparing CWLE with Blue light imaging, revealed a detection rate of 3.3% for early GC

after *H. pylori* eradication therapy. (11) We conclude from our study and others', that *H.pylori* therapy may not prevent the progression of chronic and AG to IM and dysplasia denoting that anti-*H.pylori* treatment should not give a high sense of safety for patients and follow up is recommended.

The most common endoscopic findings in a total sample population with and without IM in Gomez et al. study were chronic inflammation (137/589, 23.3%) and gastric nodularity (104, 17.7%) (3). In correlation with our study, the incidence of diffuse redness in all groups was (96, 64%), visible submucosal vessels (41/150) with a trend towards increased frequency in AG and highly statistically significant difference between the groups (p-<0.001), whitish raised plaques were more frequent in IM group 85.7% (12/26, p-<0.001) (Table 2).

Previous well-validated studies using CWLE documented the poor correlation between endoscopic and histopathological findings for the detection of precancerous gastric lesions. On the contrary, recent trials using high-definition WLE (HD-WLE) showed promising outcomes. A cross-sectional study reported overall accuracy 88% using HD-WLE for detection of IM and dysplasia with a sensitivity of 75% and specificity of 94%. Another prospective multicenter study showed a 59% sensitivity and 98% specificity for IM (12).

In a study done by Jian-Min et al. 35 out of 140 cases were diagnosed by HP to have chronic AG, only 8 by CWLE had features of AG but with ME, 33 were detected with a statistically significant difference between the two scopes p=value<0.01(14). In this project, the sensitivity and specificity of detecting AG using CWLE were 87%& 85%, respectively and ROC/AUC was 0.85.

In another study by Fukuta and others in 2013, on 163 Japanese patients indicated for EGD and biopsies were taken according to the Sydney system, 46.6% had chronic gastritis, and 16.6%had early GC by CWLE. The sensitivity, specificity, and ROC/AUC for detection of IM in gastric antrum using the standard endoscopy were 94.6%, 69.1%, and 0.82, respectively (15). In this project, the sensitivity, specificity, and ROC/AUC of IM using CWLE were 54%, 100%, and 0.77, respectively. (Figure 2).

Among the most frequent endoscopic findings in Gomez et al. research, were gastritis 23.3%, AG 10.8% of all patients and in 13.2% of patients with GIM ; while, after HP analysis, chronic gastritis was confirmed in 65.6% of GIM group and 32.3% in the group without GIM. *H. pylori* infection was detected by HP in 46/486(9.8%) in GIM and 6/171(3.5%) in non-GIM group. Multivariate analyses were [OR 3.07 (1.33, 8.20), P = 0.007] (3).

An Indian study in 2010 compared the diagnostic sensitivity of CWLE versus NBI for the detection of premalignant gastric lesions, a total of 200 patients were examined using both scopes randomly. CWLE was able to detect AG and IM in 17 patients and 31 using NBI (p-0.001) (16).

A different data elaborated in a screening study done to compare two protocols for the screening of gastritis and IM whereby the first protocol used the HD-WLE with biopsies taken from the stomach according to the updated Sydney system and targeted biopsies when needed and the second was using NBI and targeted biopsies from any suspicious premalignant lesion. Results revealed,92 out of 119 patients had chronic gastritis versus 71/119 (p 0.0001), AG 32.7% versus 23.5% (p0.03) and IM 16% versus 15.1% (p-0.7) by HD-WLE and NBI, respectively for each group (17).

In this study, the sensitivity and specificity for IM using NBI were 100&96%, respectively and for AG were 87 & 93%. But, with conventional WLE were 86% & 88% for GI with accuracy 87%, 87% & 85% for GII with accuracy 86% and for GIII 54% & 100%, respectively and accuracy 92%. So, NBI increased the diagnostic accuracy of chronic gastritis, IM and AG by 8, 2, and 4% than CWLE (p<0.001) with a highly statistically significant difference between the two scopes (Table 3).

To conclude, CWLE has high sensitivity and specificity for suspicion of chronic gastritis and AG, but low sensitivity and very high specificity for IM. Targeted biopsies with image enhanced techniques may be more practical than updated Sydney protocol, especially in a high-risk population. But, in developing and low-risk countries, we can still depend on CWLE and HD-WLE, obtaining biopsies according to the updated Sydney system and targeted biopsies from macroscopic lesions with comparable results with NBI and targeted biopsies.

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