Suez Canal University Medical Journal Vol. 22 (1), 2019
Pages 85-94

Pattern of Endoscopic Esophageal Findings in Relation to Helicobacter Pylori Infection and Histopathology: A Single Center Experience

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Abstract

Background: **Dyspepsia is a common complain among people suffering from gastrointestinal diseases. Few researches investigated the underlying causes in detail. H. Pylori is considered a major finding in patients with dyspepsia and diagnosed with gastrointestinal diseases.** ***Aim:*** **The aim of this study is to determine the pattern of Endoscopic Esophageal lesion in Relation to H. Pylori infection and histopathological features of esophageal and gastric mucosal biopsies in dyspeptic patients eligible for upper GIT Endoscopy.** ***Patients and Methods*****: all the patients presented with dyspeptic symptoms and were eligible for upper GIT endoscopy during the period from January 2016 to January 2019were included (n=60). Using endoscopy, gastric biopsies were taken for H. Pylori examination and esophageal lesions biopsies were taken for histopathological examination (n=120 specimens).** ***Results*****: the prevalence of H. pylori among patients with dyspepsia was 81.7%. The most common endoscopic esophageal pattern with H. pylori was erythema and abnormal vascular pattern (67.3%). Reflux esophagitis was the most common Histopathological finding in H. Pylori positive patients (57.1%). Chronic non-specific esophagitis was higher in H. Pylori negative (9.1%) compared with H. Pylori positive (8.2%). Adenocarcinoma was found in 16.3% of H. Pylori positive patients, however, squamous cell carcinoma was more in H. Pylori negative (27.3%) than H. Pylori positive (6.1%).** ***Conclusion*****: The majority of patient with dyspepsia has H. Pylori infection. Risk factors for malignant esophageal lesions are old age, male gender, smoking and H. pylori infection**

Keywords: esophagitis, Adenocarcinoma, squamous cell carcinoma, Helicobacter pylori

Introduction

The term Dyspepsia is used for acute, chronic, or recurrent pain or discomfort located at the upper abdomen. It may be associated with upper abdominal fullness, early satiety, and bloating, burning, belching, nausea, retching, and vomiting[(1)]. Dyspepsia is described in about 20% of the population globally [(2)] & represents up to 8.3% of all primary care physician visits and causes huge economic costs to patients and to the economy[(3)]. Despite Dyspepsia

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is a common symptom, only 25% of patients with dyspepsia have an organic cause and up to 75% have functional dyspepsia[1]. The underline causes of dyspepsia included major causes as medications, functional dyspepsia, chronic peptic ulcer disease, and malignancy[4]. Other minor causes for dyspepsia include pancreatic disease, hepatobiliary tract disease, motility disorders, infiltrative diseases of the stomach, celiac disease, metabolic disturbances, diabetic neuropathy, and hernia[4]. Researches revealed that 73% of gastroenterologists and 59% of primary care providers are aware with dyspepsia best practices. Although general practioners are the first contact with patients they lack the knowledge and practice to provide adequate treatment and to follow common dyspepsia guidelines[5]. Functional dyspepsia refers to patients with dyspepsia where organic pathology that explains the patient's symptoms has been ruled out by endoscopy and other tests [6]. Researches showed that esophagogastroduodenoscopy (EGD) is the diagnostic procedure of choice to differentiate patients with organic from those with functional dyspepsia[5]. Therefore, Endoscopy alone is insufficient because it may miss serious mucosal lesions in about 15 to 30% of cases that can be picked up later by histological examination. Biopsy is convenient procedure for accurate assessment and diagnosis of premalignant gastric lesions. Moreover, the biopsy is important for identifying and grading various mucosal pathologic lesions[7]. The American Gastroenterological Association (AGA) recommends endoscopy to be done first in patients with alarm signs and in patients >55 years. The AGA identifies alarm signs as unintended weight loss, progressive dysphagia, persistent vomiting, evidence of gastrointestinal bleeding, and family history of cancer. Patients ≤55 years of age without alarm features should be tested and treated for *H. pylori* if the local prevalence of *H. pylori* is high (>20%). Empiric acid suppressive treatments without *H. pylori* testing/treatment are recommended in areas of low prevalence for *H. pylori* (<20%)[8]. Few researches are available regarding esophageal lesions in relation to H.pylori and histopathological changes

Patients and Methods

This study was performed at the pathology department of Kafr El-sheikh general Hospital, Kafr El-sheikh governorate; Egypt; esophageal biopsies were collected from Jan 2016 to Jan 2019. All patients suffering from dyspepsia and eligible for upper GIT endoscopy were included (n=60). Patients with inadequate biopsies were excluded.

Endoscopy

Upper endoscopy was performed by two mentor gastroenterologists in our center. The patients were advised to discontinue any proton pomp inhibitor and antibiotics at least one month prior to endoscopy. After explaining the procedure to the patients, local oropharynx anesthesia with lidocaine 5% and midazolam were applied by a trained nurse. The endoscope was advanced to the second part of duodenum. The esophagus as well as stomach was evaluated carefully and any erythema, erosion, masses and ulcer were reported. Two antral biopsy samples were also taken for H. pylori testing (Presence of H. pylori was identified when rapid urease test or histology was positive). Two biopsy samples were taken from esophageal lesions for histopathological examination; During endoscopy all lesions including erythema, erosions (small superficial defect in mucosa with petechia), atrophies (whitish and thinning mucosa with or without submucosal vascular pattern), ulcer, and mass lesions were noted and biopsy samples were taken. The samples were stored in separate bottles.

Histological Evaluation

Specimen were received in 10% formalin. After adequate period of fixation, the biopsies processed in an automatic processor then embedded in paraffin. 4-5µm thick sections were cut and mounted on slide and stained with Haematoxylin and Eosin (H&E) stain and studied under microscope. All the specimens were examined by an experienced pathologist. According to Sydney System the severity and depth of inflammation were graded as 0-3[11]. Chronic inflammation was considered as the presence of inflammatory cells in lamina propria. Chronic active inflammation was considered as the presence of granulocyte in lamina propria or intraepithelial. The pres sidered as positive H. pylori.*Data collection*

The clinical data as well as upper endo scopic results for each patient enrolled in the study were recorded in each questionnaire. The histopathological data were also collected from pathology reports.

Statistical Analysis

The results were analyzed by SPSS *(version 23.0 SPSS, Chicago, Illinois USA)* software for Windows. Descriptive analysis was used for reporting the prevalence of lesions, sex, and age distributions. The association between clinical and endoscopic data and pathology findings were analyzed by chi-square test. Forward stepwise multivariate logistic regression was also applied for final estimations. P value less than 0.05 was considered as statistically significant

Table 1: Demographic data and medical history of diabetes and hypertension of the studied population

Variables	Frequency	%
**Age Groups*		
– <20 years	3	5.0%
– 20- <30 years	8	13.3%
– 30- <40 years	11	18.3%
– 40- <50 years	11	18.3%
– 50- <60 years	12	20.0%
– 60- <70 years	8	13.3%
– 70- <80 years	5	8.3%
– >80 years	2	3.3%
Gender		
– male	34	56.7%
– female	26	43.3%
Diabetes		
– diabetic	17	28.3%
– non-diabetic	43	71.7%
HTN		
– Yes	12	20.0%
– No	48	80.0%
Smoking state		
– smoker	16	26.7%
– non-smoker	44	73.3%

*Age mean (range)= 45.98±17.1 (15-83)

Results

This study included 60 patients (mean age 45.98±17.1 years). Most of cases were in the age group of 50- <60 years, while the least numbers of participants were in age group of <20 years (5.0%) followed by age group of >80 years (3.3%). More than half of cases were males (56.7%). Only 28.3% of cases were diabetics & 20% were hypertensive. About 26.7% of cases were smokers (Table 1). Regarding the clinical presentation described by the patients, 71.7% of patients complain of heart burn & epigastric pain, while 26.7% of cases complain of dysphagia, epigastric pain, regurgitation, loss of weight & loss of appetite. Only 1 case had dysphagia & loss of appetite (Table 2).

Table 2: Clinical findings among studied patients

	Frequency	Percent
heart burn, epigastric pain	43	71.7%
dysphagia, epigastric pain, regurgitation, loss of weight, loss of appetite	16	26.7%
dysphagia, loss of appetite	1	1.7%

All patients underwent diagnostic endoscopy; nine patterns were described according to the gross appearance as shown in figure 1. The common pattern was erythema and abnormal vascular pattern (66.7%) followed by lower esophageal mass (15%), while the least pattern was "erythema, ulceration and granular mucosa", "middle esophageal mass and gastric subcardial mass", "lower esophageal polyp" and "lower esophageal and gastric mass" While endoscopy, gastric biopsy was taken for H. Pylori testing and esophageal biopsy for histopathological analysis. Based on the histopatholigical appearance, nine histopathological findings were defined as presented in Figure 2. More than half of biopsies were diagnosed as Reflux esophagitis (56.7%). However, malignant changes were found in 16 cases as Adenocarcinoma, squamous cell carcinoma, adenocarcinoma in both stomach and esophagus and Gastrointestinal stromal tumor (13%, 10%, 1.7% & 1.7% respectively).

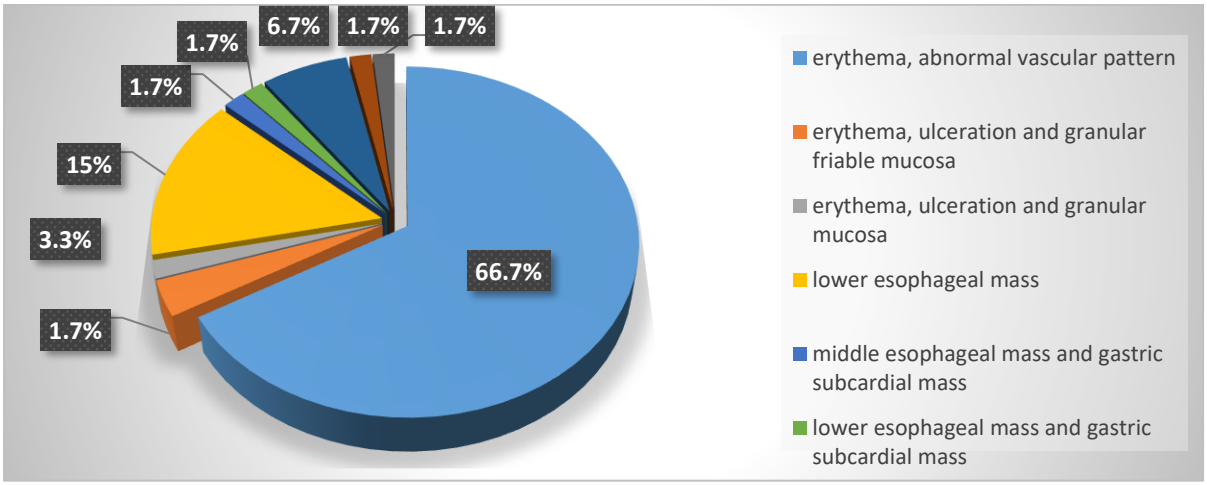

Figure 1: findings of diagnostic endoscopy among studied patients (%)

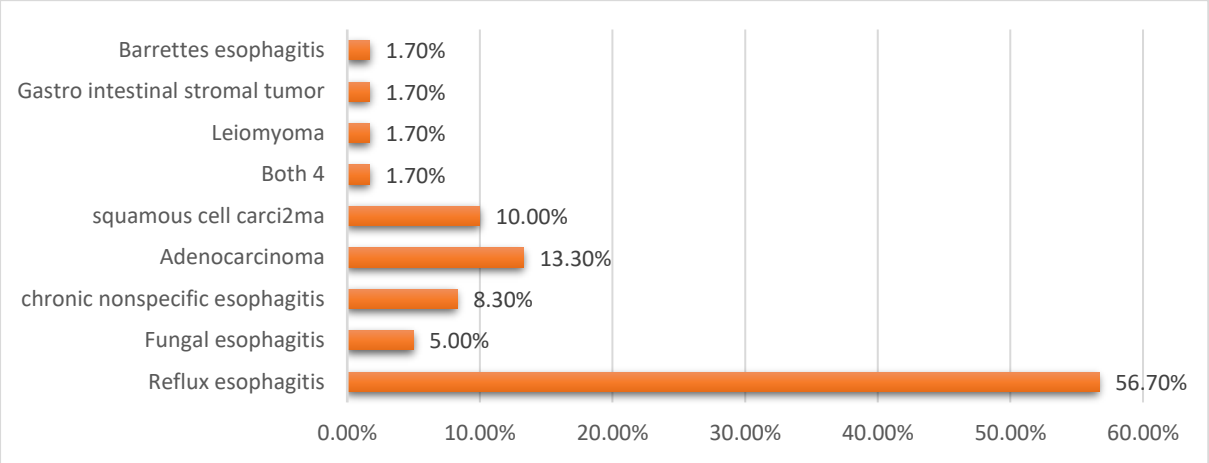

Figure 2: Histopathological findings of the taken specimens (%)

In Both 4, oegophageal adenocarcinoma extended to the stomach. We observed that 31.25% of cases with malignant lesions were in the age group of 60-70 years, followed by the age group 70-80 (18.75%) and age group 40-50 (12.5%). While most of benign esophageal diseases were in the age group of 30-40 (22.7%) and age group 40-50 (20.5%). Patients aged >60 years had a higher percentage of malignant esophageal lesions compared with less age. We also observed that females had a higher percentage for benign esophageal lesions while males had higher percentage for malignant lesions (M: F = 4.33: 1). All cases with malignant lesion were presented with dysphagia, epigastric pain, regurgitation, loss of weight & loss of appetite. However, heart burn & epigastric pain were prominent with benign diseases (97.7%). We also found that half of cases with malignant lesions were smoker. On the other hand, we found that 84.1% of cases with benign diseases had H. pylori positive test, while 75% of patients with malignant lesions were H. pylori positive. From data observed in table 3, we can define risk factors for malignant esophageal lesions namely old age, sex, clinical presentation of the patient. Other less risks factors could be smoking, infection with H. pylori. On comparing variables between whose had benign lesion & whose with malignant lesions, significant statistical deference observed regarding age, Sex, Clinical findings & Endoscopic findings (0.00, 0.02, 0.00 & 0.00 respectively), while no statistical deference were observed regarding diabetes, HTN or Gastric biopsy findings (H. Pylori) (p= 0.114, 0.567 & 0.430 respectively).

Discussion

The term esophagitis refers to an inflammatory condition of the esophageal mucosa, usually associated with characteristic symptoms, such as heartburn, chest pain and dysphagia. Esophagitis one of the most common diseases affecting the upper digestive tract caused mainly by Gastroesophageal reflux disease (GERD)[9]. In fact, the esophageal wall has low defense against gastric acid injury that can induce either erosive or non-erosive esophagitis [10]. Therefore, esophageal mucosa can be damaged by various causative agents as some infectious (e.g., Herpes simplex virus or Candida albicans in patients with a compromised immune system), systemic or chemical conditions (as caustic ingestion of alkaline liquids that results in colliquative necrosis and destruction of mucosa

within a few seconds), an immune-mediated inflammatory disease (as Eosinophilic esophagitis) or drugs (as oncologic chemotherapeutic regimens and radiotherapy)[11]. The aim of this study was to determine the pattern of Endoscopic Esophageal lesion in Relation to H. Pylori infection and histopathological features of esophageal and gastric mucosal biopsies in dyspeptic patients eligible for upper GIT Endoscopy.

Table 3: Comparison between benign and malignant gastric lesions regarding demographic, medical history of diabetes and hypertension and H. Pylori

	Benign		Malignant		t	p
	Frequency	%	Frequency	%		
Age (years)						
– <20	3	6.8%	0	0%		
– 20-30	8	18.2%	0	0%		
– 30-40	10	22.7%	1	6.25%		
– 40-50	9	20.5%	2	12.5%	-4.320	0.00
– 50-60	8	18.2%	4	25%		
– 60-70	3	6.8%	5	31.25%		
– 70-80	2	4.5%	3	18.75%		
– >80	1	2.3%	1	6.25%		
Diabetes						
– Diabetic	10	22.7%	7	43.75%	1.606	0.114
– Non-diabetic	34	77.3%	9	56.25%		
HTN						
– Hypertensive	8	18.2%	4	25%	.576	0.567
– Non	36	81.8%	12	75%		
Gender						
– Male	21	47.7%	13	81.25%	2.388	0.020
– Female	23	52.3%	3	18.75%		
Clinical findings						
– heart burn, epigastric pain	43	97.7%	0	0		
– dysphagia, epigastric pain, regurgitation, loss of weight, loss of appetite	0	0	16	100%	-12.59	0.00
– dysphagia, loss of appetite	1	2.3%	0	0		
Endoscopic findings	44	73.33%	16	26.66%	3.201	0.00
Smoking state						
– Smoker	8	18.2%	8	50%	2.556	0.13
– Non	36	81.8%	8	50%		
Gastric biopsy findings						
– H. pylori negative	7	15.9%	4	25%	.796	0.43
– H. pylori positive	37	84.1%	12	75%		

Regarding histopathological changes, we found that adenocarcinoma and fungal esophagitis was statistically higher in H. Pylori positive patients (0.00, 0.03 respectively) (Table 4). Less than 3 decades ago, Robin Warren and Barry Marshall defini-

tively identified H. pylori by culturing an organism from gastric biopsy specimens that had been visualized for almost a century by pathologists[12]. In the present study, the prevalence of H. pylori among patients with dyspepsia were 81.7%. This was higher than that reported by Alhussaini[14] (71.33%), Roshana et al[15] (68%) and Adlekha et al[16] (62.0%). Egypt is a multiracial country, the different races although living together, have exclusive habits and cultural practices peculiar to their own.

Table 4: Clinical presentation, Endoscopic findings & Histopathological Diagnosis regarding H. Pylori status

		H. pylori negative (n=11) No (%)		H. pylori positive (n=49) No (%)		P
Clinical findings	heart burn, epigastric pain	7	63.6%	36	73.5%	0.012
	dysphagia, epigastric pain, regurgitation, loss of weight, loss of appetite	4	36.%4	12	24. 5%	0.02
	dysphagia, loss of appetite	0	0	1	2.0%	0.524
Endoscopic findings	erythema, abnormal vascular pattern	7	63%.6	33	67.3%	0.001
	erythema, ulceration and granular friable mucosa	0	0	2	4.1%	0.06
	erythema, ulceration and granular mucosa	0	0	1	2.0%	0.54
	lower esophageal mass	3	27.3%	6	12.2%	0.62
	middle esophageal mass and gastric subcardial mass	0	0	1	2.0%	0.21
	lower esophageal mass and gastric subcardial mass	0	0	1	2.0%	0.14
	upper esophageal mass	1	9.1%	3	6.1%	0.01
	lower esophageal polyp	0	0	1	2.0%	0.07
	lower esophageal and gastric mass	0	0	1	2.0%	0.09
Histopatho-logical Diagnosis	Reflux esophagitis	6	54.5%	28	57.1%	0.211
	Fungal esophagitis	0	0.0%	3	6.1%	0.03
	chronic nonspecific esophagitis	1	9.1%	4	8.2%	0.01
	Adenocarcinoma	0	0	8	16.3%	0.00
	squamous cell carcinoma	3	27.3%	3	6.1%	0.415
	Upper & lower esophageal carcinoma	0	0	1	2.0%	0.02
	leiomyoma	0	0	1	2.0%	0.62
	Gastrointestinal stromal tumor	1	9.1%	0	0	0.321
	Barrettes esophagitis	0	0	1	2.0%	0.26

This made it appealing to study the prevalence of H. pylori infection and its distribution among the various ethnic groups in this country. Regarding histopathological changes, we found that adenocarcinoma and fungal esophagitis was statistically higher in H Pylori positive patients (0.00, 0.03 respectively). In 1994, H. pylori was recognized as a type I carcinogen, and now it is considered the most common etiologic agent of infection-related cancers, which represent 5.5% of the global cancer burden[13]. In our study, no difference regarding reflux sophagitis found between both H.Pylori positive and negative patients. This agree with most trials on the correlation between H. pylori infection and GERD which indicated no causal relationship [18, 22-24].H. pylori could contribute to many gastrointestinal diseases including GERD but

The role of H. pylori in developing GERD still remains a controversial issue [18, 19] and the rate of H. pylori infection in patients with GERD, wildly varies from 30-90% and it seems in some studies that about 40% of patients with GERD are infected by this bacterium[20,21]. In Helicobacter pylori infected group, we found that 73.5% of patients compliant of heart burn & epigastric pain, while less than one quarter of patients complain of dysphagia, epigastric pain, regurgitation, loss of weight & loss of appetite. It is well known that in most persons, H. pylori colonization does not cause any symptoms. However, long-term carriage of H. pylori significantly increases the risk of developing site-specific diseases[17]. It has to be reminded that our country is considered as a high prevalence area of H. pylori infection, which in turn it is not easy to exclude H. pylori factors in evaluation of patients with reflux disease. In the present study 81.7% of the patients had positive histopathological findings in esophageal biopsies associated with the dyspeptic symptoms. This finding is matching with the results reported by Dawod & Emara[4] and Nwokediuko & Okafor[27] who reported that only 29.3% of patients with functional dyspepsia had normal histology of gastric biopsies by histological examination. Nine endoscopic esophageal lesion patterns was observed in the stuied populations which are: erythema, abnormal vascular pattern (40 cases, 66.7%), erythema, ulceration and granular friable mucosa (2 cases, 3.3%), erythema, ulceration and granular mucosa (1 case, 1.7%), lower esophageal mass (9 cases, 15.0%), middle esophageal mass and gastric subcardial mass (1 cases, 1.7%), lower esophageal mass and gastric subcardial mass (1 cases, 1.7%), upper esophageal mass (4 cases, 6.7%), lower esophageal polyp (1 case, 1.7%) & lower esophageal and gastric mass (1 cases, 1.7%).In patients with Helicobacter pylori, the most common erythema and abnormal vascular pattern (67.3%) followed by lower esophageal mass (12.2%) & upper esophageal mass (6.1%). On the other hand, in patients with H. Pylori negative test, the prevalence of erythema and abnormal vascular pattern was slightly lower than H. Pylori positive (63%). lower & upper esophageal mass were higher that H. Pylori positive (27.3% & 9.1% *vs.* 12.2% 6.1%). Chronic nonspecific esophagitis was higher in H. pylori infection (4 cases *vs.* 1 case), however, our observation was less than reported by Hosam et al.[4] who found that chronic inflammation was present in 65.7% of patients with dyspepsia and was higher than that of H. pylori infections (51.4%). Regarding the Histopathological Diagnosis, the most common finding was Reflux esophagitis in 57.1% of H. Pylori positive patients. Chronic nonspecific esophagitis was higher in H. Pylori negative (9.1%) than H. Pylori positive (8.2%). We also observed that 56.7% of cases had Reflux esophagitis, 5.0% Fungal esophagitis, While Barrettes esophagitis was observed only in H. Pylori positive (2.0%). This could be explained by the presence of other causes of inflammation than H. pylori or previous ingestion of antibiotics, which are known to suppress the H. pylori infection with a slow disappearance of chronic inflammatory cells [28]. We found that adenocarcinoma was statistically higher in H Pylori positive patients16.3% (p value 0.00) which was higher than reported by Uemura et al. [29] who reported that gastric cancer developed in approximately 3% of H. pylori-infected patients, compared to none of the uninfected patients. Helicobacter pylori (H. pylori) plays a predominant role in the aetiology of GC and was characterised as a class I carcinogen by the World Health Organisation in 1994 [30]. However, other malignant lesions, we observed that squamous cell carcinoma was more in H. Pylori negative (27.3%) than H. Pylori positive (6.1%), the difference was not statistically significant

(p=0.415). Other observation was gastro intestinal stromal tumor were observed in H. Pylori negative (1 case 9.1%) while no cases were reported in H. Pylori positive. One case of in H. Pylori positive patients had Leiomyoma (2.0%). We found also only one patient has adenocarcinoma in the stomach and esophageus this may explained by that in some patients H. pylori is primarily colonized in the antrum, resulting in an antral predominant gastritis which may extend to the esophageus [25,26]. In this study we found that Risk factors for malignant esophageal lesions are old age, male six, smoking and H. pylori infection this agree with Pelayo & Blanca[31] who found that This tumor type shows a male predominance (male/female ratio of 2:1) and most cases are diagnosed during the sixth to eight decades of life.

Conclusion

H. pylori is associated with dyspepsia and increased risk for esophageal tumors, however not all cases with esophagitis are caused by H. pylori infection. Further large studies are needed to clarify H. pylori relation to esophageal malignancy

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