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ORIGINAL ARTICLE

Observational Study

Performance of American Society for Gastrointestinal Endoscopy guidelines for dyspepsia in Saudi population: Prospective observational study

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Abstract

AIM: To evaluate adherence of primary care physicians (PCPs) to international guidelines when referring patients for upper-gastrointestinal endoscopy (UGE), evaluate the importance of alarm symptoms and the performance of the American Society for Gastrointestinal Endoscopy (ASGE) guidelines in a Saudi population.

METHODS: A prospective, observational cross-sectional study on dyspeptic patients undergoing UGE who were referred by PCPs over a 4 mo period. Refer-rals were classified as appropriate or inappropriate according to adherence to ASGE guidelines.

RESULTS: Total of 221 dyspeptic patients was enrolled; 161 patients met our inclusion criteria. Mean age was 40.3 years (SD ± 18.1). Females comprised 70.1%. Alarm symptoms included low hemoglobin level (39%), weight loss (18%), vomiting (16%), loss of appetite (16%), difficulty swallowing (3%), and gastrointestinal bleeding (3%). Abnormal endoscopy findings included gastritis (52%), duodenitis (10%), hiatus hernia (7.8%), features suggestive of celiac disease (6.5%), ulcers (3.9%), malignancy (2.6%) and gastroesophageal reflux disease (GERD: 17%). Among patients who underwent UGE, 63% met ASGE guidelines, and 50% had abnormal endoscopic findings. Endoscopy was not indicated in remaining 37% of patients. Among the latter group, endoscopy was normal in 54% of patients. There was no difference in proportion of abnormal endoscopic findings between two groups (P = 0.639).

CONCLUSION: Dyspeptic patients had a low prevalence of important endoscopic lesions, and none of the alarm symptoms could significantly predict abnormal

endoscopic findings.

Key words: Dyspepsia; Primary care physician; American Society for Gastrointestinal Endoscopy guideline; Upper gastrointestinal endoscopy; Saudi population

Core tip: A prospective study looking at the practice of primary care physicians in referring dyspeptic patients for endoscopy in Saudi Arabia, such study is the first prospective study to evaluate such practice in high *Helicobacter pylori* endemic area and the adherence of general practitioners to the international guidelines for a common gastroenterology disorder, and this will shed light on the approach for such disease.

Azzam NA, Almadi MA, Alamar HH, Almalki LA, Alrashedi RN, Alghamdi RS, Al-hamoudi W. Performance of American Society for Gastrointestinal Endoscopy guidelines for dyspepsia in Saudi population: Prospective observational study. *World J Gastroenterol* 2015; 21(2): 637-643 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i2/637.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i2.637

INTRODUCTION

Dyspepsia is a complex condition comprising a spectrum of chronic and recurrent symptoms related to the upper gastrointestinal tract. The cardinal symptoms are epigastric pain, discomfort, including postprandial fullness and early satiety, which may overlap with heartburn and regurgitation[1]. These symptoms could be the result of underlying organic pathology, such as chronic peptic ulcer disease, gastro-esophageal reflux or malignancy (organic dyspepsia). Dyspepsia can also present without evidence of organic cause (functional dyspepsia). Dyspepsia is a common condition that affects up to 80% of the population at some point during an individual's lifetime[2]. Multiple studies have shown that the condition is experienced by approximately 20%-40% of the general adult population and accounts for 3%-4% of all consultations in primary care[3-5]. In Western countries, studies have suggested that dyspepsia affects approximately a one-fourth of the population[6,7]. In Japan, India, and Turkey, the prevalence of dyspepsia has been estimated to be 17%, 30.4%, and 28.4%, respectively[8-10].

Dyspepsia is the most common indication for upper gastrointestinal endoscopy (UGE)[11-13]. It has been estimated that approximately 50% of all UGE referrals are dyspepsia related[14]. In approximately half of all dyspeptic cases, the endoscopic investigation reveals no underlying organic lesion[15-17].

The overwhelming number of dyspeptic patients referred for UGE has led to prolonged waiting times for endoscopic procedures, especially in the setting of open-access endoscopy units that allow general practitioners to request an endoscopic procedure without referral to a specialist. Concerns include the high cost, unnecessary burden on available resources and long waiting lists[18]. To reduce these problems and increase the effectiveness of endoscopy, adherence to treatment guidelines has been recommended[19,20]. Despite variability in composition, the recommendations of the majority of the guidelines are similar[21]. All suggest that dyspeptic patients who are over the age of 50 years and/or those with alarm symptoms at any age need urgent referral for endoscopy as an initial management strategy because endoscopy would change the management of this subset of patients[22-24]. In young patients without alarm symptoms, however, either a "test or treat" for *Helicobacter pylori* (*H. pylori*) in high-prevalence areas or an empirical acid-suppression trial are the initial management strategies of choice[24]. Saudi Arabia is considered to be a high prevalence area and estimated to be around 50%[25].

At King Khalid University Hospital (KKUH), the endoscopy unit is an open-access unit that receives a large number of referrals from various general and specialty clinics and from in-patient wards. Annually, more than eight thousand procedures are completed in the unit. The most common indication for UGE is dyspepsia, accounting for thousands of referrals, with approximately 50% from the primary care clinics[26]. This creates a significant burden on the allocated resources and negatively impacts waiting times. In this prospective study, we aimed to evaluate the adherence of primary care physicians (PCPs) to dyspepsia guidelines, to describe the common endoscopic findings, to evaluate the importance of "red flag" symptoms and to estimate the prevalence of *H. pylori* in dyspeptic patients. To our knowledge, this is the first study to evaluate such practices in an *H. pylori* high-prevalence region.

MATERIALS AND METHODS

Prospective, cross-sectional study on dyspeptic patients undergoing UGE in an open-access endoscopy unit was conducted. Data on all adult patients referred from PCPs to the Endoscopy Unit at KKUH, Riyadh, KSA, were prospectively collected over a period of 4 mo, starting from December 2012 and ending in April 2013. Dyspepsia was defined as chronic and recurrent epigastric pain or discomfort (including postprandial fullness and early satiety) with or without heartburn and regurgitation. Patients who had gastroesophageal reflux disease (GERD) -predominant symptoms such as heartburn or acid regurgitation alone, inflammatory bowel disease, a previously diagnosed malignancy or advanced liver disease were excluded from the study.

Upon presentation to the endoscopy unit, all patients who met our inclusion criteria were enrolled in the study and provided informed consent. The participants were interviewed by an endoscopist using a pre-designed data collection sheet (Table 1).

Table 1 Study variables

Variable	Description
Age	< 50 yr of age
	⩾ 50 yr of age
Gender	Male or female
Alarm symptoms	Anemia
	Hemoglobin level
	Male: < 13 g/dL
	Female: < 12 g/dL
	Weight loss of more than 4 kg
	Vomiting
	Loss of appetite
	Dysphagia
	Gastrointestinal bleeding
	Palpable abdominal mass
Other independent variables	Smoking
	Use of NSAID
	History of *Helicobacter pylori* treatment

NSAID: Non-steroidal anti-inflammatory medications.

Endoscopic findings were noted, and gastric biopsies were obtained to rule out *H. pylori* by utilizing the rapid urease test (Lencomm trade international, Poland). The biopsy samples were inoculated immediately into the rapid urease test gel. If the gel color changed within 20 min up to a maximum of 60 min the sample was considered positive for *H. pylori*.

Referrals were classified as appropriate or inappropriate according to adherence to ASGE guidelines. These included patients over the age of 50 years or those that presented with alarm symptoms at any age. Alarm symptoms included anemia, vomiting, loss of appetite, weight loss, gastrointestinal bleeding, dysphagia or the presence of a palpable abdominal mass. The endoscopic findings were categorized as normal or abnormal. Abnormal findings included gastritis, duodenitis, peptic ulcer, varices, features of celiac disease, hiatus hernia malignancy and others. Endoscopic findings were defined as important if the abnormalities included gastric or duodenal ulcers, varices, duodenitis, adenomatous polyps or malignancy[3].

Statistical analysis

Sample size calculation: Based on an *a priori* baseline prevalence of abnormal findings on endoscopy of 60%[25], Using the rule of 10 outcome events per predictor variable, and given we wished to include up to 9 variables in our multivariable model, we estimated that 150 individuals would be needed to provide sufficient accuracy within the multivariable analysis.

Data analysis: included descriptive statistics computed for continuous variables, including means, SD, minimum and maximum values, as well as 95%CI. Frequencies are used for categorical variables. We used hypothesis testing, the *t* test with unequal variances, as well as Fisher's exact test where appropriate.

Univariable and multivariable logistic regressions were used to examine the association between independent variables and the dependent variable the presence of an abnormality at endoscopy. Independent variables included; age, gender, smoking status, the use of non-steroidal anti-inflammatory medications (NSAIDs), history of weight loss, vomiting, loss of appetite, dysphagia, gastrointestinal bleeding, history of prior endoscopy, as well as the patients hemoglobin level as well as if they were infected with *H. pylori*. OR and 95%CI were calculated. Characteristics of test procedure (sensitivity, specificity) were used to evaluate the performance of the latest ASGE guidelines in detecting abnormalities on endoscopy.

We used the software STATA 11.2 (Stata Corp, TX, United States) in our analysis. A statistical significance threshold of $P = 0.05$ was adopted. No attempt at imputation was made for missing data.

RESULTS

A total of 221 patients were screened and 161 patients met our inclusion criteria. The mean age was 40.3 years (SD ± 18.1), and age ranged from 18 years to 98 years. Females represented 70.1% of the patients, while males represented 29.9%. The proportion of patients with alarm symptoms in our study was 39%; 39% had a low hemoglobin level, 18% had weight loss, 16% had vomiting, 16% had loss of appetite, 3% had difficulty in swallowing, 3% had gastrointestinal bleeding, and 2% had an epigastric mass on physical examination (Table 2). At least one alarm feature was observed in 79.4% of the females, and one alarm feature was observed in only 20.6% of the males (*P* value < 0.01). A proportion of the patients included in the study had incurred prior endoscopic procedures (29%); 60% of those had one prior endoscopy, 20% had two prior endoscopies, 6% had 3 prior endoscopies, and 12% had 4 previous endoscopies.

The mean hemoglobin level was 12.89 ± 0.17 g/dL.

According to the ASGE guidelines, 63% of the endoscopies were considered to be indicated; the results were abnormal in 50%, while 50% were normal.

Although 37% of the endoscopies were considered inappropriate, 54% had abnormal findings. There was no difference in the proportion of abnormal endoscopic findings between the two groups ($P = 0.639$; Table 3).

The most common endoscopic findings were gastritis in 52%, duodenitis in 10%, hiatus hernia in 7.8%, ulcers in 3.9% and malignancy in 2.6% of the patients; the remaining 17% were found to have reflux esophagitis signifying GERD. Furthermore, 6.5% had endoscopic features suggestive of celiac disease (Figure 1).

The rapid urease test was positive in 22% of the patients. The majority (62%) of those was younger than 50 years of age, and 20% had a history of receiving eradication therapy for *H. pylori*.

All procedures were completed successfully, and no adverse events occurred.

Table 2 Clinical characteristics of patients stratified by presence and absence of the normal and abnormal endoscopic finding as well as univariable analysis of all corresponding variables

Characteristics	Percentage of patients	Normal	Abnormal	*P* value	Univariable analysis OR (95%CI)
Female	70.1%	53%	47%	0.399	0.7 (0.37-1.47)
Male	29.9%	45%	55%	0.711	1.02 (0.97-1.56)
Age ⩾ 50	29%	60%	40%	0.094	1.01 (0.99-1.04)
Smoker	12%	42%	58%	0.671	1.49 (0.56-3.94)
Taking NSAID	14%	35%	65%	0.094	2.16 (0.86-5.44)
Vomiting	18%	47%	53%	0.285	1.25 (0.54-2.91)
Prior endoscopy	29%	38%	62%	0.039	2.06 (1.02-4.13)
Weight loss	16%	46%	54%	0.283	1.2 5(0.54-2.91)
Loss of appetite	16%	46%	54%	0.283	1.25 (0.54-2.91)
Dysphagia	3%	20%	80%	0.161	4.32 (0.47-39.52)
GI bleeding	3%	20%	80%	0.161	4.32 (0.47-39.52)
Epigastric mass	2%	0%	100%	0.075	
Low Hb	39%	41%	59%	0.245	1.08 (0.94-1.25)
Presence of *H. pylori*	22%	36%	64%	0.044	2.2 (1.01-4.87)

H. pylori: *Heliobacter pylori*; GI: Gastrointestinal; NSAID: Non-steroidal anti-inflammatory medications.

Table 3 Findings of endoscopy according to American Society for Gastrointestinal Endoscopy guidelines

Endoscopy finding	ASGE indicated (63%)	ASGE not indicated (37%)	*P* value
Normal	50%	54%	
Abnormal	50%	46%	0.6390
Important endoscopic finding	8%	3%	0.7806

ASGE: American Society for Gastrointestinal Endoscopy.

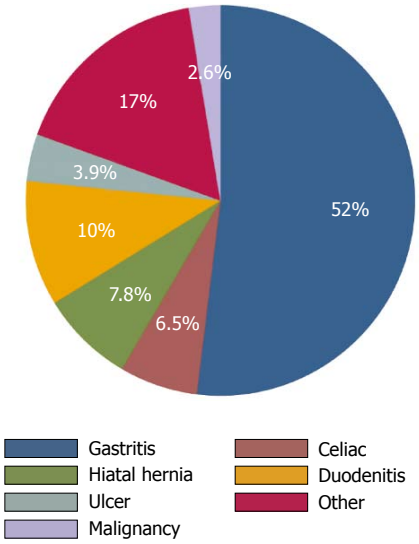

Figure 1 The distribution of abnormal endoscopic finding for the cohort.

Univariable and multivariable analysis

The only factors associated with the presence abnormal endoscopy on univariable analysis were *H. pylori* OR = 2.2 (95%CI: 1.01-4.87) and having undergone a previous endoscopy OR = 2.0 (95%CI: 1.02-4.13).

Using stepwise multivariable logistic regression, none of the variables included in the study could predict the finding of abnormalities at the time of endoscopy.

DISCUSSION

This prospective observational study found that overuse of upper gastrointestinal endoscopy is common in dyspeptic patients, between 25% and 40% of individuals with dyspepsia will consult a PCP as a result of their symptoms[27]. With such high prevalence, dyspepsia is a diagnostic and therapeutic challenge to physicians. Furthermore, most patients with dyspepsia have no detectable organic abnormality[22,28].Thus, endoscopic evaluation as an initial step in management is not recommended[9,29]. Endoscopic evaluation is recommended for older patients (older than 50 years), those with alarm symptoms, those taking NSAID, and those with persistent symptoms after acid suppression therapy and/or *H. pylori* eradication[18,30].

We found that approximately 40% of the patients complaining of upper abdominal symptoms had a normal finding according to the dyspepsia guidelines[20]. The specialty of the referring physicians affects the presumed etiology of upper gastrointestinal symptoms. The sensitivity and specificity for the diagnosis of functional dyspepsia was 61% and 84% for PCPs, respectively, while it was 73% and 37% for gastroenterologists, respectively[31]. In a large Canadian study, 1040 patients were evaluated for symptoms and underwent endoscopy within 10 d of referral. In this study, the predominant symptom was not predictive of the endoscopic findings, and the presence of alarm symptoms did not correlate with the demonstration of clinically significant endoscopic findings[16]. Another study evaluated alarm symptoms in functional dyspepsia and concluded that the value of symptoms in diagnosing functional dyspepsia was poor[32]. These data suggest that these symptoms are of limited value in the assessment of dyspepsia.

Our study confirmed that the majority of patients

with dyspepsia referred by PCPs had no important endoscopic lesion; approximately 40% were not indicated per the guidelines. Endoscopic abnormalities were found in only 48% of the patients; the majority had nonspecific gastritis, while important findings were observed in approximately 6%, with 2.6% of these patients having gastrointestinal malignancy. These results were similar to the findings of Choomsri *et al*[33] in which only important endoscopic lesions were found in 7% of the patients in the form of gastric ulcers and only 1% had gastric cancer. Moreover, in the present study, there were no clinical data such as age, smoking, NSAID use or alarm symptoms that could be used to predict the presence of important endoscopic lesions. This is in agreement with studies that found a poor positive predictive value for these symptoms[34,35]. It is thought that the presence of these alarm features are often indicative of advanced disease[36] and carry low diagnostic yield[37].

In young patients with uncomplicated dyspepsia, either a "test and treat" for *H. pylori* approach[38] or an empirical acid-suppression trial are recommended as first-line management strategies by most guidelines[20,39], depending on the prevalence of *H. pylori*.

The prevalence of *H. pylori* in the present study was 22%, and the majority of these patients were younger than 50 years (62%). Of interest, 20% of those testing positive for *H. pylori* had a previous history of receiving eradication therapy for *H. pylori*.

Abnormal endoscopic finding with important lesions were observed in only a small proportion of our study population, which is similar to a previous report[40]. The most cost-effective strategy in treating *H. pylori* is either empirical treatment or employment of a "test or treat" approach with consideration of endoscopy in a stepwise manner in dyspeptic patients, especially with the absence of alarm symptoms[41]. There is low prevalence of important endoscopic findings in *H. pylori* dyspeptic patients; therefore, a noninvasive method for diagnosing *H. pylori* would be the best modality rather than UGE because endoscopy remains a relatively expensive procedure and UGE is an invasive procedure that carries the risk of potential complications that may have grave consequences that exceed its benefit[42]. In our study, the presence of *H. pylori* was one of the predictors of an abnormal endoscopic finding. This has not been the case, however, according to multivariable analysis, which suggests the presence of an unmeasured confounder.

Gastroenterologists were found to be more likely than PCPs to comply with best practices for dyspepsia diagnosis and treatment, which could be due to PCPs having more concerns regarding long-term proton pump inhibitor use, which affects therapeutic decision making[26,43]. Studies showed an overall low dyspepsia guidelines compliance and such practice was observed in both developed and developing countries[25,33,40,43]. It is important to identify areas of disconnect between the guidelines and practices and to understand the predictors of low guideline compliance, which needs further studies employing larger populations.

The limitations of the present study included a relatively small sample size and the small number of important endoscopic lesions that were found, resulting in a low power to detect any clinically significant differences. Nonetheless, this study is one of the first prospective studies to address the appropriateness and diagnostic yield of endoscopy and adherence of PCPs to the international guidelines for dyspeptic patients in our region. We clearly demonstrate in this study the importance on adhering to the International dyspepsia guidelines when performing upper gastrointestinal endoscopy. We also believe that our hospital practices shed light on the medical approaches in our country that necessitate further studies. We, therefore advise the general practitioners to adopt these guidelines when evaluating patients with dyspepsia. Such practice would avoid unnecessary procedures and will result in an efficient utilization of resources.

In conclusion, the findings of the present study support selective UGE in patients with dyspepsia; a large number of UGE procedures in dyspeptic patients could be avoided. Further studies are needed to find prognostic markers for the abnormal findings in our patient population.

COMMENTS

Background

It's a prospective study looking at the practice of primary care physicians in referring dyspeptic patients for endoscopy in Saudi Arabia, such study is the first prospective study to evaluate such practice in high *Helicobacter pylori* endemic area and the adherence of general practitioners to the international guidelines for a common gastroenterology disorder, and this will shed light on the approach for such disease.

Research frontiers

To evaluate the adherence of primary care physicians to international guidelines when referring patients for upper-gastrointestinal endoscopy, describe the most common endoscopic findings, evaluate the importance of alarm symptoms and the performance of the American Society for Gastrointestinal Endoscopy (ASGE) guidelines in a Saudi population.

Innovations and breakthroughs

It's a first of its kind prospective study looking at the practice of primary care physicians in referring dyspeptic patients for endoscopy in Saudi Arabia, such study might change the current practice of referring system for dyspeptic patients for upper gastrointestinal (GI) endoscopy, especially those with no alarming symptoms.

Applications

This proposal might change the current practice of referring system for dyspeptic patients for upper GI endoscopy, especially those with no alarming symptoms.

Peer review

In this study, the authors have tried to demonstrate factors related to the positive endoscopic findings based on the ASGE guideline/ Study design is nice and analysis is clear. Their results should be useful for the general readers.

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