



Research Article

UNINVESTIGATED DYSPEPSIA ENDOSCOPIC EVALUATION

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ABSTRACT

Background: Dyspepsia is a frequent syndrome in our country, where there are restrictions to endoscopy and high prevalence of Helicobacter pylori (H. pylori) infection. The age indication for endoscopy has not been determined in our country. Establishment of this procedure for every dyspeptic patient may not be practical or cost effective.

Aim: To assess the endoscopic findings in uninvestigated dyspepsia syndrome, in tertiary care hospital of southern India.

Methods: Patients with uninvestigated dyspepsia, as per ROME III criteria, were screened from outpatients of gastroenterology department where they underwent esophagogastroduodenoscopy (OGD). Rapid Urease Test (RUT) was done in selected cases. Organic dyspepsia findings were analysed with different variables to verify statistically significant associations.

Results: Out of 516 patients enrolled, 500 patients underwent OGD. The mean age was 40 years and women comprised 63% of the sample. Functional dyspepsia was found in 61% and organic dyspepsia in 39%. Among organic dyspepsia, 18% had erosive oesophagitis and 13% had peptic ulcers. 21(4.2%) cases had gastric adenocarcinoma, 8(1.6%) had adenocarcinoma esophagus, 8 cases of carcinoma had no alarm symptoms. Prevalence of H. pylori is 39%.

Conclusions: Endoscopy in uninvestigated dyspepsia showed predominance of functional disease, whereas cancer is not an uncommon finding. Organic dyspepsia was associated with H pylori infection, age, male and smoking status.

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INTRODUCTION

The introduction of increasingly complex procedures in the health sector makes it necessary not only to evaluate the efficacy and cost of procedures, but also its appropriateness in the clinical setting in question. In the specialty of gastroenterology, the problem of appropriateness is particularly perceived with regard to the use of upper gastrointestinal (GI) endoscopy, because of the open access to its application all over the world. To deal with this problem, guidelines have been drawn by various associations to make the use of upper GI endoscopy more rational. The appropriation of the procedure in a clinical setting, though established in the USA and the UK where an early upper GI endoscopy is done for those above the age of 45 years, may not hold true for a distinct south Asian population. Guidelines are not yet available for our population. Dyspepsia is a prevalent complaint in general practice and gastrointestinal clinics [1-3].

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Dyspepsia represents upto 8.3% of all primary care physician visits and causes huge economic costs to patients and to the economy [4]. Rome III guideline states that dyspepsia is non-reflux predominant pain or discomfort in the upper abdomen and the patients must also have one or more of the following four symptoms: postprandial fullness, early satiation, Epigastric pain and epigastric burning. Symptom onset must have occurred at least six months prior to diagnosis [5]. Only 75% of the dyspepsia experts, 73% of gastroenterologists and 59% of primary care providers adhere to dyspepsia best practices; so “dyspepsia” means different things to different providers.

Because structural upper gastrointestinal (UGI) tract diseases, such as peptic ulcer, erosive esophagitis, luminal strictures and malignancy can course with dyspepsia, upper gastrointestinal (GI) endoscopy is the diagnostic procedure of choice to differentiate patients with organic disease from those with functional dyspepsia [06]. Although it is possible to propose endoscopy as the initial strategy for dyspepsia [07], the establishment of this procedure for every dyspeptic patient may not be practical approach, as the high prevalence of the syndrome will result in very high costs to any health system

[08]. Thus, the use of endoscopy in the management of uninvestigated dyspepsia remains a controversial issue worldwide [06]. With this background, a cross-sectional and prospective study was undertaken to assess the endoscopic findings in uninvestigated dyspepsia syndrome, in tertiary care hospital of southern India.

METHODS

This prospective observational study was carried from November 2016 to October 2017. Patients with dyspepsia, attending the outpatient clinic of the medical gastroenterology department of a large tertiary care referral centre in south India, were requested for their clinical history and subjected to a systematic examination and an upper GI endoscopy. The demographic data was recorded on a proforma. The patients were interviewed to determine the presence of alarm symptoms, including unintended weight loss (defined as decrease of more than 5% of original body weight in three months), symptoms suggestive of upper gastrointestinal bleeding and dysphagia. Older age, presence of mass or lymphadenopathy and family history of upper gastrointestinal cancer were not included as alarm characteristics. The upper digestive endoscopy was carried out with a standard electronic video endoscope by two experienced endoscopists, no later than 20 days after the interview, to allow time for the symptomatic use of antacids. H. pylori determination was performed by the Rapid Urease Test, validated in our country. Exclusion criteria included presence of systemic decompensated disease (congestive heart failure, coronary heart disease, liver failure, diabetes mellitus, thyroid disease, acute or chronic respiratory failure, haematological diseases), presence of major psychiatric disorders, impediment to endoscopy and difficulty for the patient to understand the aims and procedures of the study. Ethical committee approval taken and written informed consent was obtained from the patients prior to study participation.

Statistical analysis

Variables were measured as frequency and percentage and the association between organic dyspeptic findings and the variables was determined by chi square test, with a p value < 0.05 being considered statistically significant. Organic dyspeptic findings were analysed with the variables by simple and multiple binary logistic regressions and then odd ratios and its 95% confidence intervals were presented.

RESULTS

516 cases were enrolled for study from 15 to 80 years of age, among these 500 had undergone endoscopy. 16 cases were dropped due to lost to follow up, regularly taking PPI even 1 day before procedure, not willing for endoscopy. Patient demographic data are shown in **Table 1** and symptoms are listed in **Table 2**.

Table 1 Demographic information of study population

Patients included	516
Endoscopies performed	500 (96.8%)
Age-mean years	40
Range (age in year)	15-80
Age > 45 years	210 (42%)
Male gender	185 (37%)
Smokers	80 (16%)

Table 2 Description of the symptoms

Symptoms onset	
6 to 11 months	266 (51%)
1 to 5 years	170 (33%)
More than 5 years	77 (16%)
Type of symptoms	
Epigastric pain	196 (38%)
Epigastric burning sensation	154 (30%)
Post-prandial fullness	139 (27%)
Early satiety	26 (5%)
Alarm symptoms	206 (40%)
Weight loss	185 (36%)
Melena	21 (4%)

Table 3 General endoscopic findings

Functional dyspepsia	305 (61%)
Normal	75 (15%)
Gastritis	230 (46%)
Antral	130 (26%)
Pangastritis	100 (20%)
Organic dyspepsia	195 (39%)
Reflux esophagitis	90 (18%)
Peptic ulcer	65 (13%)
Gastric	20 (4%)
Duodenal	45 (9%)
Malignancy	31 (6.2%)
Gastric adenocarcinoma	21 (4.2%)
OG Junction malignancy	8 (1.6%)
Gastric lymphoma	2 (0.4%)
Other rare causes	9 (1.8%)
oesophageal candidiasis	2 (0.4%)
eosinophilic oesophagitis	2 (0.4%)
ascariasis	2 (0.4%)
NET of stomach	1 (0.2%)
GIST	1 (0.2%)
groove pancreatitis	1 (0.2%)
Positive H. pylori	195 (39%)

Functional dyspepsia was present in 305 (61%) of cases. Out of these 75 (15%) patients have normal endoscopic finding. 230 (46%) had gastritis which included pangastritis in 20% and antral gastritis in 26% of cases. A total of 195 (39%) patients had organic dyspepsia which included reflux oesophagitis in 90 (18%) and peptic ulcer in 65 (13%) of cases. There were 31 (6.2%) cases of upper gastrointestinal cancer (21 gastric carcinomas, 8 oesophageal adenocarcinomas and 1 gastric lymphoma) in studied population, as shown in (Table 3). Reflux disease included cases of erosive esophagitis, Barrett's esophagus and oesophageal ulcer. Other rare causes of organic dyspepsia accounts for 1.8% of cases which include oesophageal candidiasis, eosinophilic oesophagitis, ascariasis, NET of stomach, GIST and groove pancreatitis. The prevalence of H. Pylori infection in our study population is 39%. The coefficients of unilogistic regression of smoking with organic dyspepsia shown in **table 4**, which shows total 80 patients were smokers, among then 95.0% had organic dyspepsia. The coefficients of uni logistic regression of age with organic dyspepsia shown in **table 5**, which shows total 210 patients had age more than 45 years, among then 91.9% had organic dyspepsia. **Table 6**, which shows Uni Logistic Regression Analysis of SEX with organic dyspepsia shows that among 335 females, only 11.9% had organic dyspepsia. It showed that functional dyspepsia is more prevalent in females. **Table 7** showed Uni Logistic Regression Analysis of H. Pylori infection with organic dyspepsia. **Table 8** showed Multiple Logistic Regression Analysis of age, smoking, sex and H. Pylori infection. Both smoking status and age more than 45 years shows significant relationship with organic dyspepsia.

Table 4 Uni Logistic Regression Analysis of smoking with organic dyspepsia

		Organic dyspepsia		Total	
		Present	Absent		
Smoking	Yes	Count	76	4	80
		% within Smoking	95.0%	5.0%	100.0%
	No	Count	119	301	420
		% within Smoking	28.3%	71.7%	100.0%
Total		Count	195	305	500
		% within Smoking	39.0%	61.0%	100.0%

Table 5 Uni Logistic Regression Analysis of AGE with organic dyspepsia

		Organic dyspepsia		Total	
		Present	Absent		
Age	> 45 Years	Count	193	17	210
		% within Age	91.9%	8.1%	100.0%
	<= 45 Years	Count	2	288	290
		% within Age	.7%	99.3%	100.0%
Total		Count	195	305	500
		% within Age	39.0%	61.0%	100.0%

Table 6 Uni Logistic Regression Analysis of SEX with organic dyspepsia

		Organic dyspepsia		Total	
		Present	Absent		
Sex	Male	Count	155	10	165
		% within Sex	93.9%	6.1%	100.0%
	Female	Count	40	295	335
		% within Sex	11.9%	88.1%	100.0%
Total		Count	195	305	500
		% within Sex	39.0%	61.0%	100.0%

Table 7 Uni Logistic Regression Analysis of H. Pylori infection with organic dyspepsia

		Organic dyspepsia		Total	
		Present	Absent		
H. Pylori infection	Present	Count	162	33	195
		% within H. Pylori infection	83.1%	16.9%	100.0%
	Absent	Count	33	272	305
		% within H. Pylori infection	10.8%	89.2%	100.0%
Total		Count	195	305	500
		% within H. Pylori infection	39.0%	61.0%	100.0%

Table 8 Multiple Logistic Regression Analysis

VARIABLE	OR	95%CI (Lower)	95%CI (Upper)	Sig
H.Pylori positive	2.271	.801	6.435	.123
SEX	1.802	.620	5.236	.279
AGE	549.247	96.387	3129.808	.000
SMOKING	17.435	1.874	162.222	.012

DISCUSSION

Our study shows results that are consistent with the meta-analysis by Ford [09], although (considering the Rome criteria) our prevalence of reflux oesophagitis was somewhat higher than that of peptic ulcer, whereas malignancy rates were somewhat higher than those observed in that study. These differences may be due to the fact that our institution is an outpatient screening clinic in general practice of a tertiary

hospital. In patients followed in a one-year prospective general practice study, the presence of alarm symptoms significantly increased the risk of developing peptic ulcers and gastrointestinal cancer. Patients with peptic ulcer were more likely to present with gastrointestinal bleeding [10] and in our study, gastrointestinal bleeding as melena was an uncommon alarm symptom (4%), whereas the prevalence of peptic ulcer was 13% and malignancy 6.2%. It was somewhat surprising that most of our functional dyspeptic patients had alarm symptoms, while about 35% of the ulcer patients did not. It is possible that our most frequent alarm symptom (weight loss) was not specific for serious digestive tract diseases.

Upper GI bleeding and unintended weight loss were also associated with malignancy [11], but the sensitivity of alarm features in diagnosing upper gastrointestinal malignancy varied from 0% to 100%, while specificity ranged from 16% to 98% [12]. This wide variation in sensitivity may be due to the small number of cancer cases detected in many of the studies. Alarming symptoms were present in 206 (40%), out of which loss of weight in 36% and melena in 4% of cases. Eight out of 31 cases of malignancy present without any alarming symptoms, most of them are gastric carcinoma. Despite the difference between patients with and without alarm symptoms, it is known that symptoms have limited value in the diagnosis of upper gastrointestinal malignancy [13].

In this study, older age, mass or lymphadenopathy and family history of upper gastrointestinal cancer were not included as alarm features. In our study, all patients with malignancy were older than 50 years, but considering the finding of organic dyspepsia (reflux disease, peptic ulcer and malignancy) our study suggests the age of 45 as indicative of alarm symptom.

Frequent vomiting was not considered an alarm symptom, as it was disregarded when reported as a chief complaint in dyspeptic syndrome and thus, it is unlikely that this symptom, when present for at least three months, will not result in weight loss.

The presence of adenopathy or abdominal tumor changes the diagnosis of undiagnosed dyspepsia into undiagnosed adenopathy or tumor and in these cases, the best approach requires imaging assessment and not an esophagogastro duodenoscopy.

Family history of upper gastrointestinal cancer is a type of information that is difficult to obtain, when patients know the cause of the disease, they cannot provide information on its type and precise location.

Apart from peptic ulcer disease, malignancy and reflux oesophagitis, there are few other rare diagnoses that we come across while doing endoscopy in uninvestigated dyspepsia syndrome cases. These are eosinophilic esophagitis, ascariasis infestation, Neuroendocrinal tumor of stomach, gastrointestinal stromal tumor, groove pancreatitis and oesophageal candidiasis.

The prevalence of GERD has increased dramatically in recent decades, mostly in the western world, where it affects about 19% to 30% of the population, increasing the risk for oesophageal adenocarcinoma [14]. In this study, reflux oesophagitis was diagnosed in 18% of patients, similar to the findings of a recent meta-analysis, based on Rome criteria [09]. In Denmark, gastric inflammation was recently found in 11%

of the patients with upper gastrointestinal symptoms [12]; Our study includes histological examination of the gastric mucosa in selected cases, and thus, gastritis was an endoscopic diagnosis, which after the exclusion of other concurrent diagnoses showing a prevalence of 46%. Out of which antral gastritis in 26% and pangastritis in 20 % of cases.

The prevalence of *H. pylori* infection in our population was high (39%) and infected individuals had a 10-fold higher probability of having any gastric mucosa lesions than non-infected individuals [15]. Predominantly patients having antral gastritis, duodenal ulcers and bulbar duodenitis had *H. Pylori* infection. *H. pylori* infection was detected by both rapid urease test and by histological confirmation. Our finding of 65 patients (13%) with ulcer, 45 of them (9%) with duodenal ulcer, is also consistent with the high prevalence of infection. This high prevalence of infection associated with the low availability of non-invasive tests for its detection prevent the use of the proposed approach of test and treat strategy for undiagnosed dyspepsia. *H. pylori* eradication treatment is always high cost and complex, with limited efficiency of 88% [16]. The number of cases of functional dyspepsia responsive to treatment is low, as only 50% of ulcer patients attain symptom resolution [17,18], whereas the symptoms of patients with reflux disease do not improve with treatment [19]. Therefore, the test and treat strategy may not be adequate for developing countries, which usually have very high prevalence of *H. pylori* infection and low level of resources for health care. Empirical treatment for young patients without alarm signs may be the possible approach for undiagnosed dyspepsia in our country. Further studies should be performed to test this proposal, especially in center similar to ours.

CONCLUSIONS

In a developing country with high prevalence of *H. pylori* infection, the most frequent cause of uninvestigated dyspepsia is functional dyspepsia, whereas upper gastrointestinal tract cancer is not uncommon finding. Even after selecting patients according to Rome III criteria, reflux disease predominated over peptic ulcer. The suggested age for the onset of alarm signs is 45 years. Age and smoking may be useful for the indication of endoscopy as the approach in the presence of dyspepsia.

Conflict of interests: The authors declare that they have no conflicting interests.

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