

# Open access endoscopy in an epidemiological situation of high prevalence of *Helicobacter pylori* infection: applicability of the guidelines of the European Society for Primary Care Gastroenterology

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**Background.** Dyspepsia is a common syndrome and provides primary care physicians with a significant workload. To optimize the management of dyspepsia, several guidelines have been developed.

**Objective.** The aim of this study was to determine the incidence of upper gastrointestinal diseases and their relationship to *Helicobacter pylori* infection in dyspeptic patients referred for upper endoscopy by family physicians, as well as to assess the applicability of the guidelines of the European Society for Primary Care Gastroenterology (ESPCG).

**Methods.** A total of 168 unselected dyspeptic out-patients (mean age 38 years, range 18–75), 88 male and 80 female, were included. Two biopsies from the antrum and two from the corpus were taken for histological assessment, and one from the antrum and one from the corpus were taken for culture.

**Results.** Half of the patients had clinically significant findings at endoscopy: peptic ulcer which occurred in 35% of the patients under the age of 30 years, in 45% of the patients in the age group 30–44 years and in 36% of the patients over 45 years of age. The prevalence of *H. pylori* infection in these age groups was 67, 87 and 89%, respectively. Duodenal ulcer was 12 times more common than gastric ulcer.

**Conclusions.** The overall incidence of upper gastrointestinal disease, especially among young dyspeptic patients, was high compared with that observed in Western countries. The characteristics of dyspeptic patients, consulted in primary care, should be used for adaptation of the ESPCG guidelines to local needs.

**Keywords.** Dyspepsia, guidelines, *Helicobacter pylori*, primary care.

## Introduction

Dyspepsia is a common syndrome in the general population. It provides a significant workload for GPs, accounting for 2–5% of all family practice consultations and up to 40% of referrals for gastroenterology out-patients.<sup>1–3</sup> *Helicobacter pylori* infection is widespread,

and it is also recognized as an important cause of gastrointestinal morbidity. Previous seroepidemiological studies have revealed an extremely high prevalence of *H. pylori* infection among the normal population in Eastern Europe.<sup>4,5</sup>

Although upper gastrointestinal endoscopy was considered the investigation of first choice in patients with dyspepsia until recently, not all dyspeptic patients in primary care may need endoscopic investigation. To optimize the management of dyspeptic patients, various guidelines have been published, based on detailed interviewing, written or computerized patient history questionnaires, as well as on data from clinical investigations,

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especially those which determine the patient's *H. pylori* status.<sup>2,6-8</sup> These recommendations are drawn up mainly by gastroenterologists and rely on the data obtained from hospitals and referral centres. The majority of dyspeptic patients are treated in primary care, where the management strategy is often different from that of a specialist or at the hospital level. Therefore, the European Society for Primary Care Gastroenterology (ESPCG) identified the key issues for primary care in management of *H. pylori* infection and developed evidence-based guidelines.<sup>9,10</sup>

The aim of this study was to determine the incidence of upper gastrointestinal diseases and their relationship to *H. pylori* infection among dyspeptic patients referred for upper endoscopy by family physicians and assess the applicability of the ESPCG guidelines in a situation of high prevalence of *H. pylori* infection.

## Patients and methods

Over a period of 20 months, 168 unselected out-patients (mean age 38 years, range 18–75), 88 male (mean age 37 years, range 18–75) and 80 female (mean age 39 years, range 18–68), referred for upper gastrointestinal endoscopy by their family physicians, were included in the study. Family physicians used open access endoscopy with a short waiting list (1–6 days) without secondary selection by a gastroenterologist. Three experienced endoscopists participated in the study, which allowed inclusion of patients during three morning sessions per week.

Dyspepsia was defined as persistent or recurrent abdominal pain or abdominal discomfort, centred in the upper abdomen, with duration of at least 3 months. Discomfort was characterized by early satiety, post-prandial fullness, nausea, retching, upper abdominal bloating, anorexia, heartburn and/or regurgitation. Use of antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), bismuth compounds or proton pump inhibitors 4 weeks prior to endoscopy, as well as current anti-coagulant therapy, suspected alcohol abuse, jaundice, bleeding, vomiting, anaemia or non-compliance, served as the exclusion criteria.

### *Upper endoscopy and diagnostic criteria*

The patients were examined using an Olympus Q21 endoscope. Endoscopic characteristics of inflammation were based on the Sydney classification. A circumscribed break in the mucosa with a considerable depth (>5 mm), covered with exudate, present in the prepyloric, pyloric or duodenal bulb region, was classified as duodenal ulcer (DU). Gastric ulcer (GU) was diagnosed when the above-described mucosal defect was located at the angulus or above it. Gastric or duodenal ulcer was diagnosed in the case of either an active ulcer or a deformity of the duodenal bulb. Visibility of the vascular pattern described a situation where vessels were visible even in a slightly

distended stomach. Oesophagitis was diagnosed in the case of apparent (haemorrhagic, erosive or ulcerative) mucosal alterations. In the case of specific findings (gastric ulcer, polyps, erosions, cancer), biopsies were taken for histological assessment.

### *Histology*

Two biopsies from the corpus (one from the greater curve, ~8 cm from the cardia, and the other from the lesser curve, ~4 cm proximal to the angulus) and two from the antrum (at least 2 cm from the pyloro-duodenal junction, one from the anterior and one from the posterior wall) were taken for histological assessment. Formalin fixation, Giemsa and haematoxylin–eosin staining were used. Gastritis was scored according to the Sydney classification. The presence of *H. pylori* was evaluated as follows: mild colonization (score 1) when single organisms or groups of organisms (<20 microbes per field) were present; moderate colonization (score 2) when bacteria (20–60 microbes per field) were found focally or diffusely; and severe colonization (score 3) in the case of diffuse involvement (>60 microbes per field).<sup>11,12</sup>

### *Culture*

For culture, one antral and one corporal specimen were obtained. Stuart's transport medium was used. The interval between obtaining specimens and *H. pylori* culturing did not exceed 4 hours, being in most cases 1–2 hours. Selective (one) and non-selective (one) medium plates were incubated in a microaerobic atmosphere (5–6% O<sub>2</sub>, 8–10% CO<sub>2</sub>, 80–85% N<sub>2</sub> and relative humidity at least 95%) at 37°C for up to 7 days. Microscopy of a specimen for detection of *H. pylori* was done with Gram stain. The patient was regarded as *H. pylori* positive when histology, culture or both methods were positive for *H. pylori*.

### *Ethics*

The study was carried out in accordance with the Helsinki Declaration and was approved by the Ethics Committee of the University of Tartu.

### *Statistical methods*

Statistical analysis was done using SPSS 8.0 for Windows. Student's *t*-test was used for continuous variables, and the significance of differences between the groups was tested with Fisher's exact test.

## Results

There was no difference between male and female mean age in the study group. Among the 168 included patients, 115 (68%, 61 male, 54 female) were younger than 45 years of age. The endoscopic findings and diagnoses of the included patients and their *H. pylori* status are presented in Tables 1 and 2.

TABLE 1 Endoscopic findings of 168 dyspeptic patients referred for upper endoscopy by family physicians

Diagnosis	Age group			Total
	18–29 years	30–44 years	≥45 years	
Peptic ulcer	20	26	18	64
Gastric ulcer	0	0	3	3
Duodenal ulcer	20 <sup>a</sup>	26 <sup>a</sup>	13 <sup>a</sup>	59
Duodenal and gastric ulcer	0	0	2	2
Other findings	8	11	15	34
Gastric cancer	0	1	0	1
Reflux oesophagitis	0	3	3	6
Gastric erosions	5	6	6	17
Hiatal hernia	1	1	1	3
Visible vascular pattern	0	0	5	5
Gastric polyp	2	0	0	2
Normal findings	29	21	20	70
Total	57	58	53	168

<sup>a</sup>One person in each age group of duodenal ulcer patients had a duodenal deformity or an ulcer scar, but not an active ulcer at endoscopy.

TABLE 2 Prevalence of *H. pylori* infection according to the results of histology and culture

<i>H. pylori</i> status	Age group		
	18–29 years	30–44 years	≥45 years
<i>H. pylori</i> -positive	38	49	47
<i>H. pylori</i> -negative	19	9	6
Prevalence of <i>H. pylori</i> infection	67%	86%	89%

### Endoscopic findings

Among the 168 patients, 64 (38%) had peptic ulcer (PU), while 70 (42%) had normal findings on endoscopy. For patients under the age of 45, the respective figures were 46 (40%) and 50 (43%). Among 61 male patients younger than 45 years, DU was diagnosed in 33, and among 54 female patients of the same age, DU was found in 13. The frequency of endoscopic findings depending on patient age and sex is shown in Table 3.

*Helicobacter pylori* positivity was predictive of DU rather than non-ulcer dyspepsia. Altogether, there were only 22 (19%) *H. pylori*-negative patients with normal findings at endoscopy in the group of patients younger than 45 years (Table 4).

All 64 newly diagnosed PU patients were infected by *H. pylori*. This indicator is significantly higher ( $P < 0.0001$ ) than the 63% prevalence for the 70 patients with normal findings. *Helicobacter pylori*-negative patients were significantly younger than *H. pylori*-positive patients (mean age 32 versus 40 years,  $P = 0.003$ ). The prevalence of *H. pylori* infection among the youngest age group was significantly lower than the overall prevalence of infection ( $P = 0.0085$ ).

## Discussion

The aim of our study was to analyse the data of patients referred for upper endoscopy by family physicians, as well as to assess the applicability of the EPCGE guidelines. More than two-thirds of included patients were younger than 45 years, an age at which, according to different guidelines, referrals are not indicated because organic diseases are rare.<sup>2,7,8</sup> Our findings showed a high incidence of PU in all age groups, including those aged less than 45. Similar results were obtained in a joint Estonian–Finnish study on the epidemiology of acute

TABLE 3 Peptic ulcer in different age and sex groups and the relative risk of peptic ulcer in male patients

	Age group							
	18–29 years		30–44 years		≥45 years		Total	
	Male	Female	Male	Female	Male	Female	Male	Female
No. of patients with peptic ulcer	15 (47%)	5 (20%)	18 (62%)	8 (28%)	13 (48%)	5 (19%)	46 (52%)	18 (23%)
No. of patients with normal findings	13 (41%)	16 (64%)	6 (21%)	15 (52%)	5 (19%)	15 (58%)	24 (27%)	46 (58%)
Relative risk of male patients having peptic ulcer	$P = 0.0448$		$P = 0.0084$		$P = 0.0084$		$P = 0.0001$	
OR	3.692		5.625		7.800		4.898	
95% CI	1.059–12.878		1.594–19.855		1.838–33.100		2.348–10.219	

TABLE 4 Age, sex and *H. pylori* status of patients with normal findings at endoscopy

Age group	Male		Female		Total
	<i>H. pylori</i> -positive	<i>H. pylori</i> -negative	<i>H. pylori</i> -positive	<i>H. pylori</i> -negative	
18–29 years	6	8	8	7	29
30–44 years	5	1	9	6	21
≥45 years	3	2	13	2	20
Total	14	11	30	15	70

upper gastrointestinal haemorrhage (UGIH).<sup>13</sup> The overall incidence of UGIH as well as the incidence rates in younger age groups were considerably lower in Finland than in Estonia. The most frequent cause of haemorrhage in both countries was PU. Differences between our findings and those obtained in Western countries<sup>1,2,10</sup> can be explained by geographical differences in the prevalence of *H. pylori* infection.<sup>4,5,10</sup> The prevalence of *H. pylori* infection is >60% in Eastern European populations and <50% in Western communities.<sup>4,5,10</sup> In Estonia, the prevalence among the population is >80%, while it was not higher among the investigated dyspeptic patients.<sup>4,5</sup>

According to the ESPCG guidelines, *H. pylori* testing and referral should be considered for patients who present with recurrent symptoms but not on the first presentation with dyspepsia.<sup>6</sup> Previous studies from the UK have shown that fewer than half of all patients complaining of dyspepsia seek medical aid, and the consultation rate in the case of chronic dyspepsia depends on factors other than the severity or duration of symptoms.<sup>1</sup> Patients with complaints lasting no less than 3 months were included in our study, and the number of their earlier endoscopies but not their consultations was registered. The risk of having PU was very high among male patients even in the young age group, but PU was also diagnosed in >20% of female patients. Where the recommended strategy is followed, the diagnosis of PU will be delayed for many patients. As almost all (99%) PU patients were *H. pylori* positive, non-invasive testing for *H. pylori* appears to be an option for selecting patients for endoscopy. Non-invasive tests should be performed with care, especially when commercial serological kits are used, as high infection prevalence renders negative tests unreliable.<sup>14</sup> In our population, non-invasive tests can be applied mainly for patients under the age of 30 years. Considering the 100% sensitivity and specificity of tests, approximately a quarter of endoscopies could be avoided. Another important issue at present is that the carbon urea breath test, which can achieve the highest sensitivity (96–100%) and specificity (86–100%), is more expensive than endoscopy in Eastern European countries and is not widely available for family physicians even in Western countries.<sup>14</sup> In Estonia, the cost of upper gastrointestinal endoscopy without biopsy and histological

examination, according to the price list of the Estonian Sick Fund is ~12EUR, while the addition of biopsy and histology will double the price if ordinary staining methods are used. The [<sup>13</sup>C]urea breath test has been used for research purposes only, with an approximate cost of 48EUR.

A 'test and treat' strategy, or prescription of eradication without testing *H. pylori*, cannot be resorted to in countries with high infection prevalence for several reasons, such as the large number of persons to be treated as well as the existing and developing resistance to antimicrobials.<sup>10,15</sup> Furthermore, the cost of *H. pylori* eradication therapy exceeds that of upper endoscopy by 4- to 5-fold in Estonia. It is also unclear whether patients with normal or minor findings, diagnosed as having non-ulcer dyspepsia, will remain symptom free after eradication.

According to different standards, age less than 45 years is taken as a cut-off for endoscopy, because the relative risk of gastro-oesophageal malignancy among younger people is low. The incidence of gastric cancer and the prevalence of PU have declined markedly in most developed countries during recent decades.<sup>1,16</sup> Despite the 36% decrease in the incidence and the 42% decrease in the mortality of gastric cancer from 1968 to 1992, Estonia ranked sixth among 67 European populations with respect to the incidence of gastric cancer (incidence rates 42.3 for males and 20.6 for females).<sup>17</sup> The incidence of gastric cancer was already higher than 10.0 for both sexes in the age group 35–40 years, and increased with age.<sup>17</sup> Although only one case of gastric cancer in the present study group is insufficient for analysis, it indicates that the proportion of gastric cancer among patients investigated at out-patient referral centres is similar to the respective figures reported from other countries (1–2%).<sup>2</sup> This can be explained by a further decrease in cancer incidence in our country as well as by the fact that patients with curable malignancy seldom present with uncomplicated dyspepsia.

Introduction of *H. pylori* eradication therapy in patients with newly diagnosed DU, as well as in patients with previously diagnosed DU who become symptomatic or are on long-term acid suppression therapy, would diminish the need for repeat endoscopies, since the frequency of exacerbations and ulcer complications

diminishes markedly after *H. pylori* eradication. Eradication therapy can be prescribed for patients with DU without detection of *H. pylori*. To eliminate NSAIDs as a risk factor for PU, and antimicrobials as a confusing factor in detection of *H. pylori* infection, patients who had taken these medicines recently were not included in our study.

Patients with GU should be tested for *H. pylori* infection, as recommended in guidelines, and should be provided with appropriate eradication therapy. Since all GU patients in our group were *H. pylori* positive, pre-treatment testing for *H. pylori* is not needed in primary care. Similar results were obtained in Southern China<sup>18</sup> where all GU patients were *H. pylori* positive, and the GU:DU ratio was 1:10.2 versus 1:12 for our group. As patients with GU are at risk of gastric malignancy, both ulcer healing and *H. pylori* eradication should be confirmed.

In conclusion, when using open access endoscopy in a region of high *H. pylori* infection prevalence, we found a high overall incidence of upper gastrointestinal disease, particularly DU, among young dyspeptic patients. The diagnostic performance of open access endoscopy was good when used by family physicians. When adapted to local data, the ESPCG guidelines for the management of *H. pylori* infection would meet the needs of family physicians in countries with a high prevalence of *H. pylori* infection.

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