

***Helicobacter pylori* infection diagnosis and management: current practices of Greek gastroenterologists**

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Abstract

Background The diagnosis and management of *Helicobacter pylori* (*H. pylori*) infection vary significantly, depending on country, area, and specialty. The aim of this study was to record the current practices of Greek gastroenterologists in the screening and treatment of *H. pylori* infection.

Method An anonymous questionnaire consisting of 19 questions about the management of *H. pylori* infection was sent with the aid of the Hellenic Society of Gastroenterology to all members of the Society.

Results The questionnaire was completed by 180 gastroenterologists, with a response rate of 31.4%. Diagnostic tests to confirm *H. pylori* infection are ordered by >90% of the gastroenterologists for patients with current peptic ulcer disease, gastric lymphoma, family history of gastric cancer, and an endoscopic appearance suggestive of gastritis. Most gastroenterologists (55.8%) also tested for *H. pylori* in patients with gastroesophageal reflux disease (GERD). Histopathology was the most preferred (60.6%) method when testing was decided during endoscopy, while urea breath test was the most preferred method (67.8%) regardless of endoscopy. Most gastroenterologists use quadruple eradication regimens supported by international guidelines (90%), while 65.6% of the physicians answered that they systematically recommend the addition of probiotics to standard therapy. Most physicians (82.8%) answered that they always confirm the eradication of the pathogen.

Conclusions The majority of Greek gastroenterologists conform to the recommendations of international guidelines regarding the diagnosis and management of *H. pylori* infection, except for the screening of patients with GERD. A considerable number of doctors use probiotics in addition to standard therapy.

Keywords *Helicobacter pylori*, questionnaire, gastroenterologists, survey, practices

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Introduction

Helicobacter pylori (*H. pylori*) infection is considered a significant public health hazard because of its association with various health conditions, including peptic ulcer disease (PUD) and gastric cancer. As a matter of fact, *H. pylori* is considered by the International Agency for Research on Cancer, World Health Organization (IARC/WHO) as a class 1 biologic carcinogen, in a category that includes hepatitis virus B and C, human immunodeficiency virus, and human papillomavirus [1]. *H. pylori* infection constitutes the most prevalent chronic infection worldwide, with studies estimating the worldwide prevalence at 50%, rising as high as 90% in some countries [2,3]. In Greece, a recent study, albeit geographically limited, estimated local prevalence at 34% [4].

In order to effectively detect and treat *H. pylori* infection, there are recent guidelines in place, both international

(Maastricht VI/Florence consensus report [5]) and local (Hellenic consensus on *H. pylori* infection [6]). Adherence to these guidelines is crucial to minimize the impact of *H. pylori* infection by employing cost-effective resources. However, the extent to which physicians follow these guidelines varies from country to country, and according to the physician's specialty, age and expertise [7-9]. Although studies investigating physician practices regarding *H. pylori* management have taken place in many countries, there has never been a study to examine the adherence of Greek gastroenterologists to *H. pylori* guidelines.

Our study aimed to investigate the current practices of Greek gastroenterologists regarding *H. pylori* screening, diagnosis, and management. We hope that the results may serve as an indicator of the adherence of Greek gastroenterologists to society guidelines and be used to detect potential areas that require improvements to further optimize the management of *H. pylori* infection in Greece.

Materials and methods

We created an electronic questionnaire that included questions about gastroenterologists' personal data, the cases in which they test for *H. pylori*, the preferred test method (depending on whether the decision to screen is taken during or outside endoscopy), the preferred eradication regimen, the frequency of confirmation of eradication, and the method used to perform it. The Hellenic Society of Gastroenterology, the scientific society responsible for the gastroenterology specialty in Greece, granted permission for the study and sent the questionnaire to all its members. The questionnaire and its approval by the Society are provided in the Supplementary material section. Responses were recorded anonymously, with no respondent information retained beyond the questionnaire components.

Statistical analysis

The questionnaire results were statistically analyzed and expanded using IBM SPSS Statistics for Windows software, version 25 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to test the normality of the investigated variables. Variables with normal distribution were expressed as mean \pm standard deviation and variables without normal distribution as median with interquartile range. The Student's *t*-test was used to compare continuous variables when they concerned 2 groups, and the ANOVA test when they concerned 3 or more groups. The chi-square test was used for the comparison of frequencies of categorical variables. Probability values of $P < 0.05$ were defined as statistically significant.

Results

Demographics

We received 180 responses from a total of 574 questionnaires sent, corresponding to a response rate of 31.4%. The majority of the responders were men (77.2%), and almost half of the responders practiced gastroenterology in Athens (46.1%). Most gastroenterologists were engaged in the private sector (66.7%). The mean age of the physicians was 48.9 ± 9 years, and they had practiced gastroenterology for a mean time of 15.6 ± 10.5 years. Demographic data are presented in Table 1.

Screening and diagnostic tests

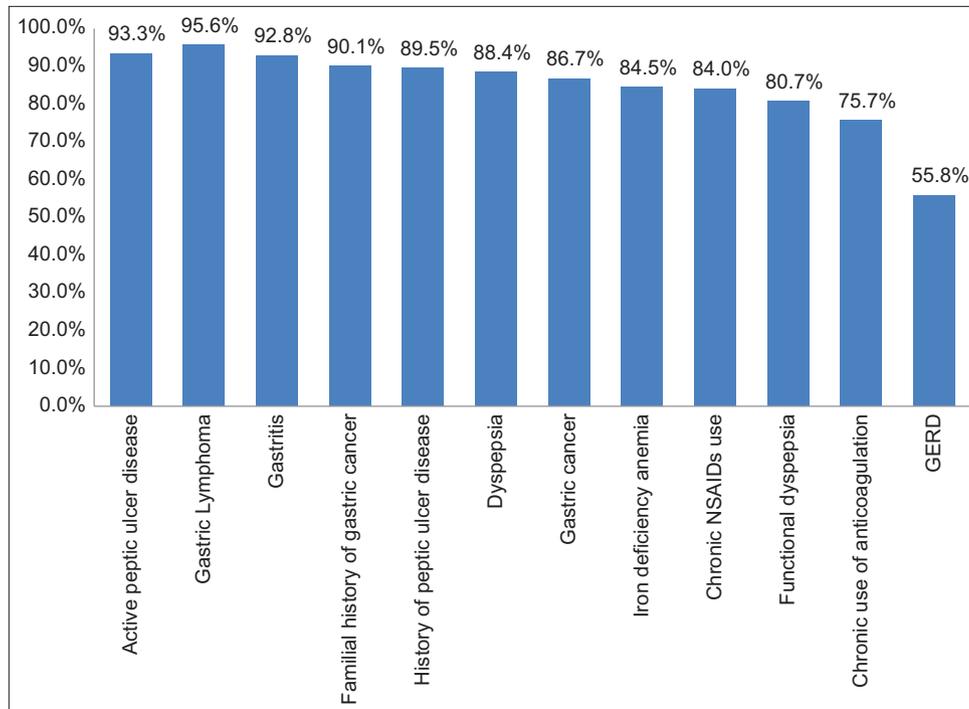
When asked in which cases they screen for *H. pylori*, 98.3% of physicians proceed in cases of active PUD, and 89.5% in patients with a history of PUD. Regarding other conditions, 95.6% of responders proceed to *H. pylori* screening in patients with gastric lymphoma, 86.7% in patients with gastric cancer, and 90.1% in patients with a familial history of gastric cancer. More than 80% of the responders proceed to screen for *H. pylori* infection in patients with gastritis, dyspepsia (even in patients with normal endoscopic findings), or iron deficiency anemia. Finally, 55.8% of the physicians declared that they screen for *H. pylori* infection in patients presenting with gastroesophageal reflux disease (GERD). There was no statistical difference in terms of screening with regard to the type of practice. Percentages of reported *H. pylori* screening in a variety of health conditions are outlined in Fig. 1.

Regarding *H. pylori* screening during endoscopy, the majority of gastroenterologists perform it via histologic assessment (60.6%), while a significant minority (33.9%) use a rapid urease test. On the other hand, *H. pylori* screening outside of endoscopy is mainly via the urea breath test (UBT) (67.8%), with significantly fewer physicians using fecal antigen detection (13.3%), serology (8.3%), or by performing endoscopy and histological assessment (8.3%). Physicians in the public sector were more likely to use UBT for *H. pylori* screening outside of endoscopy than physicians in the private sector ($P = 0.012$). Regarding the reasoning behind the choice of test (each physician was given 2 answers), most doctors cited sensitivity (60.2%) and simplicity (40.3%), with fewer doctors citing availability (28.2%), timeliness (22.1%), and economic burden (19.9%).

With regard to screening of relatives, almost half of the physicians (48.3%) screen family members of patients with *H. pylori* only in specific situations, with 22.2% routinely recommending screening of relatives and 29.4% not doing so. There was a statistically significant difference according to the type of practice, with private sector physicians being more likely to recommend screening to relatives, either routinely or under specific circumstances.

Table 1 Demographic data

Characteristics	Values		
Sex	Male: 139 (77.2%)	Female: 41 (22.8%)	
Practice location	Athens: 83 (46.1%)	Thessaloniki: 26 (14.4%)	Rest of Greece: 71 (39.4%)
Type of practice	Private sector: 120 (66.7%)	National Health System: 53 (29.4%)	Academic: 7 (3.9%)
Age	48.9±9 years		
Years of practice	15.6±10.5 years		

**Figure 1** Percentages of reported *Helicobacter pylori* screening according to health condition
NSAIDs, nonsteroidal anti-inflammatory drugs; GERD, gastroesophageal reflux disease

Treatment

The majority (61.7%) of Greek gastroenterologists showed a preference for a concomitant regimen for the eradication of *H. pylori*, consisting of clarithromycin, amoxicillin, metronidazole and a proton pump inhibitor (PPI). A small percentage (17.2%) preferred a sequential regimen (amoxicillin and PPI initially, then clarithromycin and metronidazole and PPI), while only 10% supported the use of the classic triple regimen (clarithromycin, amoxicillin, and PPI). The regimens used are depicted in Fig. 2. A statistically significant difference was observed regarding age and years of professional practice in relation to the choice of treatment ($P=0.002$ and $P=0.003$, respectively), with older and more experienced physicians being more likely to prefer the classic triple therapy regimen.

With regard to treatment duration, most preferred 10-day regimens (51.7%), while a significant percentage preferred 14-day regimens (44.4%). A statistically significant difference was

observed in relation to sex ($P=0.003$), region ($P=0.045$), and type of employment ($P=0.032$).

In case of failure of the first regimen, the overwhelming majority of respondents (87.2%) preferred a combination containing a fluoroquinolone, specifically levofloxacin, combined with amoxicillin and a PPI. There was a statistically significant difference in terms of age and years of professional practice ($P<0.001$ and $P=0.005$, respectively), with older and more experienced doctors being more likely to prescribe a concomitant regimen as second-choice therapy.

Regarding probiotics, 65.6% reported that they recommend the simultaneous intake of probiotics, while 30.6% do not. A statistically significant difference was observed regarding the type of employment ($P=0.008$), with private sector individuals prescribing probiotics in a much higher percentage than doctors working in the National Health System (NHS; 74.8% vs. 52.8%). Finally, a statistically significant difference was observed regarding the use of probiotics depending on the first-line treatment used by the physician ($P=0.002$). Physicians

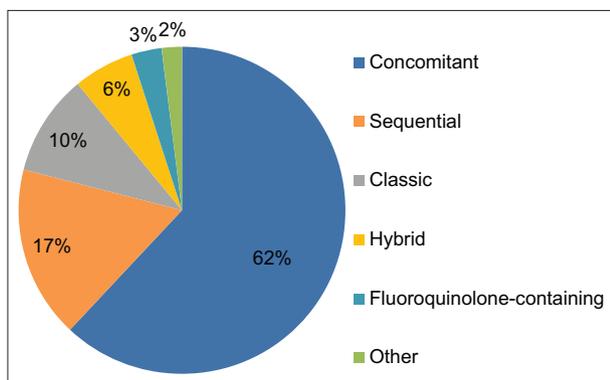


Figure 2 Prevalence of first-line *Helicobacter pylori* eradication regimens

using triple therapy were less likely to prescribe probiotics (55.5%) than physicians prescribing any quadruple regimen (68.1%).

Eradication confirmation

When asked whether they confirm the eradication of *H. pylori* after the end of treatment, most (82.8%) physicians answered that they always or almost always, 13.9% that they usually, and only 3.3% that they rarely or never confirm eradication. The preferred method of confirming eradication was the UBT (79.4%), with fewer preferring detection of *H. pylori* antigen in the stool (14.4%) and 5.6% preferring re-endoscopy (Fig. 3). Again, a statistically significant difference was observed in terms of age and years of professional practice ($P=0.008$ and $P=0.019$, respectively), with older and more experienced doctors being more likely to confirm eradication by means of endoscopy. A statistically significant difference was found depending on the doctors' employment type ($P=0.022$), with NHS doctors almost exclusively using the UBT as a method to verify eradication (90.6%), in contrast to the private sector where, in addition to this test (75%), a significant percentage used fecal antigen detection (20.8%). The most important criteria for choosing a diagnostic eradication test (with the possibility of choosing 2) were the sensitivity of the method (59.7%), ease of execution (48.6%), availability (25.4%), immediacy (19.3%), and cost (16.6%).

Discussion

This study covered a wide range of gastroenterologists' activities related to diagnosing and treating *H. pylori* infection. The answers can offer us multiple conclusions, whether analyzed as an individual study or compared to similar international studies.

Regarding the participation rate in the study, this is quite large compared to other similar studies on the specific topic. In a recent study in the USA, the corresponding rate was 19% [8],

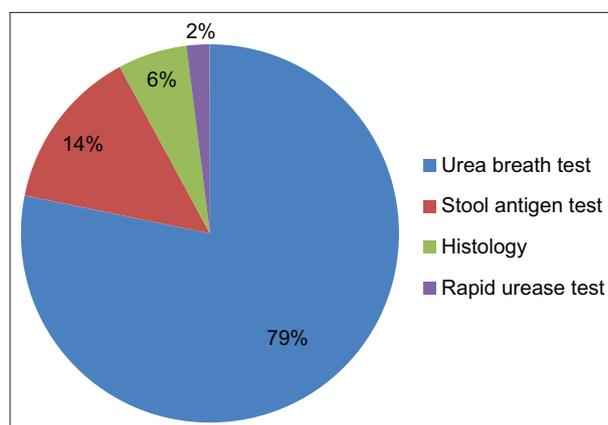


Figure 3 Predominant methods of confirmation of *Helicobacter pylori* eradication

while in a study of German gastroenterologists, the response rate was at the same level as ours (36%) [10].

Regarding gastroenterologists' awareness of which patients should be screened for *H. pylori* infection, rates are satisfactory, with >85% of physicians screening for *H. pylori* in cases of active ulcer, history of cancer, lymphoma, and previous ulcer or family history of cancer, and >75% screening patients who are taking antiplatelet/anticoagulant drugs or nonsteroidal anti-inflammatory drugs, rates at the same or higher level compared to a recent equivalent American study [8]. Although recent guidelines have emphasized the lack of correlation between GERD and *H. pylori*, stating that diagnostic testing for *H. pylori* is not recommended in patients with GERD [11], a significant percentage of Greek gastroenterologists proceed to test this group of patients (55.8%); this should be considered unsatisfactory, especially compared to the very low percentage in a recent USA study (15%).

Regarding the initial diagnostic test, our study had the innovation of introducing 2 options, performing a diagnostic test based on findings during endoscopy and performing it regardless of endoscopy. As expected, histological identification was the first choice during endoscopy, as has also been confirmed in similar studies abroad [8,10]. This preference may be related to 2 factors: taking biopsies regardless of *H. pylori*, for histological identification of lesions (e.g., ulcer, cancer, gastritis, dysplasia) and the possible unavailability of the rapid urease test in many endoscopy rooms. In the case of diagnosis regardless of endoscopy, a clear preference is observed for the UBT. This is in agreement with the practices of German doctors [12], but contrasts with the practices of American doctors, where a similar study highlighted a preference for the fecal antigen detection test [8]. Physicians justified their choices by citing the test's sensitivity as the primary reason, with ease of performance as a secondary criterion. In contrast, no particular importance seems to be attached to the immediacy of the method and the potential financial burden. This is probably related to the lack of urgency for diagnosing *H. pylori* infection, while the public coverage

and low cost of almost all methods practically eliminate the financial burden from the factors that will influence a physician's choice.

Most responses indicated that only under specific circumstances is *H. pylori* testing recommended for family members of someone positive for *H. pylori* infection. Particular emphasis was placed on screening individuals with a family history of gastric neoplasia. It is striking that a significant percentage of Greek gastroenterologists (40%) would recommend testing for *H. pylori* in relatives of patients who developed a peptic ulcer, a practice not promoted by any set of official guidelines.

The questions about the first line of treatment showed particularly positive results, with the concomitant regimen being used as the first line of treatment by most physicians, while even more importantly, only 10% reported using the classic triple regimen, a regimen that is no longer recommended by local and international guidelines [5,6,11]. The preference for the concomitant regimen can be justified, in that it is simpler for the patient than regimens that require a change of formulations in the middle of treatment, thus increasing the likelihood of compliance. However, it appears that older and more experienced physicians are more likely to choose the classic triple regimen than younger and less experienced physicians. This may be because older doctors have not updated their knowledge, or prefer to stick to old practices that have proven to be effective until today. This is in striking contrast to a corresponding Spanish study published in 2019 [7], in which 56.4% of Spanish general practitioners used the triple treatment regimen, even though national guidelines suggest quadruple treatment regimens [13]. This probably reflects a difference between the 2 health systems and who is called upon in each system to diagnose and treat *H. pylori* infection. Additionally, a significant number of physicians use the sequential regimen (17%). This regimen is not supported by local and international guidelines [5,6] and should be avoided, given its lower efficacy vs. metronidazole-resistant and metronidazole plus clarithromycin-resistant strains [14,15], which are common in Greece [16-18]. With regard to the duration of treatment, 95% of physicians prefer 10 or 14 days of treatment, an answer compatible with international guidelines. Nevertheless, 2 recent meta-analyses provide clear evidence that prolonging treatment to 14 days provides a therapeutic benefit for the patient [19,20].

Regarding the second line of treatment, an overwhelming percentage choose treatment with a regimen based on levofloxacin, which is fully justified by the guidelines, based on the lack of bismuth formulation in our country. The doctors who do not choose this regimen as a second line are, in a large percentage (66.6%), doctors who use the classic triple regimen as the first line of treatment, subsequently choosing the concomitant regimen as a second-line regimen. At the same time, most physicians use probiotics as an adjunct to standard therapy, with recent guidelines focusing on certain probiotic strains as potentially helpful in terms of treatment success and adverse event reduction [5,6].

Another positive result of the study is that the vast

majority of doctors answered that they systematically check to confirm the eradication of *H. pylori*. In this aspect of the treatment of *H. pylori* infection, Greek doctors are much more consistent and methodical than those in similar studies in Germany and the USA [8,9]. As in the case of diagnosis with noninvasive methods, Greek gastroenterologists prefer the UBT, with only a tiny percentage preferring re-endoscopy for confirmation. Accordingly, as in the initial diagnosis, Greek physicians show similar preferences to German colleagues regarding their preference for the UBT [10]. However, this differs significantly from the practices of American doctors, where the stool detection test showed a much higher frequency [8].

In making comparisons of doctors' practices depending on their country, it is essential not to fall into a number of pitfalls that may affect the conclusions that will be drawn. First, it is important to consider the timing of the study, as even a short interval can produce significant differences in physician practices, especially when guidelines or studies that change daily clinical practice emerge during that time. An even more critical pitfall is the non-separation between medical specialties. This is also evident from the studies that addressed gastroenterologists and general practitioners and found significant differences in the practices of the 2 specialties. The medical procedures each doctor can perform, the available medical procedures, and the medical training physicians receive depending on their specialty, are factors that lead to these differences [21]. The results change according to the conditions in each country, and it is important to consider which group of doctors mainly undertakes each part of *H. pylori* diagnosis and management.

The present study represents the first attempt to approach the specific topic on this scale in Greece. An important health issue is being addressed: *H. pylori* infection is now considered an infectious disease that should be treated regardless of symptoms and complications [22], as *H. pylori* is classified as a class 1 carcinogen by the IARC/WHO [1]. Therefore, this study may be an initial step towards the adoption of health policies regarding the diagnosis and treatment of an infection that is a major national health issue. An important advantage of this study is the channel through which it was carried out. The involvement of the Hellenic Gastroenterology Society, the official society for the relevant specialty in Greece, ensured that almost all Greek gastroenterologists were invited to participate. Furthermore, the fact that this invitation was made through an official body that carries the necessary prestige reinforced the reliability of the study in the eyes of the participants. Importantly, complete anonymity was maintained during the completion of the questionnaires. Finally, satisfactory participation was achieved, with a response rate that exceeded that of similar initiatives abroad [8-10,23].

Of course, our study also had some important limitations. The main one is that, although there were satisfactory response rates, the overall study population was relatively small, making it difficult to draw firm conclusions when comparing distinct subpopulations. Another important limitation of the study is the limitation of the questions to the preference of a single

diagnostic method, rather than offering a selection of multiple diagnostic methods and asking about the conditions that support the use of each, so as to determine the reasoning of the physician performing the test. In a similar study conducted in the USA, physicians were asked about the frequency with which they used each method, with 5 possible answers ranging from never to always [8].

H. pylori infection is a disease that shows constant rearrangements in terms of both its diagnosis and treatment. Consequently, it is difficult for the clinician to be constantly up to date with the ongoing changes in the *H. pylori* landscape. Nevertheless, Greek gastroenterologists seem to achieve this to a significant extent, possibly showing greater credibility than their colleagues in countries with more developed health systems. The impression is that they have a good understanding of the indications for a diagnostic test for *H. pylori*, and that if it turns out to be positive, they must treat the patient. At the same time, a considerable percentage seem to follow the latest guidelines on eradication therapy, immediately changing their practices and realizing the inability of the regimens used until a few years ago to deal with the global epidemic of *H. pylori* infection. Of course, we observe many minor differences between the subgroups of doctors, the main one being the type of employment. In the Greece of the financial crisis and the overloaded hospitals, it is to be expected that some practices of hospital doctors differ from those of their private counterparts. Importantly, these differences are not between acceptable and unacceptable practices, but between practices considered equally acceptable by the scientific community and the latest guidelines. There are, of course, areas where there is potential for improvement, with the main problem probably being the excessive effort of doctors to diagnose and treat *H. pylori* infection (resulting in testing in groups that are not recommended), rather than indifference about screening and applying appropriate treatment.

In summary, this study highlights the awareness of some Greek gastroenterologists of the particular characteristics of *H. pylori* infection, the population in which testing for the infection is deemed necessary, the appropriate diagnostic tests, the treatment regimens recommended by international guidelines as first- and second-line, and the need to confirm eradication. The next step is the creation by the state of the appropriate conditions that allow doctors to apply this knowledge in practice, whether they work in the public or the private sector.

Acknowledgment

The Hellenic Society of Gastroenterology approved the study and distributed the questionnaire to its members via e-mail.

Summary Box

What is already known:

- *Helicobacter pylori* (*H. pylori*) infection remains a significant health hazard, due to its connection with peptic ulcer disease and gastric cancer
- There are guidelines in place for the management of *H. pylori* infection
- Practice patterns with regards to *H. pylori* diagnosis and management are constantly evolving and vary from country to country

What the new findings are:

- Greek gastroenterologists conform with the vast majority of current *H. pylori* guidelines
- A significant number of Greek gastroenterologists screen for *H. pylori* infection in the presence of gastroesophageal reflux disease
- Most Greek gastroenterologists include probiotics in their standard *H. pylori* eradication regimen

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