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Original article

# Eradication of *Helicobacter pylori* with First-Line Treatment at a High-Complexity Hospital in Southwestern Colombia

Mauricio Sepúlveda-Copete,[1] Nelson Enrique Rojas-Rojas,[2] Carlos Julio Vargas-Potes,[2] Carolina Agudelo-Gutiérrez,[3] Heidy Lizeth Benavides,[4] Ana Fernanda Mejía,[5] David Alejandro Pantoja,[6] Leidy Johanna Hurtado-Bermúdez,[7,8*] Stefanía Cruz-Calderón,[9] Michelle González-Hurtado,[10] Carlos Arturo Rojas-Rodríguez.[1]

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[1] Gastroenterologist and Endoscopist, Department of Gastroenterology, Hospital Universitario Fundación Valle del Lili. Cali, Colombia.
[2] Internist, Hospital Universitario Fundación Valle del Lili. Department of Internal Medicine, School of Health Sciences, Universidad ICESI. Cali, Colombia.
[3] Internist, Hospital Universitario Fundación Valle del Lili. Department of Public Health, School of Health Sciences, Universidad ICESI. Cali, Colombia.
[4] Medical Student, Department of Public Health, School of Health Sciences, Universidad ICESI. Cali, Colombia.
[5] Nurse, Master in Epidemiology, Department of Public Health, School of Health Sciences, Universidad ICESI. Epidemiologist, Clinical Research Center (CIC), Hospital Universitario Fundación Valle del Lili. Cali, Colombia.
[6] General Practitioner, Clinical Research Center (CIC), Hospital Universitario Fundación Valle del Lili. Cali, Colombia.
[7] Epidemiologist, Clinical Research Center (CIC), Hospital Universitario Fundación Valle del Lili. Cali, Colombia.
[8] Epidemiologist, Department of Public Health and Community Medicine, School of Health Sciences, Universidad ICESI. Cali, Colombia.
[9] Internal Medicine Resident, Hospital Universitario Fundación Valle del Lili. Department of Internal Medicine, School of Health Sciences, Universidad ICESI. Cali, Colombia.
[10] Physician, Research Assistant, Clinical Research Center (CIC), Hospital Universitario Fundación Valle del Lili. Cali, Colombia.

**Correspondence:** Leidy Johanna Hurtado-Bermúdez.
leidy.hurtado.be@fvl.org.co

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## Abstract

**Introduction and Objectives:** Confirming the eradication of *Helicobacter pylori* is essential due to increasing antimicrobial resistance to various treatment regimens. The primary objective of this study is to determine the eradication rate of *H. pylori* using the carbon-14 ($^{14}C$) urea breath test. **Materials and Methods:** A cross-sectional study with an analytical component was conducted by retrospectively reviewing medical records of patients who received eradication treatment for *H. pylori* and subsequent confirmation of eradication through the $^{14}C$ urea breath test. The study was carried out at Hospital Universitario Fundación Valle del Lili between January 2019 and June 2022. **Results:** A total of 360 patients met the inclusion criteria. Women represented 66.9% of the sample, with a median age of 51 years (interquartile range [IQR]: 39–61). A negative $^{14}C$ urea breath test result was obtained in 84.4% of cases, with a median interval of eight weeks (IQR: 5–12) between the end of treatment and test performance. Almost all patients received 14 days of treatment. **Conclusions:** An acceptable eradication rate was observed in our setting, even with the standard triple therapy, which remains the most commonly used regimen. Antimicrobial susceptibility studies are needed to guide treatments based on local epidemiology.

## Keywords

*Helicobacter pylori*, eradication, breath test, microbial resistance, treatment adherence.

## INTRODUCTION

The significance of *Helicobacter pylori* lies in its classification as a Group I carcinogen by the International Agency for Research on Cancer, making it a critical agent in public health[1]. In addition, it has the potential to cause pathologies such as chronic gastritis, peptic ulcer, MALT lymphoma, unexplained iron deficiency anemia, refractory thrombocytopenia and vitamin $B_{12}$[2]. Globally, the prevalence of *H. pylori* infection in the six regions defined by the



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World Health Organization (WHO) has decreased from 58.2% (1980–1990) to 43.1% (2011–2022). This reduction is more pronounced in younger populations, in high-income countries, and in settings with universal health coverage[3]. In Colombia, studies report a prevalence of *H. pylori* ranging from 36.4% to 83.1%, with variations depending on the geographic region studied[4–7].

Guidelines and consensus documents of the greatest impact strongly recommend the eradication of *H. pylori* due to the aforementioned effects[8–15]. The eradication rate varies depending on the treatment regimen used and the local pattern of antimicrobial susceptibility. By the late 20th century, triple eradication therapy (proton pump inhibitor [PPI], amoxicillin, and clarithromycin or metronidazole) was the first-line treatment. However, a concerning decrease in susceptibility has been observed, based on studies of antimicrobial resistance, genetic polymorphisms, and metabolomics. Currently, there is an urgent need to implement treatments that achieve at least an acceptable eradication rate[16].

Confirmation of eradication is recommended for all treated patients. The most widely used and guideline-recommended non-invasive test is the breath test, which is based on the chemical reaction of *H. pylori* urease. This enzyme cleaves urea to produce carbon dioxide ($CO_2$) and ammonium hydroxide ($NH_4OH$); these compounds then react with a labeled carbon isotope, which is exhaled and subsequently measured[17]. Two carbon isotopes ($^{13}C$ and $^{14}C$) are used for the breath test. The $^{13}C$ isotope requires more complex equipment (including a mass spectrometer), which makes the test more challenging to perform compared to the less complex and less costly $^{14}C$ isotope[18]. Importantly, this does not compromise the sensitivity and specificity of the test, which are 96% and 93%, respectively[19–22].

The objective of this study was to describe the results of *H. pylori* eradication using the $^{14}C$ breath test in adult patients who received various treatment regimens at a high-complexity institution.

## MATERIALS AND METHODS

This was a cross-sectional study with an analytical component, involving retrospective data collection through a review of medical records. The study was conducted at Fundación Valle del Lili and approved by the institution's Biomedical Research Ethics Committee. Patients over 18 years old diagnosed with *H. pylori* infection via biopsy obtained through upper gastrointestinal endoscopy (performed either at the institution or externally) were included. After receiving treatment (whether or not provided by the institution), these patients underwent a confirmatory urea breath test between January 2019 and June 2022. Patients with more than one year between the end of treatment and the breath test were excluded.

### Procedure Description

As part of the institutional protocol, the following pre-procedure checks were conducted: verification of fasting status, allergies, absence of antibiotic, PPI, or antacid use in the past 30 days, no smoking in the last 8 hours, and the date of the last *H. pylori* treatment dose. If the patient was pregnant, suspected to be pregnant, or exhibited signs of acute or recent gastrointestinal bleeding, the procedure was postponed. The required materials included the Heliprobe® system (Kibion AB, Uppsala, Sweden), which uses the 37kBq HeliCap™ capsule (2.5 µSv of radiation per capsule), the Heliprobe® BreathCard® (a device to capture exhaled $^{14}C$), and the Heliprobe® Analyzer (for detecting $^{14}C$ radioactivity in the BreathCard®).

The patient was seated and instructed to swallow the HeliCap™ capsule with a glass of water, then wait for 10 minutes. After this time, the patient was asked to exhale into the Heliprobe® BreathCard® until the color indicator changed from orange to yellow. Finally, the BreathCard® was inserted into the Heliprobe® Analyzer for measurement.

### Result Interpretation

The cut-off points for determining infection status were as follows:

- Heliprobe 0: non-infected/negative
- Heliprobe 2: infected/positive

The results were interpreted in writing by an institutional gastroenterology and endoscopy specialist.

### Statistical Analysis

The institutional database was searched using the Unified Classification of Health Procedures (CUPS in Spanish) code corresponding to the [$^{13}C$ urea] breath test. This search identified approximately 1,300 procedures.

The sample size was calculated based on an *H. pylori* eradication rate of 80%, with a precision of 5% and a power of 80%, requiring a sample size of 360 patients.

A simple random sampling strategy was employed using the list of 1,300 procedures recorded during the study period. From this list, 360 procedures were selected using a random number table to meet the desired precision and power. Patients who underwent the breath test one year or more after treatment were excluded. The results of the breath tests and other relevant variables were then collected through a review of medical records in the institutional

system. All data were recorded in a database maintained by the Clinical Research Center.

Descriptive statistics were used to evaluate sociodemographic variables, clinical symptoms, treatment types, time before testing, treatment duration, and breath test results. Absolute numbers and percentages were reported for qualitative variables, while medians and interquartile ranges (IQR) were reported for quantitative variables. Bivariate analysis was performed using chi-square or Fisher's exact tests for qualitative variables, Mann-Whitney U tests for non-normally distributed quantitative variables, and Student's T tests for normally distributed variables. Variables with a statistical significance of $p < 0.05$ were considered statistically significant. All analyses were conducted using RStudio statistical software, version 2022.07.2.

### Ethical Considerations

This research adheres to the international agreements on biomedical research established by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the WHO, as well as Resolution 8430 of 1993 in Colombia. The study is classified as risk-free and is retrospective in nature; therefore, informed consent was not required. It is important to note that this article does not contain any personal information that could lead to the identification of patients involved.

## RESULTS

The breath test results after antibiotic treatment were negative in 84.4% of patients. A total of 360 patients were analyzed, of whom 241 (66.9%) were women. The median age of the patients was 51 years (IQR: 39–61). The most commonly reported symptom was dyspepsia (79.4%), followed by gastroesophageal reflux (24.1%), and 22.0% of patients reported other symptoms such as diarrhea, gastrointestinal bleeding, halitosis, vomiting, and belching. No statistically significant differences were observed regarding symptoms. The median time between the end of treatment and the breath test was eight weeks (IQR: 5–12). No statistically significant differences were found in the test results based on the time interval studied. However, a higher proportion of positive results was observed in tests performed before week 8. After this period, the proportion of positive results varied but was generally lower. No patients exceeded 10 months between the end of treatment and the breath test. The treatment duration was 14 days for both groups (**Table 1**).

Eighty-six point one percent of the patients in the study received a triple regimen of amoxicillin/clarithromycin/PPI; among these, 86.4% had a negative result. The treatment regimens of amoxicillin/clarithromycin/PPI/bismuth, amoxicillin/levofloxacin/PPI, and amoxicillin/levofloxacin/PPI/bismuth yielded negative results in 83.3%, 72.4%, and 54.5% of cases, respectively. All four patients treated with the regimen of metronidazole/clarithromycin/bismuth/PPI had negative results (**Table 2**).

Regarding the time interval between the end of the treatment regimen and the breath test, among the 296 cases with available data, negative results exceeded 80% across all groups: 80% for the group tested at 4 weeks, 87.9% for the group tested between 5 and 12 weeks, and 80.2% for the group tested after more than 12 weeks (**Figure 1**).

## DISCUSSION

This study identified an overall eradication rate (encompassing all treatment regimens) of 84.4%. Currently, there are uncertainties and a lack of consensus on fundamental aspects such as what constitutes an acceptable eradication rate. The most recent guidelines from the World Gastroenterology Organization propose a minimum acceptable eradication rate of 80% by intention-to-treat, although this value is described in the document as "arbitrary"[23]. Previously, Graham and colleagues proposed categorizing treatment efficacy as excellent (≥95% eradication), good (≥90%), borderline acceptable (85%–89%), or unacceptable (<85%)[24]. Other authors suggest that treatment regimens should be based on therapies achieving cure rates above 90%[11,25]. Antimicrobial resistance plays a significant role and varies geographically. A systematic review and meta-analysis across WHO regions reported global bacterial resistance rates of *H. pylori* (based on genotypic and phenotypic testing) to metronidazole, amoxicillin, clarithromycin, and levofloxacin as 91%, 38%, 15%, and 14%, respectively. According to international guidelines, a resistance rate above 15% is considered high[1]. Previously, amoxicillin resistance was thought to be low; however, in Colombia, it has been reported to range from 3.8% to 20.5%[26–28]. Resistance to clarithromycin is much more variable, ranging from as low as 2.2% in cities like Pereira[29] and Armenia, to as high as 63.1% in Bogotá[26–28,30,31], mostly associated with point mutations in the 23S rRNA gene. Metronidazole has the highest resistance rate, reaching up to 97.6%[27,31–33].

The most recent Maastricht VI/Florence Consensus recommends that in the absence of susceptibility testing, first-line treatment in areas with high (>15%) or unknown resistance to clarithromycin should be quadruple therapy with bismuth. In areas with low resistance and locally confirmed efficacy rates above 90%, triple therapy with amoxicillin/clarithromycin/PPI may still be recommended[11]. In this study, triple therapy remains the most commonly used regimen in our setting (86.1%), with a negative breath test

**Table 1.** Patient Characteristics According to Breath Test Results

| Característica | n | Overall n = 360 | Negative n = 304 | Positive n = 56 | *p*-value* |
|---|---|---|---|---|---|
| **Age** | 360 | 51 (39-61) | 51 (39-60) | 55 (39-62) | 0.24 |
| **Sex, n (%)** | 360 | | | | 0.43 |
| Female | | 241 (67.0) | 201 (66.1) | 40 (71.4) | |
| Male | | 121 (33.0) | 103 (33.9) | 16 (28.6) | |
| **Symptoms** | | | | | |
| **Dyspepsia, n (%)** | 350 | | | | 0.9 |
| Negative | | 72 (20.6) | 61 (20.7) | 11 (20.0) | |
| Positive | | 278 (79.4) | 234 (79.3) | 44 (80.0) | |
| **Gastroesophageal reflux, n (%)** | 349 | | | | 0.73 |
| Negative | | 265 (75.9) | 223 (75.6) | 42 (77.8) | |
| Positive | | 84 (24.1) | 72 (24.4) | 12 (22.2) | |
| **Other symptoms, n (%)** | 359 | | | | 0.19 |
| Negative | | 280 (78.0) | 240 (79.2) | 40 (71.4) | |
| Positive | | 79 (22.0) | 63 (20.8) | 16 (28.6) | |
| **Time between treatment and breath test (weeks)*** | 351 | 8 (5-12) | 8 (6 -12) | 8 (4-20) | 0.817 |
| **Duration of treatment (days)*** | 354 | 14 (14-14) | 14 (14-14) | 14 (14-14) | 0.054 |

*Median (interquartile range [IQR]). **Wilcoxon rank-sum test (Mann-Whitney U test); Pearson's chi-square test; Fisher's exact test. Author's own research.

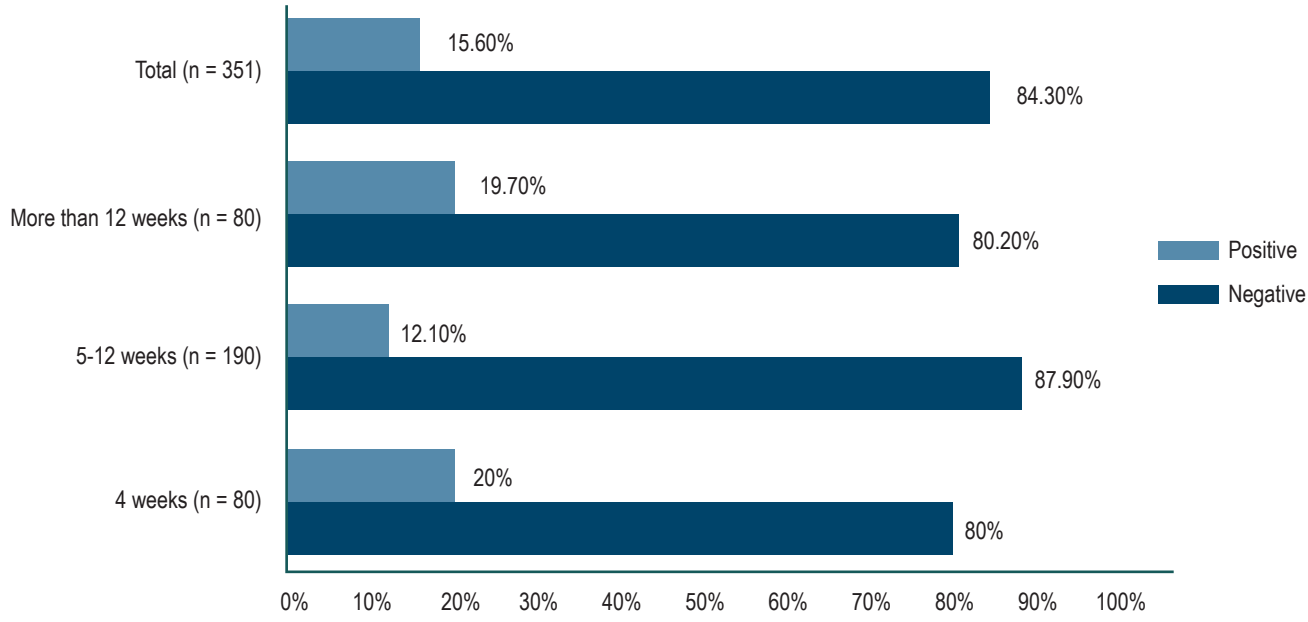



**Figure 1.** Breath Test Results by Time Interval Between End of Treatment and Breath Test. Author's own research.

**Table 2.** Breath Test Results by Treatment Regimen

| | n | % |
|---|---|---|
| Total (n = 360) | | |
| - Negative | 304 | 84,4 |
| - Positive | 56 | 15,5 |
| Amoxicillin/clarithromycin/PPI (n = 310) | | |
| - Negative | 268 | **86,4** |
| - Positive | 42 | 13,5 |
| Amoxicillin/levofloxacin/PPI (n = 29) | | |
| - Negative | 21 | **72,4** |
| - Positive | 8 | 27,6 |
| Amoxicillin/clarithromycin/PPI/bismuth (n = 6) | | |
| - Negative | 6 | **54,5** |
| - Positive | 5 | 45,4 |
| Amoxicillin/levofloxacin/PPI/bismuth (n = 4) | | |
| - Negative | 5 | **83,3** |
| - Positive | 1 | 16,6 |
| Metronidazole/clarithromycin/bismuth (n = 4) | | |
| - Negative | 4 | **100** |
| - Positive | 0 | 0 |

Author's own research.

rate of 86.4%, classifying it as an acceptable eradication therapy. Interestingly, quadruple therapy with metronidazole/clarithromycin/bismuth/PPI achieved the highest eradication rate (100%), which is inconsistent with the extremely high resistance rates reported for metronidazole. However, the number of patients receiving this regimen was limited. Additionally, quadruple therapy with amoxicillin/clarithromycin/PPI/bismuth showed a notable eradication rate below 85%.

It is evident that treatment regimens containing levofloxacin have eradication rates as low as 54.6% and 72.4%, consistent with the increasing resistance to levofloxacin reported by Trespalacios and colleagues in Bogotá (from 11.8% in 2009 to 27.3% in 2014), which would preclude its use as first-line therapy[34]. The same study discusses that even in *H. pylori*-naive patients, the widespread use of this antibiotic for urinary, respiratory, and gastrointestinal infections may influence resistance. To date, there are no antimicrobial susceptibility studies for *H. pylori* in Valle del Cauca, and considering the epidemiological significance, it is imperative to conduct bacterial resistance studies to determine whether it remains safe to continue using triple therapy, currently the most widely employed regimen.

The second most important factor influencing treatment success is poor adherence, which is affected by factors such as treatment complexity, potential side effects, patient willingness and motivation, and socioeconomic status[35]. In Colombia, Salazar and colleagues reported an adherence rate of 84%, which is suboptimal. Factors most significantly impacting adherence included adverse drug reactions, dosing frequency, and the number of tablets taken during the treatment period[36]. Adherence is considered excellent if it reaches or exceeds 90%. In our study, nearly all patients underwent a 14-day treatment regimen; however, this was not evaluated using validated strategies to confirm adherence. Only four patients received treatment lasting less than 14 days, three of whom had positive follow-up tests. This finding aligns with the Maastricht consensus, which states that shorter treatment durations are associated with lower effectiveness[37].

In a prospective study conducted in Peru by Vargas-Cárdenas and colleagues, a much lower adherence rate (65%) was reported using the Morisky-Green test. Poor adherence was more frequent in patients under 50 years of age, those with lower education levels, and those experiencing adverse reactions[38]. These factors could be extrapolated to the Colombian context, as it is also a developing country, highlighting the need for a prospective study on treatment adherence using validated strategies. Other factors that reduce the likelihood of eradication include disparities in healthcare access, age-related changes in the gastrointestinal microbiota, and prior exposure to specific antibiotics and *H. pylori* strains. These factors warrant further study in our local context.

The median age was 51 years, consistent with findings by Correa and colleagues, who reported that individuals aged 40 to 59 years accounted for nearly 40% of positive cases[6]. Some studies have described no significant differences in infection rates between sexes, with prevalence being similar in both men and women[39,40]. However, in our study, there was a notable predominance of women regardless of the breath test result. This finding aligns with reports from Sepúlveda and colleagues in Cali, where diagnostic positivity for *H. pylori* was based on upper gastrointestinal endoscopy and, in some cases, post-treatment follow-up[7]. Conversely, a study in China by Ren and colleagues found a slight predominance in men (44.9% compared to 42.0%)[41].

The median time between the end of treatment and the breath test was eight weeks for both positive and negative cases, with no statistically significant differences. This

value exceeds guideline recommendations. It is important to note that no studies have reported potential diagnostic performance alterations when more than four weeks elapse between the end of treatment and testing, and there is no consensus on the maximum tolerable interval. Additionally, the characteristics of the local healthcare system often do not allow adherence to the specified timelines. In our study, no significant differences were observed among the subgroups of 4 weeks, 4 to 12 weeks, and more than 12 weeks (as outlined in guidelines); in all cases, the percentage of negative results was equal to or greater than 80%. However, it is crucial to consider various causes of false positives, such as the presence of other urease-producing bacteria, including *Helicobacter heilmannii*, *Proteus mirabilis*, *Citrobacter freundii*, and *Staphylococcus aureus*, as well as false negatives due to factors like antibiotic and bismuth compound use within the last four weeks, proton pump inhibitor (PPI) and sucralfate use within the last two weeks, testing conducted less than four weeks after treatment, infection predominantly in the gastric body, and previous gastric surgery[42,43].

Given the results of this study and the high variability in clarithromycin resistance rates, triple therapy with amoxicillin/clarithromycin/PPI remains a potentially acceptable first-line treatment option in our setting while awaiting local epidemiological data on antimicrobial susceptibility.

## STRENGTHS AND LIMITATIONS

This study represents one of the first descriptive analyses of *H. pylori* eradication with first-line treatment in a high-complexity hospital in southwestern Colombia, providing valuable insights into eradication outcomes via the breath test and addressing an informational gap in the region. However, some limitations must be noted. In several cases, both the diagnosis and the indication for a specific eradication treatment were made outside our institution, with patients visiting Fundación Valle del Lili solely for the post-eradication breath test. Nevertheless, the physician conducting the procedure collected detailed information on the type and duration of the treatment received. Additionally, due to administrative issues with their health insurance providers (EPS in Spanish), some patients did not undergo the follow-up test within the recommended time frame (less than one year). Finally, it was not possible to measure treatment adherence due to the retrospective nature of the study and the reliance on patient-reported information, which could affect the accuracy of some collected data.

## CONCLUSION

In our setting, the eradication rate aligns with the acceptable threshold proposed by the World Gastroenterology Organization, even with standard triple therapy, which remains the most widely used regimen. The findings of this study highlight the high variability in clarithromycin resistance rates. Against this backdrop, triple therapy including amoxicillin, clarithromycin, and a PPI emerges as a potentially acceptable first-line treatment option in our context, where epidemiological data on antimicrobial susceptibility are still being gathered.


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### Conflict of Interest

The authors declare no conflicts of interest.

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