

The Role of the Breath Test in Monitoring the Eradication of Helicobacter Pylori Infection: Insights from The Chu of Brazzaville

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Received: 28 Nov 2024; Accepted: 22 Dec 2024; Published: 03 Jan 2025

Citation: Mikolélé Ahoui Apendi C, Ngaguene Volobanda UL, Itoua-Ngaporo NA, et al. The Role of the Breath Test in Monitoring the Eradication of Helicobacter Pylori Infection: Insights from The Chu of Brazzaville. *Gastroint Hepatol Dig Dis.* 2025; 8(1): 1-5.

ABSTRACT

The aim of the study was to evaluate the performance of the breath test in monitoring Helicobacter Pylori eradication in Brazzaville.

Patients and Methods: *we carried out a cross-sectional analytical study over a nine-month period at the Brazzaville University Hospital and Bio-santé laboratory, and in a medical analysis laboratory in Brussels. Patients over 18 years of age with H. pylori infection who had received treatment for its eradication were included. Diagnosis was made by urease testing of gastric biopsies and/or stool antigen testing. Socio-demographic, diagnostic and evolutionary variables were studied.*

Results: *Our sample comprised 30 patients with a mean age of 39.6 ± 13.7 years, extremes of 22 and 72 years, and a sex ratio of 0.7. Compared with fecal antigen testing, the sensitivity, specificity, PPV and NPV of the carbon-13 urea breath test were 100%, 72%, 41.7% and 100% respectively. Accuracy was 65%.*

Conclusion: *The labelled urea breath test is a reliable test that can be used in Congo for post-therapeutic monitoring of Helicobacter pylori infection. However, when interpretation must be conducted outside the country, challenges related to its cost and the time required to obtain results are factors that limit its feasibility.*

Keywords

Infection, Helicobacter pylori, Eradication, Control, Breath test.

Introduction

Helicobacter pylori (Hp) infection poses a significant public health challenge due to its high prevalence, particularly exceeding 90% in Africa [1,2], with a notable incidence in Congo [3,4], and its potential severity. The infection can lead to complications such as peptic ulcers and gastric cancer [5]. Diagnosis and monitoring of eradication efficacy involve several tests, categorized into invasive tests like urease assays and histological examinations, and non-invasive tests such as serology, fecal antigen tests, and

the carbon-13 labeled urea breath test (13C-UBT). Due to the increasing resistance to treatment, confirming eradication is crucial to mitigating the risk of progression to severe complications [6,7]. Histological examination of gastric biopsies is the standard reference test, although it necessitates prior upper gastrointestinal endoscopy. The carbon-13 labeled urea breath test is employed both for initial diagnosis and post-treatment monitoring. The selection of a control test is based on factors such as availability, performance metrics (sensitivity, specificity, predictive values), and cost [1,2]. Numerous scientific societies advocate for the urea breath test as the first-line option, conducted at a suitable interval after treatment, to verify therapeutic efficacy [1,8]. Nonetheless,

its availability in Africa is limited and even non-existent in certain countries such as Congo. The primary aim was to assess the role of the breath test in verifying the eradication of *Helicobacter pylori* in Congo and to evaluate its feasibility.

Patients and Methods

This study was an analytical investigation with a prospective data collection approach conducted over nine months, from February 1 to October 31, 2022. The research was performed at the Gastroenterology and Internal Medicine Department (GEMI) of the University Hospital Center of Brazzaville (CHUB), alongside the Bio-Health laboratory in Brazzaville, Congo, and a laboratory in Brussels, Belgium. The study's general population included all patients, whether symptomatic or asymptomatic, hospitalized or seen in outpatient gastroenterology consultations at CHUB. The target population focused on individuals with *H. pylori* infection, diagnosed through either a urease test on gastric biopsies or the detection of *H. pylori* antigen in stool samples. The source population comprised patients who underwent eradication treatment for *H. pylori* infection, involving a fixed combination of two antibiotics (Amoxicillin and Clarithromycin) and a proton pump inhibitor (Omeprazole) over a 14-day regimen. The inclusion criteria encompassed all consenting patients of both genders, aged over 18 years, who had ceased treatment at least two weeks prior to the control test. Excluded were those who withdrew consent. Patients treated based on positive *H. pylori* serology and those lost to follow-up before the control examination were not included. The sample size was calculated using Schwartz's formula [$1.96^2 p(1-p)^2/d^2$], assuming an 80% prevalence of *H. pylori* infection in Africa, with a 5% margin of error and a 95% confidence interval, resulting in a target of 49.1 participants. However, due to financial constraints, the study was limited to 30 patients. We employed consecutive sampling of patients meeting the inclusion criteria, with data collected via a pre-designed survey form. The variables examined included sociodemographic factors (age, gender, occupation, individual income as per national definition, housing type), diagnostic factors (consultation reasons, endoscopic lesions, diagnostic test results), and clinical, endoscopic, and biological evolution (13C-UBT breath test, fecal test), along with the performance metrics of the breath test (sensitivity, specificity, positive and negative predictive values). Eradication verification was based on stool antigen testing for *H. pylori* conducted at the Bio-Health laboratory and a breath test performed in Brussels. The breath test exploits *H. pylori*'s ability to convert urea into ammonia and carbon dioxide. The medi Gastro® kit from the Louise Medical Center laboratory in Brussels was used, comprising a 75 mg carbon-13 labeled urea capsule, a straw, five glass tubes (one for T0 min, two for T15 min, and two for T30 min to collect exhaled air at baseline, 15, and 30 minutes post-ingestion of the labeled urea), a form for patient identification, physician signature and stamp, and a packaging bag (Photo 1).

Sampling was conducted at the Bio-Health laboratory in Brazzaville with patients fasting (no food, drink, or smoking) for at least six hours, following three steps: ingestion of the carbon-13

labeled urea capsule with water, collection of exhaled air by blowing through a straw into each tube, gradually removing the straw during expiration, slowly and continuously, across the five tubes for a minimum of 15 seconds (Photo 2), followed by rapid sealing of the tubes post-expiration.

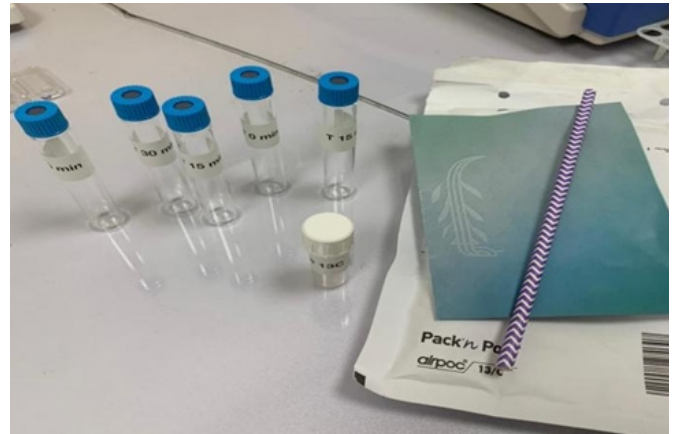


Photo 1: Breath test kit (taken at the Bio Santé laboratory).



Photo 2: Exhalation in the collection tubes (done at the Bio Santé laboratory).

Each sample batch, consisting of five clearly identified tubes per patient, was placed in a specific packaging bag, carefully sealed, and stored at room temperature (between +15°C and +25°C). Transportation was conducted by air, with the samples placed in the hold within a cardboard box. Sample analysis was performed in Belgium at the Louise Medical Center laboratory in Brussels. A test was considered positive if the amount of carbon-13 labeled CO₂ collected exceeded 0.80. The cost per test is 57 euros, which is approximately equivalent to 40,000 CFA francs. This cost did not include the transportation fees for the samples. All these costs were our responsibility. The samples were dispatched in two separate batches. The results of the breath tests were communicated via email. Due to the necessity for secure transportation, there was an average waiting period of two weeks from sampling to result acquisition. The *H. pylori* eradication control tests were disposed of according to the standard procedures of each analysis center. Data management, including database creation, data entry, and graph construction, was carried out using Excel 2016. Statistical

analysis was performed using Epi Info version 7.5.2.

Results

The study included thirty patients, comprising 13 males and 17 females, yielding a sex ratio of 0.7. The mean age was 39.6 ± 13.7 years, with ages spanning from 22 to 72 years. Socio-economic status (SES) was classified as low in 10 patients (33.3%), medium in 13 patients (43.3%), and high in 7 patients (23.4%). Abdominal pain emerged as the most common presenting symptom.

The study examined cases of epigastric pain (n=26) and right hypochondrium pain (n=4), characterized by burning sensations (n=14), cramping (n=10), a feeling of compression (n=4), or a combination of burning and compression (n=1) or burning and cramping (n=1). Patients with dyspepsia reported symptoms of gastric fullness (n=14) and early satiety (n=10). Ulcers were the most frequently identified endoscopic lesions (Figure 1). The endoscopic duodenal histology (EDH) appeared normal in 66.7% of the cases.

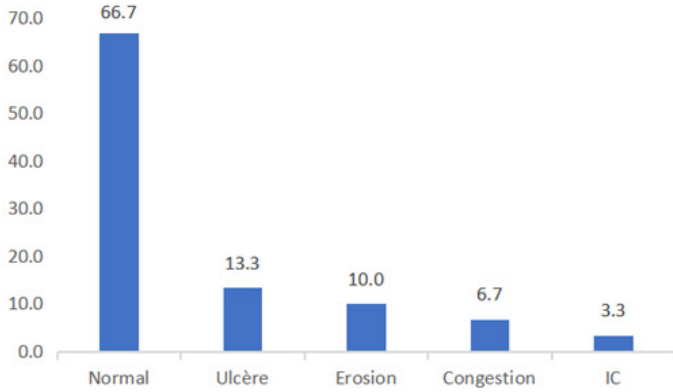


Figure 1: Distribution of patients according to endoscopic results.

Diagnosis was established through the detection of fecal antigen and the rapid urease test on gastric biopsies in 29 cases (96.7%) and six cases (20%), respectively, with five patients undergoing both tests. Helicobacter pylori eradication assessment showed that 18 patients tested negative with the breath test, while 25 patients tested negative with the fecal antigen test, indicating eradication rates of 60% and 83.3%, respectively (Figure 2a and Figure 2b). The concordance between these two tests was moderate, with a Cohen's Kappa coefficient of 0.45.

Following eradication treatment, 16.6% of patients continued to exhibit clinical signs (Figure 3). Nevertheless, their follow-up endoscopic examinations were normal. The detection of fecal antigen in stool samples served as the benchmark test for evaluating the efficacy of the carbon-13 labeled urea breath test.

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 100%, 72%, 41.6%, 100%, and 65%, respectively.

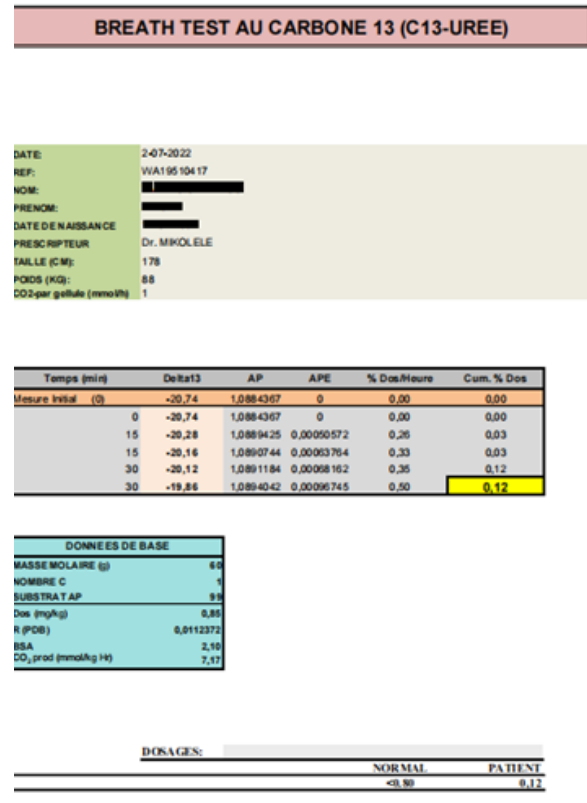


Figure 2a: Negative breath test result.

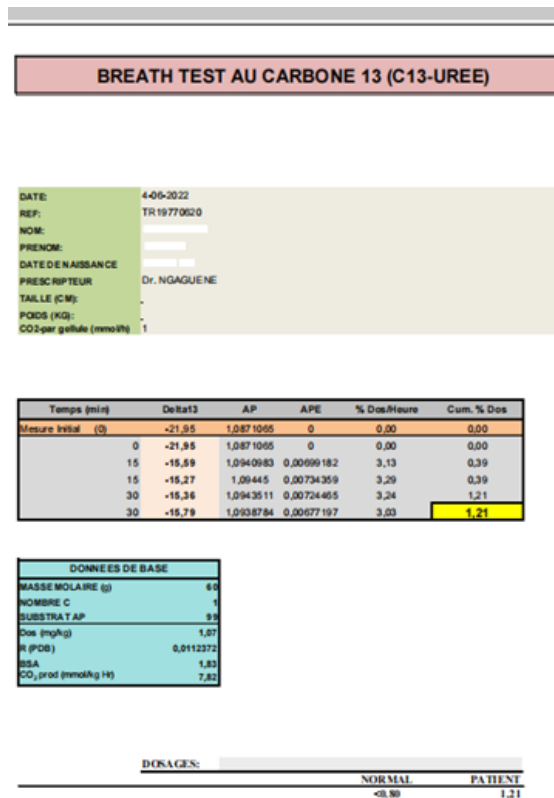


Figure 2b: Positive breath test result.

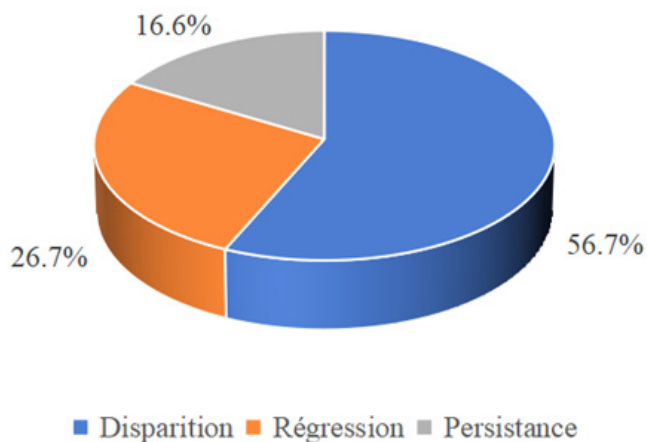


Figure 3: Evolution of signs after treatment.

Discussion

The predominance of *Helicobacter pylori* infection among females has been documented by several researchers. Specifically, studies by Ilboudo in Burkina Faso and Itoudi Bignoumba in Gabon have reported a female predominance of 52% and 58%, respectively [9,10]. In the Congo, this trend might be attributed to the generally higher female population, as outlined in the Congo Demographic and Health Survey (DHS). Regarding the younger age group of patients, similar findings have been reported by researchers in Cameroon and Madagascar [11,12]. This may be due to the fact that *H. pylori* infection is mainly acquired during childhood [13]. The high prevalence of *H. pylori* infection among patients from middle and lower socioeconomic backgrounds is likely due to poor living conditions, a common scenario in resource-limited countries [9,10,12,14]. Abdominal pain is among the few indicative symptoms of *H. pylori* infection, as noted by Bagny et al. in Lomé, Konaté et al. in Bamako, and Dia et al. in Dakar [15-17]. The gastric complications associated with *Helicobacter pylori* account for the frequent occurrence of epigastric abdominal pain [16]. Routine upper gastrointestinal endoscopy is not typically required for monitoring *Helicobacter pylori* infection, except in cases of severe initial endoscopic lesions or when there is resistance to treatment necessitating an antibiogram [18]. When endoscopy is conducted, studies by Konaté et al. in Mali and Jmaa et al. in Tunisia have shown a predominance of gastric congestive lesions, whereas ulcers were the most common lesions observed in our series [16,19,20]. Bemajo et al., in a study involving 76 patients, along with Ianonne et al., reported a high concordance between fecal antigen detection, serology conducted six months post-eradication therapy, and gastric biopsy histology, with a kappa coefficient of 83% and an accuracy rate of 95% [21,22]. The limited size of our sample may account for the moderate concordance observed in our findings. When compared to the reference standard of gastric biopsy histology, some studies have demonstrated that the breath test exhibits high sensitivity, specificity, and overall accuracy exceeding 95% for assessing therapeutic effectiveness [23,24]. In a study involving 115 patients, Rawaa et al. in 2021 in Iraq

reported sensitivity, specificity, and accuracy rates of 97.5%, 97%, and 97.3%, respectively [25]. The discrepancy between these results and ours is primarily in the higher specificity and accuracy reported in their study. In 2020, Hamed Alzoubi et al. in Jordan found sensitivity, specificity, PPV, NPV, and accuracy values of 94.1%, 76.9%, 84.2%, 90.9%, and 86.7%, respectively, using the UBT to diagnose and monitor the eradication of *H. pylori* infection in a cohort of 67 patients [8]. In Italy, Francesco Perri et al. in 2005, conducted a study on 250 patients for eradication monitoring, reporting sensitivity, specificity, PPV, and NPV values of 91%, 100%, 100%, and 97.4%, respectively [26]. Other researchers have compared serology with the breath test, demonstrating sensitivity and specificity greater than 95% [27,28]. In the absence of the reference test, the stool antigen test was employed in our study to evaluate the breath test's performance. It demonstrated good sensitivity and PPV, suggesting its efficacy for eradication monitoring. However, the low specificity and PPV values could be attributed to the different nature of the comparison test used and the limited sample size in our study. This limited sample size was due to the high cost of the examination, 40,000 CFA francs per test (excluding transport costs), compared to the locally available antigen test priced at 15,000 CFA francs. Thus, the limitations of this study included the sample size, the monocentric nature of the study, and the cost of the breath test.

Conclusion

The clinical manifestations are diverse, predominantly characterized by epigastric pain. Research on the performance of breath tests for the eradication control of *Helicobacter pylori* infection remains scarce in Africa. The carbon-13 labeled urea breath test, which is the standard reference, demonstrates good sensitivity and a good negative predictive value. It can be employed for eradication control in Congo. However, when interpretation must be conducted outside the country, challenges related to its cost and the time required to obtain results are factors that limit its feasibility.

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