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Assessment of the accuracy of the rapid test for the diagnosis of *Helicobacter pylori* in patients that didn't undergo previous eradication therapy and who went through endoscopy

Gianluca Z **ROVARIS**[1], João V **BACK**[1], Maria Paula **RONCHI-COLOMBO**[1], Vitória S **ROSA**[1], Manoel C B **CARDOSO**[2,3] and Emilio C **BERGER**[4]

[1] Curso de Medicina Universidade do Extremo Sul Catarinense, Criciúma, SC, Brasil. [2] Universidade da Região de Joinville, Joinville, SC, Brasil. [3] Hospital Dia Clinigastro, Criciúma, SC, Brasil. [4] Programa de Pós-Graduação em Ciências da Saúde, Criciúma, SC, Brasil.

HIGHLIGHTS

- *Helicobacter pylori* infection can cause potentially serious diseases.
- Serological tests are based on the detection of antibodies immunoglobulin G against *Helicobacter pylori*.
- Serological tests for the diagnosis of *Helicobacter pylori* infection are low cost tools and have easy application.
- Rapid serological test is a reasonable choice for screening large populations.

ABSTRACT – Background – *Helicobacter pylori* infection is widely spread globally and is known to cause potentially serious diseases. Several diagnostic methods exist to identify and treat carriers of this bacterium. Serological tests for the diagnosis of infection are based on the detection of antibodies immunoglobulin G against *H. pylori*, a non-invasive, inexpensive, and easy-to-perform option. **Objective –** This research aims to ascertain the accuracy of an immunochromatographic serological test to verify the feasibility of using this method in patients who have not undergone previous eradication therapy. **Methods –** Rapid tests and questionnaires were applied to 53 patients that underwent upper digestive endoscopy with research for *H. pylori* between the period of September and October 2021. The results were compared with histopathology. **Results –** In the rapid tests, seven positive and 46 negative results were obtained. When compared with the gold standard, the following values were described: sensitivity 54.5%, specificity 97.6%, positive predictive value 85.7%, and negative predictive value 89.1%. **Conclusion –** In the present study, the immunochromatographic serological tests had an accuracy close to the values found in other similar studies. Therefore, it may be concluded that the rapid serological test remains a reasonable choice for screening large populations due to its low cost and ease of application, especially in those individuals who have not undergone previous treatment.

Keywords – Diagnosis; *Helicobacter pylori;* serological tests.

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Corresponding author: Maria Paula Ronchi Colombo. E-mail: mariapaulacolomboo@gmail.com

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a gram-negative bacillus that colonizes the gastrointestinal mucosa of nearly half of the global human population with varying prevalence in different geographic regions[1]. In the early 1980s, Marshall and Warren were the first to isolate *H. pylori* in the gastric mucosa of a patient with chronic gastritis[2].

The viability of the survival of the bacterium on the mucosal surface depends on colonization factors such as urease, motility, chemotaxis, membrane proteins, and the helical shape. Moreover, *H. pylori* has well-developed mechanisms to neutralize the effects of acidic pH. Nevertheless, the exact role of virulence factors, as well as environmental factors, remains in need of further explanation, furthermore, how these factors are involved in the survival of the bacterium in the acidic environment is still unknown[3]. In most patients, *H. pylori* infection remains asymptomatic, yet it can progress to a variety of gastrointestinal diseases including chronic gastritis, peptic or duodenal ulcers, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (MALT)[4]. Patients with dyspepsia and *H. pylori* should be subjected to eradication therapy. The main cause for eradicating this bacillus in patients with dyspepsia, besides the relief of symptoms, also a lower risk of developing clinical sequelae, and the interruption of transmission of the bacteria[5].

Standard triple therapy consisting of a proton pump inhibitor (PPI) and a therapeutic plan using amoxicillin and clarithromycin was recommended for eradication. However, there was a reduction in suppression rates caused by bacterial resistance[6]. Despite the indications for PPIs having increased, many studies document inappropriate prescriptions for PPIs[7]. They are often used without discretion for long periods, which calls into question their long-term use[8]. In contrast, quadruple therapy includes a PPI, associated with clarithromycin, amoxicillin, and metronidazole or tinidazole, in sequential or concomitant therapy[9].

Currently, there are several diagnostic methods available for the detection of this infection. The choice of the method must take into consideration the clinical conditions of the patient, access to the exams, and cost-benefit[10]. Among the designated invasive exams are the urease test, culture, histopathology, immunohistochemistry, fluorescent hybridization technique, and molecular tests (such as polymerase chain reaction (PCR). Besides, the non-invasive tests include serology, breath test with urea containing labeled carbon, and fecal antigen research[11].

The most commonly used serological tests are the immunoabsorbent assay (such as ELISA - Enzyme-linked immunosorbent assay), immunochromatographic assay (rapid test), and immunoblot[5]. Nonetheless, serology can be positive due to the presence of active infection at the time of testing, previous infection, or due to cross-reaction with nonspecific antibodies[12].

The serological test has a sensitivity greater than 95% and specificity of 60 to 90%. Its advantages are low cost, simple and safe; it is not affected by gastroduodenal bleeding; it does not present false negatives due to the use of PPIs and antibiotics; it identifies virulence factors. Still, it has the following limitations: it does not offer data on antibiotic resistance; fails to distinguish between active and past infection; isn't useful to confirm *H. pylori* eradication[10].

Because this bacteria is a widespread pathogen that causes potentially serious complications in humans, early diagnosis is essential, since chronic colonization by *H. pylori* is associated with conditions like gastric atrophy and gastric cancer. This study aims to determine the accuracy of the rapid test in patients who have not undergone previous eradication therapy, thus enabling its use in public health as a tool for diagnostic screening in primary care, providing cost reduction, better choice of drugs, avoiding bacterial resistance and optimization of endoscopy services. The present study has the purpose to evaluate the accuracy of a rapid test for diagnosis of *H. pylori* in patients not submitted to previous eradication therapy, submitted to high digestive endoscopy in a private clinic in the city of Criciúma-Santa Catarina (SC).

METHODS

Study design

In this study, 56 patients who had not undergone previous eradication therapy, subjected to upper digestive endoscopy and search for *H. pylori* by gastric biopsy underwent a cross-sectional analytical obser-

vational study, with primary and secondary data collection and quantitative approach, in a private clinic in Criciúma, Santa Catarina, Brazil, between September and October of the year 2021.

All individuals characterized in the target population were included in the research, considering the procedure as census collection.

Variables investigated and analyzed included the presence of *H. pylori* in the gastrointestinal mucosa, age, sex, previous *H. pylori* eradication therapy, previous upper digestive endoscopy, smoking, alcoholism, endoscopic findings (non-ulcer dyspepsia, gastroesophageal reflux disease, gastric ulcer, duodenal ulcer, normal mucosa, atrophic gastritis, intestinal metaplasia, enanthematous gastritis, erosive gastritis, nodular gastritis, among others), biopsy with *H. pylori*, rapid test for *H. pylori*.

Data collection

The data were collected through self-administered questionnaires answered by the patients between September and October 2021. The histopathology reports of the gastric biopsies of the included patients were analyzed through their medical records.

Performing the rapid serological test by immunochromatography.

Patients who met the inclusion criteria underwent the biopsy with *H. pylori* investigation in the determined period and answered the questionnaire were submitted to a rapid serological test by immunochromatography (MedLevensohn®) before the procedure.

A small portion of blood collected by digital puncture was placed in the rapid test hole, and a drop of buffer solution was added. After that, the result was read within 10 minutes. The validity of the result was confirmed by the appearance of the control line in the test.

Statistics

The data collected were analyzed with the help of IBM Statistical Package for the Social Sciences (SPSS) software version 21.0. Qualitative variables were expressed as frequency and percentage. The investigation of the existence of an association between qualitative variables was carried out using the likelihood ratio, with subsequent analysis of residuals when statistical significance was observed.

Ethical considerations

After being approved by the Ethics in Human Research Committee, under opinion number 4,874,651 and CAAE 48145021.6.0000.0119. Patients were only interviewed and tested after signing the informed consent form (ICF) and and there was informed consent to patients.

RESULTS

The final sample consisted of 53 individuals, 36 (67.9%) of were female with a mean age of 45.6 years. Thirty-five (66.0%) participants had already undergone previous endoscopic examination. The risk factors smoking and alcoholism were present in 3 (5.7%) and 10 (18.9%) study participants, respectively. Regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) was seen in 15 (26.8%) individuals. About recent chronic use of PPIs, 23 (43.4%) make chronic use of PPIs, among this group 12 (52.2%), use daily, 5 (21.7%) every other day, and 6 (26.1%) less than 3 times a week (TABLE 1).

TABLE 1. Clinical-epidemiological characteristics of patients undergoing the study.

	n (%)
Sex	
Female	36 (67.9)
Male	17 (32.1)
First Endoscopy	18 (34.0)
Recent PPI use	23 (43.4)
Every day	12 (52.2)
Every Other day	5 (21.7)
At least three times a week	6 (26.1)
Alcoholic	10 (18.9)
Smoker	3 (5.7)
Continuous use of NSAIDs	15 (28.3)

PPI use and presence of *H. pylori* TABLE 2 correlates by likelihood ratio, the presence of *H. pylori*, and the use of PPIs. Nevertheless, no statistically significant difference was observed between the variables considered.

TABLE 2. Correlation between PPI use and the presence of *H. pylori.*

	Gastric biopsy, Mean ± DP		*P*-value
	Positive	Negative	
	n=11	n = 42	
Recent PPI use			0.379*
No	7 (63.6)	23 (54.8)	
Yes, Every day	2 (18.2)	10 (23.8)	
Yes, Every Other day	-	5 (11.9)	
Yes, less than three times a week	2 (18.2)	4 (9.5)	

*Value obtained after applying the likelihood ratio test.

Endoscopic findings and the presence of *H. pylori*

TABLE 3 correlates endoscopy findings (GERD, erosive gastritis, gastric ulcer, atrophic gastritis, nodular gastritis, and normal examination) with biopsy positivity/negativity for *H. pylori*. Among all findings, there was a statistically significant correlation between the presence of nodular gastritis and positivity for *H. pylori* in gastric biopsy (*P*=0.04).

Immunochromatographic rapid serological test compared to biopsy.

It was verified through seven positive and 46 negative results in the immunochromatographic rapid serological test (IgG), and 11 positive and 42 negative results in the gastric biopsy, showing a sensitivity of 54.5% and specificity of 97.6%. Besides, the findings appoint a positive predictive value of 85.7%, a negative predictive value of 89.1%, and an accuracy of 88.7%, in the diagnosis of *H. pylori*, compared to gastric biopsy (TABLE 4).

DISCUSSION

In the present study, nodular gastritis was the only endoscopic finding that was statistically significantly correlated with the presence of *H. pylori*. Similarly, studies conducted in 1995[13], 2013[14] and 2019[15] noted sensitivity (32.1%, 5.3%, 6.4%) and specificity (95.8%, 98.8%, 98.3%) respectively. Higher titers of serum *H. pylori* antibodies correlate with the presence of modularity on endoscopy examination.

The present study obtained, through the application of rapid serological tests (IgG) immunochromatographic for detection of *H. pylori*, seven positive and 46 negative results resulting in a sensitivity of

TABLE 3. Correlation between endoscopic findings and the presence of *H. pylori.*

	Biopsy (%)		*P*-value
	Positive	Negative	
	n=11	n=42	
Enanthematous Gastritis			
Yes	4 (36.4)	25 (59.5)	0.194†
No	7 (63.6)	17 (40.5)	
GERD			
Yes	2 (18.2)	16 (38.1)	0.296†
No	9 (81.8)	26 (61.9)	
Erosive Gastritis			
Yes	5 (45.5)	9 (21.4)	0.134†
No	6 (54.5)	33 (78.6)	
Normal			
Yes	0 (0.0)	6 (14.3)	0.324†
No	11 (100.0)	36 (85.7)	
Gastric Ulcer			
Yes	0 (0.0)	3 (7.1)	0.999†
No	11 (100.0)	39 (92.9)	
Atrophic Gastritis			
Yes	0 (0.0)	2 (4.8)	0.999†
No	11 (100.0)	40 (95.2)	
Nodular Gastritis			
Yes	2 (18.2)*	0 (0.0)	0.040†
No	9 (81.8)	42 (100.0)*	
Gastric Atrophy			
Absent	8 (72.7)	37 (88.1)	
Discrete	3 (27.3)	4 (9.5)	0.294††
Moderate	0 (0.0)	1 (2.4)	
Intestinal Metaplasia			
Absent	10 (90.9)	39 (92.9)	
Discrete	1 (9.1)	2 (4.8)	0.696††
Moderate	0 (0.0)	1 (2.4)	

Values obtained after applying the tests: †Fisher's Exact; *Statistically significantvalues after residual analysis.

TABLE 4. Immunochromatographic rapid serological test compared to biopsy for diagnosis of *H. pylori.*

	% (CI95%)
Rapid test	
Negative	46 (86.8)
Positive	7 (13.2)
Biopsy	
Negative	42 (79.2)
Positive	11 (20.8)
Sensibility	54.5 (25.1–84.0)
Specificity	97.6 (93.0–100.0)
Positive predictive value	85.7 (59.8–100.0)
Negative predictive value	89.1 (80.1–98.1)
Accuracy	88.7 (80.1–97.2)

54.5% and a specificity of 97.6%, positive predictive value (PPV) of 85.7%, negative predictive value (NPV) of 89.1%, and accuracy of 88.7%, when compared to the gold standard (gastric biopsy).

A similar study published by the Journal of Gastroenterology, conducted in Israel in 1999[16], selected older patients and compared the immunochromatographic (IgG) serological test with gastric biopsy. It achieved sensitivity, specificity, PPV, and NPV of 84%, 52%, 76%, and 63%, respectively. The low values of sensitivity and negative predictive value may be related to a site of infection in the stomach different from the site where the biopsy was performed, failure to detect antibodies due to gastric atrophy and intestinal metaplasia, and the possibility of previous infection and maintenance of high serum antibodies. The absence of antibodies in *H. pylori*-positive patients has also been reported in elderly patients[17].

Another research conducted in Minas Gerais, Brazil[18] in 1998, evaluated adult patients and by using the Elisa method and selecting culture with carbofuxin and urease as the gold standard, obtained sensitivity, specificity, PPV, and NPV of 95.4, 100, 100, 91.4%, respectively. In another study conducted in Seoul, South Korea[19], among adults, in the year 2015, three different serological tests by the Elisa method were compared, achieving sensitivity of 89.7%, 100%, 100%, and specificity of 85.5%, 75.4%, 80.7%. In this research, the Urea Breath Test was used as the gold standard. Moreover, another comparative study between 29 brands of tests, conducted in France[20], showed a significant difference between tests that used different serological methods, so that the ELISA method, when compared to immunochromatography, showed higher sensitivity, specificity, PPV, and NPV.

On the other hand, a study conducted in 2018 in Surubaya, Indonesia[21], among pediatric patients using gastric biopsy as Standard-Our, achieved sensitivity, specificity, positive predictive value, and negative predictive value of 100%, 15.38%, 15.38%, and 100% respectively. The low specificity obtained in the study can be explained by the occurrence of cross-reactions between different bacteria that can stimulate the production of antibodies similar to those produced by *H. pylori*[22]. Another research among minors, a Japanese study published in the journal Digestion in 2019[23], conducted among 13- and 14-year-old students obtained specificity of 99.5% and sensitivity of 93.3%; The justification for antagonistic results between the two studies may be associated with the use of different cutoff values, since antibody production may differ between adults and children[24].

Another non-invasive, low-cost method available, approved and indicated by the FDA (food and drug administration) for primary diagnosis and post-treatment monitoring, is the Monoclonal Fecal Antigen Test. A meta-analysis of 22 studies and 2499 patients published in 2006 by the American Journal of Gastroenterology found this method's sensitivity and specificity to be 94% and 97%. Until very recently, the urea breath test was the only noninvasive method available that was accurate for confirmation of eradication since serology requires a few months to show good accuracy for the drop in antibody titer[25].

CONCLUSION

The accuracy of the rapid test was similar to results already found in previous studies. A slight superiority of the ELISA method compared to immunochromatography can be observed.

The present study has some experimental biases, such as a few participants (sample bias) and the use of a kit with antigens not geographically validated. However, as in previous studies, the test proved to be inferior to other widespread invasive and noninvasive diagnostic methods. Nevertheless, this method still seems to be the option of choice for mass screening, due to its low cost, ease of application of the test, and speed in obtaining results.

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Authors' contribution

Rovaris GZ, Back JV, Ronchi-Colombo MP, Rosa VS, Cardoso MCB, Berger EC. Rovaris GZ, Back JV: article author, survey execution, data collection, writing of the text, statistical analysis. Ronchi-Colombo MP: article author, writing of the text. Rosa VS: text review. Cardoso MCB: text review, lead research. Berger EC: lead research.

Orcid

Gianluca Z Rovaris: 0009-0003-5885-9846.
João V Back: 0009-0002-2754-4502.
Maria P Ronchi Colombo: 0000-0003-4158-7197.
Vitória S Rosa: 0009-0009-4907-7029.
Manoel C B Cardoso: 0000-0003-2239-6387.
Emilio C Berger: 0009-0008-3017-8789.

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RESUMO – Contexto – A infecção pelo *Helicobacter pylori* apresenta-se amplamente difundida globalmente e é comprovadamente causadora de patologias potencialmente graves. Diversos métodos diagnósticos existem com o propósito de identificar e tratar os portadores dessa bactéria. Testes sorológicos para diagnóstico da infecção se baseiam na detecção de anticorpos imunoglobulina G anti-*H.pylori*, sendo uma opção não-invasiva, barata e de fácil realização. **Objetivo –** O objetivo dessa pesquisa é determinar a acurácia de um teste sorológico imunocromatográfico para verificar a viabilidade do uso desse método em pacientes que não realizaram terapia de erradicação prévia. **Métodos –** Foram aplicados testes rápidos e questionários em 53 participantes que realizaram endoscopia digestiva alta com pesquisa de *H. pylori* entre o período de setembro e outubro de 2021. Os resultados foram comparados com a histopatologia. **Resultados** – Foram obtidos nos testes rápidos 7 resultados positivos e 46 negativos. Ao comparar com o padrão-ouro, os seguintes valores foram descritos: Sensibilidade 54,5%, especificidade 97,6%, valor preditivo positivo 85,7% e valor preditivo negativo 89,1%. No presente estudo, os testes sorológicos imunocromatográficos tiveram acurácia próxima aos valores encontrados em outros trabalhos semelhantes. **Conclusão –** Sendo assim, conclui-se que o teste rápido sorológico permanece como escolha razoável para *screening* de grandes populações devido ao seu baixo custo e facilidade de aplicação, especialmente naqueles indivíduos que não realizaram tratamento prévio.

Palavras-chave – Diagnóstico; *Helicobacter pylori*; testes sorológicos.

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