Diagnostic Methods in *H. pylori* Infection

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Helicobacter pylori (*H. pylori*) develops potentially life-threatening conditions in adults if not appropriately treated. Helicobacter pylori is a common human pathogen that was first described in the stomach many years ago.

H. pylori children diagnostics test chronic gastritis

1. Introduction

Among the most widespread childhood infections, *Helicobacter pylori* (*H. pylori*) develops potentially life-threatening conditions in adults if not appropriately treated. *H. pylori* is a common human pathogen that was first described in the stomach many years ago [1]. In 1983, *H. pylori* was isolated from the gastric antrum by Marshall and Warren and described as a Gram-negative, flagellated, and microaerophilic bacterium [2]. The discovery of *H. pylori* is of crucial importance in gastroenterology; this bacterium is associated with chronic gastritis, peptic ulcers, gastric cancer, and lymphoid tissue lymphoma associated with the gastric mucosa [3].

2. Noninvasive Diagnostic Tests

2.1. Urea Breath Test

The urea breath test (UBT) was the first method of diagnosis and still represents the most popular noninvasive test for diagnosing *H. pylori* infection. UBT presents multiple advantages in detecting *H. pylori* infection, especially in children and teenagers, being a simple, non-invasive, and reliable method, with a sensitivity and specificity of 75% to 100% [4].

A recently published meta-analysis evaluating the diagnostic accuracy of *H. pylori* infection using UBT in adult patients with specific dyspeptic symptoms revealed a sensitivity of 96% and a common specificity of 93% [5].

UBT is also helpful for epidemiological studies and for evaluating eradication therapy efficiency [6].

2.2. Stool Antigen Test

The stool antigen test (SAT) is a noninvasive method with remarkable sensitivity and specificity, 94% to 97%, used to diagnose *H. pylori* infection [7].

Also used to confirm eradication after anti-infective therapy, the cumulative sensitivity and specificity for the monoclonal SAT were 93% and 96%, respectively, according to data published in global meta-analyses [7].

The accuracy of the stool antigen diagnosis is influenced by factors such as the use of antibiotics, PPI, or other drugs such as N-acetylcysteine, and the coexistence of complications such as upper digestive hemorrhage. Before testing, sample preservation, temperature, and transport time can influence the diagnostic accuracy of the SAT [8][9].

2.3. Serological Tests

Currently, numerous serological tests are available based on the detection of anti-*H. pylori* IgG antibodies; the EIA test is the most used. Serological tests are frequently used in the screening of epidemiological studies due to their acceptability for patients, prompt result, and inexpensive cost.

The accuracy of serological tests is not affected by digestive hemorrhaging, gastric atrophy, antibiotics, or PPIs, which cause false negative results in other methods.

The disadvantage of serological tests is the impossibility of evaluating the efficacy of the eradication therapy because the levels of anti-*H. pylori* antibodies can persist in the blood for a long time, even after the eradication of the infection. Antibody-based tests do not distinguish between active infection and previous exposure to *H. pylori*, so further confirmation is required before the initiation of eradication therapy [6].

The determination of *H. pylori* antibodies has a decisive role in studies related to the pathogenesis of the infection and the assessment of virulence factors because specific antigenic proteins can be detected via immunological techniques, thus conferring an additional diagnostic value. Potential biomarkers have been tested to identify subjects infected with *H. pylori* strains with a high risk of developing complications and assess the prognosis of diseases associated with *H. pylori* infection.

Thereby, in patients affected by *H. pylori*, the detection of serum CagA, VacA, and GroEL antibodies was correlated with the development of gastric precancerous lesions and even gastric cancer, making these serum markers potential predictive factors for patients infected with high-risk strains [10][11].

2.4. Polymerase Chain Reaction

A PCR test detects *H pylori* in stool and is a reliable and fast technique that offers the advantage of identifying specific genotypes, with a possible role in determining the antibiotic resistance of bacteria [12][13].

The detection of infection through PCR in the oral cavity uses *H. pylori*-specific primer sets based on specific complete genome sequences of 48 *H. pylori* strains, increasing the diagnostic accuracy [14].

3. Invasive Tests

3.1. Endoscopy

Conventional endoscopic examination is routinely performed to evaluate lesions associated with *H. pylori* (chronic atrophic gastritis, peptic ulcers, MALT lymphomas, and gastric cancer). Endoscopy is also used for taking biopsy samples from the gastric mucosa for further determinations, such as rapid urease tests, histopathological examinations, cultures, and molecular methods. The biopsy is preferably performed from the gastric antrum.

Chromoendoscopy with phenol red is a method used for detecting *H. pylori* infection due to the specific urease activity of the bacterium, but its sensitivity (73–81%) and specificity (76–81%) are low [15][16].

Confocal laser endomicroscopy (CLE) represents an endoscopic method that allows the histological examination of the gastric mucosa. Characteristic for the positive diagnosis of *H. pylori* infection is the presence, at laser confocal endomicroscopy, of white spots, neutrophils, and sometimes micro-abscesses. The accuracy, sensitivity, and specificity of this method have been evaluated in various studies at 92.8%, 89.2%, and 95.7%, respectively [17].

3.2. Histological Examination

The histological examination is the gold standard for diagnosing *H. pylori* infection. The examiner's experience influences the accuracy of the diagnosis, size, site, number of biopsies, and staining procedures, as well as the use of inhibitors of the proton pump (PPI) and antibiotics.

3.3. The Rapid Test with Urease

The rapid urease test (RUT) is considered the most useful invasive test in the diagnosis of *H. pylori* infection because it is quickly available, not expensive, easy to perform, and, in particular, has a sensitivity of over 85–95% and a specificity between 95% and 100%, with increased accuracy with the number of gastric biopsies [18].

3.4. Microbiological Culture

The cultivation of *H. pylori* from the gastric biopsy sample is a diagnostic method with a specificity of approximately 100% but less sensitivity, with variability between 85% and 95%. Culturing allows the isolation of *H. pylori* for subsequent phenotypic and genotypic characterization, with a role in the efficiency of the therapeutic scheme. The cultivation of *H. pylori* provides the ability to manage and assess antibiotic resistance in extensive observational studies [6].

3.5. Polymerase Chain Reaction

PCR is widely used to detect *H. pylori* infection from gastric biopsy samples, saliva, and stool. Compared to conventional tests, PCR offers a sensitivity and specificity above 95%. PCR provides information on *H. pylori's*

virulence factors by detecting specific mutations that determine antibiotic resistance, such as resistance to macrolides and fluoroquinolones [19][20].

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