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LABORATORY SCREENING FOR H.Pylori AMONG HIGH RISK POPULATION

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Abstract:

Helicobacter pylori is a highly motile bacteria with numerous unipolar flagella that generates urease. H. pylori's virulence components consist of its flagella and urease. H. pylori frequently causes a chronic infection in the stomach, which can result in gastric and duodenal ulcers, gastric malignancies, and gastric lymphomas, as well as other gastrointestinal illnesses. For H. pylori, there are numerous invasive and noninvasive clinical laboratory testing. Laboratory testing is not recommended for asymptomatic patients and should only be considered if H. pylori infection therapy is planned. If an endoscopy is done on the patient, invasive testing for H. pylori, including as tissue histology, culture, and fast urease assays, are utilized. Patients whose symptoms do not require endoscopy are advised to undergo noninvasive tests for H. pylori, such as enzyme antibody and urea breath tests. Therefore, comprehensive search through literature using electronic databases; PubMed and Embase to search all relevant studies to our review topics, that were published in English language and limited to human subjects up to June 2022.

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INTRODUCTION:

Helicobacter pylori is likely the most successful human pathogen, as it has colonized the stomachs of roughly half of the world's population [1]. In several regions of the world, the incidence is even higher, such as 80% or more in portions of China and some Eastern European and South American countries, although it is decreasing in the United States and Western European nations [2,3]. Less-developed areas are more likely to have high H. pylori prevalence and higher rates of recurrence of infection after treatment [4]; rates of infection are correlated with socioeconomic characteristics such as level of education and living standards.

Despite a reducing prevalence, gastric cancer was the fifth most prevalent cancer and the third leading cause of cancer-related deaths globally in 2012 [5], accounting for over three-quarters of a million fatalities annually. The current accepted model for stomach carcinogenesis is an extension of the original model published in 1975 by Correa et al. [6]. This model proposes that gastric cancer is the end result of a series of mutations that begin with an unknown environmental trigger in early life, now known to be infection with H. pylori, resulting in a superficial gastritis, followed by chronic non-atrophic gastritis, gastric atrophy, and achlorhydria [7]. The development of gastric intestine metaplasia, which assumes increasingly basic forms, is followed by cell change, dysplasia, and ultimately cancer (Figure 1) [6].

H. pylori generates a pattern of gastritis known as acute-on-chronic inflammation, which leads to chronic progressive gastric damage and, eventually, gastric atrophy [8]. Stomach cancer is a malignancy associated with inflammation in which the infection directly and indirectly causes progressive genetic damage to the gastric epithelium, which may finally develop to gastric adenocarcinoma. In H. pylori-infected patients, the risk of developing gastric cancer can be calculated based on the degree and extent of mucosal damage and atrophy, identified as metaplastic epithelia with or without intraepithelial neoplasia or dysplasia. Eradication of H. pylori reduces the risk of gastric cancer, which is proportional to the extent of genetic and epigenetic changes existing at the time of H. pylori eradication [9,10]. The translation of this basic and clinical information into public health intervention through population-wide screening and eradication of H. pylori, which would ultimately prevent the development of stomach cancer, is, however, lacking. First, we need up-to-date information on the worldwide disease burden of H. pylori infection and stomach cancer, and we must better define the target groups for screening and eradication initiatives. Second, the implementation of mass screening requires consideration of the choice of non-invasive test, when to proceed to endoscopy, whether and how to test for eradication efficacy and how to survey those with advanced atrophic gastritis, how to implement this programmed, how to treat asymptomatic H. pylori-infected subjects for gastric cancer prevention, and how to identify subjects at higher risk of gastric cancer for endoscopic examination [10,11].

DISCUSSION:

Numerous studies have demonstrated that H. pylori infection is a key factor in the etiology of peptic ulcers, gastric ulcers, noncardia gastric cancer, low-grade mucosa-associated lymphoid tissue (MALT) lymphoma of the stomach, and other diseases, including non-ulcer dyspepsia and gastrointestinal reflux diseases. H. pylori is a gram-negative spiral bacterium that colonizes the gastric epithelium [12,13], but not the duodenal epithelium. The organism possesses specific, crucial characteristics: A) H. pylori create high quantities of urease, which is essential for colonization, pathogenicity, and neutralizing the effects of an acidic environment via the production of ammonia [14,15]. B) In vivo, H. pylori promotes epithelial cell growth and apoptosis. Nevertheless, infection with bacteria of the CagA genotype results in greater proliferation than apoptosis [16]. C) The production of a vacuolating toxin and the presence of the CagA gene, which encodes virulence genes involved in the stimulation of epithelial chemokine response, are the primary determinants of H. pylori [16]. The body of the stomach becomes highly inflamed at initial infection with H. pylori, and acid output is blocked [12]. With H. pylori infection, the inflammation migrates to the antrum, resulting in antral gastritis and increased acid output. Reduced bicarbonate secretion, intestinal inflammation, and ulceration are observed in the duodenum [12,16]. Those infected with H. pylori who develop acid hypersecretion are susceptible to developing duodenal ulcers. If duodenal ulcer is evident, eradication of the H. pylori bacteria from the gastric mucosa is curative [12]. Most infected individuals may develop a symbiotic connection with the H. pylori organism. Nonetheless, a few patients with illness in the stomach body may have normal or reduced acid secretion and develop gastric ulcers [14,15]. H. pylori is implicated

in the pathophysiology and development of both adenocarcinoma and stomach MALT lymphoma, according to substantial evidence. H. pylori's mechanism and significance in the etiology of gastric cancer and lymphoma remain undefined. H. pylori infection is a risk factor. However, only a small fraction of H. pylori-infected patients actually develops cancers. Therefore, H. pylori must interact with additional environmental and genetic cofactors [15,16].

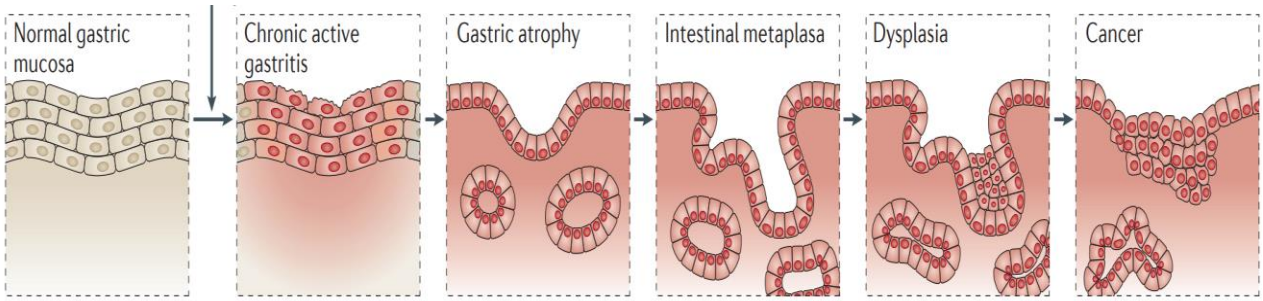

FIG. 1: A model for the development of gastric cancer [6].

Indications for Diagnostic Testing:

Currently, the diagnostic gold standard for H. pylori infection necessitates the histologic inspection of two specifically stained stomach antral biopsy specimens (28,29). Sampling and observer error have the potential to restrict the utility of routine histology in normal clinical practice. Currently, there are no clearly and reliably defined indications or guidelines for determining whether a child or an adult should undergo definitive testing for H. pylori infection [17,18]. H. pylori testing should only be deemed appropriate if treatment is planned. Currently, there is no evidence that H. pylori eradication is beneficial for asymptomatic children, adults, or adults [19]. Therefore, the physician should utilize a meticulously documented history of gastrointestinal complaints and symptoms to determine H. pylori diagnosis indicators (TABLE.1). If H. pylori is detected by a credible test, the infection is presumed to be treated [19].

General Diagnostic Testing

The reference method (gold standard) for the diagnosis ofactive *H. pylori* infection is esophago-gastro-duodenoscopy with gastric biopsies. At present, there are numerous other accurate detection assays, which can be categorized as invasive or noninvasive. The primary invasive technique is endoscopy with biopsy, which enables histological examinations to identify the microorganisms directly. Most of the noninvasive techniques rely on the detection of biochemicalproperties of *H. pylori* (the ability to hydrolyze urea), or the response of the immune system with the production of specific antibodies [19].

Histological testing:

For the diagnosis of H. pylori infections, histological staining of stomach biopsies is still regarded as the gold standard. Two specifically coloured gastric antral biopsy specimens are examined [20,21]. In the hands of professionals, Giemsa, Warthin-Starry, and Genta stains can be as accurate as 98%, according to studies [18,21]. These two stains increase the percentage of organisms that can be positively identified. Histological investigation necessitates expensive intrusive procedures, such as endoscopy. In regular clinical practice, sampling error is cited as a source of inaccurate histological diagnosis; hence, some authors have suggested that additional specimens be collected from the lesser curvature and/or the stomach body to improve diagnostic accuracy [19,21].

Culture as testing method:

H. pylori is a microaerophilic bacterium that must be cultured as a testing method. Culture of biopsies is the most specific approach for diagnosing H. pylori infection [18,19]. Due to the organism's sensitivity, however, the culture method is exceedingly insensitive; hence, routine culture cannot be considered an appropriate gold standard for general clinical practice.

In tissue culture, H. pylori grows slowly and requires 2–5 days to become positive. Identification is based on Gram stain morphology in addition to positive urease, catalase, and oxidase reactions.

Due to the organism's sensitivity, the culture yield may decrease if the stomach biopsies are not performed correctly. Consequently, a negative culture result does not exclude H. pylori infection. With the culture

approach, experienced laboratories have demonstrated sensitivities of at least 90 percent [22,23].

The major advantage of utilizing culture as a diagnostic method is that culture and isolation of the H. pylori bacterium can help select the choice of antibiotic [23].

Rapid Urease Tests

Owen et al. [24] reported in 1985 that H. pylori exhibited a quick urease hydrolysis reaction that differentiated it from other bacteria. Several diagnostic kits based on the urease reaction have been developed.

The test requires the addition of a gastric mucosal biopsy to a urea substrate and a pH-sensitive marker in order to detect the ammonia produced by the urease reaction during pH rise [19].

At 1 hour, the test endpoint is measured. When read after more than one hour, there are several false-positive results, and specificity drops to 68% [25]. Rapid urease tests are straightforward to administer, however they require endoscopic biopsies.

The sensitivity of highly sensitive fast urease tests was shown to be comparable to that of culture regardless of testing time, but lower than that of histology a few months after treatment [26]. However, the very sensitive fast urease test was accurate in verifying treatment success [26] when utilized many months following therapy.

Polymerase Chain Reaction-Based Molecular Diagnosis (PCR):

Molecular assays, such as PCR, may be utilized for the exact diagnosis of H. pylori infections. Testing bacteria with molecular techniques does not require that they be alive. Numerous PCR techniques are highly accurate at diagnosing H. pylori from clinical biopsies. It is widely recognized that PCR adds little to other procedures when used to biopsy samples [27]. The combination of culture and histology detects H. pylori in about the same proportion of patients as PCR [28,29]. Gastric juice, which can be obtained through nasogastric catheter, demonstrates the principal advantage and utility of PCR. Westblom et al. [30], utilizing PCR on specimens of 5 mL gastric juice, detected H. pylori infection with a sensitivity of 96% and a specificity of 100%. With the use of a highly sensitive semi-nested PCR assay on stomach juice samples taken with capsulated strings, Yoshida et al. [31] found 97% of cases of recurrent infection of H. pylori within 8 wk following antimicrobial therapy.

TABLE. 1: Diagnostic tests for Helicobacter pylori

Tests	Advantages	Disadvantages
Non-invasive		
Serology	Widely available, relatively inexpensive	Cannot be used to confirm eradication after treatment; does not
Urea breath test	High sensitivity and specificity; no specific transport conditions; good test to use to confirm eradication of *H. pylori* infection after treatment	permit antimicrobial sensitivity Cannot do antimicrobial sensitivity; use ^{14}C radioactive-labeled material
Stool *H. pylori*	Useful to confirm eradication of *H. pylori* a few weeks	Collection of stool specimen
antigen test	after treatment	
Invasive		
Histology	Can estimate presence of *H. pylori* and extent of inflammation and damage; can do etrospective examination	Endoscopy to obtain samples; performance depends on experience of pathologist; cannot do antimicrobial susceptibility studies
Culture	100% specific; allows testing for antimicrobial sensitivity; permits typing of strains	Endoscopy needed to obtain samples
Rapid urease test	Close to 100% specific; results within serial	Endoscopy needed; no antimicrobial sensitivity studies can be
	hematoxylin-eosin-stained tissue sections 1–2 hours	done
Molecular methods	High sensitivity and specificity; can do retrospective	Does not permit antimicrobial susceptibility testing; requires skills
(PCR)	analysis; applicable to special samples such as oral	in testing personnel

	and gastric fluids, stool, environmental samples	

CONCLUSION:

It is estimated that around fifty percent of the world's population is infected with H. pylori. Humans appear to be the infection's natural host and source. For in vivo proliferation, H. pylori requires gastric-type mucosa, and eating appears to be the most prevalent route of infection. Numerous investigations have shown that H. pylori infection has a significant role in the etiology and pathophysiology of gastric and duodenal ulcers, gastric cancer, gastric MALT lymphoma, and other gastrointestinal illnesses. There are numerous diagnostic tests available for H. pylori infections (Table 1). In general, laboratory testing in asymptomatic children and adults is not indicated. Testing should only be considered if H. pylori infection therapy is planned. The most crucial factor is whether or not the patient will undergo endoscopy.

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