Characteristics of intestinal microflora in gastroduodenal pathologies related to helicobacter pylori and some aspects of its diagnostics

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Abstract.
The need to clarify the interaction between H. pylori and the intestinal microflora and its role in the pathogenesis of the disease is explained by the prospect of considering the changes in the intestinal microflora in the treatment of diseases related to H. pylori. Also, the identification of non-invasive methods that can determine the nature (gastritis or gastroduodenal ulcer) and localization of H. pylori-related gastroduodenal pathologies offer opportunities in the diagnosis of H. pylori-related diseases.

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About 50% of the world's population is infected with Helicobacter pylori infection, and the prevalence of this infection in developing countries is 70-80% [1, 2]. This microorganism is not only the main causative agent of gastritis and gastric ulcer, but also a risk factor for gastric adenocarcinoma. Thus, H. pylori have an etiological role in approximately 50-60% of gastritis, 90% of duodenal ulcer disease, 50-80% of gastric ulcer disease, and 60-70% of gastric cancer cases [3].

More than 80% of peptic ulcer diseases are caused by H. pylori infection, and the risk of death in such patients is about 15%. Gastric cancer is the third leading cause of cancer-related deaths in the world, and 74.7% of this problem is caused by H. pylori [1, 4]. Statistics show that peptic ulcers and stomach cancer together kill more than one million people worldwide every year, and therefore H. pylori infection always remains an important health problem [5].

In addition, recent studies have focused on studying the effects of H. pylori and its metabolism on the stomach and intestinal microflora [6, 7, 8, 9]. At present, the idea that this bacterium causes pathologies in the host body by changing the normal microflora is increasing. As a result of research, it was found that there is a significant relationship between H. pylori and the microflora of the stomach and duodenum [10, 11]. In various studies, during H. pylori colonization, Enterococcus spp., and Staphylococcus aureus increased in the stomach and duodenum, while lactobacilli decreased in the normal microflora of the stomach [12, 13]. Bifidobacterium spp., Bacteroides spp., and a significant change in the amount and localization of other bacteria were observed [14, 15]. However, the research conducted so far could not unambiguously explain the nature of changes in intestinal microflora in diseases caused by H. pylori. Also, the interaction between H. pylori and intestinal microflora and its role in the pathogenesis of the disease has not been clarified.

It is known that the normal microflora of the gastrointestinal tract can be changed under the influence of various factors, and dysbiotic conditions can occur for many reasons. Thus, the role of intestinal parasites and helminths is undeniable. However, the possible relationship between
H. pylori and dysbiotic conditions has hardly been studied [16, 17, 18].

There are many invasive and non-invasive examination methods for the diagnosis of H. pylori infection. Invasive methods include the following methods applied based on endoscopy and biopsy: direct microscopic examination, culture method, rapid urease test, cyto-histological examinations, and molecular-genetic method (polymerase chain reaction - PCR). Non-invasive methods include the serological method, urea breath test (UNT), determination of carbon isotope (13C) in urine or blood, antigen test with saliva and stool, as well as molecular genetic method (PCR) [19, 20, 21, 22].

As mentioned, Helicobacter pylori cause chronic active gastritis, atrophic gastritis, peptic ulcer disease, gastric cancer, mucosa-associated lymphoid tissue lymphoma (mucosa-associated lymphoid tissue - MALT), etc. causes such diseases. Currently, more than half of the world's population is infected with H. pylori infection, but the frequency of this spread depends on geographical area, socio-economic conditions, age, race, etc. such factors also play an important role [23]. In this regard, accurate diagnosis of H. pylori infection is one of the important conditions for the effective treatment of many gastroduodenal diseases. Considering the recommended indications for H. pylori eradication therapy and the wide range of available diagnostic methods, choosing a reliable diagnostic method before and after eradication treatment is a necessary condition. Taking this into account, only high-precision tests should be used in clinical practice, and the sensitivity and specificity of the corresponding test should be more than 90%. When choosing tests, the clinical condition of the patient, the probability ratio of positive and negative results, the usability of the tests, finances, etc. factors should be considered [24].

There are several invasive and non-invasive diagnostic methods for the detection of H. pylori, and each method has advantages and disadvantages in different clinical situations. Invasive examinations are performed based on endoscopic biopsy samples and include histological and cultural methods, rapid urease tests, and molecular-genetic methods. The cultural method is considered the "gold standard"
because it is used to obtain a pure culture of H. pylori from a biopsy sample of the stomach and to determine its sensitivity to antibiotics. The improvement of endoscopy tools also helps in the "real-time" diagnosis of H. pylori during this examination. Despite all these advantages, the main drawback of invasive methods is endoscopic intervention, i.e. swallowing the probe, which causes serious anxiety, discomfort, and additional stress in patients.

Non-invasive examination methods include urea breath test (UNT), serological method, stool antigen test, and molecular-genetic methods. UNT and stool antigen tests are the most common non-invasive methods, and stool antigen testing is more commonly used as an alternative when UNT cannot be administered. However, more serological methods are used in primary research (screening) and epidemiological studies [23].

Stool antigen test (Stool Antigen Test). It is a non-invasive method used in the diagnosis of H. pylori infection with 94% sensitivity and 97% specificity in a global meta-analysis. Like all methods, this method has its advantages and disadvantages. The main advantage of the test is its non-invasiveness, cost-effectiveness, routineness, accessibility, the possibility of use in any age group, etc. As mentioned above, its disadvantages are the lack of 100% sensitivity and specificity and the possibility of false positive results due to the sensitivity of the test to various adverse effects.

A stool antigen test is used to detect the presence of H. pylori antigen in stool samples. There are two variants of the H. pylori stool antigen test - enzyme immunoassay-EIA and immunochromatography assay-ICA. These tests are based on the use of polyclonal or monoclonal antibodies. In general, monoclonal antibody-based tests are more accurate than polyclonal antibody-based tests, in other words, enzyme immunoassay-based tests provide more reliable results than immunochromatography-based tests [25].

EIA-based serological tests with stool antigen testing are more accurate and sensitive than ICA-based tests. To prove this, a study compared the results of 29 commercial serological tests (17 EIA-based and 12 ICA-based) and found
that 9 of the 17 EIA-based tests had an accuracy greater than 90%, while only one of the 12 ICA-based tests' accuracy was >90%. EIA-based tests ranged in sensitivity from 57.8% to 100% and specificity from 58.7% to 96.8%; In ICA-based tests, the sensitivity ranged from 55.6% to 97.8% and the specificity ranged from 60.3% to 96.8%. All this suggests that serological tests should be selected according to their parameters to achieve different goals, such as research, preliminary diagnosis, or confirmation of other tests [26].

The molecular-genetic method is mainly important in determining the antibiotic resistance of bacteria. This method uses saliva, gastric juice, gastric mucosa biopsies, etc. can be implemented with other examples as well [24].

Although all these methods are used in different frequencies, the determination of H. pylori in patients with gastroduodenal pathology by non-invasive methods still retains its relevance. The ideal method is one with high sensitivity and specificity, easy to apply, relatively quick response, minimally invasive, and financially inexpensive. An examination method that can fully meet all these requirements has not yet been discovered. However, among non-invasive methods, stool antigen testing is simple and easy to apply and is also useful for detecting active infection. This test can also be used to detect the incidence of H. pylori infection in asymptomatic individuals for epidemiological studies and control purposes after treatment (usually after 4 weeks). The sensitivity and specificity of the method are 95% [27, 28].

However, the most important drawback of non-invasive methods is the impossibility of isolating bacteria and determining their sensitivity to antibiotics due to the inability to directly interfere with the digestive tract. Therefore, it is usually recommended to use two methods together in initial recognition. The use of non-invasive tests to detect H. pylori in patients with ulcer-like dyspepsia or other gastrointestinal symptoms or suspected peptic ulcer is appropriate [3].

One of the non-invasive examination methods we mentioned is the serological method. Serological methods include latex agglutination, complement fixation reaction (CBR), ELISA
(enzyme-linked immunosorbent assay), Western blot, and enzyme-linked immunosorbent assay (ELISA). It has been known that both local and the general immune response is formed in the body against H. pylori. However, the determination of antibodies (IgM, IgG) against H. pylori in blood serum cannot provide accurate information about the nature of gastroduodenal pathologies caused by H. pylori in all cases. In other words, it cannot distinguish gastroduodenitis, gastric and duodenal ulcers, as well as other pathologies.

Thus, the research conducted on this topic in gastroduodenal pathologies (gastritis, gastric and duodenal ulcer, and cancer) related to H. pylori allows a deeper study of the nature of the changes in the normal microflora of the intestine, as well as the interaction between H. pylori and the intestinal microflora and its pathogenesis, shows the need to clarify its role. This is explained by the perspective of considering changes in intestinal microflora in the treatment of diseases related to H. pylori. Also, the identification of non-invasive methods that can determine the nature of H. pylori-related gastroduodenal pathologies (gastritis or gastric-duodenal ulcer) and localization offers opportunities in the diagnosis of H. pylori-related diseases.

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