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HELICOBACTER PYLORI, TRANSMISSION, SYMPTOMS, DIAGNOSIS AND TREATMENT (ARTICLE REVIEW)

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Abstract
Helicobacter pylori is a type of bacteria that is grame-negative, microaerophilic, and has a helical shape (Figure .1). About half of the world's population typically has it in their stomachs. Those who are infected may develop chronic gastritis, which often remains symptomless in 85 percent of cases.

Introduction

However, in some instances, it can lead to various conditions, such as stomach cancer or peptic ulcers. Sadly, gastric adenocarcinoma takes the lives of more than 800,000 people worldwide each year. H. pylori is widely recognized as the primary culprit behind stomach ulcers, duodenal ulcers, gastritis, and various forms of stomach cancer, such as mucosa-associated lymphoid tissue carcinoma (MALT) and adenocarcinoma (1). Gastric cancer has emerged as a result of the interplay betwien the geinetic makeup of host gastric epithelial cells and H. pylori virulence factors. The bacteria possess vareous vierulence factors, such as cytotoxin gen A (CagA), the cellular toxin responsible for vacuolization (VacA), and the production of the urease enzyme, which breaks down urea into ammonia, providing an antacid effect on the stomach lining. H. pylori releases CagA, a toxin that can do many things.There are various diagnostic procedures available for identifying H. pylori inefection, divided as invasive or non-invasive. Invasive methods include the rapid urease test (RUT),(3 microbiological culture and polymerase chain reaction based on biopsies. A number of well-established non-invasive techniques exist, such as urea breath tests (UBT), enzyme-linked immune sorbent assays (ELISAs), and stool antigen testing (SAT) for serology (4).

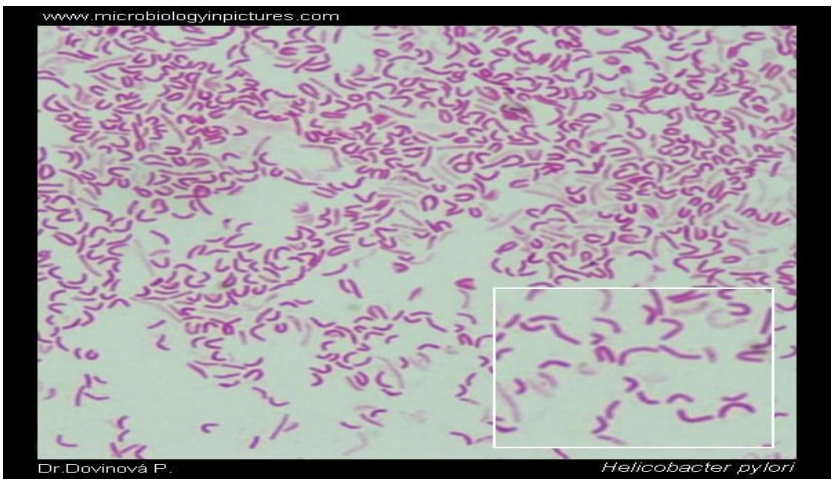

Fig.1. Helicobacter Pylori bacteria (Rimbara et al., 2019).

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Properties of the Helicobacter pylori

Humans and other primates frequently have the bacteria H. pylori in their stomachs.. It is thrives in low-oxygen conditions and is well-suited to the acidic environment of the stomach. Its curved or spiral shape enables it to penetrate the stomach's mucus layer and attach to the cells lining the stomach. This bacterium possesses several unipolar flagella, enabling it to navigate through the mucus layer and establish itself in the stomach (Fig. 2). This bacteria, known as H. Pylori, possesses certain characteristics that contribute to its ability to affect the stomach. It is oxidase and catalase-positive, meaning it has the ability to undergo certain chemical reactions. Additionally, it is motile and produces a powerful enzyme called urease, which alters thestomach mucus and reduces the effectiveness of acid in passing through the mucous membrane. Furthermore, it also produces a protease, as mentioned by (5). The bacterium thrives in an environment with specific oxygen and carbon dioxide levels, typically around (5-7%) O2 and (5-10%) CO2. It also prefers to grow on various culture media at a temperature of 37 ˚C, in a humid setting (6). The phenomena of polymorphism in these organisms is fascinating, as it can take on various forms such as a seagull wing or bacilli. In more mature cultures, they can even appear as spheres, and their movement is driven by their unique, unipolar monolithic whips. In certain circumstances, H. pylori has the ability to transform from a spiraling bacillary to a coccoid shape. The bacteria in question exhibit a unique characteristic when they form colonies, they take on a convex and transparent appearance. They do not produce spores and do not cause any blood haemolysis, in fact, they resemble a droplet of water (7).

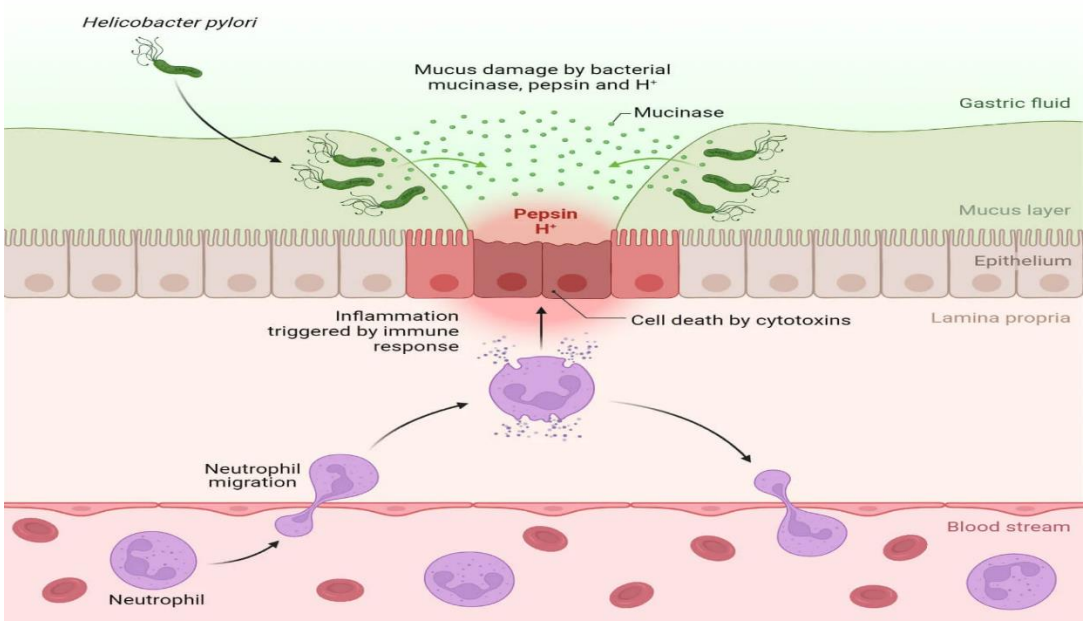

Fig. 2. Helicobacter Pylori infection. (Hirukawa., 2022).

Transmission of *H. pylori*

The transmission of H. pylori occurs through various routes, although the exact mechanism is still not fully understood. The most common mode of transmission is person-to-person, believed to occur through direct contact between individuals. This often happens in close

personal settings, such as among family members or individuals living in crowded conditions. This information explains how the bacterium can be transmitted from one person to another. It can be spread through oral-oral or fecal-oral routes, which means that an infected person can pass it on through saliva, vomit, or faecal matter (8). There have been multiple studies indicating that contaminated water. H. pylori was detected (9). The United States conducted epidemiological investigations to study the spread of H. pylori bacteria through contaminated water or food. Through the use of 16SrRNA and other genes, researchers discovered the presence of H. pylori in wastewater and water samples, indicating the potential transmission of the bacteria through water (10).

Epidemiology

Examining the prevalence and underlying causes of health-related diseases or events within a certain population is the main goal of the science of epidemiology.. It is worth noting that H. pylori has been found to inhabit the bodies of individuals across the globe. Various significant factors, including socioeconomic status, age, gender, and geographic area, have greatly influenced the risk of colonization and disease development. Childhood colonization is a prevalent issue, especially in developing countries (11). Studies have indicated that around half of adults in developed countries and the majority of adults in developing countries are seropositive for H. pylori (12). The prevalence of gastritis, duodenitis, gastric ulcer, and duodenal ulcer in Kuwait was found to be 50.98% among patients, as compared to Iraq where (13). Studies have indicated that the rate of infection among children in developed countries is relatively low and tends to rise as they grow older (14). It's worth noting that the prevalence of this condition tends to increase with age in Middle Eastern countries. Additionally, the rates in these countries are similar to group rates across different age groups. Interestingly, the prevalence tends to be significantly higher in adults compared to children (15).

Symptoms of *H.pylori* infections

Because Helicobacter pylori has a variety of adhesion molecules, it can connect to the stomach epithelium and endure the harsh conditions by interacting with receptors on cells. antigen , which binds to fucosylated Lewis B group antigen (Leb) present on host gastric epithelial cells, is one of the important adhesions. then H. pylori first infects the gastric of a human, it enters the host cells alongside other virulence factors and toxins such cagA or vacA. Through inflammatory or immunological reactions, this process encourages harm to the host tissue, either directly or indirectly. Based on research done by Hassan et al. (16It was proposed that the expression of BabA in stomach tissue might work as a biomarker for infection (17). Both the stomach mucosa and the oral cavity mucosa exhibit BabA binding to its receptors. Studies have demonstrated a direct correlation between the degree of gastritis in the gastric antrum and the expression of BabA. Then bacteria are less able to attach to the Leb and express less BabA, they can separate from gastric mucus and create duodenal ulcers, which raises the risk of gastrointestinal conditions such as stomach tumor or stomach ulcer disease. Additionally, it has been discovered to be connected to elevated mucosal inflammation.(18). Members of the outer membrane protein (OMP) family, sialic acid-binding adhesions (SabA) are another class of adhesion molecules. By attaching to the Lex antigen, these molecules facilitate contact

bacteria to host . Research has revealed that SabA is present in around 40% of H. pylori strains and tumor in stomach , intestinal metaplasia, bacterial colonization, and gastric atrophy. Gastrointestinal diseases have been related to the regulation of several outer membrane proteins (OMPs) such as OipA, BabA, and SabA (19). The cag A is a crucial component of bacteria pathogenesis . The presence of the bacteria pathogenicity (Cag PAI) has been linked to the cagA gene (20). Produced by cagA, the cagA protein is associated with more severe clinical diseases such as gastric adenocarcinoma and duodenal ulcer, and it also sets off a robust immunological response. It was discovered in a study by Orsini et al. (21), that some strains of H. pylori, which are known to be harmful, can cause mucosal inflammation by inducing epithelial cells to secrete IL-8. According to research done by Lima et al. (22), the existence of cag-PAI genes is essential for the growth and (22), it was found that the presence of cag-PAI genes role a crucial role in the occuer and severity of stomach cancer associated with H. pylori infection. In western countries, the prevalence of cagA-positive H. pylori strains was approximately 60%, compared to around 90% in Asian countries (23).

Diagnosis of Helicobacter pylori

Researchers have made numerous attempts to accurately detect H. pylori infection. These methods include invasive tests. PCR is another method that can be two types, depending on the type of specimen. On the other hand, non-invasive tests like UBT, SAT, and serology tests have also been used (24). The primary rationale for opting for noninvasive tests is to circumvent the need for endoscopy. Numerous guidelines have advocated for noninvasive tests as the preferred initial option (25).

Non – Invasive Tests

There are four types of non-invasive tests: the passive tests cannot determine if the infection is still ongoing. (26).

1. Urea Breath Test (UBT)

The urea breath test is a commonly used way for identifying the presence of an active bacteria infection. Helicobacter pylori is recognised as the sole bacterium that can withstand the harsh acidity of the stomach and has the ability to conceal itself within the gastric mucosa and reproduce there. The test relies on the natural capacity of bacteria to proeduce urease enzyme and convert absorbed C13 or C14-labeled urea into CO2 in the acidic conditions of the stomach.(Fig .2) When someone is colonised with bacteria, the uriea is metabolised into amimonia and labellied bicarbonate [C14-CO12]. The labelled becarbonate is transferred within the lungs, resulting in the production of labelled carbon dioxide. This allows the mechine to detect and conferm the presence of the infection. The level of labelled CO2 is influenced by the urease activity, which sirves as an cases for the presence or absence of infection (27). Due to its high specificity and sensitivity, UBT is a method that has garnered significant interest among microbiologists and clinicians for measuring active H. pylori infection. This method is considered highly reliable and accurate, as it eliminates any potential errors that may arise from sampling or the absence of endoscope surgery. It was crucial for clincians to veriefy H. pylori eradication, particularly in aseymptomatic individuals who were elderly or paediatric subjeicts

(28). The diagnostic specificity was found to be 95% and the sensitivity was 100%, which was good test . Nevertheless, there have been reports suggesting that his method may be less dependable for patients who have undergone gastric surgery or are taking proton pump inhibitors or ranitidine (29). Recently, there has been an increasing acceptance tests for detecting active bacterial infection. The International Consensus Report recognises UBT and SAT research as the primary diagnostic methods, with sensitivity and specificity levels exceeding 90%. (30).

Figure 3."YH04E" H. pylori test system

2. The Test of Stool Antigen (SAT)

Determine tool commonly employed bacterial infections is the bacterial stool antigen test, which helps identify the presence of bacterial antigens in human faeces. This test for H. pylori has been widely adopted and utilised by numerous clinical laboratories and researchers worldwide. Its effectiveness as a tool for studying the privalence and epedemiology of bacterial has been well-established (31). There are two primary types of SATs utilised for H. pylori detection: enzyme immunoassay (EIA) and immune chrematography asseay (ICA)-based methods. These methods involve the use of either polyclonal or monoclonal antibodies. (32). In a study conducted by Zhou et al. in 2014 It is important to note that SAT results may sometimes yield false negatives, particularly when the bacterial load is low or when certain medications like antibiotics, PPIs, and bismuth are being used (33).

There have been recent advancements in the development of monoclonal antibodies that are not affected by PPIs. Several studies have demonstrated the ability of SATs to effectively differentiate between actively infection and threatening patients, and evaluate the success of bacterial eradication. These findings highlight the advantages of SATs over UBT as a diagnostic test. (34). This test is valuable for both diagnosing the infection and assessing its eradication, even as early as four weeks after treatment. It involves a straightforward laboratory examination using monoclonal antibodies. This method is highly feasible, cost-effective, and can be easily performed by regular laboratory personnel.(35).

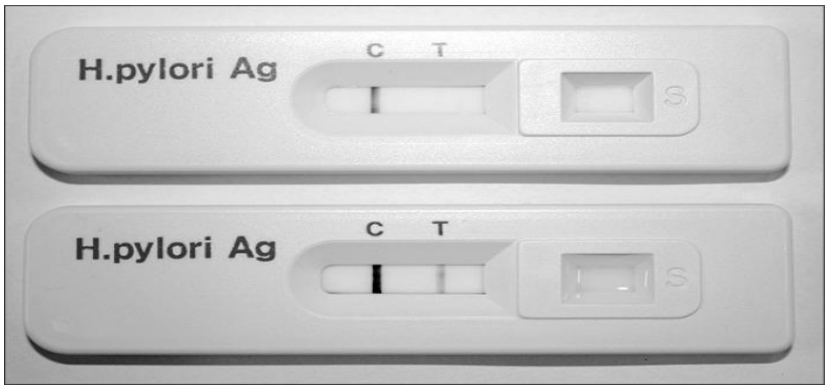

Fig.4. Stool Antigen Test (SAT)

3. Serum Antibody Test

Serological tests are commonly used in H. pylori epidemiological studies due to their cost-effectiveness, simplicity, and wider availability. These tests are non-invasive and provide valuable diagnostic information for H. pylori infection (36). Another benefit of serological tests is that their accuracy remains unaffected by gastric atrophy and ulcer bleeding, which can lead to false-negative results in other types of experiments, whether invasive or non-invasive , Individuals with H. pylori infection typically exhibit distinct circulating antibodies (IgG, IgM, and IgA), which can be identified through specialised serological tests like ELISA, latex agglutination techniques, and Immunochromatography assay (ICA). The sensitivity and specificity of these methods range from 76-84% and 79-90%, respectively. (37). False-negative results may occur during the early stages of infection, as the levels of antibodies may not be elevated enough at that time. It is worth noting that IgG antibodies can still be detected for an extended period of time following treatment, leading to continued positive results, even after the bacteria have been eliminated (38).

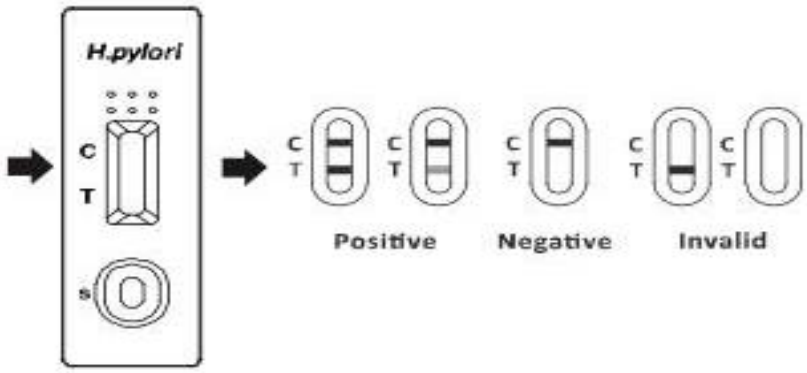

Fig.5. Serum Antibody Test (SAT)

4. Polymerase chain reaction (PCR)

In recent years, the use of poilymerase chein reaction (PCR) for detecting infection has become widespread. It has been extensively applied in diagnosing H. pylori from various samples such

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as gastric beopsy specimens, fluid, and other specimens. PCR offers exceptional sensitivity and specificity, surpassing 95%, when compared to other traditional tests. It provides highly accurate results in identifying H. pylori in patients experiencing bleeding. The use of molecular detection has greatly impacted the clinical understanding of numerous infectious diseases (39). PCR is a highly effective molecular technique utilised in various clinical applications, including identifying antibiotic resistance, genotyping bacteria, detecting broad-spectrum infections, and conducting epidemiological studies. , This method demonstrates exceptional sensitivity and specificity, with accuracy exceeding 95%. It is characterised by its simplicity, speed, automation, and overall proficiency in detecting H. pylori(40).

Treatment of Helicobacter pylori

For the past 20 years, the conventional triple therapy has been extensively advised as a means of eliminating H. pylori. Proton pump inhibitors, ranitidine bismuth citrate, clarithromycin, amoxicillin, or metronidazole are used in this treatment (41). With eradication rates surpassing 90%, these treatments gained widespread acceptability among clinicians in the 1990s due to their efficacy and safety (42). This is explained by H. pylori being resistant to significant medicines including levofloxacin, metronidazole, and clarithromycin (43). This research conducted a meta-analysis of nine randomised controlled trials to compare the efficacy of bismuth quadruple therapy versus clarithromycin triple therapy. According to the findings, 78.3% of patients responded to bismuth quadruple therapy, whereas 77% of patients responded to clarithromycin triple therapy. When used as the main course of treatment for bacterial infection, quadruple and triple therapies have been shown to have eradication rates that are comparable. However, the results showed a 77% eradication (44). Recent research has shown that probiotics are drawing more attention as scientists investigate their potential as a medicinal strategy. Probiotics are living microorganisms with disease and improve intestinal microecology and public health (45).

Conclusion

Various factors, such as cigarette smoking, diets, and alcohol consumption, have been identified in epidemiological studies as having an impact on the risk of acquiring peptic ulcer disease and gastric cancer in people infected with H. pylori bacteria.

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