ABSTRACT

*Helicobacter pylori* is a spiral bacterium that causes gastric ulcers that affect the gastrointestinal tract. It inhabits the stomach, colonizes the gastric epithelium, and leads to multiple digestive system ailments. Diagnostic techniques for identifying *H. pylori* infection differ in invasiveness, sensitivity, and specificity, and can be invasive or non-invasive. The choice of which diagnostic test(s) to use may depend on clinical circumstances, clinician expertise, cost, and test accuracy. On the other hand, anemia is a condition in which the number of red blood cells or the hemoglobin concentration within them is lower than normal, a common disease that affects people all over the world. The distinction between iron deficiency anemia and other causes of anemia is unclear. Recent studies on *H. pylori*’s possible contribution to the development of various gastrointestinal problems, including iron deficiency anemia is currently underway.

**Keywords:** *H. pylori*, iron deficiency, Anemia.
Anemia and iron deficiency

Anemia occurs when a person has lower than normal levels of either red blood cells or hemoglobin, resulting in an insufficient amount of oxygen for their body's needs. This condition is a significant problem worldwide, affecting people of all ages. Recent statistics indicate that in 2019, for example, almost 30% of women aged 15-49 years, nearly 40% of children aged 6-59 months, and over 60% of African children in this age range suffered from anemia (World Health Organization, 2021). Helicobacter pylori infection is linked to this public health issue. Discovering the link between anemia and H. pylori infection is critical for developing evidence-based treatment and prevention plans.

Approximately one-third of the global populace is affected by anemia, a condition characterized by low iron levels. This deficiency has negative consequences on immunity, reproductive health, overall well-being, social growth, and economic development. Specifically, women and children are at increased risk of morbidity and mortality, impaired birth outcomes, reduced work productivity, and hindered cognitive and behavioral development. Preschool children and women of reproductive age experience disproportionate effects. Moreover, anemia also heightens susceptibility to infections and lowers physical and mental capacity and productivity. (Wieczorek et al., 2022), (Gonzalez-D’Gregorio et al., 2018), (Philip et al., 2020). According to the WHO, over 2 billion people worldwide are anemic.

The prevalence

It is known that the rate of infection with H. pylori reaches a percentage of 50% of the total population and approximately one-third of all children around the world. Over the past 30 years, the incidence of H. pylori infection in children has decreased by more than half, from 42.2% in the pre-2000 era to 31.9% between 2000 and 2009, and 19.3% in 2010 and beyond. H. pylori infection rates were consistent across genders, with higher rates in rural areas compared to urban areas. Older children had a higher prevalence of H. pylori than younger children, with the highest rates in the African region and the lowest in the Western Pacific region. Low- and middle-income countries had almost double the incidence of H. pylori compared to high-income countries. Children from lower economic status households, those with siblings or more children, infected mothers or siblings, or who shared rooms had a higher risk of contracting H. pylori. However, study limitations such as incomplete country data and various diagnostic methods across populations should be considered. While global development has led to a decrease in H. pylori infection rates, large prevention and treatment programs are still necessary to tackle this public health issue (Yuan et al., 2022).

Helicobacter pylori

Helicobacter pylori is a microaerophilic flagellated bacterium contained by a majority of the world’s population in the sterile gastric mucosa. It is considered as a significant pediatric gastroenterology pathogen that is acquired in early infancy. It is estimated that over half of the world’s population has been infected with Helicobacter pylori, the first formally recognized bacterial carcinogen. Colonization usually lasts for the rest of one's life unless it is treated (Takahashi-Kanemitsu et al., 2020).

Although H. pylori is commonly known for causing gastrointestinal issues, recent studies suggest that it may also contribute to a variety of extra gastric diseases such as neurological, dermatological, hematologic, ocular, cardiovascular, metabolic, hepatobiliary, and even allergies. H. pylori has various mechanisms for adapting to its acidic gastric and gastrointestinal environment, including its ability to form biofilms. While approximately half of the world's population is infected with H. pylori, the majority of infected individuals are asymptomatic and without long-term side effects. The prevalence of H. pylori is significantly higher in developing countries than in developed ones, and it is a major factor in the onset of gastric cancer. H. pylori's pathogenicity
depends on the specific strain and genotype, as well as the associated expression of virulence factors that facilitate its interaction with the host microenvironment (Baj et al., 2021).

**Morphology**

Helicobacter pylori are gram-negative, helical or curved cells 2.5-5µm with rounded ends. Non-capsulated. Polyphosphate granules are seen in cells under certain conditions. Cells transform to coccid forms with age. Motile by 4-7 unipolar sheathed flagella which are used to swim in aqueous solutions as well as in gastric mucin (Bansil et al., 2023).

**Cultural Characteristics of *Helicobacter pylori***

Colonies are non-pigmented, translucent, and 1-2 mm in diameter. Grow in Brain Heart Infusion, Brucella broth and Mueller Hinton broth. Positive for urease and oxidase. Due to their small size, they require a small amount of CO2 and high humidity to survive. Grow best at 37°C, but not at 43°C or below 30°C. They are fastidious bacteria. After 2-5 days of incubation, growth is better with Chocolate and Blood agar. Circular, convex, and translucent colonies can grow up to 2 mm across. On Columbia blood agar they give small, dome-shaped translucent, and sometimes weakly hemolytic colonies. With Modified Columbia Urea Agar (MCUA medium, the inoculated tubes are incubated microaerophically at 37 ºC for 24 hours, after which the color changes from orange to pink in the solid phase, indicating urease activity. The addition of Vancomycin, Nalidixic acid, and Amphotericin give discrete dome-shaped colonies on Marshall's Brain Heart Infusion medium. Colonies should be large (3mm) and red against a yellow background on Egg Yolk Emulsion Agar (EYA) (Andersen and Wadström, 2001), (Rojas and Martin, 2013).

**Helicobacter Pylori Tests**

Testing for *Helicobacter pylori* is used to detect an infection in the stomach and upper small intestine caused by *H. pylori*. Peptic ulcers can be brought on by the presence of *H. pylori* in the stomach. However, *H. pylori* infection does not usually result in stomach ulcers in healthy individuals.

**Diagnosis of *H. pylori* infection**

The presence of a *H. pylori* infection can be detected through the use of a variety of tests and procedures. Testing is critical not only for identifying the presence of *H. pylori* but also for following up on the treatment to ensure the infection has been completely eradicated.

Many gastro duodenal diseases can be effectively managed if *H. pylori* infection is accurately diagnosed. *H. pylori* can be detected using a variety of invasive and non-invasive diagnostic tests, each with advantages and disadvantages depending on the clinical setting. Many techniques have been developed to provide more reliable results despite the lack of a single gold standard in clinical practice. A patient's clinical condition, the level of laboratories, and the likelihood ratio all play a role in determining which method should be used. Invasive and noninvasive diagnostic tests are the two main types of tests used in medicine. Diagnosis can be achieved by invasive (endoscopic-based) and non- invasive (urea breath test, *H. pylori* stool antigen test and IgG antibodies) methods. (Hussein et al., 2021).

**A) Invasive methods**

**Endoscopy:**

Upper endoscopy exams require sedation of patients. Endoscopy involves inserting a long flexible tube with a small camera (endoscope) down the throat and esophagus as well as into the stomach and duodenum during the examination. This device makes it possible to see and collect tissue samples from the upper digestive tract if there are any abnormalities (biopsy). Depending on
the results of the first endoscopy and whether or not symptoms persist after *H. pylori* treatment, the test may be repeated (Chatrangsun and Vilaichone, 2021).

To diagnose *H. pylori*-associated diseases such as peptic ulcer disease, atrophic gastritis, MALT lymphoma, and gastric cancer, conventional endoscopic examination is usually carried out. Further study on other invasive tests such as the rapid urease test, histology, culture, and molecular methods using endoscopy is routinely used. The specimens obtained are usually gastric mucosa from the biopsy (Sabbagh et al., 2019).

As an additional option to conventional endoscopy, researchers have looked into using Chromoendoscopy with phenol red to diagnose *H. pylori* infections. (Yang and Hu, 2021). Using magnification endoscopy, researchers can see the surface microstructure of the gastric mucosa up close, and high-resolution endoscopic patterns of the mucosa are highly correlated with histopathological changes, including infection with *H. pylori* (Lee, 2021).

When combined with magnifying endoscopy and indigo carmine staining, magnifying endoscopy accurately predicted *H. pylori*-positive gastritis in 97.6% of patients. However, in patients with *H. pylori*-positive antral gastritis, the sensitivity and specificity fell to 88.4% and 75.0%, respectively (Yang and Hu, 2021).

Recent advances in endoscopic technology allow detailed observation of the gastric mucosa. Today, endoscopy is used in the diagnosis of gastritis to determine the presence/absence of *H. pylori* infection and evaluate gastric cancer risk. In 2013, the Japan Gastroenterological Endoscopy Society advocated the Kyoto classification, a new grading system for endoscopic gastritis. The Kyoto classification organized endoscopic findings related to *H. pylori* infection. The Kyoto classification score is the sum of scores for five endoscopic findings (atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness with or without regular arrangement of collecting venules) and ranges from 0 to 8 (Toyoshima et al., 2020).

**Histology Tests:**

When it comes to finding *H. pylori* infection, histology is the gold standard. It is also the first method used to find *H. pylori*. Histology's diagnostic accuracy is affected by many factors, including the biopsy site, size, and the number, staining methods, Proton Pump Inhibitors (PPIs), antibiotics, and the pathologist's experience. Histology has excellent sensitivity and specificity. (Alkhamiss, 2020). Different histopathological staining methods have been used for many years to detect *H. pylori* in gastric biopsies, including routine haematoxylin & eosin (H&E) stain and other special stains such as Giemsa, periodic acid Schiff - Alcian blue (PAS-AB), Gimenez, Steiner, Warthin-Starry, Toluidine blue and immune stain (Elias et al., 2017).

In ordinary clinical practice, even though the immunohistochemical stain is more sensitive and specific, HE stain is frequently sufficient for the diagnosis of *H. pylori* infection. Additionally, if an auxiliary stain is chosen to detect *H. pylori*, the immunohistochemical stain should be the first option (Lee and Kim, 2015). Many *H. pylori* organisms transformed into coccoid forms, after therapy, are not detected routinely by H and E/MGS.

In general, all the studies reveal that Giemsa stain has a lower sensibility compared to H&E but with higher specificity and more important issues with a lower false-positive rate. To further reduce this rate, it is necessary to use IHC in lab practice. *H. pylori* infection can typically be identified through histochemical staining and a stomach sample. Immunohistochemical methods may be used if the histochemical method fails to detect the infection in chronic gastritis cases.

For accurate identification of clarithromycin-resistant HP, fluorescent nucleic acid peptide in situ hybridization (PNA-FISH) is recommended due to its ability to identify undetectable forms. However, it requires specialized equipment and experience in preparation reading, which can be laborious. In comparison to the reference method, PNA-FISH has a specificity and sensitivity of 90.9% and 84.2%, respectively. It also has a sensitivity of 80.0% and a specificity of 93.8% for detecting clarithromycin resistance in *H. pylori* (Benoit et al., 2018), (Glickman et al., 2015).
By using PNA-FISH, the coccoid form of *H. pylori* can be identified, which is normally missed during a conventional histological exam. PNA-FISH's shortcomings, such as tedious preparation, requiring a fluorescent microscope and specialized knowledge to read the slides, may prevent this technology from being widely used despite the benefits of simultaneously monitoring *H. pylori* and clarithromycin resistance.

**Rapid Urease Tests**

Endoscopy and gastric biopsy are among the methods used, which are followed by either a rapid urease test (RUT), histology, culture, or molecular methods on biopsy samples. Each invasive test offers a distinct clinical benefit. The RUT is the fastest method, providing a chance to begin treatment promptly (Sabbagh, 2019).

Because it is cheap, quick, easy to conduct, highly specific, and widely available, the rapid urease test (RUT) is the most useful invasive diagnostic for diagnosing *H. pylori* infection in ordinary clinical practice. As a result of *H. pylori* urease enzyme activity, the presence of *H. pylori* in biopsy material causes an increase in pH and a change in the pH monitor's color to indicate the presence of the ammonia test reagent, which is then converted back to urea Fig. (1).

![Rapid Urease Test](image)

**Fig. 1: Rapid Urease Test**

Today, there are numerous commercially-available urease testing options available, including gel-based testing (CLOtest, HpFast), paper-based testing (PyloriTek, ProntoDry), and liquid testing (UFT300, EndoscHp). Varying commercial RUTs have different reaction times deliver results.

When it comes to closets, the average turnaround time is 24 hours, while PyloriTek takes just an hour, and UFT 300 takes just five minutes to deliver results. If you do the urease test earlier than suggested, you run the risk of getting a false negative (Vaira, 2010). There are other factors affecting RUT reaction time and diagnostic accuracy besides commercial kit design, such as bacteria density in the biopsy specimen. A minimum of 10,000 organisms is usually required for a positive RUT result. H2-receptor antagonists, PPI, bismuth compounds, antibiotics, achlorhydria, and the presence of blood can all affect the diagnostic accuracy of urease tests, increasing the risk of false-negative results. Furthermore, the sensitivity of RUTs is reduced when biopsy tissues are contaminated with formalin.

Generally speaking, commercial fast urease tests are highly specific (over 95% accuracy) and sensitive (over 85% accuracy). RUT sensitivity could be improved by performing more gastric antral biopsies, and dual biopsy specimens from the gastric corpus and antrum are preferred to single antrum biopsy specimens because additional corpus biopsies improve diagnostic accuracy and prevent bias in sampling caused by the uneven distribution of *H. pylori* in the stomach. The use of PPI for two weeks and antibiotics for four weeks before RUT will lower the number of false negatives. Medications that alter urease activity should be avoided. In this clinical scenario, bleeding reduces the sensitivity and specificity of RUTs, making them a less trustworthy test than other tests.

**Culture**

*H. pylori* can be cultured from stomach biopsy specimens, but this approach is less sensitive than others. Culturing has a high degree of specificity; however, the sensitivity of the culture varies
widely, ranging from 85% to 95%. To cultivate *H. pylori* in vitro, specialized transport mediums, growth media, and incubation environments are required due to its delicate and exacting nature. Samples from biopsies can be stored at 4°C for up to 24 hours in a transport medium such as Portagerm pylori or Stuart's transport medium. After isolating *H. pylori*, a variety of agars can be employed to cultivate it. Pylori agar, Skirrow agar, Columbia blood agar, Brucella agar (Fig. 2), Brain heart infusion, and Trypticase soy agar are some of the more often used media. These media are often supplemented with sheep or horse blood. At 35-37°C, the agar plates are incubated for at least 5 days since *H. pylori* have been deemed a microaerophile (80%-90%) in an anaerobic environment (50%-10%) CO2, 50%-10% O2. An interesting new study found that atmospheric oxygen levels stimulate the growth of *H. pylori* even in the presence of 10% CO2, suggesting that the bacteria may be a capnophilic aerobe (Park *et al.*, 2011).

Fig. 2: *Helicobacter pylori* colony morphology on Brucella agar (Khafri, 2005).

As well as positive results of the tests for urease and catalase, microbiological laboratories should be equipped and staff should be well-trained to identify *H. pylori* in culture media. Poor specimen quality, late delivery, exposure to an aerobic environment, and unskilled microbiologists all have a negative impact on culture performance and diagnostic precision. A new transport medium, the GESA transport medium, has just emerged in the transportation industry. *H. pylori* may be quantified at a recovery rate of 90.7% when using the GESA transport medium, a semi-solid medium that can retain gastric biopsy specimens at 4 °C for up to 10 days (Cellini *et al.*, 2014). For cultivating *H. pylori* in stomach biopsies, researchers devised a new biphasic test that combines the selective enrichment broth with a biochemical test on urea agar in a single vessel.

H2- receptor antagonists, PPI, and antibiotics have an unfavorable effect on the percentage of cultures that test positive when the host has a high activity of gastritis, low bacterial load, bleeding, and alcohol use. Except for antibiotics, which should be avoided for at least 4 weeks, these drugs should also be avoided for at least 2 weeks before culture was indicated. At least two antrum and two corpus biopsy specimens were also recommended to avoid sampling bias due to the patchy distribution of *H. pylori* in the stomach (Abadi, 2018).

**Polymerase chain reaction**

*H. pylori* infection was first detected using Polymerase Chain Reaction (PCR), which has since been widely used to diagnose *H. pylori* from stomach biopsy specimens, saliva, and stool samples. More reliable findings can be obtained when using PCR to detect *H. pylori* in patients with bleeding than other conventional tests, which have a sensitivity and specificity of less than 95% each (Wang *et al.*, 2015).

Multiple genes, including UreA, glmM, UreC, 16S rRNA, 23S rRNA, HSP60, and VacA, have been identified as potential targets for the drug, *H. pylori* detection employing two separate conserved target genes can boost specificity, which in turn prevents false-positive results, especially for material other than gastric biopsy specimens, which are employed in the test. Clinical decision-making can be accelerated and improved due to the advantages of PCR such as the requirement for fewer bacteria in the sample, the speed of the results, and the lack of additional processing supplies or transportation. Another benefit is the ability to detect antibiotic resistance as well as virulence
Patients of *Helicobacter pylori*………

factors such as CagA and VacA using PCR at the same time, which is particularly useful when testing for drug resistance to macrolides or fluoroquinolones. (Cardos *et al*., 2022). Real-time PCR (RT-PCR) has significant advantages over the conventional agar dilution method (Etest), which is often considered the gold standard in antibiotic susceptibility testing. One advantage of PCR over Etest is that it is faster, more convenient, and more sensitive when utilizing formaldehyde-fixed paraffin-embedded stomach tissue. Furthermore, RT-PCR results for antibiotic susceptibility testing were comparable to Etest in this situation. Since false-negative results in Etest are common, and because PCR is more accurate, it can provide more accurate information to clinicians before the initiation of antibiotic treatment (Monno *et al*., 2012).

Identification of virulence factors by PCR aids in evaluating the genetic variation within *H. pylori*’s virulence factors and provides more information in understanding the clinical disparities between patients infected with various *H. pylori* strains. *H. pylori* may be detected in environmental samples by using PCR, which is very useful in epidemiological investigations. More information on *H. pylori* transmission through the water was gleaned through PCR detection of high *H. pylori* prevalence in drinking water samples. Apart from PCR's ability to detect *H. pylori* infection and antibiotic-resistant bacteria more quickly and with greater accuracy, issues regarding cost, locally available equipment and molecular method competence necessarily limit the practicality of PCR in rural laboratories. (Chomvarin *et al*., 2017).

**B: Noninvasive Tests**

Endoscopic diagnostic procedures have been avoided for a variety of reasons. An endoscopic operation is inherently painful and unsuitable for patients with preexisting medical conditions or contraindications of any kind. In addition, endoscopy costs can be substantial, as can the costs of disposable forceps and anesthetics that are used in conjunction with endoscopy. Finally, because of the uneven distribution of *H. pylori* in the stomach, bias in biopsy-based approaches is practically unavoidable (Pichon *et al*., 2020).

Nearly 30 years after its invention, the Urea Breath Test (UBT) remains the most widely used and most accurate noninvasive method for the identification of *Helicobacter pylori* infection (HP). *H. pylori*’s urease activity hydrolyzes the patient’s 13C- or 14C-labeled urea into labeled CO2 in the stomach, which is then absorbed into the blood and expelled through breathing, allowing for the measurement of labeled CO2 (Cardos *et al*., 2022).

Other urease-producing infections in the stomach can induce false-positive results, although this is rare. Even though UBT's accuracy in pediatric patients isn't as good as it is in adult patients (particularly for children less than 6 years old), it is a useful approach for detecting *H. Pylori* infection in pediatric patients due to its many advantages, such as simplicity, noninvasiveness, and safety (Seo *et al*., 2018).

Even though 14C-UBT is safe for children and pregnant women because the radiation from 14C-UBT is lower than radiation received from the natural environment, 13C-UBT is preferable to 14C-UBT for avoiding radiation exposure. 14C-UBT is more common in underdeveloped nations since 13C-UBT is costly and not widely available. No significant difference exists in the diagnostic accuracy between the noninvasive tests used to diagnose *H. pylori* infection using 13C-UBT and 14C-UBT (Jambi, 2022). Oral injection of 14C-urea for *H. pylori* diagnosis uses two protocols: nonencapsulated and encapsulated. Encapsulated 14C-UBT was initially created to prevent the problem of 14C-urea hydrolysis caused by oral flora that produces urease, and this approach eliminates the issue of false-positive results in early breath samples. (Pathak *et al*., 2012).

**Stool Antigen Test**

The other noninvasive approach for diagnosing *H. pylori* infection had a sensitivity and specificity of 94% and 97%, respectively, in a global meta-analysis (Wang *et al*., 2015). Using this procedure, you may check if you have *H. pylori* in stool for antigen. Enzyme immunoassay (EIA)
and Immunochromatography Assay (ICA) based approaches use polyclonal antibodies or monoclonal antibodies to detect *H. pylori*, respectively.

It is also possible to utilize monoclonal Stool Antigen Test (SAT) as a quick, non-invasive way to diagnose *H. pylori* infection in pediatric patients, in addition to evaluating the effectiveness of eradication therapy (Qiu et al., 2021). Scanners are valuable in epidemiological research and screening programs, as well. In terms of cost and equipment, SAT is better suited for large-scale surveys than UBT. Compared to serological tests, which are commonly used for screening, *H. pylori* infection diagnosis appears to be more reliable with SAT. Several factors, such as antibiotics, PPI, N-acetylcysteine, bowel movements, and upper gastrointestinal hemorrhage, alter the SAT’s precision. The diagnostic accuracy of SAT is also affected by specimen preservation measures such as temperature and transport time before testing. (Al-Hilfi et al., 2021).

**Antibody-Based Tests**

Numerous serological tests based on the detection of anti-*H. pylori* IgG antibodies are widely available for *H. pylori* diagnosis. Serological tests have also frequently been used in screening for epidemiological studies because of their inexpensive, rapid, and acceptability. It is possible to identify anti-*H. pylori* IgG antibodies using a variety of serological tests, although enzyme immunoassay (EIA) testing is the most commonly used because of its high sensitivity and specificity. Because they are low-cost, quick, and well-tolerated by patients, serological tests are often employed in epidemiological screening. Additionally, serological tests can be used to determine whether or not a child has *H. pylori* infection (Elias, et al., 2017).

Correct antigens should be validated locally before studying the population, either by using antigens from local strains or by pooling antigens from several strains. A credible cutoff value for serological tests should also be established locally. Many immunogenic proteins have been proposed as potential diagnostics for infections such as CagA, VacA, UreA, Omp, and GroEL. The *H. pylori* FliD protein is an essential element in the assembly of the functional flagella. protein is required for the proper assembly of functioning flagella in *H. pylori*, the protein is a new marker for the diagnosis of *H. pylori* infection by serology and is 97% sensitive and 100% specific (Gholi et al., 2013).

RecomLine IgG, a revolutionary line immunoassay for diagnosing *H. pylori* infection, was recently established using six highly immunogenic virulence factors (CAG, VACA, GROEL, GGTP-GGT-HCP-UreA, and UreA) for serological detection. The accuracy of serological tests is not impacted by ulcer bleeding, stomach atrophy, or the use of PPI or antibiotics, which is a benefit of serological testing. Because antibody levels might stay in blood for years after an infection has been eradicated, serological testing is not a good way to know if treatment is working (Idowu et al., 2019). Before eradication therapy can be started, additional testing is needed to identify whether a patient has an ongoing infection or has been exposed to *H. pylori* in the past.

Like SAT, serological tests based on EIA have superior accuracy to those using ICA. A correct selection of serological tests based on their specific performance criteria should be made to achieve various screening, initial diagnosis, or confirmation of another test goal (Miftahussurur, 2020). The use of serological tests in pathogenesis and virulence investigations is critical because immunological techniques can identify numerous antigenic proteins, providing extra diagnostic value.

**Diagnosis of *H. pylori* in Other Specimens**

As a noninvasive test, PCR can be an appealing option for children who have trouble with *H. pylori* infection due to its reliability and speed. Additionally, the advantages of stool PCR include the ability to identify specific bacterial genotypes and drug resistance (Qiu et al., 2021). There is some evidence to suggest that the oral cavity is a source of re-infection for people with *H. pylori* or a channel of transfer for those already infected.
Recent research has relied heavily on saliva and dental plaque specimens for detecting \textit{H. pylori} in the oral cavity, with PCR being the most common and most accurate method. Early research used RUT and culture to find oral \textit{H. pylori}. Its prevalence in the oral cavity varies widely, possibly because of the varying techniques, populations, and primers utilized in the various investigations (Rahman et al., 2020).

**Association of anemia with \textit{Helicobacter pylori} infection**

The discovery of \textit{H. pylori}, a helical bacterium found in the human stomach, was made by Barry Marshall and Robin Warren about two decades ago. After this discovery, they received the 2005 Nobel Prize in Physiology or Medicine for their "discovery of the bacteria \textit{H. pylori} and its role in gastritis and peptic ulcer disease." (Warren and Marshall, 1983).

\textit{H. pylori} is a stomach-colonizing bacteria that is acquired in early life. Infection with \textit{H. pylori} is normally asymptomatic, but in around 20% of cases, clinical illness develops, usually in maturity. Having \textit{H. pylori} in your system raises your risk of developing chronic gastritis, peptic ulcers, and gastric cancer (Reshetnyak et al., 2021). Adults and children with \textit{H. pylori} infection have lower iron reserves. \textit{H. pylori} infection has been linked to an increased incidence of iron deficiency anemia by a factor of 2.8 and an increased prevalence of iron insufficiency by a factor of 1.38.

\textit{H. pylori} colonization in the stomach can last for years or even decades if nutrients necessary for bacterial development are not provided. \textit{H. pylori} infection has been linked to anemia, iron shortage, and vitamin B12 deficiency recently (Asiimwe et al., 2023).

The study by Rostami-Nejad et al., showed that even in celiac disease patients, \textit{H. pylori} was linked to iron deficiency anemia, which had a strong evidentiary base, but was only weakly reflected in actual practice. Epidemiological and clinical research has found a link between anemia and \textit{H. pylori} infection, and these findings have been corroborated. Anemia and \textit{Helicobacter pylori} infection has been linked in several studies, but the evidence is inconsistent across regions and nations (Rostami-Nejad et al., 2015).

Anaemiaigenic pathways associated with \textit{H. pylori} infection and anemia include various potential hypotheses. Gastrointestinal blood loss caused by \textit{H. pylori}-induced gastritis or duodenitis is the most likely explanation (Sullivan et al., 2019).

Another suggestion is that the \textit{H. pylori} bacterial sequestration of free iron affects iron transporter molecules, hence limiting free iron absorption and inducing dietary cobalamin malabsorption (Xu et al., 2017).

Both Betesh (2015) and Campuzano-maya (2016) found a link between illness and anemia because chronic gastritis, which induces stomach hypochlorhydria, impairs iron absorption, resulting in dietary iron conversion from ferric to ferrous form that is impaired (Betesh et al., 2015), (Campuzano-maya, 2016).

Almost all dietary iron is in the ferric form, and to absorb it, you need an acidic intragastric pH and ascorbic acid. Since chronic superficial gastritis results in atrophy of the gastric glands due to \textit{H. pylori} infection, less stomach acid is secreted (Waldum et al., 2016). Iron is taken up by \textit{H. pylori} through competition with their host and decreased iron release from macrophages and entrecote due to increased hepcidin synthesis related to \textit{H. pylori} infection (Mendoza et al., 2019). Anemia of inflammation or chronic disease might develop from the acute-phase reactant hepcidin, which is produced in the gastric mucosa in response to the inflammation. Iron loss through hemorrhagic gastritis and active bleeding peptic ulcers are two further possibilities.

According to (Timerga et al., 2021), anemia and \textit{H. pylori} infection are significantly associated with adult dyspeptic patients. Those infected with \textit{H. pylori} had a 1.77-times greater chance of being anemic than those who were not, China and the United States supported these findings. Adult dyspeptic individuals with \textit{H. pylori} infection are more likely to have anemia, which could be explained by the organism consuming iron (Bianca and Francesco, 2018). Higher amounts of neutrophil-derived lactoferrin were seen in patients with \textit{H. pylori}-induced gastrointestinal ulcers.
and gastritis; this infection, which contains a lactoferrin-binding protein receptor, is thought to result in increased iron losses due to bacterial turnover. Iron may be lost in feces as dead bacteria due to the rapid turnover of these bacteria. The physiology of the stomach can be altered by *H. pylori* chronic gastritis in the form of reduced gastric acid secretion, although acidic intragastric PH was necessary for iron absorption from food, preventing iron absorption from food. One of the most common underlying causes of anemia in adults is blood loss from the gastrointestinal tract.

*H. pylori* Infection is linked to anemia because chronic gastritis promotes stomach hypochlorhydria, which hinders the reduction of dietary iron from its ferric to ferrous form, resulting in impaired iron absorption (Betesh *et al.*, 2015).

In summary; three mechanisms are involved in the association of *H. pylori* with iron deficiency anemia:

1. *H. pylori*-induced histopathological alterations in the stomach reduce the intestinal absorption of iron, which reduces ferric iron’s conversion to ferrous iron.
2. The bacteria must have iron to multiply, so they compete with the host for it.
3. This lowers intestinal iron absorption and macrophage iron recycling by increasing hepcidin synthesis.

Wang *et al.*, 2012 reported an intriguing discovery, showing that the host's genetic features, notably the ABO blood group, increase the vulnerability to *H. pylori* infection. When it comes to adhering to type A blood cells, *H. pylori* has a stronger grip than it does on cells from people with other blood types. *H. Pylori* continually absorbs iron from the food Fig. (3). At the same time, *H. pylori* collects on the epithelial surface and absorbs the iron from the host's epithelial cells, resulting in an iron deficiency in the host.

**Fig. 3:** Diagram of the novel mechanism for iron-deficiency anemia caused by *H. pylori*. In the case of infection, the demand for the iron element of Helicobacter is increased (Wang, 2012).

Even though *H. pylori*-associated peptic ulcers and stomach cancer can induce bleeding, resulting in an iron deficit, the majority of people infected with *H. pylori* do not have either. Their persistent gastritis is generally unaccompanied by gastrointestinal hemorrhage. After a gastrointestinal evaluation, about 35% of people with iron deficiency anemia still have no idea why they have the condition. *H. pylori* has recently been linked to the development of extra-gastrointestinal illnesses, such as iron deficiency anemia, according to new research (Haile *et al.*, 2021).

**Cognitive development**

When iron deficiency is widespread throughout important developmental periods, such as the fetal and early postnatal stages, cognitive and socioemotional impairments develop in infants and children that persist into adulthood (Georgieff, 2020).

*H. pylori* has also been proposed to be a factor in the development of chronic neurological conditions. Many believe that *H. pylori*-induced cytokines and chemokines promote systemically and CNS inflammation and dysfunction, which could explain how it contributes to neurological illness (Gorle *et al.*, 2021).
CONCLUSION

Iron deficiency anemia associated with H. pylori infection is a common and significant health problem worldwide. The bacterium is known to cause chronic inflammation of the stomach lining, leading to a reduction in stomach acid secretion and destruction of the gastric mucosa. This condition impairs the absorption of dietary iron, thus leading to iron deficiency anemia. Early detection and treatment of H. pylori infection in patients with iron deficiency anemia may help prevent further complications and improve overall health outcomes. Therefore, healthcare providers should be aware of this association and consider screening for H. pylori infection in patients with iron deficiency anemia.

Chronic and widespread, H. pylori infection can lead to chronic inflammation and atrophy, ultimately resulting in Gastric Cancer (GC). However, clinical practice is hindered by challenges such as false-negative results, antibiotic resistance, decreased eradication rates, and low retesting rates. Noninvasive methods for real-time detection of H. pylori during endoscopy are being studied to replace biopsies. Additionally, PCR development can aid in determining antibiotic resistance and eradication rates after treatment. The relationship between H. pylori infection and iron-deficiency anemia is not yet clear, but prevention should be a priority when dealing with refractory moderate to severe cases associated with gastrointestinal symptoms. Technology optimization and innovation hold promise in the better diagnosis, management, and prevention of H. pylori infection and GC.

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مرضى عدوى Helicobacter pylori

يسري يحيى اغا
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الملخص

هي بكتيريا حزازنية الشكل وتعد هذه البكتيريا إحدى مسببات القرحة المعدية التي تصيب الجهاز الهضمي، تستوطن هذه البكتيريا المعدة وتحديداً في الطبقة المبطنة للأنسجة، وذلك تؤدي إلى العديد من الأعراض المرضية. التقنيات المتاحة لتشخيص الإصابات بهذه البكتيريا تختلف فيما بينها من ناحية الشدة، الحساسية، والخصوصية وتتطلب إلى طرق شديدة وغير الشديدة، اختبار الطريقة الصحيحة للاستخدام قد يعتمد على الحالة السريرية، خبرة الطبيب، الكفالة، واخيراً دقة الاختبار.

من ناحية أخرى، فإن فقر الدم هو عبارة عن حالة يكون فيها عدد كريات الدم الحمراء أو تركيز الهيموغلوبين أقل من الطبيعي. ويعتبر من الأمراض الشائعة التي تصيب الأشخاص في جميع أنحاء العالم، مما يجدر الإشارة إليه هو أنه من الصعب التمييز بين فقر الدم الناتج عن نقص الحديد وفقر الدم الناتج عن أسباب أخرى، ولكن هناك دراسات حديثة قد تتبع حول في الإصابات المعوية المختلفة وبعضها فقر الدم الناتج عن نقص الحديد. Helicobacter pylori: نقص الحديد، فقر الدم.