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Research Article

The pathogenicity of the gastric bacteria and its potential threat to humans

Hussein Kazim Jakhir [1,*], Ahmed Mohammed [1], Zainab Sattar [1], Haider Karim [1], Amjad Saffah [1], Risan Taleb [1], Haider Saad [1], Hamid Alwan [1], Hassan Jamal [1]

[1] *Department of Community Health Technologies, Middle Euphrates University Technical Institute - Samawah, Iraq.*

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ABSTRACT

Following the initial identification of Helicobacter pylori in the stomach and the following recognition of its detrimental effects, contemporary gastroenterology has advanced significantly. Research undertaken over nearly forty years has revealed that the bacteria is linked to the natural history of several upper gastrointestinal illnesses. Epidemiologic studies reveal a greater prevalence of autoimmune disorders occurring during or subsequent to infections with certain germs. Research findings indicate that H. pylori may act as a catalyst for infectious autoimmunity and might be linked to several autoimmune illnesses, both innate and acquired.

This research aims to deliver sufficient preventive and community information while rectifying misconceptions about H. pylori infection, and to examine the existing resistance related to H. pylori as a potential contributor to autoimmune disorders, including autoimmune thyroiditis, inflammatory bowel disease, and analogous conditions. This study focuses on several investigated and analyzed autoimmune illnesses.

1. INTRODUCTION

The thyroid gland is a vital organ in the human body that synthesizes essential hormones: triiodothyronine (T3) and tetraiodothyronine (T4), which are crucial for regulating metabolic processes and development. Thyroid dysfunction impacts several essential functions, stemming from thyroid activity or hyperthyroidism, which causes fluctuations in the levels of thyroid hormones T3 and T4 [1].

Hypothyroidism (Hashimoto's thyroiditis) and hyperthyroidism (Graves' disease) are the predominant autoimmune thyroid diseases, representing a frequent consequence of thyroid malfunction. Autoimmune diseases manifest when the immune system erroneously targets its own antigens. A defining characteristic of autoimmune thyroid diseases is the presence of autoantibodies directed against thyroid antigens. These conditions can arise from various factors, including infectious agents like the spiral bacterium Helicobacter pylori.

A significant proportion of persons diagnosed with thyroid illness were concurrently discovered to be infected with H. pylori, indicating that this bacteria plays a crucial role in the pathogenesis of these conditions. Helicobacter pylori is a prevalent bacterial infection in people globally, typically acquired in childhood and persistently harbored throughout life if untreated with antimicrobial treatments. Considering the significant significance of H. pylori in the etiology of autoimmune disorders Research is necessary on thyroid dysfunction and the ulcerogenic bacterium H. pylori, particularly in Iraq and other regions experiencing thyroid and human abnormalities.

This study was formulated to achieve the following research objectives:

1- Investigating the relationship between the occurrence of thyroid disorders and H. pylori.

2-Studying the pathogenesis of the stomach bacteria and the reasons for its danger to the human body and the body's lack of response to treatment.

2. REVIEW OF THE LITERATURE:

2.1. Historical Review about H.pylori

Two centuries ago, epidemiologists and clinical pathologists were doing research to determine the cause of peptic ulcer disease [2]. It was during this investigation that H. pylori was first discovered. The bacterium known as Helicobacter pylori was discovered by the Italian anatomist Giulio Bizzozero in the year 1892. This bacteria lives in the stomachs of dogs, which

*Corresponding author email: h.Jakhir82@gmail.com
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are very acidic. In the year 1899, Professor Warley Jaworski discovered a spiral-shaped bacteria in the sediments of the stomach wash. He named this bacterium Vibrio rugula and indicated that it may be involved in the pathogenic process of a number of different gastric illnesses. In addition, in the year 1896, a scientist named Salmonn claimed that these bacteria may be transmitted from diseased dogs and cats to mice. This idea was essential in the creation of vaccinations against H. pylori [23].

During the course of their study, a number of researchers discovered that the stomachs of carnivorous animals, such as dogs and cats, contained urease enzyme. The findings were broadened to include the human stomach, where it was discovered that the urease enzyme was present. It is believed that the urease enzyme is secreted by the epithelial cells that line the stomach. The use of the antibiotic tetracycline results in a reduction in the effectiveness of the urease enzyme. Particular microorganisms were found to be the origin of the urease enzyme that is found in the stomach. This was shown by the fact that the stomachs of germ-free animals did not have any urease activity. According to the findings of Steer (1975), who investigated the relationship between H. pylori infection and gastritis, the majority of instances of gastric ulcers and gastritis may be traced back to the colonization of the stomach by H. pylori bacteria.

2.2 General Characteristics of H.pylori:

H. pylori is a Gram-negative, S-shaped bacterium that is curved, measuring between 2.5 and 4.0 µm in length and around 0.5 to 1.0 µm in diameter. According to Mandell et al. (2010), this bacterium is present in vivo and, under optimal conditions, in vitro. This bacterium has a tuft of five to seven polar encircling flagella [21]. Despite variations in the size and number of flagella, they remain constant. Two and one of the figurines. Spiral bacteria are microaerophilic, indicating that they need oxygen, but at far lower concentrations than those seen in oceanic environments. This delineates both the configuration and the quantity of flagella they possess. These bacteria contain the enzyme hydrogenase, which they utilize to derive energy by oxidizing molecular hydrogen (H2) generated by intestinal bacteria. Their colonies stand out for their diminutive size and convexity, displaying transparency similar to a droplet of water. Additionally, they are motile due to sheathed unipolar flagella that facilitate their movement and penetration of the gastric mucous membranes.

Polymorphism is a phenomenon defined by its manifestation in both bacillary and coccoid forms. This bacterium is the primary etiological factor for ulceration of the stomach and duodenum, and these conditions are becoming more frequent due to its dissemination, affecting over fifty percent of the global population. The virulence genes possessed by certain genotypes of these bacteria account for the occurrence of illnesses attributed to them. The virulence genes especially pertinent to gastrointestinal disorders are vacA and cagA. These bacteria have evolved a way to withstand microbicidal acid to evade the severe circumstances present in the stomach lumen. They do this by populating a confined region of the stomach antrum and secreting the enzyme urease. Urease catalyzes the decomposition of urea in the medium into ammonia, which influences the acidity surrounding the stomach lining. This process enables the germs to persist in the human stomach indefinitely if untreated with antibiotics. Numerous illnesses, such as chronic gastritis, gastric and duodenal ulcers, gastric cancer, mucosa-associated lymphoid tissue lymphoma, Cotter's disease, and Hashimoto's disease, are associated with Helicobacter pylori.

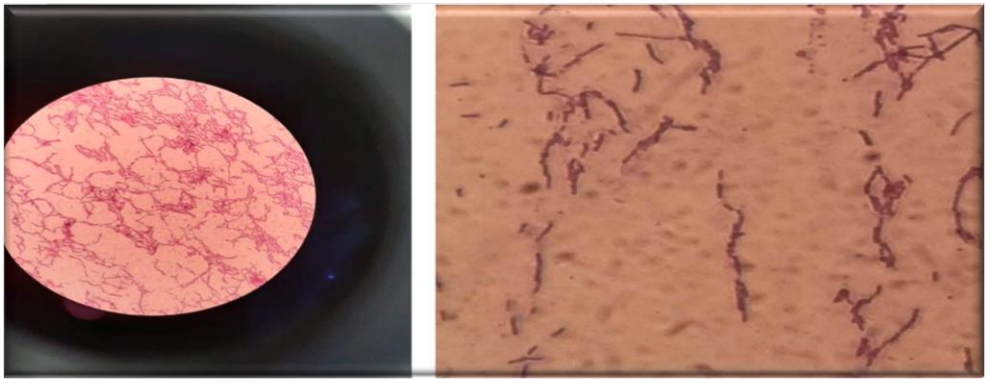

Fig .1. The microscopic appearance of Helicobacter pylori (Helicobacter pylori appears microscopically as a V-shaped curved rod and is Gram-negative).

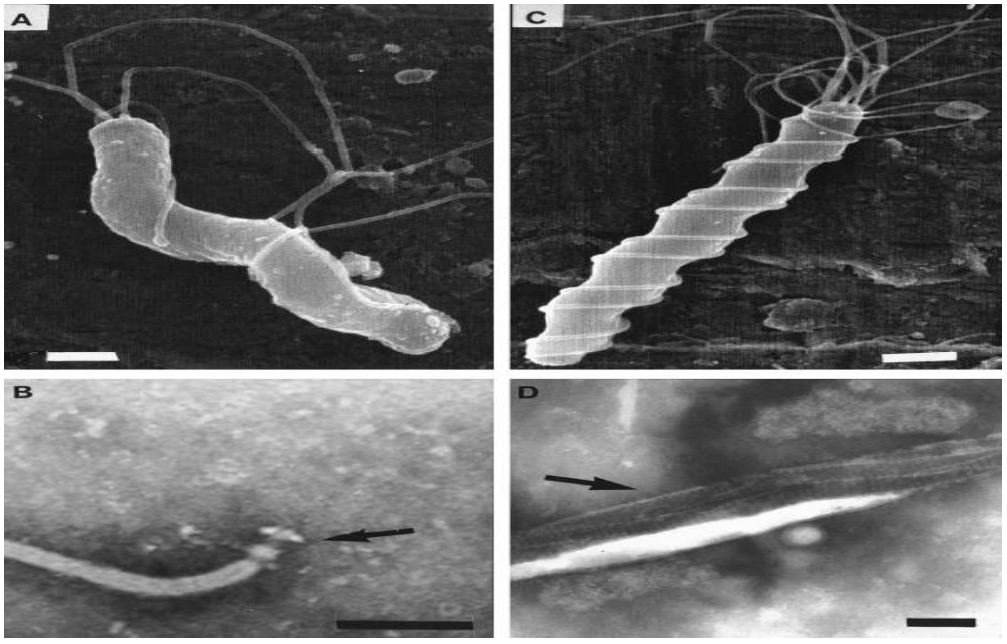

Fig .2. S-shaped portal malleus with five to seven coated polar flagella.

2.3 Pathogenicity of H. pylori:

H.pylori is the only bacterial pathogen that can survive in the stomach's highly acidic environment because it lives in the pyloric region and has a pH concentration of less than 2. It uses its flagella to penetrate the mucous layer and reach the right place in the stomach [3]. Hwang et al. (2015) Chemotaxis allows them to detect pH in the mucosal layer and swim toward a neutral environment at the stomach epithelial cells [20] [30].

These bacteria cling to stomach epithelial cells and create significant quantities of urease, which breaks down urea into CO2 and NH3. The urease enzyme degrades urea into ammonia, which is harmful to epithelial cells. Other H. pyori products, including as protease and an enzyme that vacuolates, are similarly cytotoxic. [26] H. pylori symptoms range in intensity. About 80% of people infected with the bacteria do not show any symptoms, while acute infection appears as acute gastritis with abdominal pain and nausea and can develop into chronic inflammation with dyspepsia, acidity, vomiting, abdominal pain, and weight loss.

2.4 H. pylori virulence factors

H. pylori cause chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue malignancy, and gastric cancer. Gastric cancer Important H. pylori infection feature Most H. pylori infections are asymptomatic, but a tiny number develop tissue inflammation that leads to Peptic Ulcer and Gastric Lymphoma. An imbalance between host defense systems and bacterial virulence factors causes H. pylori illnesses. The bacteria's key virulence genes, including cag A and cag A, make H. pylori strains extremely pathogenic and disease-prone. Vacuolizing Cytotoxin (VacA) and Urease (Yamazaki et al., 2003). acidic media [21].

1. flagella: Because of its wrapped form and polar flagella, H. pylori is able to hide in the stomach's mucous layer and avoid the acidic effect. It then spreads to the gastrointestinal tract, which is not as acidic, and begins colonizing the area. The flagella are encased in a bilayer sheath that continues the outer membrane of the bacterial cell wall; this sheath keeps the flagella flexible and allows them to move freely in acidic media [21].
2. Production of a number of exoenzymes: H. influenzae produces a number of exoenzymes; two of these, catalase and protease, affect the bicarbonate of the gastric mucosa and harm the surface epithelial cells; and a third, superoxidase, protects bacteria from neutrophil killing. In addition to creating phospholipase, an enzyme that dissolves the lipid layer present in the stomach's epithelial membrane, these enzymes play an important role in encouraging bacteria to infiltrate the gastric mucosa [5].
3. Urease Enzyme: - The initial step in an infection is the production of an enzyme called urease. This enzyme starts by breaking down the naturally secreted urea in the stomach into ammonia and carbon dioxide. Then, ammonia becomes ammonium by removing the positive hydrogen proton from water, leaving only negative hydroxyl ions (OH). The hydroxyl ions then react with carbon dioxide (CO2) to produce bicarbonate (HCO3), which neutralizes stomach acidity and provides a basic medium that protects bacteria from stomach acidity. In 2018, Levinson, Jawetz, and Levinson collaborated. Encoding the urease complex is another crucial function of the ureC gene [25].
4. Cytotoxic associated protein: It is a key component of H. pylori's pathogenicity. Since the majority of H. pylori strains in Asia are cag-positive, the exact nature of the association between cag-positive infection and clinical diseases is unclear in Asian countries, although numerous studies have shown that cag-positive strains are linked to chronic gastritis, gastric cancer, and a high prevalence of peptic ulcers in Western countries [40].

5. Vacuolating cytotoxin A (VacA): Vacuolating cytotoxin Vaca is synthesized by the majority of pathogenic strains; this protein constitutes one of the virulence factors that enhance the pathogenicity of gastric ulcers. The vaca gene encodes this protein under standard conditions. The polymorphism in the vaca gene sequence is delineated into three distinct regions: the signal region, the s-region, the middle region (m-region), and the intermediate region, which lies between the signal region and the middle region. The Vaca protein induces the formation of vacuoles among infected epithelial cells, resulting in the discharge of their contents and subsequent cell death [5].
6. Outer Membrane Proteins: Surface proteins on the surface of bacteria called outer membrane proteins (OMPs) trigger an inflammatory response by stimulating the release of interleukin-8 (IL-8). Intensity of leukocyte depletion, bacterial density, and the severity of disorders such stomach cancer and duodenal ulcers are all reflected in the gene expression of the proteins. Increased colonization and adhesion (2013) are results of increased gene expression in bacteria that have additional virulence factors [33]. Baba adhesion and Sab adhesion are two of the most significant proteins on the cell surface because they link to receptors on host cells; their sticky characteristics allow the bacteria to invade. Bacteria with these sticky proteins are more dangerous [13].
7. Biofilm Forming: The ability of certain bacteria, like H. Pylori, to form biofilms communities of bacteria that are closely bound to a surface by wet matrices of extracellular polymeric materials is a key component of bacterial pathogenicity because biofilms shield the bacteria from environmental hazards like dehydration, antibiotics, heavy metals, UV radiation, and the host immune system's defenses. One way to treat bacteria is by removing their capacity to create biofilms, which may happen if the bacteria are resistant to Amoxicillin, Clarithromycin, and Metronidazole [14].
8. Host immune response: Helicobacter pylori has evolved several strategies for interacting with and surviving within its host cells. In addition to causing stomach ulcers and cancer, H. pylori trigger the production of inflammatory cytokines, tumor necrosis factor, and interleukins inside gastric host cells via a variety of signaling pathways. The immunological response to Helicobacter pylori is triggered when the bacteria adhere to the host epithelial cells. This attachment triggers regulatory T lymphocytes, which secrete inflammatory chemokines after binding to complex molecules of major histocompatibility complex class II [8].

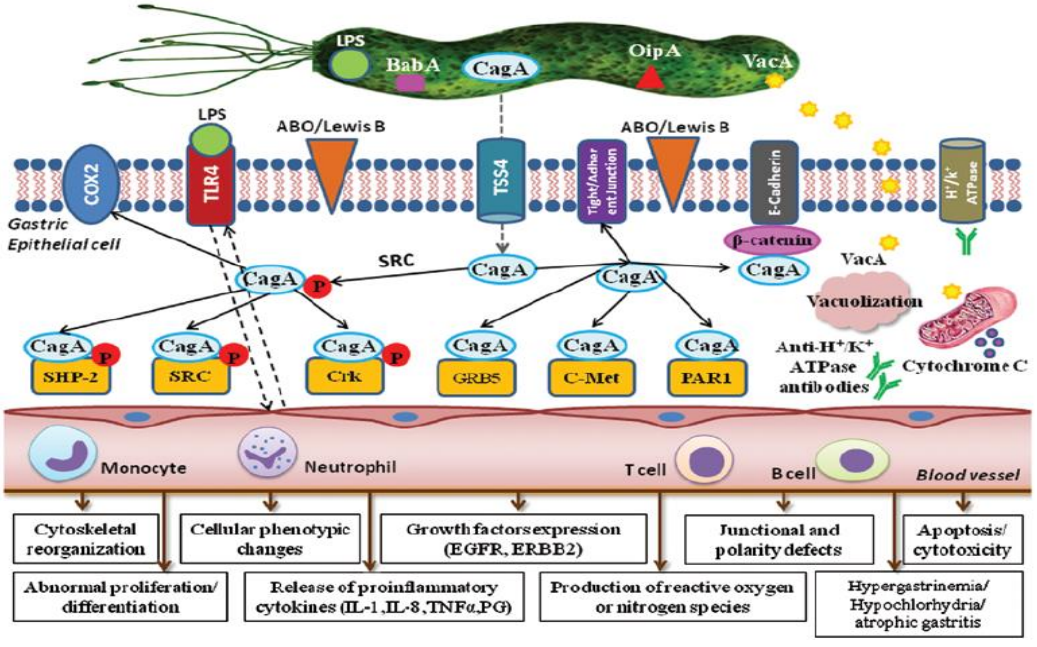

Fig .3. Molecular consequences of agA cytotoxicity in gastric epithelial cells (Atherton, 2006)

2.4.1 Epidemiology and transmission

Helicobacter pylori is more common as people become older. Infection with Helicobacter pylori is a worldwide problem, according to epidemiologic research. Place of residence, parental education, poor socioeconomic level, overcrowding in dwellings, and an unclean water supply are some of the several variables linked to the passing on and spread of H. pylori [6].

A. Oral-oral transmission: This route of transmission is mostly seen in industrialized nations owing to overpopulation, resulting in diminished living conditions and the proliferation of harmful practices. Research has verified the extraction of H. pylori bacteria from saliva, dental plaques, the oral cavity, tonsillar tissue, and the esophagus. This transmission method may be augmented by certain dietary practices, such as mothers chewing food before to feeding their infants [15].
B. Fecal-oral transmissions are prevalent in poorer nations because to inadequate cleanliness and insufficient information. H. pylori has been extracted from the feces of infected children, suggesting potential fecal-oral transmission, and has also

been isolated from adult feces, albeit to a lesser degree. However, the isolation process is complicated by the toxic effects of feces on these bacteria or the inadequacy of the employed isolation methods [24].

C. Water Route Transmissions: Contaminated water containing fecal matter may serve as a possible source for H. pylori transmission. Environmental data about H. pylori contamination in water suggests that H. pylori may be spread by water due to the contamination of water supply sources with fecal matter, a primary transmission route, mostly reported in poor countries. A research, the first of its kind in Basra, Iraq, using polymerase chain reaction (PCR) technology, documented the presence of H. pylori in treated drinking water [26].
D. Person-to-Person Transmissions: Research indicates that bacterial infections can propagate directly between individuals or indirectly from an infected individual to the environment. Currently, direct personal transmission pathways are more prevalent than environmental exposure methods, as infections are primarily transmitted through oral or fecal routes. This mode of transmission is particularly common among medical personnel, especially those handling endoscopic devices or specializing in gastrointestinal disorders, as well as through interactions among infected siblings and other family members, which facilitates infection spread and heightens transmission risk. Additionally, insufficient health awareness among infected individuals exacerbates the situation.

2.5 Diagnosis of Helicobacter pylori infection:

A variety of invasive and non-invasive diagnostics exist for the detection of H. pylori infection. Invasive procedures will undergo endoscopy followed by mucosal biopsy for culture, fast urease testing, and histological analysis. Endoscopy is costlier and less comfortable for patients, with a significant risk of complications. Consequently, the use of non-invasive tests for diagnosing H. pylori infection has gained prevalence owing to their high accuracy, cost-effectiveness, accessibility, and inability to differentiate between ongoing and past infections with the organism.

2.6 Therapeutic Intervention:

In cases of persistent illness, bacterial decolonization necessitates the use of an antimicrobial drug, with triple therapy being the conventional treatment for eradicating H. pylori infection. The conventional treatment for H. pylori is triple therapy, comprising a proton pump inhibitor (PPI), amoxicillin, and clarithromycin. However, the contemporary approach for resistant strains is termed quadruple therapy, which includes the same components as triple therapy with the addition of metronidazole [27] (Metronidazole). Antibiotic resistance is a prevalent problem among bacterial infections, and new research reveal the rise of antibiotic-resistant strains of H. pylori in clinical samples. In such instances, when triple and quadruple therapies are ineffective, an alternative treatment may be administered, including tetracycline and fluoroquinolones. Regrettably, tetracycline and fluoroquinolone-resistant strains have evolved from this bacteria. Research indicates that bacteria may alter their genome in response to the selection pressure imposed by antimicrobial treatment [22].

2.7 Pathogenesis of Helicobacter pylori:

The H. pylori bacterium utilizes its flagella to pierce the mucous layer and reach the right location, which is close to the stomach's epithelial cell layer, in order to live within the stomach. The bacteria must be able to withstand the stomach cavity's extreme acidity. The chemotaxis feature of H. pylori bacteria allows it to detect the pH of the mucous layer and move away from its acidic composition and toward a more moderate environment on the surface of the epithelial cells. The stomach epithelial cells' inner surface and sometimes their interiors are home to H. pylori bacteria. [30]. The bacteria in question generate adhesions to help in their attachment to the stomach's epithelial cells. Subsequently, they generate significant quantities of the urease enzyme, which is present both inside and outside of the bacteria. Urea, which is distributed throughout the circulation, is broken down by urease into carbon dioxide (CO_2) and ammonia (NH_3). By gaining a proton (H), ammonia is changed into ammonium (NH_4), which balances the stomach's acidity. The urease enzyme is necessary for the H. pylori bacteria to survive in the stomach. Along with other byproducts of the H. pylori bacteria that may be toxic to cells, such as the enzyme protease, vacuolating cytotoxin A (Vaca), and certain phospholipid enzymes that break down cells and are associated with severe pathogenesis, ammonia produced by the breakdown of urea by the enzyme urease is toxic to epithelial cells. I'll quickly discuss the following conditions that are brought on by spiral twisters that affect the stomach and duodenal regions. These conditions may evolve into acute or serious infections.

2-7-1 Gastritis:

H. pylori infection causes acute and chronic gastritis. Acute inflammation [4] occurs as a result of the colonization of this bacterium in the mucosal layer of the gastric cavity, and thus neutrophils and polymorphonuclear cells accumulate. This results in an acute inflammatory response and a decrease in the acid level in the stomach (Hypochlorohyra). As a result of

acute inflammation, if this initial response fails to eliminate the infection, other immune cells, including T cells and B cells, and macrophages, accumulate in the gastric mucosa and produce chronic gastritis [9].

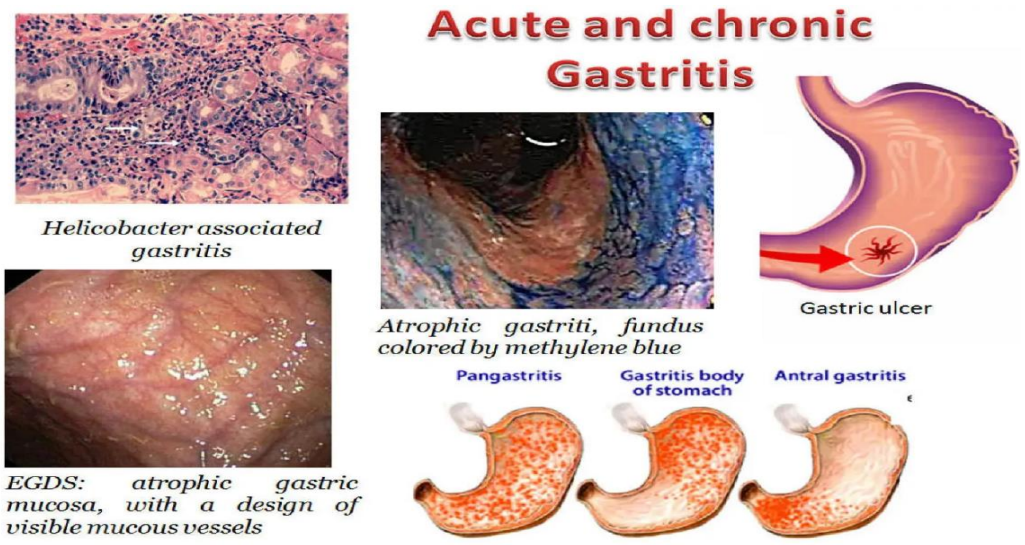

Fig .4. Helicobacter pylori: acute chronic gastritis

2-7-2 Gastric Ulcer:

Studies have shown that Helicobacter pylori bacteria, which can withstand the stomach's acidic environment, is a primary cause of peptic ulcers, or ulcers of the duodenum or stomach. Additionally, there is a link between the bacteria and a higher risk of stomach cancer. Approximately 80% of stomach ulcers and over 90% of duodenal ulcers are caused by H. pylori. Using pili as a point of attachment, H. pylori colonizes the stomach's epithelial cells. Urease, which is produced by these bacteria, causes ammonia, gastritis, and maybe the gradual development of ulcers. Urease also triggers an immunological response. Toxin activity is another factor that might lead to the development of ulcers. According to reports, the toxin VaCa, which induces the development of a vacuole in host cells, is present in measurable amounts in 50% of clinical isolates of H. pylori [10].

Weight loss, bloating, belching, nausea, and appetite loss are among the warning signs and symptoms. Stools from bleeding ulcers may be black in color. If the ulcer is not treated, it may deepen, damage more tissue, and eventually cause a hole in the stomach. It is a highly severe illness because a hole enables digestive enzymes and acids to escape into the body.

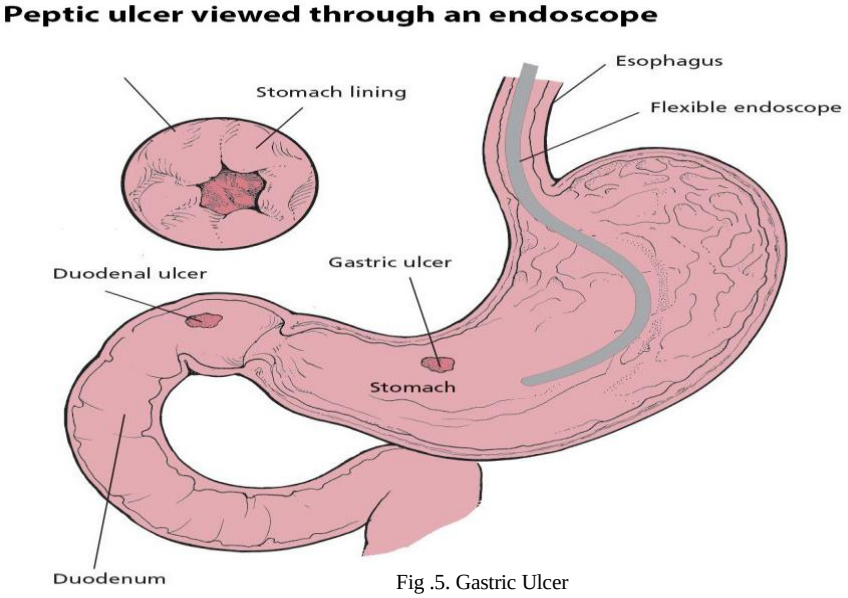

Fig .5. Gastric Ulcer

2.7.3 Mucosa-associated tissue lymphoma lymphoid:

H.pylori infection stimulates the aggregation of lymphoid cells in the submucosa to become lymphoid follicles, which form lymphoid tissue. This lymphoid tissue is essential for the development of malignant gastric MALT lymphoma. In a study of 110 patients with mucosa-associated tissue lymphoma, H.pylori was found in 101 cases, or 92%. [41].

2.8 Autoimmune thyroid disease (ATD):

According to Canaris (2000), autoimmune thyroid disease (ATD) is more prevalent in middle-aged women and its prevalence rises with age. The disorders that comprise ATD include hyperthyroidism (also known as Graves' disease), goitre, postpartum thyroiditis, atrophic autoimmune hypothyroidism, thyroid-associated orbitopathy, and others. Other forms of thyroiditis may emerge over time, however the immune system is involved in the majority of HT and GD cases. Autoimmune reactions targeting several thyroid-related proteins and receptors are the hallmark of autoimmune thyroid disease (ATD)[42].

2.8.1 Non-toxic goiter or goiter:

The word is used to describe a situation where the thyroid gland is bigger than usual; it may also signify goiter. Visual inspection, palpation, or imaging studies may detect goitre. Anterior measurements range from 0.8 cm to 1.6 cm, width from 1 to 1.8 cm, and cross-sectional area from 4 to 4.8 cm for a normal thyroid gland. According to ultrasonography estimates, this corresponds to a weight of 10–20 grams and a volume of 7–10 ml. The thyroid gland becomes larger as a person gets older and heavier. Its size is greater in men than in women. As iodine consumption rises, the size falls. The enlargement of the thyroid gland may occur for a number of reasons, both normal and abnormal. Some of the most common reasons for physiological goitre are adolescent goitre, pregnancy, and infections that induce autoimmune illnesses. Either hyperthyroidism, hypothyroidism, or euthyroidism may be accompanied with a goiter.
Dispersed, nodular, or multinodular forms are possible. Since the enlarged thyroid gland is not constrained by weak anterior cervical muscles, subcutaneous tissue, or skin, it often expands at the front of the neck. A goiter is a medical word for an enlarged thyroid gland located in the cervix. The enlargement of the thyroid gland to the point that it goes through the thoracic inlet is known as substernal or retrosternal goiter. [45]
Chronic gastritis is usually caused by an infection with Helicobacter pylori. Because Helicobacter pylori lowers stomach acid output, it may decrease the effectiveness of oral thyroid hormone absorption. We set out to see if there was a difference in thyroid function tests between before and after H. pylori eradication in patients who had previously failed to show improvement with high-dose thyroid hormone treatment. When hypothyroidism develops, the ineffectiveness of therapy might be due to H. pylori gastritis. Patients taking large dosages of thyroid hormone run the risk of developing thyrotoxicosis if they undergo H. pylori eradication [7].

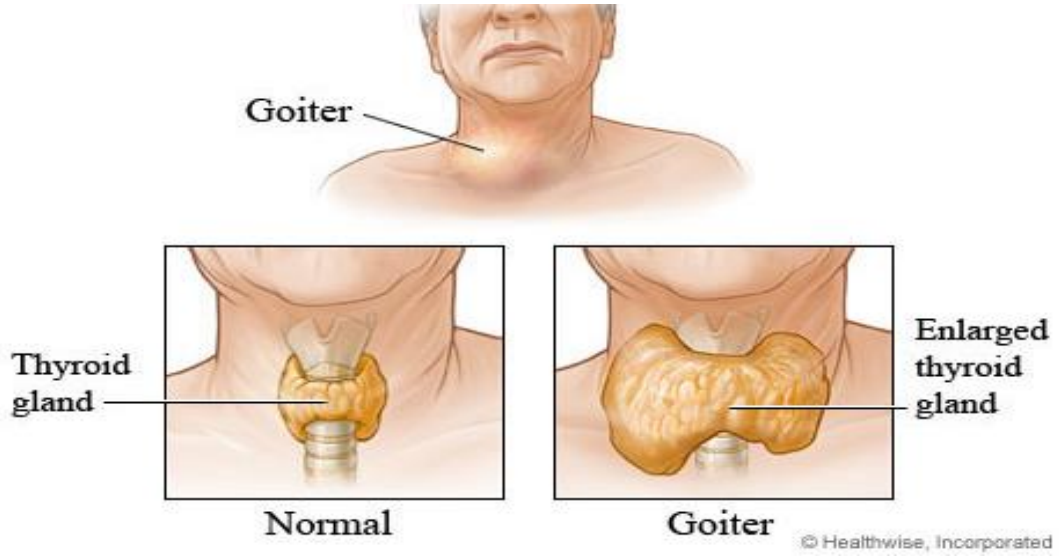

Fig.6. Goiter

2.8.2 The relationship between Helicobacter pylori and autoimmune thyroid disease (ATD) development. Inflammatory thyroid disease pathophysiology.

Hypothyroidism and hyperthyroidism are symptoms of Graves' illness, which is caused by thyroid-stimulating hormone (TSH) receptor antibody (TRAB). However, many parts of the immune system, including B- and T-cell activity, are affected by immunological dysfunction. After T cells become sensitive to antigens from the thyroid gland, B lymphocytes in Graves' disease begin producing antibodies against these antigens. In hyperthyroidism, an antibody binds to the thyroid surface

TSHR, which in turn targets the TSH receptor area [11]. Although hyperthyroidism patients' blood TRAB concentrations do not correlate with their serum thyroid hormone concentrations, the existence of these antibodies is positively linked to both current illness and disease recurrence [2][12].

Over time, Hashimoto's thyroiditis (HT) destroys the natural design of the thyroid, leading to hypothyroidism. Apoptosis is involved in the pathophysiology of HT. While FAS is expressed by normal thyroid cells, FASL is not. Although both HT thyroid cells and those with Graves' illness have FAS and FASL, only HT thyroid cells undergo apoptosis. Increased FAS-mediated apoptosis is brought about by Thl-type cytokines, which are the most common in HT thyroids. Apoptosis was later shown to be associated with the activation of the caspase pathway, which was largely caused by the external permeabilization of the mitochondrial membranes of the target cells [16] [17].

2.8.3 The correlation among autoimmune thyroid disease (ATD) & the presence of Helicobacter pylori infection.

Both genetic and non-genetic factors, including environmental influences and microbial infections, contribute to the genesis of autoimmune thyroid disease (ATD). Helicobacter pylori is associated with the onset of ATD, as noted by Jueckstock and Mylonas (2010). The genesis of ATD may be ascribed to hereditary and non-genetic factors. Genetic variables include thyroid-specific genes and genes that govern the immune system. Non-genetic variables include elements such as tobacco usage, psychological stress, iodine intake, pharmaceuticals, gestation, and infections from bacteria and viruses.

Extensive research has associated Helicobacter pylori infection with autoimmune thyroid diseases (ATD) and several other thyroid disorders. Consequently, data indicates that both adults and children with ATD are predisposed to Helicobacter pylori infections, which correlate with elevated levels of thyroid autoantibodies, potentially impairing stomach secretory function. Another idea posits that the predominant form of Hashimoto's thyroiditis is induced by Cag A+ Helicobacter pylori strains, which likewise elevate the incidence of autoimmune thyroid disease in women. This is based on the discovery of monoclonal antibodies that target the Cag A+ pathogenic islets, which express an endogenous peroxidase gene.

Additional evidence suggesting that Helicobacter pylori antigens may significantly contribute to the development of autoimmune atrophic thyroiditis includes a strong correlation between anti-Helicobacter pylori IgG antibodies and thyroid autoantibodies, as well as the observation that thyroid autoantibody levels progressively decline following the eradication of Helicobacter pylori infection. An increased susceptibility to Helicobacter pylori infection may be linked to the autoimmune characteristics of this condition.

The absorption of levothyroxine may be affected by malabsorption disorders or conditions that reduce gastric acidity. These data suggest that pre-existing malabsorption may impair levothyroxine bioavailability. The association seems to be more pronounced with Helicobacter pylori infection.

2.8.4 Hyperglycemia, Helicobacter pylori, and lipid profiles in the blood:

Some disorders, such as diabetes, alter the quantity of fat in the body. Due to insulin resistance's effect on the primary enzymes and fat metabolism pathways, Ozder (2014) found a direct correlation between lipid problems and type 2 diabetes. According to Sreenivas et al. (2014), lipid problems in type 2 diabetes are associated with elevated total cholesterol (TC), triglycerides (TG), and low levels of high-density lipoproteins (HDL), making them a major risk factor for cardiovascular illnesses. When the levels of HDL drop, LDL-C and VLDL levels rise in tandem. Elevated VLDL levels contribute to elevated TG, a single risk factor for diabetes, particularly when combined with low HDL levels. There is strong evidence that type 2 diabetes is closely linked to coronary heart disease (CHD). According to Hashim (2015), although low HDL levels are related with an increased risk of coronary heart disease, they are inversely proportional to the risk of developing type 2 diabetes. Thanks to its high lipoprotein content, particularly HDL, it shields the heart from harm and helps prevent heart diseases. Lipid levels are affected and the risk of cardiovascular disease and atherosclerosis is increased by an infection with the H. pylori bacterium [37-38]. According to a study conducted by Sung et al. (2005) [39], the lipopolysaccharides found in H. pylori bacteria are responsible for the role of atherosclerosis. These bacteria stimulate the production of various cytokines, such as TNF and IL-6, which in turn inhibit the activity of the lipase enzyme. As a result, the metabolism of lipids in the tissues is affected, with an increase in harmful fats and a decrease in good fats. Atherosclerosis may develop in people with diabetes and H. pylori infection for a number of reasons, one of which is the high prevalence of a particular blood lipid condition known as diabetic dyslipidemia, according to several research. Symptoms include decreased HDL-C levels, tiny dense particles, elevated TG, and triglyceride-rich lipoproteins (TRLs). Patients with type 2 diabetes often have this pattern of lipid abnormalities, but those with type 1 diabetes have a lower prevalence.

2.9 Diagnostic procedures for Helicobacter pylori infection:

According to Garza-Gonzalez et al. (2014), there are two types of diagnostic testing for H.pylori infection. One kind of test requires endoscopy and involves invasive procedures including tissue tests, bacterial cultures, polymerase chain reactions, and quick urease tests. The other type of test does not include endoscopy and is non-invasive and involves serological tests and stool tests.

A. Histology Test: H. pylori infection can be precisely diagnosed through histological examination utilizing specialized dyes. The extent of gastritis offers insights into the risk of infection with this bacterium when tissue biopsies are

obtained from the antrum or body of the stomach. Additionally, histological alterations that may result in stomach cancer or gastric atrophy are identified [35] (Gastric atrophy).

B. Bacterial Culture: Tissue biopsy samples obtained via endoscopy may be cultivated on specialized medium to identify H. pylori bacteria, ensuring optimal environmental conditions while necessitating precision, diligence, and expertise to isolate colonies of this bacterium. This test is regarded as the least reliable among diagnostic tests since medications that suppress the development of this bacterium might provide a negative culture result. It is regarded as a crucial diagnostic test for assessing the susceptibility of this bacterium to various antibiotics, which is vital for selecting these particular medicines in cases of prior treatment failure [18] [19].

C. Polymerase Chain Reaction (PCR) assay This approach is the most used in molecular genetics labs and is described as the enzymatic amplification of DNA outside the body millions of times. This approach is distinguished by its excellent diagnostic sensitivity and may be used in conjunction with endoscopy or alone, as shown in the detection of H. pylori DNA in the feces and saliva of infected individuals. Falsafi, 2009 This technology's significant advantage lies in its capacity to diagnose the bacteria without endoscopy, enabling the detection of bacterial DNA in the gastric juice and saliva of infected individuals, as well as in gastric tissue biopsy samples and stool specimens. Another advantage is its capacity to differentiate between hazardous and non-toxic strains, since it has unique genes associated with the virulence of these bacteria [31][36].

D. The rapid urease test (RUT) demonstrates an accuracy over 90% in identifying bacterial infections, so sufficing for diagnosis and the commencement of therapy. The test is straightforward, cost-effective, and very specific, since it may be conducted at the patient's bedside. This assay is extensively used to identify urease enzyme activity in tissue biopsies [29]. This test is a dependable method for detecting H. pylori bacteria in tissue biopsies. The tissue biopsy sample is used in accordance with the manufacturer's directions by positioning it on the examination kit in the specified locations. The test result is available within one hour and is contingent upon the color transition of the biopsy on the kit from yellow to dark pink, which occurs due to the urease enzyme produced in abundance by bacteria, facilitating the decomposition of urea into two ammonia molecules and one carbon dioxide molecule.

E. Serological examination These tests include the identification of antibodies specific to H. pylori. Nonetheless, its precision is contingent upon the specific serological test used. Serological tests are mostly used to assess individuals with early dyspepsia and those with ulcers for the presence of antibodies to H. pylori in bodily fluids. Serological tests provide positive results over an extended period post-recovery from H. pylori infection; however, they are not used to confirm effective therapy, since antibodies in the bloodstream diminish gradually [27].

- Serological assays for the detection of H. pylori bacterial infection. The most renowned assessments used are:
  1. Accelerated Assessment One Step H. pylori Ab: A serological assay used for the diagnosis of H. pylori bacteria. It is defined by its simplicity and rapidity, and is offered as a commercially accessible immunoassay kit. This test typically consists of a strip including an aperture for the insertion of the contaminated serum. This serum comprises antibodies generated in response to the germ, as the reaction transpires with the bacterial antigen affixed to the surface of the aperture in the strip. Adjacent to the cavity housing the serum, there exists a large aperture with the letters C and T. In the event of a good result, two red lines are shown; conversely, a negative result is indicated by the presence of one red line.
- Enzyme-linked immunosorbent assay (ELISA) test
  One of the serological assays used to identify H. pylori bacteria examines the concentration of particular antibodies, including IgM and IgG. This assay relies on the interaction between specific antibodies in the serum of the infected individual and the antigens located in the wells of the test plate, and it is regarded as one of the most reliable serological tests in terms of usability and precision [33][34].
- Assay for the identification of antibodies against H. pylori bacteria in saliva: Detection of H. pylori Antibodies in Saliva. Salivary antibodies are produced in response to infection with this bacterium, and a commercial kit is used to identify the IgG antibody in saliva. The saliva collection procedure involves depositing the patient's saliva into a clean, sterile, and securely sealed tube. A specialized apparatus for collecting saliva from the gums is used to provide improved results; nonetheless, the test is limited by its inadequate sensitivity [28].
- Assay for the identification of antibodies against H. pylori bacteria in urine Detection of H. pylori Antibodies in Urine Test. This assay may identify particular IgG antibodies in urine at low concentrations. The ELISA device is applicable for this test and the rapid serological test, exhibiting a sensitivity range of 89.7-93.3, contingent upon the concentration or presence of the bacteria, which is influenced by elevated IgG levels. However, urine samples cannot be frozen due to protein degradation at low temperatures; thus, they must be processed while fresh. Consequently, this test did not attain the requisite optimal sensitivity for routine testing [32].

3. CONCLUSIONS

1. Thyroid diseases escalate with patient age, and females exhibit greater susceptibility than men.
2. There exists a correlation between thyroid problems and elevated body weight.

3. Cholesterol was identified as being correlated with high-density lipoprotein (HDL) levels in individuals with thyroid problems.
4. Patients with thyroid problems exhibited increased susceptibility to H. pylori infection.
5. The prevalence of Helicobacter pylori infection is greater in individuals with hypothyroidism compared to those with hyperthyroidism.
6. In individuals with diminished iodine levels, namely those with hypothyroidism, the presence of Helicobacter pylori gastritis could lead to the insufficient response to therapy. The eradication of Helicobacter pylori in individuals given high dosages of thyroid hormone entails the risk of thyrotoxicosis.

4. RECOMMENDATIONS

1- The association between hypothyroidism and Helicobacter pylori-induced peptic ulcers requires further research.
2- Research on the correlation between diabetes, thyroid issues, and H. pylori infection is urgently needed.
3- More research on the link between H. pylori infection and subclinical hypothyroidism is required.
4- Genetic research into the link among thyroid problems and H. pylori-induced stomach cancer is urgently needed.

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Conflicts of Interest:

The authors declare no conflicts of interest in relation to this study.

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