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Helicobacter Pylori: An Overview and Facts

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ABSTRACT

Infection with *Helicobacter pylori* is one of the most common human infections as more than half of the world's population suffers from infection with *H. pylori*. The role of *H. pylori* in gastroduodenal diseases became more confirmed. in the advanced stages of Infection, *H. pylori* can cause stomach and duodenal ulcers and gastric cancers. In this review, we introduce a comprehensive view of pathogenesis mechanisms of *Helicobacter pylori* and the good management of infection.

KEY WORDS: *Helicobacter pylori*, ulcers, gastric cancer, Pathogenesis, Vaccine.

1. INTRODUCTION

Helicobacter pylori are one of the wildest human infections. Infected people with *Helicobacter pylori* are usually asymptomatic, but about 30% of patients may develop symptoms to severe gastrointestinal diseases such as stomach and duodenal ulcers, gastric cancer and MALT lymphoma (Fuccio, 2008; Shigeru and Steffen, 2019, Tang, 2005).

A recent report estimates that more than half the world's population is infected with *H. pylori* with a variation in the prevalence of it between regions and countries (Hooi, 2017). The highest rate was in Africa about 79.1% followed by Latin America with 63.4%, in Asia the rate was 54.7% but the lowest prevalence of *H. pylori* was in Northern America and Oceania (37.1%, 24.4%) respectively (Eric, 2019).

At the beginning of the twenty-first century, the prevalence of *H. pylori* decreased in industrialized countries in west and concentrate in developing countries, this is according to urbanization, good sanitation management, provides to clean water, socioeconomic status (Hooi, 2017). There are differences in the *H. pylori* prevalence within the same country. for example, the rate in non-whites ranged from 34.5% to 61.6% while in non-Hispanic whites was 18.4% - 26.2% (Fuccio, 2008; Everhart, 2000; Cardenas, 2006; Ina S Santos, 2005).

Helicobacter pylori prefer regions with low acidity. In normal conditions of the stomach, the antrum, which is less acidic region than the stomach body, is often the site of *H. pylori* in infected people. the Evidence of that when infected people are given a drug to reduce acid production in the stomach, the distribution of infection gathers on this area. In addition to the easily infected children who have less acidity than adults in their stomach, this is suggested that stomach acidity determines *H. pylori* growth (Marguerite, 1995; Shamshu and Yoshio, 2018; Sachs, 2000).

Pathogenic Mechanisms: *Helicobacter pylori* are gram-negative bacteria belonging to the family Helicobacter Figure.1, it's found mainly in the gastrointestinal tract of the patient. *H. pylori* protect itself from the acid by providing a buffer zone, it produces an enzyme called urease that converts urea that secreted by the stomach cells into ammonia and carbon dioxide in addition to alpha-carbonic anhydrase (α-CA). both enzymes contribute to deacidification in the stomach by turning carbon dioxide produced by urease into bicarbonate, this compound is another weakly basic chemical used to moderate the stomach's acidity. When *H. pylori* infect the stomach, it penetrates the mucus layer and links to the surface of the epithelial cell where obtaining nutrients (Stephanie, 2008; Elizabeth, 2005).

To pass these stages, *H. pylori* uses several mechanisms such as producing urease enzyme that has a role in *H. pylori* protection from stomach acid. in addition to that, some strains of *H. pylori* produce a protein called cytotoxin associated gene A (CagA). These strains are highly associated with the development of infection into ulcers or stomach cancer. When *H. pylori* produce the CagA, it injects this protein into the mucosal cells by pilus. once entering the cell, CagA destroys the structure of cells in tight junctions where it takes its nutrients causing damaging in the protective layer. Also, *H. pylori* produce a protein called Vacuolating cytotoxin (VacA), this protein attaches to the outer membrane of stomach cell forming regions where nutrients leak or making inside the epithelial cells a vacuole that contained substances such as polysaccharides, ions, etc. Figure.2 (Shigeru and Steffen, 2019; Philip and Hazel, 2010; Steffen and Yoshio, 2016; Alojz and Marija, 2014; Breno, 2019; Nicole and Steffen, 2017; Gu, 2017; Alzahrani, 2014).

As a result, the immune system is induced to produce cytokines by the injured cells leading the immune cells to transfer into the tissue Figure.3. This tissue becomes inflamed that resulting in a loss in lining cells and mucus layer. all of that lead the stomach acid to access to the epithelial cells causing an ulcer.

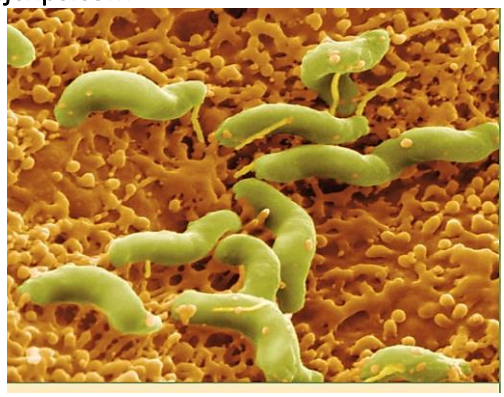

Figure.1. *Helicobacter pylori* bacteria

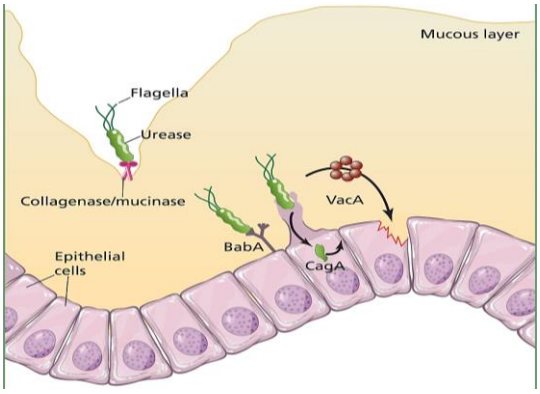

Figure.2. *H. pylori* proteins that used to maintain its presence in the stomach

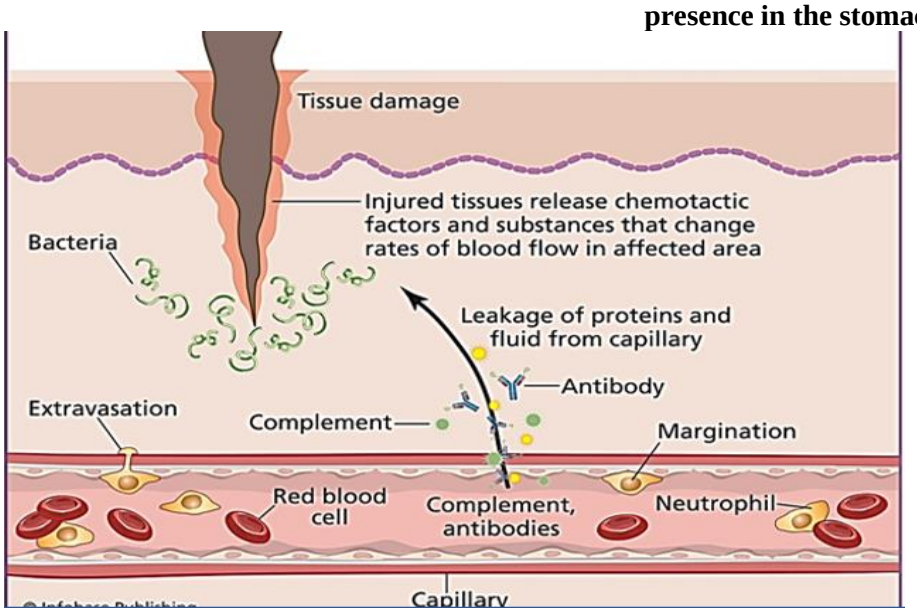

Figure.3. The infection of *H. pylori* induces the immune system

How *Helicobacter Pylori* avoids the Immune System: *H. pylori* have developed its defences against the immune system to become the infection chronic. With the continuous infection, damaged cells induce the immune system by a cytokine called Interleukin-8 Figure.3. Then macrophages begin their attack, but bacterial proteins such as VacA protein reduce the responding of T cells to cytokine and limit the interaction with B cells so reduce the production antibodies of *H. pylori* (Philip and Hazel, 2010). In addition to the effects of *H. pylori* on the activities of the immune system, *H. pylori* can survive using immune cells themselves. Some of *H. pylori* strains can live inside the immune cell (more than 24 hours) by surrounding themselves by vacuole inside of the macrophages. It is thought that these macrophages are reservoirs of re-infection. Also, *H. pylori* use the hiding strategy in the epithelium as a mechanism for avoiding the immune system using CagA to breaks down the barriers between the cells of epithelial (Shigeru and Steffen, 2019; Nicole and Steffen, 2017; Tummala, 2004; Xia, 2005).

***Helicobacter Pylori* and Ulcers**: It was thought that ulcers are caused under the effect of emotional stress and according to bad lifestyle customs such as (drinking alcohol, smoking, etc.), but now, it is known that the ulcers are caused as the effect of *H. pylori* infection. it's worth to mention that the *H. pylori* infect over than half of the world's population, but the infection develops to ulcers in only about 10 per cent of them. the differences in the response of a human to *H. pylori* are caused according to the type of infecting strain and the immune system responding to it (Shigeru and Steffen, 2019; Johannes, 2006; Matsumoto, 2014).

***Helicobacter Pylori* and Cancers:** In the infected tissue, Macrophages and neutrophils produce substances such as nitric oxide, these substances are considered as antibacterial and destroy the nearby cells that are lead to mutations in the DNA of tissue cells. Furthermore, it is a high oxidizing agent, the activity of these oxidants causes breaks in the DNA of the cells which surround the neutrophil. These breaks cause a loss in genes as tumour suppressors, mutations or maybe cause rearrangement of genes. the disorder is in the stomach cells leads to gastric atrophy that can then develop to another condition called intestinal metaplasia leading to the replacement of gastric glandular cells by intestinal and fibrous tissues. The possibility of gastric cancer increases according to increasing worsens of gastric atrophy and intestinal metaplasia (Steven, 2017). In addition to gastric cancer, *H. pylori* infection causes other cancers such as MALT lymphoma. The inflammation, resulting from the bacterial presence, leads to disturbances in resident lymphocytes (especially T or B cells) and cell division. lymphocytes concentrate in high level and they

displace normal cells leading to function reduced (Shigeru and Steffen, 2019; Johannes, 2006; Nicole and Steffen, 2017; William, 2017; Sebastian and Pierre, 2002).

Diagnosis: There are a lot of tests used to diagnose *H. pylori* infections. These tests differ in their accuracy, sensitivity and its suitableness to the patients. One of these tests is Histological Examination by esophagogastroduodenoscopy which allows to observe the oesophagus, stomach and then collect biopsy from tissue and culture it (Shigeru and Steffen, 2019; Johannes, 2006; Breno, 2019; Ashwini, 2015; Bjorn, 2008; Wang, 2015; Nishizawa, 2012).

Rapid Urease Test is another test that uses a small piece of biopsy then put them in the liquid containing urea and a chemical whose colour changes depending on the pH in the solution. If *H. pylori* are present, the area is metabolized to ammonia with changes in chemical colour. the result of this test can be obtained between 20 minutes to 24 hours (Johannes, 2006; Breno, 2019; Ashwini, 2015; Bjorn, 2008; Hidekazu, 2016).

As mentioned earlier, the immune response to the infection with *H. pylori* produces antibodies we can be detected in the blood. So, Blood tests accompanied by symptoms of indigestion give the possibility of infection with *H. pylori*. the problem of this test is that the presence of antibodies does not necessarily suggest that the patient has an active infection, as antibodies can remain for up to a year after healing from infection (Shigeru and Steffen, 2019; Johannes, 2006; McColl KEL, 2012).

Urea Breath Test is an effective test to detect *H. pylori*. In this test, patients take a capsule containing a small amount of ^{13}C-labeled urea which is a special form of carbon that is a little heavier than normal carbon. Patients who haven't infections with *H. pylori* will produce little or no ^{13}CO2 and the urea will be metabolized and disposal in the faeces and urine. Despite the success of this test, its reliability in children is not yet confirmed (Shigeru and Steffen, 2019; Breno, 2019; Ashwini, 2015; Wang, 2015; Hidekazu, 2016). One of the most suspected ways of transmission of *H. pylori* is the faecal-oral route (McColl KEL, 2012). So, the faecal test is sensitive and specific and used to detect proteins and other antigens in the faeces of patients. is used to detect *H. pylori* proteins and other antigens in the faeces of patients who are suspected of having *H. pylori* infection. This test is sensitive and good for children (Ashwini, 2015).

Treatment: In several cases, eradication was effective in healing from ulcers and preventing recurrence. However, it is not sure whether the eradication of H pylori infection can reduce the risk of gastric cancer (Fuccio, 2008; Johannes, 2006; William, 2017; Sebastian and Pierre, 2002; Bjorn, 2008).

Triple-combination therapy has been proposed when *H. pylori* infection is diagnosed, this therapy consists of two antibiotics plus a proton pump inhibitor. There are common antibiotics that are used in this case such as amoxicillin, clarithromycin, metronidazole, and tetracycline, etc. Triple-combination therapy has been proposed when *H. pylori* infection is diagnosed, this therapy consists of two antibiotics plus a proton pump inhibitor. There are common antibiotics that are used in this case such as amoxicillin, clarithromycin, metronidazole, and tetracycline, etc. the triple-combination treatment affects in two ways, two antibiotics are used proceeding from the fact that *H. pylori* can resistant the antibiotics through changes in its DNA, so *H. pylori* can escape from one antibiotic but it is hard to do that when two antibiotics are used. Secondly, the proton pump inhibitor extends the antibiotics life This is because antibiotics do not be stable in an acidic environment. Figure.4 (Fuccio, 2008; Johannes, 2006; Nicole, 2017; Sebastian and Pierre, 2002; Bjorn, 2008; Hidekazu, 2016; Fernando, 2001; Venerito, 2013; Selgrad, 2013).

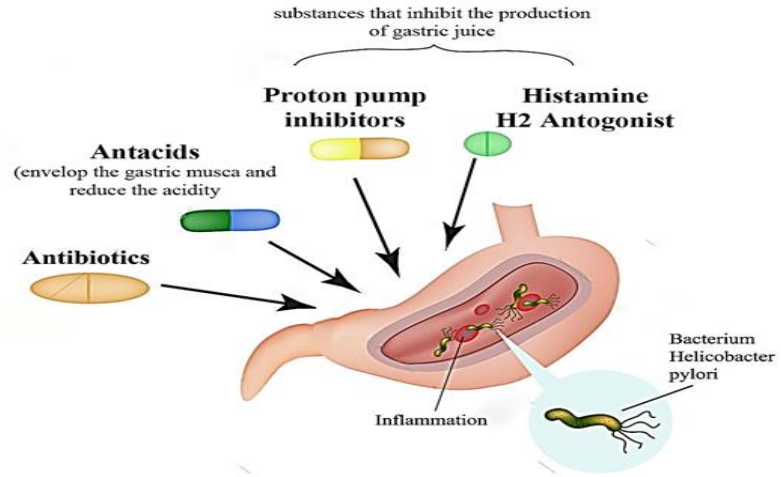

Figure.4. Treatment of *H. pylori*

Efforts are still underway to develop the vaccine that is a mixture of proteins and other molecules to stimulate the immune system to produce antibodies fort those proteins and molecules. this vaccine can be used before the infection to eliminated before it is confirmed, or after the infection to stimulate the immune system against *H. pylori* infection (Johannes, 2006; Nicole, 2017; Songhua, 2011).

2. CONCLUSION

Although the *H. pylori* infection characteristics have been studied extensively, researchers are still having to discover the more about the diagnosis and management of *H. pylori* infection to reduce health expenditure and to develop vaccine aiming to reduce the infection prevalence.

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