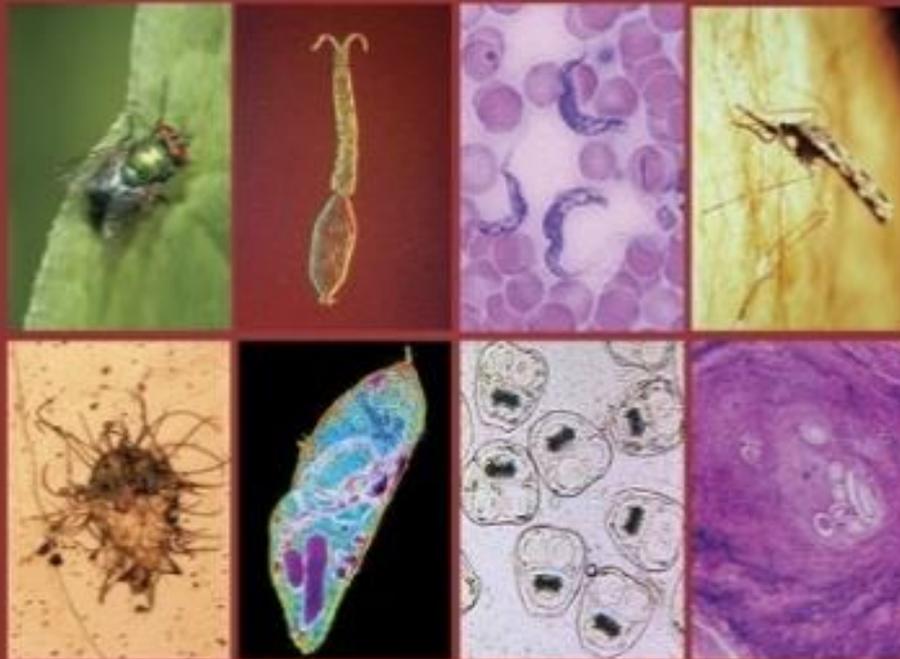




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Helicobacter pylori Infection and Intestinal Parasites; A Brief Review

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ABSTRACT

Human infection by *Helicobacter pylori* (*H.pylori*) and intestinal parasites simultaneously is a common health problem, especially in developing countries. *H.pylori* infection often leads to the development of different gastrointestinal complaints. Both groups of pathogens have the same predisposing factors and play an important role in gastrointestinal pathology in individuals having these co-infections, furthermore, it can affect the host's immune response. However, data on the magnitude and risk factors of these co-infections are limited. Here we tried to spot the light on this important relationship.

INTRODUCTION

Helicobacter pylori is a type of gram-negative bacterium found in the stomach's mucus layer of humans leading to chronic gastric inflammation (Alfarouk *et al.*, 2019). It affects 70–90% of the population in developing countries (Gillespie & Hawkey, 2006). In Africa, this bacterium infects 80% of the population as the infection is acquired during childhood (Smith *et al.*, 2019). Also in Egypt, the seropositivity of anti-*Helicobacter* IgG was found to be 79.8% when compared with the controls (Hanafi *et al.*,2017).

The infection by *H.pylori* commonly occurs by three different routes: oral-oral infection, gastro-oral infection and feco-oral infection. Also, the infection can occur through contaminated water and food or infected animals. (Eusebi *et al.*, 2014; Khalifa *et al.*, 2010). Low socioeconomic status, overcrowding and contaminated water supplies are important risk factors for this infection (Crowe, 2019 and Mezmale *et al.*, 2020). It is a well-known cause of peptic ulcers and it is an important risk factor for gastric carcinoma (Lesbros-Pantoflickova *et al.*, 2007). This type of cancer is considered the sixth most common cancer worldwide and the third most common cause of cancer death (Lee *et al.*, 2022).

Colonization of *H. pylori* in the stomach modulates the host immune system stimulating the release of inflammatory cytokines with neutrophils, lymphocytes, plasma cells and macrophage infiltration and contributing to the development of malignant complications of infection (Chan *et al.*, 2004). Oster *et al.*, (2022) found a negative impact of this immunomodulation leading to the consideration that this infection can decrease the results of cancer immunotherapies.

H. pylori also leads to many extra-gastrointestinal manifestations such as idiopathic thrombocytopenic purpura, iron-deficiency anaemia, chronic liver and cardiovascular diseases (Pellicano *et al.*, 2008& de Korwin *et al.*, 2017). Mohammad *et al.*, (2008) reported that *H. pylori* infection was extremely high among Egyptian school children.

As regards Parasitic infections, they are more or less neglected to constitute a global health problem (Taghipour *et al.*, 2021), especially among children (Harhay *et al.*, 2010). The World Health Organization estimated that in areas with high parasite transmission, about 600 million children are at risk (Sitotaw *et al.*, 2019; Melese *et al.*, 2019). The prevalence of infections is increased by geographic, ecology, socioeconomic factors, poor water supplies, decreased general sanitation and low income (Amer *et al.*, 2018). Contamination of food and water is a common source of infection by different intestinal parasites (Moses *et al.*, 2013).

Co-infection with many types of parasites affecting the gastrointestinal tract is usually seen in developing countries. This co-infection leads to damage in the intestinal mucosa of the affected patient resulting in malnutrition and also the affection of the immune system may take place. (Harhay *et al.*, 2010). In spite of the increased improvement in sanitation and hygiene in Egypt, intestinal parasites are still a significant Challenge (Monib *et al.*, 2016).

Co-infection of *Helicobacter pylori* with intestinal parasites is common as they share the same modes of infection and the same environmental conditions (Abd El Hameed *et al.*, 2021). Common risk factors include contaminated water supplies, defecation in the soil and low personal hygiene (Awuku *et al.*, 2017; Hernández *et al.*, 2019; Sitotaw *et al.*, 2019). Parasitic infection and *H. pylori* should be considered with low hygiene style and impaired immunity in diabetic children (Rady *et al.*, 2019).

The urease production by *H. pylori* facilitates the crossing of the stomach by these intestinal parasites (David *et al.*, 2006). The increased production of pro-inflammatory cytokines such as *IL-2* and *IFN-γ* caused by *H. pylori* leads to changes in the gastric environment, and diminished acid production (Padol and Hunt, 2004). As

a result of this diminished acid production, infection of the stomach by other organisms becomes much easier (Hosni *et al.*, 2012; Windle *et al.*, 2007). This reduction in gastric acid secretion occurs when *H. pylori* are present in the corpus region of the stomach. However, it was found that when these bacteria are present in the antrum region of the stomach, the production of gastric acid is increased. (Konturek *et al.*, 2006). Abd Elbagi *et al.*, (2019) concluded that gastrointestinal parasites are more common in *H. pylori*-infected patients compared to non-infected ones. Different consequences can occur as a result of this co-infection such as malnutrition and dehydration (Awuku *et al.*, 2017; Smith *et al.*, 2018; Melese *et al.*, 2019; Sabet *et al.*, 2009; Sitotaw *et al.*, 2019; Hernández *et al.*, 2019; Queiroz *et al.*, 2013).

***H. pylori* and Protozoal Intestinal Infections:**

Protozoa are microorganisms that are formed of a single rapidly growing cell, they may live intracellular or extracellular in the host resulting in many adverse effects such as fatigue, malnutrition, abdominal pain, or even ulcerations in the digestive tract (Abdullah *et al.*, 2016). Both *H. pylori* infection and protozoa infection leads to the recruitment of Th1 cells. This exacerbates the damage to the gastric mucosa (Haque, 2007; Maizels & Yazdanbakhsh, 2003).

In children in Africa, it was found that infected patients with *G. lamblia* had three times increased risk of infection with *H. pylori* (Ankarklev *et al.*, 2012). Kibru *et al.*, (2014) in Ethiopia found that there was a significant association between intestinal parasites and *H. pylori* infection. Schmid *et al.*, (2021) in Switzerland found that *G. lamblia* and *H. pylori* were important common causes of gastrointestinal disorders. Also, Yakoob *et al.*, (2018) found a strong correlation between *H. pylori* and common protozoal infections (*E. histolytica* and *Blastocystis* sp infections) in affected people suffering from chronic diarrhoea. Ahmed *et al.*, (2018) found a significant

correlation between them in patients with gastrointestinal complaints ($P \leq 0.005$). *Entamoeba histolytica/dispar* (55.5%) was the commonest parasite detected in positive cases with *H. pylori*.

H. pylori and *G. lamblia* were found among organic causes of recurrent abdominal pain, with different prevalences mainly in developing countries (Eldash *et al.*, 2013). Consequently, the early diagnosis helped patients to escape chronic gastritis complications (Sigthorsson *et al.*, 2001), and progression into painful stomach ulcers due to the excessive release of gastrin hormone (Gulcelik *et al.*, 2005). Zeyrek *et al.*, (2008) found that 22.4% of patients with recurrent abdominal pain were infected with both *Giardia* and *H. pylori*. In several studies, it was found that *H. pylori* infection increased the co-infection by *Giardia lamblia* by three times, and in another study, *Giardia lamblia* infection represented 22.3% of co-infecting parasites found among *H. pylori*-infected patients (Ankarklev *et al.*, 2012; Seid *et al.*, 2018).

In our country, Egypt, Abou Holw *et al.*, (2009) studied the effect of such an association on fifty *giardiasis* patients. Results showed significant upper gastrointestinal symptoms (epigastric pain and anorexia) in patients co-infected with *H. pylori*. Also, endoscopic and histopathologic examinations showed significant gastric lesions in this category of patients when compared to those infected with *G. lamblia* only. In a study done in Tanta, the co-infection between *H. pylori* and *E. histolytica* or *G. lamblia* was high affecting nearly half of the patients included in the study (Sabah *et al.*, 2015). El-Badry *et al.*, (2017) found that among 63 cases of *giardiasis* by both microscopy and PCR, 52.5% were co-infected with *H. pylori*. Co-infection was more frequent with assemblage B (50.9%) than assemblage A (40%) and concluded that this co-infection is common in school-age children. Ghallab and Morsy, (2020) showed a significant association between *H. pylori* and protozoan-causing diarrhea. These

protozoan parasites were with *G. lamblia*, *E. histolytica/dispar*, *Cryptosporidium parvum* and *Blastocystis hominis*. (Nasr *et al.*, 2022) found that the prevalence of *H. pylori* co-infection with parasites was 2%.

***H. pylori* and Helminthic Intestinal Infections:**

Unlike protozoa that stimulate Th1 recruitment, helminthic infections lead to Th2 polarization. A study held on mucosal samples from the stomach showed reduced expression of pro-inflammatory cytokines and predominant Th2 response (higher level *IL-4*) among patients with this co-infection (Fuenmayor-Boscán *et al.*, 2020). So, the infection of a human with *H. pylori* and helminths may protect against inflammations within the gastrointestinal tract and is linked with the enhancement of the regenerative processes (Haque, 2007; Maizels & Yazdanbakhsh, 2003). Concurrent helminthic infections in animal models showed to decrease the severity of gastritis induced by *H. pylori* (Fox *et al.*, 2000). *H. pylori* infection was considered a cause of gastric carcinoma in humans but on the contrary, large human populations living in Africa infected with *H. pylori* have low gastric cancer rates. This was called the "African enigma" (Bravo *et al.*, 2002). In spite of the high prevalence of *H. pylori* and helminthic infections in humans living in Venezuela and India, a low risk of gastric cancer was found (Fuenmayor-Boscán *et al.*, 2020; Hussain *et al.*, 2020). In one study in China, there was a decreased prevalence of *H. pylori*-induced atrophy due to concurrent helminthic infections (Du *et al.*, 2006). Another study reported that populations from the low-risk place of gastric carcinoma were infected with helminths (Whary *et al.*, 2005). So, there are differences in the prevalence of gastric cancer in spite of the high prevalence of *H. pylori* infection in some countries due to many reasons such as genetics, diet and helminthic infections (Kumar *et al.*, 2021)

Treatment of Helicobacter pylori Infection and Intestinal Parasites:

Treatment for *H. pylori* infection depends on either a triple or quadruple treatment according to the patient location and socioeconomic status. Triple therapy is the common treatment for *H. pylori* infections which consists of amoxicillin, clarithromycin, and a proton pump inhibitor (PPI) and this regimen is given to the patient for 14 days. Recent guidelines support also 14 days of quadruple treatment, which contains three antibiotics and a proton pump inhibitor (Chey *et al.*, 2017; Fallone *et al.*, 2016 and Malfertheiner *et al.*, 2017).

Benzimidazoles such as albendazole and mebendazole are the first line for the treatment of nematodes and tapeworm infections. Ivermectin is effective against adult and migrating larval stages of nematodes. Praziquantel is considered the drug of choice for most food-borne trematodes (Al-Wasidi *et al.*, 2021). Metronidazole is the standard treatment for protozoal infections such as *Entamoeba histolytica*, *Giardia lamblia*, blastocysts, and *Balantidium coli*. The drug nitazoxanide is used for the treatment of cryptosporidiosis. Cyclosporiasis and isosporiasis are treated with trimethoprim-sulfamethoxazole (Petri, 2003).

Conclusion:

Co-infection with many intestinal parasites is usually seen in developing countries including Egypt, and human infection by these parasites and *H. pylori* and is also a common phenomenon. Predisposing factors for this co-infection include low socioeconomic and contamination of water supplies. Co-infection of *H. pylori* and protozoa lead to the recruitment of Th1 cells leading to exacerbating the damage to the mucosa of the stomach. On the other hand, during co-infection of *H. pylori* and helminth infection, recruitment of Th2 cells occurs to protect against inflammations within the gastrointestinal tract. So, we should work on improving environmental sanitation, educating people and providing safe water supplies in order to control *H. pylori* and parasites.

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