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Serum Level of IL -6, CRP and PCT among Food Handlers Patient Infected with *Helicobacter Pylori*

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Annotation: The current study aimed at determining the prevalence of Helicobacter pylori in food handlers and the effect of the infection on the choice of serum and hematological parameters. The empirical work was done in the laboratories of Kirkuk Teaching Hospital, and it was conducted during the period between November 7, 2022, and March 28, 2023. The researchers used a sample of 150 food handlers including personnel of restaurants and cafes. The samples were also stratified into two cohorts. The first group was 45 persons who were diagnosed to have been colonized by the above bacterial pathogen, and the second group was a control group of 20 persons as part of the experimental set-up. The highest level of infection was observed in the age group of 20-30 years. Diagnostic tests were conducted using the following bacterial tests: Urea Breath Test (UBT), Stool Antigen Test (SAT), and the Antibody Test in Serum (ATS).

The highest rate of symptoms was found among those infected with H. pylori was associated with loss of appetite (53.3%), followed by dyspepsia (44.45%), stomach pain (31.1%), and gastroesophageal reflux

disease (20%). The least common symptom was gastritis (15.5%). The studied criteria included a set of immunological tests, where the levels of high sensitivity C-reactive protein (HSCP), procalcitonin, and interleukin6 (IL- 6) were measured. This was found to differ statistically significantly (P<0.01) between the level of the serum of both high-sensitivity C-reactive protein (HSCP) and procalcitonin in infected patients compared to the control cohort. Moreover, the results showed a strong rise (P<0.01) in the serum levels of IL 6 in the infected group.

Introduction

Helicobacter pylori is a Gram-negative, microaerophilic, spiral-shaped bacterium with polymorphism and may take the form of coccoid or bacillary. It is the primary cause of duodenal and gastric ulcers. The prevalence of these diseases has increased in recent times because of the proliferation of this kind of bacteria that is a highly pathogenic bacterium that has a prevalence rate of over half of the global population (Liu *et al.*, 2024). The bacteria is contracted by touching infected persons, and by eating and drinking contaminated food and water (Duan *et al.*, 2023). They can enter the stomach wall because of the spiral form of the bacteria and the flagella which shields the stomach lining against mucus. This helps to prevent the immune cells of the body to access them hence disrupting the immune attack and thus allowing them to survive. This causes ulcers of the stomach wall. Such bacteria are also capable of modifying the environment around them and making it less acidic to allow their survival (Gupta *et al.*, 2019).

Those are regulatory proteins secreted by the cells of immune system it participates in the process of inflammatory response, as well as helps to regulate the inflammatory immunity, Infection with H. pylori results in the secretion of a number of cytokines, including IL-1, IL-6, IL-12, and IL-17, which are released by the inflamed mucosa, which causes local inflammation in the stomach, and triggers a humoral immune response. IL-6 is relevant to the acquired immune mechanism because it enhances the formation of antibodies, It differentiates the effector T cells and helps in the differentiation of a large number of immune cells (Atrisco-Morales *et al.*,2022). Proteins of the acute stage are significant and powerful biomarkers of inflammation during H.pylori infection, one of them being C-reactive protein (CRP) and IL-6, whose elevation or reduction is evidence of the disease (Al-Karawi *et al.*, 2023).

- Procalcitonin is a hormone which is stimulated by C cells in the thyroid gland in cases of inflammatory stimulus. It is regarded to be influential in primary diagnosis of H. pylori infection and it serves as a biomarker to distinguish between bacterial and viral infections (Schuetz *et al.*, 2018)

Identification

1- Detection of antibodies in blood serum (Ab test in serum)

Using the *H. pylori* Ab test kit, from Hightop Biotech, made in China

2- Detection of antigens in stool (Ag stool test)

Using the *H. pylori* Ag test kit, from Boreal Biotech, made in China

3- Detection of the urease enzyme (Urea breath test) from Hidway Bio, made in China

Distribution of the study groups

The target population of the present study was 45 males with H. pylori and working as food handlers (restaurants and cafes). Figure (4-3) of the diagnosed utilizing a urea breath test (15 cases), Ag stool test (30 cases), and Ab rapid test (80 cases) of the two cases out of 150 males aged between (20-45 years), and 20 healthy people (control group) not infected by H. pylori indicated the infection rate of (47%), (21%) respectively.

Prevalence of symptoms among those infected with *H. pylori*

The present research paper has established the commonness of the symptoms in patients with H. pylori. The symptoms included loss of appetite (53.3%), indigestion (44.4%), stomach pain (19%), and gastroesophageal reflux disease (GERD) (20.1%). Figure 1-1 shows that chronic gastritis (15.5%) was the least prevalent symptom.

Loss of appetite (53.3% was the most common symptom and chronic gastritis (15.5) was the least common symptom. This could be associated with the development of the disease whereby appetite and indigestion are affected and later on mature into chronic gastritis. This remains in line with a research done by scholars (Kouitcheu Mabeku, Noundjeu Ngamga and Leundji, 2018), who reported that the prevalence of all symptoms was 64.39 percent in all the patients. The research documented chronic gastritis in patients of gastritis. Investigators (Alhadi, 2001) documented the existence of the chronic gastritis symptoms in individuals infected with H.pylori, and the documented rate was 41%. This study has results that are congruent with a study by researcher (Ali *et al.*, 2021), who validated the prevalence of symptoms in patients who had H. pylori infection that leads to symptoms of ulcers, chronic gastritis and indigestion.

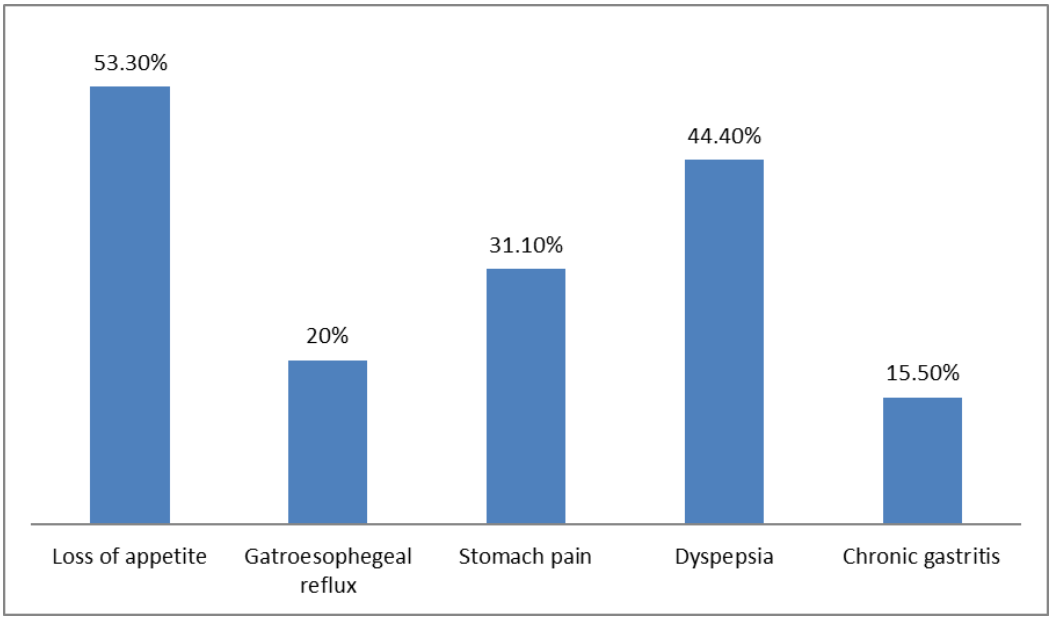

Figure (1-1): Percentage of symptoms among those infected with *H.pylori*

***H. pylori* infection rate by age group**

The study group rate of H. pylori infection (according to the age group) is presented in Figure (1-2). The table results indicate that the age group with the highest infection rate was 20-30 with the

rate of 57.8% and the lowest infection rate was 41-50 with 17.8%. The percentage of the age bracket (31-40) years was 24.4%.

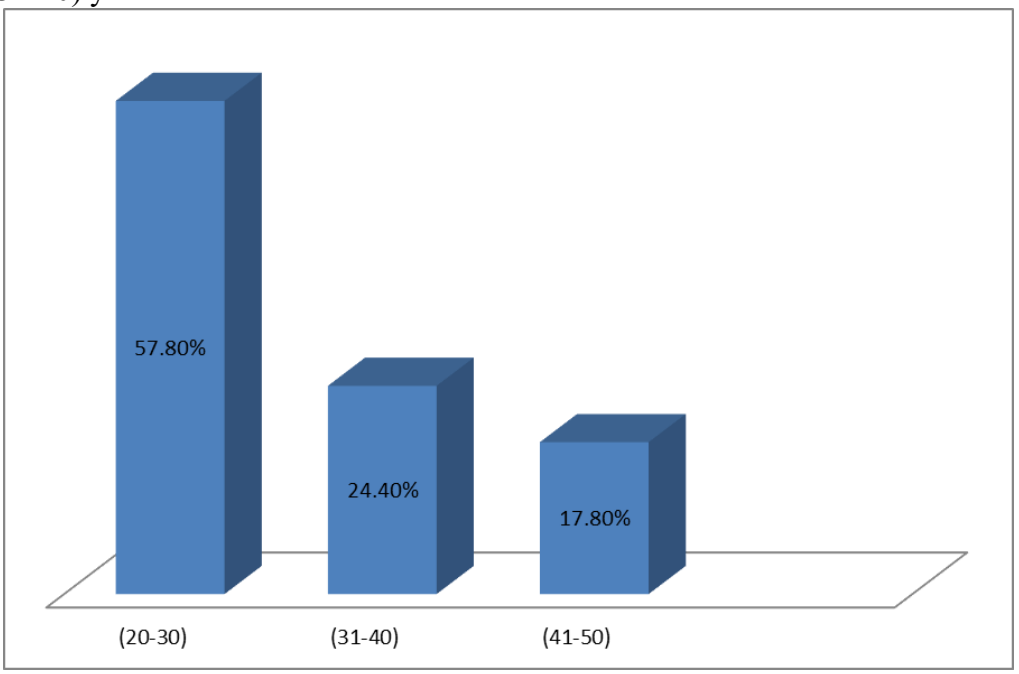

Figure (1-2): Infection rate by age group.

The findings of the present study are in line with those of a research that has been carried out by researchers (Hussein *et al.*, 2022), that indicated that the mean age of H. pylori contracting was more common among the age group less than 33 years. The study by (Ashwaq, 2017) also indicated that the age group (21-30) recorded the highest rate of infection. Age was also discovered as one of the risk factors of an H. pylori infection that is due to smoking, frequenting cafes, eating fast foods, use of non-steroidal anti-inflammatory drugs, alcohol, emotional stress, and hygiene among others, as well as hygiene, which plays a role in the prevention of an H. pylori infection.

Measuring serum levels of high-sensitivity C-reactive protein (hs-CRP) in both study groups.

The current study showed a significant increase (P<0.01) in hs-CRP levels in patients infected with H. pylori (2273±1837 pg/ml) compared to the control group (426±195 pg/ml).

Study groups	HS-CRP (pg/ml)	
	Average± Standard Error	P – value
pateints	2273 ±1837	<0.01
control	426±195	

Table (3-1) serum level of HS-CRP in both study groups

The results of this study are consistent with those of(Temesgen *et al.*, 2022)

(Abbas *et al.*, 2020; Makhlouf *et al.*, 2021), where they reported a large influx of the level of CRP hs- in serum of H. pylori infected patients and a positive correlation between H. pylori infection and serum levels of inflammatory markers, including C- reactive protein and the cytokine IL-6, the inflammatory response in addition to the accumulation of neutrophils, T and B lymphocytes, plasma cells and macrophages (Bagheri *et al.*, 2015; Al-Karawi *et al.*, 2023).

H. pylori is a Gram-negative bacterium and has a lipopolysaccharide component which triggers the expression of numerous pro-inflammatory cytokines like IL-6, IL-1 and TNF- 6. The effects of these cytokines are chronic intestinal damage and systemic diseases. Thus, IL-6 acts of cytokines in stimulating the production of C-reactive protein by the liver which is an inflammatory

indicator, and inflammatory reactions also occur in the vascular endothelium, because infection of the gastric mucosa layers of the stomach by H. pylori bacteria leads to inflammatory reactions, and CRP is an inflammatory indicator (Al-Karawi *et al.*, 2023). Secretion of different virulence factors such as CagA and VaC may be responsible of the inflammatory action of H. pylori as they cause the stimulation of the inflammatory process through activation of nuclear factor kappa-B (NF-kB) which activates the production of the cytokines IL-6 and TNF-a. Although it was stated that the serum level of hs-CRP rises in patients with chronic gastritis, and it is deemed as an indicator of the severity of acute and chronic inflammation and the existence of H. pylori infection, (Jafarzadeh *et al.*, 2009) also verified that an important rise in the level of CRP and the hs-CRP exists with the presence and extent of infection In gastritis caused by H. pylori infection, a study by (Kocazeybek *et al.*, 2003), proved that CRP is an effective mediator of immune cellular activities because of its binding to such protein and presentation to the receptors of phagocytic cells.

Procalcitonin (PCT) Level Measurement

The results of the current study showed an increase in procalcitonin levels in patients infected with *H. pylori* (0.0194±0.0131) compared to the control group (0.0453±0.0165 ng/ml), with a statistically significant difference (P<0.01).

Study groups	PCT(pg/ml)	
	Average±Standard Error	P – value
pateints	0.0453±0.0165	<0.01
control	0.0194±0.0131	

Table (3-2) serum level of procalcitonin in both study groups

The results of this study are consistent with those of (Makhlouf *et al.*, 2021) who discovered that there were significant differences in the amount of PCT in the serum of H. pylori infected persons and the control population in the study. The findings of this paper were also similar to the findings of (Oktay *et al.*, 2015), who verified an increased level of PCT in serum of patients infected with H. pylori that possess the CagA gene positive than H. pylori that lack CagA gene negative. The infection of the Helicobacter pylori causes chronic infection of the gastric epithelial cavity that causes the development of gastritis symptoms (de Korwin, 2008). One of the key peptide hormones that are significant in calcium equilibrium in the body is procalcitonin. It is a 116-amino acid molecule that is produced in the thyroid gland and endocrine cells within the intestine and lung. Its level augments when there is an inflammatory stimulus when its source is bacterial, in which case the product is produced by the lung, intestine, liver, pancreas and kidney. (Schuetz *et al.*, 2018)) denoted that it multiplies its production at least more than 100-1000 times, in the presence of endotoxins in peripheral blood or because of the secretion of cytokines, like IL-6, TNF-alpha and IL-1B, which target the various tissues. It is affected by the production of INF-alpha that suppresses its production due to viral infection and the production of INF-alpha (Mohamed *et al.*, 2020)) indicated that there is a high positive correlation between the severity of H. pylori infection and both CRP and procalcitonin (r: 0.929; p<0.001) and (r=0.928; p<0.001), respectively, and concluded that each of the above variables is considered an effective marker in diagnosis. First infection with *H.pylori*

Measuring serum levels of interleukin-6 (IL-6)

The results of the current study showed an increase in the serum level of the interleukin-6 (IL-6) in patients infected with H. pylori (13.37±4.02 pg/ml) compared to the control group (2.82±1.58 pg/ml), with a statistically significant difference (P<0.01).

The findings of the present research upheld the upsurge of the amount of cytokine IL-6 in the serum of the H. pylori infected patients. The current research findings were in line with the findings of the previous research (Haghazali et al., 2011; (Yu *et al.*, 2023). which validated the rise in the amount of cytokines IL-6 in the serum of individuals infected with H. pylori as compared to the control group.

The rise in the concentration of cytokines IL-6 in individuals who are infected with H. pylori is

attributed to the immunological reaction of the gastric mucosa to the H. pylori bacteria. This is different among patients and is determined by the stage of infection. During the chronic and acute phases, secretion of cytokines is elevated as it is anticipated that in this condition, the immune cells are highly infiltrated into the area of infection caused by H. pylori (Rasool *et al*, 2022). which increases the severity of inflammation due to the secretion of proinflammatory cytokines in the cells of the infected stomach lining ((Jafarzadeh *et al*, 2019)

(Yu *et al.*, 2023) reported that the infection of Helicobacter pylori and gastric cancer is correlated with the improved levels of the cytokine IL-6, which was demonstrated to rise in the region related to the appearance of the infection because of the elevated level of inflammatory cytokines released by immune cells at the site of infection. H.pylori infection leads to gastritis, peptic ulcers and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. (Milic *et al.*, 2019) demonstrated that the level of the proinflammatory cytokine IL-6 in the serum of patients with H.pylori infection was extremely high, in contrast to healthy people (the control group). The reason is in the fact that the H. pylori mucosa infection triggers a cascade of events culminating in an inflammatory response involving the release of proinflammatory cytokines and Maastricht-Ansterdam-Londen-Tiel cells activation.

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