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Correlation between CD14 and CD163 in duodenal ulcer and gastric cancer patients infected with *Helicobacter Pylori*

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Abstract---Most people around the world are infected with *Helicobacter pylori* (*H.pylori*); it can lead to duodenal ulcer (DU) and gastric cancer (GC). The main objective of this study is to determine the correlation between CD14 and CD163 in individuals with DU and GC infected with *H.pylori*. Sixty nine individuals were included in this work; 27 patients infected with *H.pylori* only (*H.Pylori*+), 22 patients infected with *H.pylori* with DU and 20 patients infected with *H.pylori* with GC. CD14 and CD163 were measured in all individuals' serum using the Enzyme-Linked Immunoassay (ELISA) test. The results proved there was negative correlation between CD14 and CD163 in *H.pylori*-positive patients ($y = -0.0263x + 1.4179$). While, there was positive correlation in *H.pylori*-positive patients with DU ($y = 0.0932x + 1.6647$) and with GC ($y = 0.0607x + 1.9824$). In conclusion: CD14 and CD163 have a synergistic protected effect in *H.pylori*-positive patients with DU and GC.

Keywords---Correlation, CD14, CD163, *Helicobacter pylori*, duodenal ulcer, gastric cancer.

Introduction

Infection with *H. pylori* causes many post-infection complications such as duodenal ulcers, peptic ulcers, and stomach cancer because it is a spiral, motile, gram-negative bacteria that are resistant to stomach acid. *H. pylori* is found in about half of the world's population, mainly in developing countries (Hou et al., 2019; Alhasnawi and Aljanaby, 2022a). When *H. pylori* invade the host, it causes chronic inflammatory reactions in the mucosal lining of the stomach, resulting in

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chronic indigestion, gastritis, and anemia (Lehours and Robinson, 2020). Several kinds of immune markers, such as IL-10, IL-2, CD14+, and CD163+, play a pivotal role against this pathogen, originating primarily from macrophages and monocytes (Zhu et al., 2020). CD14+ is an essential innate immune factor produced mainly by macrophages and monocytes. When macrophages switch to alternate suppressed and activated phenotypes in inflammation, one of the primary changes is an increase in CD163 (a macrophage-specific protein) (Youssefi et al., 2021). Macrophages expressing high levels of CD163 are associated with inflammatory tissues (Etzerodt et al., 2013). Globally, more than 8.2% of cancer deaths are attributable to gastric malignancies in less developed countries (Raza et al., 2020). In underdeveloped countries, 70% to 90% of people have *H.pylori* by age, while infection rates range from 25 to 50% in wealthy countries (Ansari et al., 2020). The main objective of this study is to determine the correlation between CD14 and CD163 in individuals with DU and GC infected with *H.pylori*.

Methods

Study design and patients

This study was carried out in AL-Sader Medical City, microbiology department, in AL-Najaf Governorate, Iraq. Twenty seven *H. Pylori*-positive patients, 22 duodenal ulcer patients, 20 gastric cancer patients were included in this work.

Diagnosis of *H.Pylori*-positive patents

Stool antigen tests have been used in the diagnosis of *H. Pylori*-positive patients with 94% sensitivity and 97% specificity with a 100% positive detection rate at 1 ng/mL of pylori antigen in stool specimens (Pichon et al., 2020; Alhasnawi Aljanaby, 2022b). The test was done according to the kit provided by the manufacturing company (CTK Biotech, Inc. China).

ELISA

Five ml of blood were collected from each individual and centrifuged at 7,000 rounds per minute for 15 min. Two mL of serum have been obtained to measure the concentration of human CD16 (Cat. No E0283Hu) and human CD163 (Cat. No E0246Hu) by an ELISA test (Aljanaby et al., 2022a; Alhasnawi and Aljanaby, 2022a) according to the kits provided by the manufacturing company (BT LAB, CO. China).

Statically analysis

The correlation between CD14 and CD163 has been made by Graphpad-prism V.10 computer software. The mean standard error value of CD14 and CD163 has been measured using the T-test, unpaired, one-tailed, and significant digits at 0.05. P-values less than 0.05 were considered statistically significant (Alhasnawi and Aljanaby, 2022b; Aljanaby et al., 2022a; Aljanaby et al., 2022b).

Ethics approval

We confirmed that we obtained all ethics approvals from all individuals in this work, which includes blood and stool sample collection and all tests related to patients infected with *H.pylori* (Hasan et al., 2021).

Results

The results of the current study proved that there was negative correlation between CD14 and CD163 in *H.pylori*-positive patients (P-value < 0.0001, $y = -0.0263x + 1.4179$) (Figure 1). While, there was positive correlation between CD14 and CD163 in *H.pylori*-positive patients with duodenal ulcer (P-value 0.0631, $y = 0.0932x + 1.6647$) (Figure 2) and positive correlation between CD14 and CD163 in patients of *H.pylori* positive with gastric cancer (P-value 0.1421, $y = 0.0607x + 1.9824$) (Figure 3).

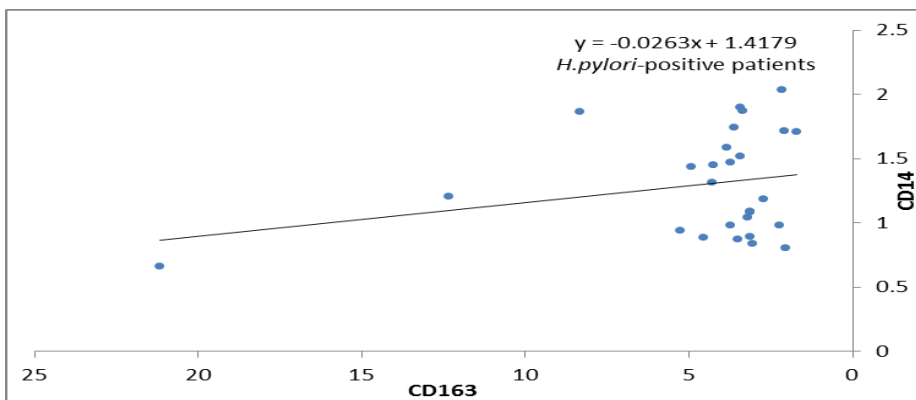


Figure 1. Correlation between CD14 and CD163 in patients infected with *H.pylori*.

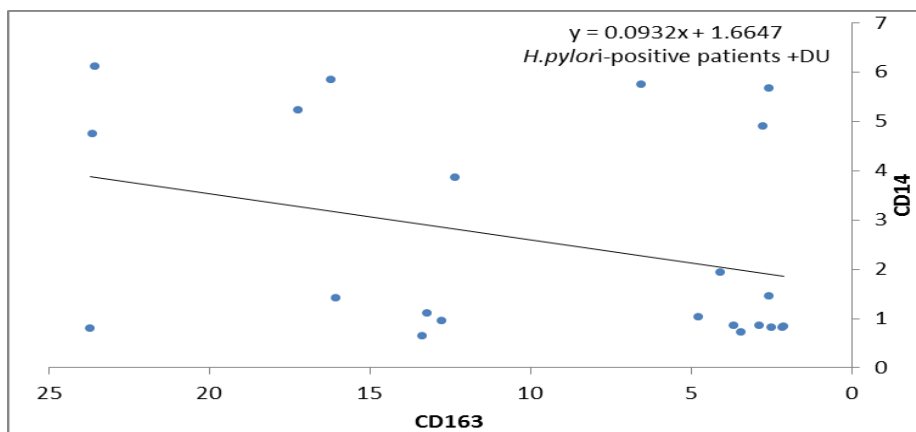


Figure 2. Correlation between CD14 and CD163 in patients infected with *H.pylori* and duodenal ulcer

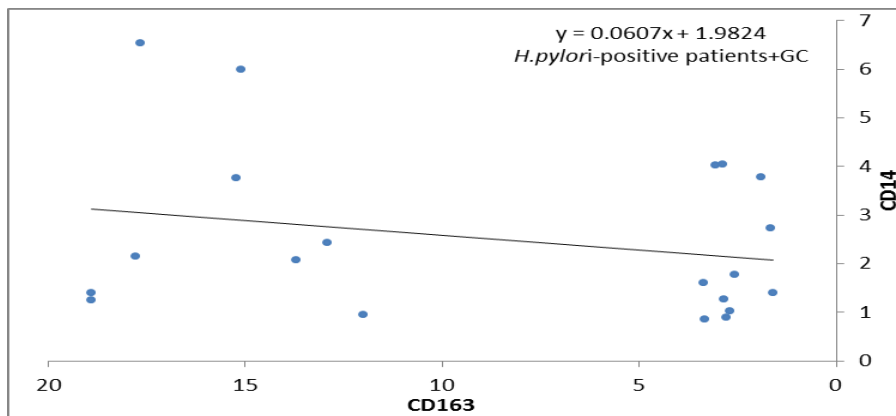


Figure 3. Correlation between CD14 and CD163 in patients infected with *H.pylori* and gastric cancer

Discussion

Changing acid levels in the stomach causes the infection to change, so when Marshall inhibited acid in his stomach before swallowing HP, the illness disappeared after two weeks when acid secretion had returned to normal (Hobsley et al., 2008). The results of the current study proved that there was negative correlation between CD14 and CD163 in patients infected with *H.pylori* (Figure 1). While, there was positive correlation in patients infected with *H.pylori* and duodenal ulcer (Figure 2) and in patients infected with *H.pylori* and gastric cancer (Figure 3). A TH-1 immune response is triggered by *H.pylori* in the host, as can the production of pro-inflammatory cytokines by M1-like monocytes during TH-1 immunity (Zhang et al., 2018). IL-6, IL-8, tumour necrosis factor, IL-1, and IL-12 are among the cytokines released by gastric epithelial cells in response to the *H.pylori* infection (Chonwerawong and Ferrero, 2017). The cytokines that cause reactive oxygen species and nitrogen species are of particular interest to neutrophils, B and T lymphocytes, natural killer cells, natural killer T cells, macrophages, mast cells, and dendritic cells (Zhang et al., 2016). Inflammation and elevated reactive oxygen species are both caused by dysregulation of autophagy, a mechanism for getting rid of damaged cells, linked to host gene polymorphisms, which are associated with an increased risk of disease (Eslami et al., 2019). A great example of the complex relationship between human cells, microbes, and their environment is *H.pylori*'s colonization of the human stomach, and its role in the development of gastric cancer. This is also a significant medical issue owing to the widespread incidence and lethality of gastric cancer around the world (Sugano, 2019). In gastric cancer, it seems that bacterial genotypes interact in a more detailed fashion. On the bacterial side, the *cag* pathogenicity island is a well-characterized and well-studied virulence factor of *H.pylori*; strains containing the *cag* pathogenicity island have been found to be linked to a higher risk of distal gastric cancer than those lacking it (Waskito et al., 2018). Genetic studies have shown that polymorphisms in genes encoding inflammatory cytokines in patients infected with *H.pylori* CagA strain dramatically increase the risk of gastric cancer (Amieva and El-Omar, 2008).

Conclusions

CD14 and CD163 can be considered potential biomarkers for *H. pylori* infection and as immune therapy for patients infected with *H. pylori*.

A conflict of interest

A conflict of interest does not exist in this work

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