Study Of Some Immunological Parameters With Helicobacter Pylori Infected Patients

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Abstract

Helicobacter pylori is a spiral-shaped bacterium classified as gram-negative. Its primary mode of transmission is through oral-oral and fecal-oral routes. This bacterium induces mucosal damage and inflammation, potentially progressing from acute to chronic inflammation, ultimately increasing the risk of gastric cancer.

A study involving 35 patients (14 men and 21 women) utilized the Fecal Antigen Test and Serological Test to analyze peripheral blood leukocyte count and differential. Among the findings, it was observed that the total leukocyte count and neutrophil count were significantly higher in H. pylori-positive patients (N = 24) compared to those negative for H. pylori (N = 11). Interestingly, while there was a significant difference in the total leukocyte count between H. pylori-positive and negative females, this difference was not significant in males. However, there was a notable increase in neutrophil count in both males and females with H. pylori infection, suggesting the potential utility of neutrophil count as an indicator for prognosis and diagnosis of H. pylori infection.

Conversely, there was no significant correlation observed between eosinophils, lymphocytes, and other immune cells

with bacterial infection, indicating minimal variation among immune cell populations in response to H. pylori infection.

Keywords: Helicobacter pylori - Immunological parameters – Antibodies - Immune cells - Gastric cancer - Immune profiling - Clinical outcomes

Introduction

Helicobacter pylori stand as one of the most prevalent bacterial pathogens affecting humans globally [5]. Shockingly, over a third of a million deaths worldwide each year may be attributed to this potentially lethal microorganism. H. pylori, a gram-negative, microaerophilic bacterium, has adeptly infected approximately half of the world's population over centuries. Often, individuals acquire this infection during childhood, and if left untreated, it persists throughout life. [10]

This pathogen is notorious for instigating various gastric disorders and has also been linked to extra-gastric conditions such as anemia, dyspepsia, and certain immunological disorders [1-2]. Nearly all infected individuals develop chronic gastritis, with a significant portion progressing to ulcer disease or gastric cancer. [3]

Figure 1. Helicobacter pylori.

H. pylori is a gram-negative bacterium characterized by its helical rod shape. It possesses prominent flagella, which aid in its penetration of the thick mucus layer lining the stomach. [7]

Study Terms

Helicobacter pylori

Helicobacter pylori is a type of bacteria that infects the stomach lining, particularly the mucus layer that protects the stomach from the acidic digestive juices. [4] It's one of the most common bacterial infections worldwide, affecting about half of the world's population. [31]

Here are some key points about Helicobacter pylori: [20]

- Transmission: The exact route of transmission is still not entirely clear, but it's believed to spread through oral-oral or fecal-oral routes. It often infects individuals during childhood and can persist for many years if left untreated. [6]
- Pathogenesis: H. pylori infection can lead to various gastrointestinal diseases, including gastritis (inflammation of the stomach lining), peptic ulcers (sores in the stomach lining or the upper part of the small intestine), and even stomach cancer. However, many infected individuals may remain asymptomatic. [8]
- Diagnosis: Several methods are used to diagnose H. pylori infection, including breath tests, blood tests to detect antibodies against the bacteria, stool tests, and endoscopy with biopsy to directly visualize the bacteria in the stomach lining. [11]
- Treatment: Antibiotics are the primary treatment for H. pylori infection, usually combined with proton pump inhibitors (PPIs) or bismuth salts to help eradicate the bacteria and heal any associated ulcers. However, antibiotic resistance is a growing concern and can make treatment more challenging. [9]
- Prevention: Preventive measures for H. pylori infection include practicing good hygiene, avoiding contaminated food and water, and possibly vaccination (though no widely available vaccine exists yet). [32]

H. pylori infection is a significant public health issue due to its association with various gastrointestinal diseases, and ongoing research aims to better understand its pathogenesis, improve diagnostic methods, and develop more effective treatments. [36]

Aim of study

The aim of this study is to elucidate the correlation and conduct statistical analysis among various immune cells in patients infected with H. pylori. [23]

Objectives of study

The objectives of the Study may include: [9]

- Investigating the immune response of individuals infected with Helicobacter pylori: This involves understanding how the immune system reacts to the presence of the bacteria, including the production of antibodies and activation of immune cells. [12]
- Identifying specific immunological markers associated with Helicobacter pylori infection: The research aims to pinpoint particular markers within the immune system that are indicative of H. pylori infection, which could aid in diagnosis or monitoring of the infection. [15]
- Assessing the impact of Helicobacter pylori on immune function: This objective involves examining how H. pylori infection influences overall immune function, including any potential alterations in immune cell activity or cytokine production. [25]
- Exploring potential correlations between immunological parameters and clinical outcomes: The research may seek to establish links between specific immune responses and the severity of H. pylori-associated diseases or symptoms, such as gastritis, peptic ulcers, or gastric cancer. [30]
- Providing insights for the development of immunotherapeutic strategies: By elucidating the immunological aspects of H. pylori infection, the research aims to contribute to the development of novel immunotherapeutic approaches for managing or treating H. pylori-related conditions. [13]

Epidemiology & Transmission

Infection with H. pylori is widespread globally, yet its prevalence varies significantly among countries and within different population groups within the same country. The overall prevalence of H. pylori infection is strongly linked to socioeconomic conditions. [35] In many developing countries, the prevalence among middle-aged adults exceeds 80 percent, while in

industrialized countries, it ranges from 20 to 50 percent. [33] The primary mode of transmission is through oral ingestion of the bacterium, mainly occurring within families during early childhood. In industrialized nations, direct person-to-person transmission via vomitus, saliva, or feces is likely predominant, with potential additional transmission routes such as water being more significant in developing countries. [34] Although H. pylori is present in some nonhuman primates and occasionally in other animals, there is currently no evidence of zoonotic transmission. In adults, H. pylori infection tends to be chronic and requires specific therapy for resolution, whereas spontaneous clearance of the bacterium in childhood is relatively common, possibly aided by the use of antibiotics for unrelated reasons. The prevalence of H. pylori infection in a community is influenced by three main factors: the rate of acquiring the infection (incidence), the rate of losing the infection, and the prolonged persistence of the bacterium in the gastroduodenal mucosa between infection and eradication. [29]

Pathogenicity

Each day, humans ingest numerous microorganisms, yet most fail to colonize the stomach successfully. One of the stomach's primary antibacterial defenses is its acidic pH. In fasting conditions, the gastric luminal pH in humans is <2, preventing bacterial proliferation within the gastric lumen. [21] A pH gradient exists within the gastric mucus layer covering the gastric epithelial cells, ranging from approximately 2 at the luminal surface to between 5 and 6 at the epithelial cell surface. [19] Upon entering the stomach, H. pylori breaches the gastric mucus layer and encounters a less acidic environment than that of the gastric lumen. Typically, H. pylori does not breach the epithelial barrier and is considered a noninvasive bacterium. Within the gastric mucus layer, most H. pylori organisms are free-living, but some attach to the apical surface of gastric epithelial cells and may occasionally be internalized by these cells. [14]

Chronic Helicobacter pylori infection prompts a gastroduodenal response characterized by the infiltration of plasma cells, lymphocytes, neutrophils, and monocytes into the mucosa. Eradication studies have revealed that this inflammatory response is a specific reaction to H. pylori. [16] H. pylori infection induces not only specific local T and B cell responses and a systemic antibody response but also a local pro-inflammatory cytokine

response. Interleukin-8 (IL-8), expressed and secreted by gastric epithelial cells, may be a significant host mediator, inducing neutrophil migration and activation. IL-8 mRNA and protein secretion in gastric epithelial cell lines can be upregulated by cytokines such as tumor necrosis factor-alpha and IL-1, as well as by type I strains of H. pylori expressing the vacuolating toxin and cytotoxin-associated protein, CagA. Hence, the gastric epithelium actively participates in mucosal defense. Bacterial factors directly and indirectly via host-derived cytokines, products of complement activation, and bioactive lipids induce neutrophil activation and the production of reactive oxygen metabolites. Strain variation in the induction of IL-8 from epithelial cells and the oxidative burst in neutrophils may influence the extent of mucosal injury. [18]

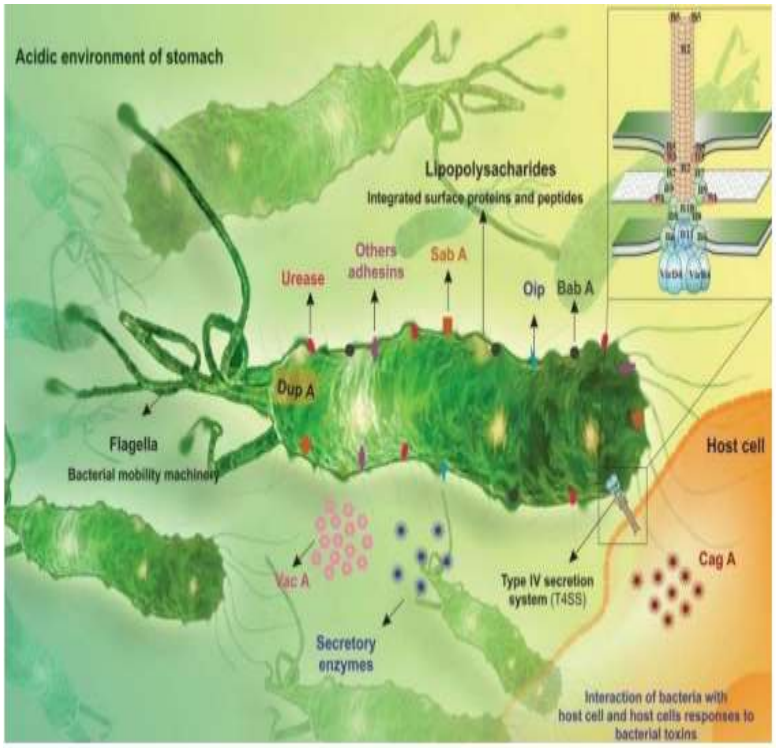

Fig. 2 Helicobacter pylori structure and its infection mechanism

Several bacterial components, including toxins and enzymes, play crucial roles in the interaction between bacteria and host cells, aiding evasion from immune system surveillance. Flagella provide motility, allowing bacteria to grow beneath the mucosal membrane. [17] Lipopolysaccharides (LPS) and membrane proteins adhere to host cell receptors. The urease enzyme combats the acidic stomach environment by generating ammonia.

The VacA exotoxin damages the mucosal membrane. The Type IV secretion system (T4SS) utilizes a pilus to inject effectors into host cells. CagA induces actin remodeling and inhibits apoptosis. Outer proteins such as BabA, Oip, SabA, and others function as adhesins, adhering to host cells. [22]

Complication of H. pylori

H. pylori without treatment for a long time can cause the following: [24]

- gastritis
- gastric ulcers
- duodenal ulcer
- Gastric cancer
- Mucosa associated lymphoid tissue (MALT) lymphoma.

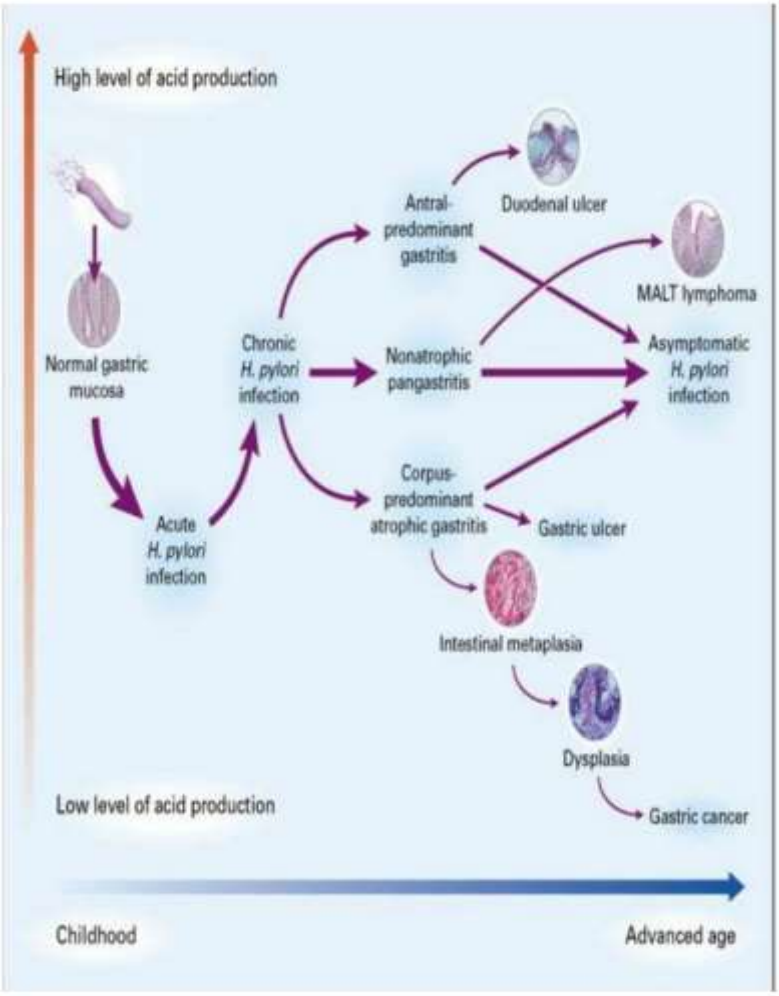

Fig 3: complication of H. pylori

Tests used for examination of H. pylori

Since the identification of Helicobacter pylori (H. pylori) in 1983, numerous methods for detecting the presence of the bacterium have been developed, each with its own advantages and disadvantages. Clinicians often prefer noninvasive tests such as serology, the 13C urea breath test (UBT), and stool antigen tests. [29]

1. Serological Test

Immune responses against H. pylori are harnessed for infection detection by analyzing patients' blood or serum for IgG and IgA antibodies. Serology stands out as the only test unaffected by local stomach changes, which could otherwise lead to low bacterial loads and false negative results. [12] These non-invasive tests are both easy and cost-effective. Serology holds promise for developing rapid diagnostic tests, particularly beneficial for populations in areas with limited access to medical facilities. [28] With automated approaches, large cohorts can be swiftly tested, facilitating population-based studies with improved sensitivity and specificity. Moreover, the decline in antibody responses can serve as a clinical indicator to confirm treatment success, as evidenced by various studies. [30]

2. Fecal Antigen Test

Fecal antigen tests detect antigens in stool samples, and current guidelines consider them equivalent to the urea breath test (UBT) when a validated laboratory-based monoclonal antibody is utilized. However, the sensitivity and specificity of these tests can vary widely, ranging from 48.9% to 92.2% and 88.9% to 94.4%, respectively, depending on the test format. While they are fast and easy to use, fecal antigen tests may provide less reliable results compared to other methods. [22] Nevertheless, available stool antigen tests have demonstrated the ability to distinguish between infected and treated patients, facilitating treatment confirmation. [8] Challenges such as antigen degradation in the intestine and subsequent loss of epitopes may lead to false negative results. Additionally, sample handling procedures can be cumbersome for patients. False negative results may also occur when the bacterial load is low, possibly due to proton-pump inhibitors, recent antibiotic use, or bismuth administration. [5]

3. Urea Breath Test

The urea breath test relies on the presence of the urease enzyme in live H. pylori bacteria, which metabolizes urea into ammonia and carbon dioxide. [7] Following ingestion of urea labeled with either 13C or 14C, breath samples are collected for up to 30 minutes by exhaling into a carbon dioxide-trapping agent. [16] This test is typically conducted by the clinician or the clinician's assistant and has been widely employed for diagnosing H. pylori infection. [19]

4. Rapid urease Test

The Rapid Urease Test (RUT) is a commonly used invasive diagnostic method for detecting H. pylori infection. [10] It is known for its speed, affordability, and simplicity. The test works by detecting the presence of urease enzyme in or on the gastric mucosa. [20] Optimal results are achieved when biopsies are taken from both the antrum and corpus of the stomach. Additionally, the biopsy samples used for RUT can also be utilized for other tests, such as molecular-based assessments of microbial susceptibility. [17]

5. PCR

Tests used for the detection of pathogenic genes and antibiotic resistance offer high sensitivity and specificity. However, their effectiveness is influenced by factors such as the local availability of equipment and technical expertise. [33] While these tests can provide valuable information, they are often time-consuming and carry a risk of contamination. [36]

6. Histology

The initial method for detecting H. pylori infection was the histological examination, which remains the gold standard for infection detection. [35] Various factors such as the location, size, and quantity of samples, staining procedures, and the use of proton pump inhibitors (PPIs) or antibiotics can influence the diagnostic accuracy of histology. [24]

7. culture

A culture test involves placing a tissue sample in a specialized dish or tube containing nutrients similar to those found in the organism's natural environment. If H. pylori bacteria are present in

the sample, they will grow until they are visible under a microscope or in a liquid solution. While culture testing is less sensitive, it is highly specific (with a specificity of 100%) for diagnosing H. pylori infections. Other advantages of this method include providing evidence of active infection, which is recommended whenever possible in cases of therapy failure. [18]

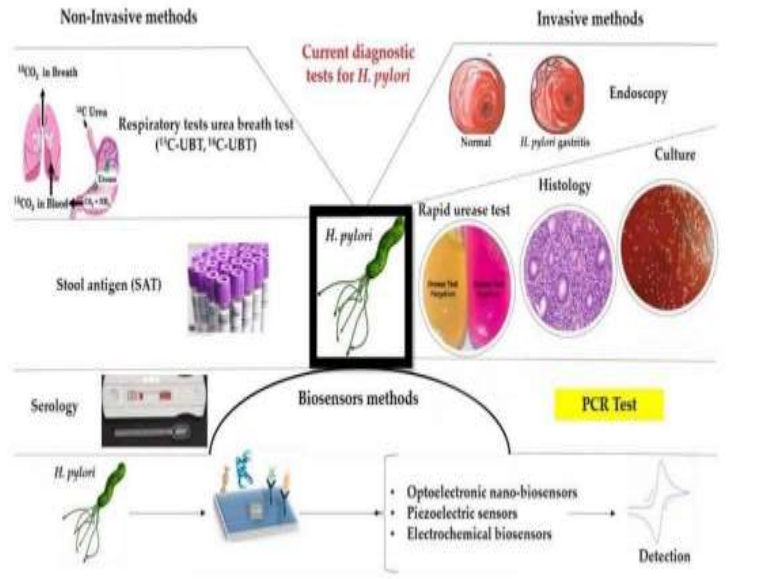

Fig 4 tests and detection H. pylori

Materials and Methods

In this case-controlled study conducted from December 2023 to March 2024 at King Saud Hospital, Kingdom of Saudi Arabia, thirty-five patients diagnosed with peptic ulcer (PU) disease were included. Inclusion criteria for subjects comprised symptoms indicative of peptic disease such as burning abdominal pain, chronic vomiting, or hematemesis. [15] The H. pylori status of PU patients was determined using fecal antigen tests and serological assessments of anti-H. pylori IgG antibodies. Positive results for both fecal antigen tests and anti-H. pylori IgG serology confirmed H. pylori infection in the PU patients. [29] The control group comprised 11 asymptomatic individuals with negative serology for anti-H. pylori IgG and no history of gastrointestinal disease. Exclusion criteria included a history of pulmonary disease, cardiovascular disease, diabetes mellitus, hypertension, renal failure, anemia, asthma, or neoplasia. Subjects in the non-infected groups were healthy individuals who had not undergone

endoscopy. Serum samples were collected from all subjects for analysis. [1]

H. pylori antibody Rapid Test

The H. pylori Rapid Test Device (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay designed for qualitatively detecting antibodies to H. pylori in whole blood, serum, or plasma. It is intended to aid in the diagnosis of H. pylori infection in adults aged 18 years and older. [3]

Principle

The H. pylori Rapid Test Device (Whole Blood/Serum/Plasma) is a qualitative membrane-based immunoassay designed for detecting H. pylori antibodies in whole blood, serum, or plasma samples. [2] In this test, anti-human IgG is immobilized in the test line region. When the specimen is added to the specimen well, it reacts with H. pylori antigen-coated particles present in the test. This mixture then migrates chromatographically along the test length and interacts with the immobilized anti-human IgG. If the specimen contains H. pylori antibodies, a colored line will appear in the test line region, indicating a positive result. Conversely, if the specimen lacks H. pylori antibodies, no colored line will appear in this region, indicating a negative result. Additionally, a colored line will always appear in the control line region, serving as a procedural control to confirm that the proper volume of specimen has been added and membrane wicking has occurred. [4]

Test Procedure

1. Remove the cassette from the sealed pouch. Add 1 drop (25 µl) of serum/plasma/whole blood vertically into the sample hole. [9]
2. Add about 2 drops (80 µl-100 µl) of sample buffer into the sample hole.
3. Read the result within 10-20 minutes. Results are considered invalid if read after 20 minutes.

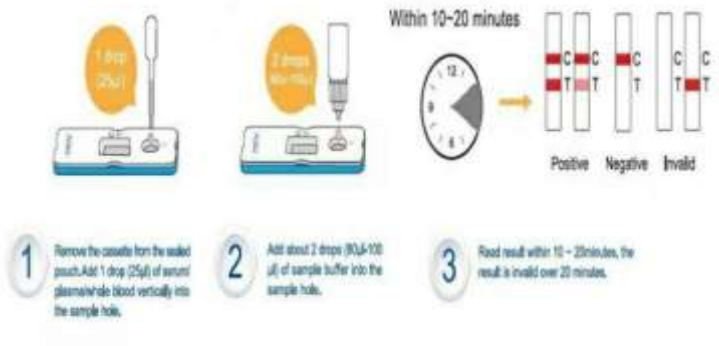

Fig 5: H. pylori antibody Rapid Test procedure

H. pylori Antigen Rapid Test

The cassette is a rapid chromatographic immunoassay designed for the qualitative detection of H. pylori antigens in human feces specimens. Its purpose is to aid in the diagnosis of H. pylori infection. [7]

Principle

The H. pylori Antigen Rapid Test Cassette is a qualitative lateral flow immunoassay designed for detecting H. pylori antigens in human fecal specimens. In this test, the membrane is pre-coated with anti-H. pylori antibodies in the test line region. During testing, the specimen reacts with particles coated with anti-H. pylori antibodies. [20] This mixture migrates upward on the membrane via capillary action to react with anti-H. pylori antibodies on the membrane, producing a colored line. The presence of this colored line in the test region indicates a positive result, while its absence indicates a negative result. [14] Additionally, a colored line will always appear in the control line region to serve as a procedural control, confirming that the proper volume of specimen has been added and membrane wicking has occurred. The storage conditions for the test cassette are between +2°C to +30°C. [34]

Test Procedure

1. Collect the feces sample.
2. Transfer 50 mg of feces into the dilution buffer and mix well.
3. Leave the tube alone for 2 minutes.
4. Unscrew the tip.
5. Place 2 drops of the specimen onto the cassette.

6. Read the result within 10 minutes. Results are considered invalid if read after 20 minutes.

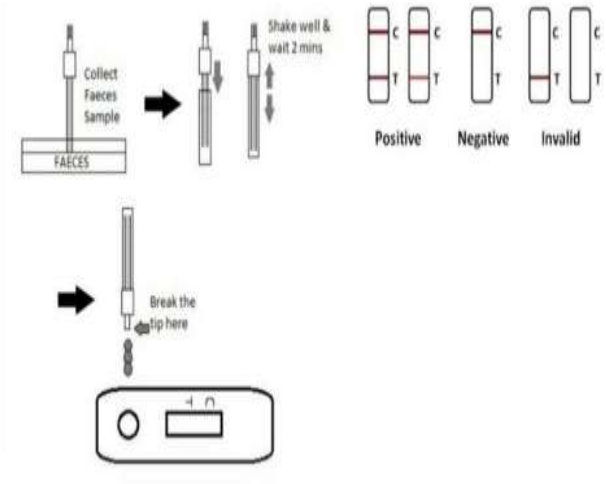

Fig. 6: Procedure of H. pylori Antigen Rapid Test

Complete blood count

A CBC (complete blood count) measures the quantities of red blood cells, white blood cells, and platelets in a blood sample. It provides measurements that represent both the actual number of cells and the percentage or concentration of each cell type compared to the total blood volume. [16]

The principle of CBC analyzers initially relied on Coulter's Principle, which involves passing the blood through a small aperture and measuring changes in electrical impedance to count cells. However, modern CBC analyzers have advanced to incorporate various techniques such as flow cytometry and spectrophotometry. [11] These techniques allow for more accurate and comprehensive analysis of blood cell populations, enabling healthcare professionals to diagnose and monitor a wide range of conditions. [19]

The Procedure of CBC Test

Here are the steps for collecting and analyzing a blood sample using a hematology analyzer: [20]

1. Collect approximately 2 ml of the blood sample in a lavender top tube (EDTA vial).

2. Gently shake the tube to ensure thorough mixing of the blood with the EDTA anticoagulant to prevent clotting.
3. Turn "ON" the rotor.
4. Place the vial on the rotor to mix the blood sample with the anticoagulant.
5. Turn "ON" the hematology analyzer.
6. Click on "New Sample" on the analyzer interface.
7. Click on "ID 1" and enter the unique ID of the sample, then click "OK."
8. Click on "ID 2" and enter the name of the patient, then click "OK."
9. Introduce the blood sample to the hematology analyzer (CBC machine).
10. Wait for 1-2 minutes for the analyzer to process the sample and display the results on the screen.
11. Print the results and turn off the machine.

Following these steps ensures proper sample collection, analysis, and recording of results using the hematology analyzer.

Results and Discussion

It seems like you're describing the findings of a study investigating the relationship between H. pylori infection, gastric mucosal inflammation, and peripheral blood leukocyte count. [13] The study involved 35 patients, consisting of 14 men and 21 women, who underwent Fecal Antigen Test and Serological Test to determine H. pylori infection status. The severity of inflammation in both the antral and body mucosa was assessed. [23]

The study found that patients positive for H. pylori infection (N = 24) exhibited a significant increase in both total leukocyte count and neutrophil count compared to those negative for H. pylori (N = 11). Additionally, there was a correlation between the total leukocyte count and the numbers of neutrophils in the gastric mucosa. [33]

These findings suggest that mucosal inflammation resulting from H. pylori infection is reflected in the peripheral blood leukocyte count. [25] The figure below likely illustrates this relationship in detail, providing insights into the mechanisms underlying the systemic effects of H. pylori infection and gastric mucosal inflammation. [7]

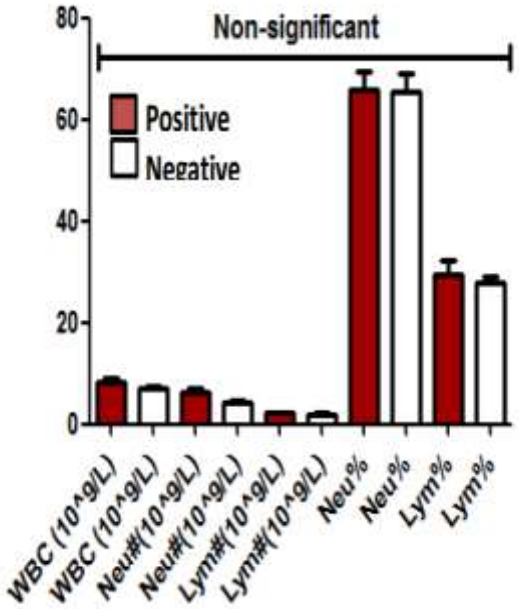

Fig. 7: Relationship between WBC, neutrophil, lymphocyte in meal and female with H. pylori infected patient

As shown in the (figure7) that summarized the amount and percentages of different immune cells like WBC, neutrophils, and lymphocytes, comparing positive and negative individuals for H. pylori infection. The results indicated non-significant differences in these immune cell counts between the two groups. [1]

However, it's noted that the small sample size may have limited the ability to detect any significant effects of H. pylori on immune cells, as measured by automated complete blood count (CBC). [8] It's also mentioned that other studies have reported different findings, suggesting that further research may be needed to fully understand the impact of H. pylori infection on immune cell populations. [24]

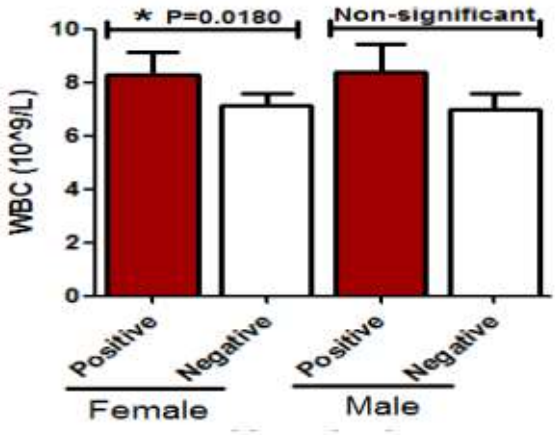

Fig. 8: Relationship between WBC in meal and female with H. pylori infected patient

The comparison of H. pylori infection between control and infected individuals, stratified by gender, revealed a significant difference in white blood cell (WBC) counts among females, regardless of infection status, whereas in males, no significant difference was observed. [8]

Recent studies suggest that women possess a more robust immune system against infections compared to men, attributed to genetic structural disparities. Specifically, this genetic divergence involves microRNAs located on the X chromosome in females. MicroRNAs (miRNAs) play a pivotal role in immune function, encompassing both innate and adaptive immune responses, as well as the development and differentiation of immune cells in response to pathogens, thereby mitigating the risk of autoimmunity. Consequently, these microRNAs confer women with a distinct advantage in immunity over men. [18]

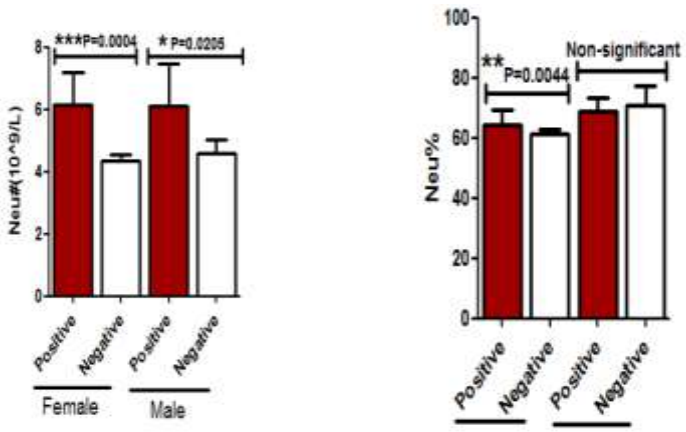

Fig. 9: Relationship betwen neutrophil in mel and femal with H. pylori infected patient

When each type of immune cell was examined as an indicator of H. pylori infection among both healthy and infected patients, the figure above demonstrates a significant increase in neutrophil count among females, regardless of infection status. This suggests that neutrophil count could serve as a reliable indicator for prognosis and diagnosis of H. pylori infection. Similar trends were observed among males, with significant variations in neutrophil count between positive and negative H. pylori infections, yielding a p-value of 0.02. [16]

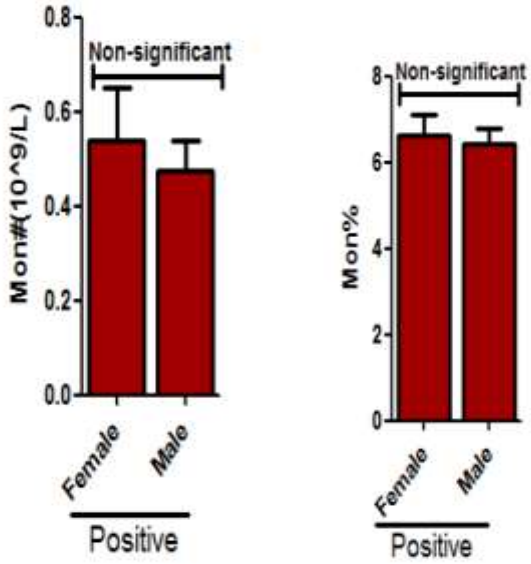

Fig 10: mon#, mon% in H. pylori infected patient

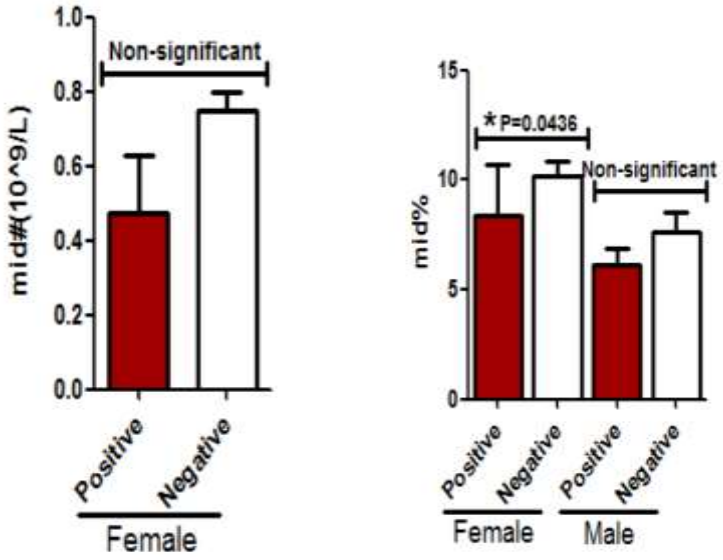

Fig 11: mid#, mid% in H. pylori infected patient

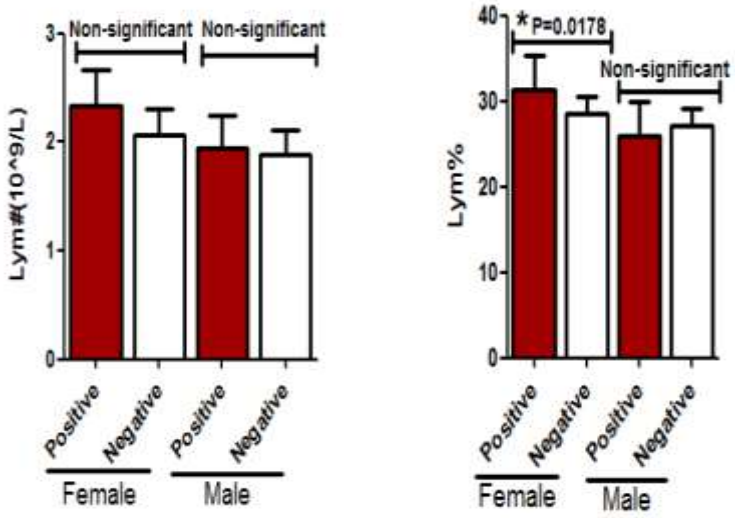

Fig 12: lym#, lym% in H. pylori infected patient

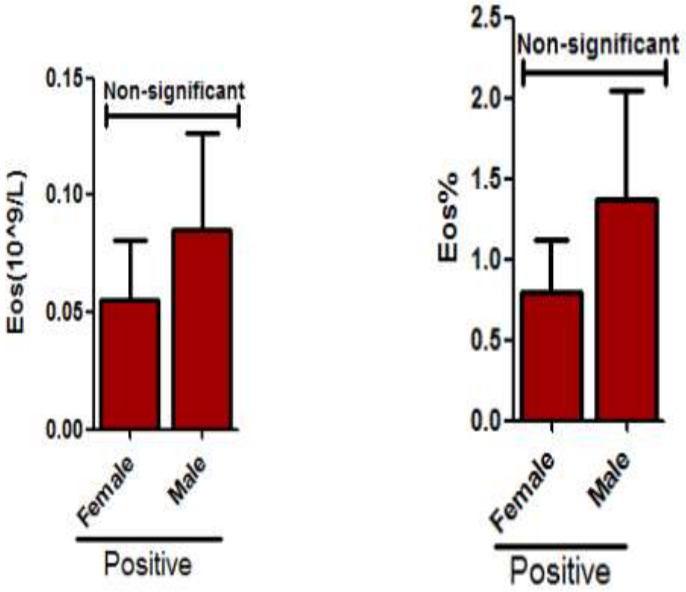

Fig 13:Eso#, Eso% in H. pylori infected patient

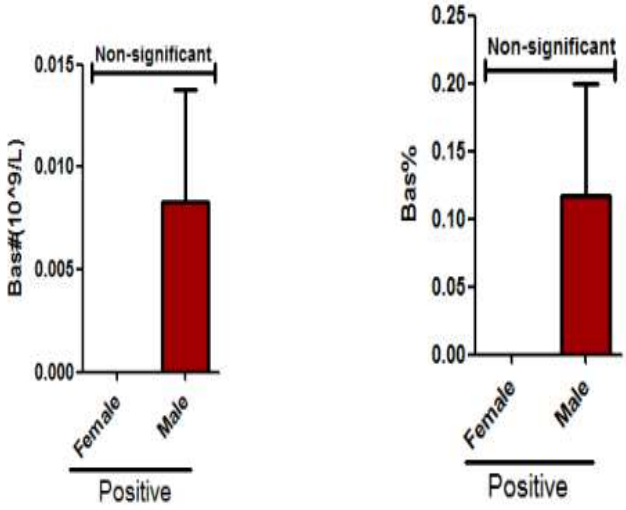

Fig 14 : Bas#, Bas% in H. pylori infected patient

The current study aligns with the scientific understanding of immune response concerning Eosinophils, Lymphocytes, and other immune cells, which are not correlated with bacterial infection. Consequently, as depicted, there is no significant variation observed among these cells.

While other studies appeared (A Jafarzadeh, V Akbarpoor, M Nabizadeh, M Nemati and MT Rezayati)

Among the control group, total white blood cell (WBC) counts ranged from 5,000 to 10,000 cells/mm3. Leukocytosis (WBC >10,000 cells/mm3) can indicate various conditions such as infection, inflammation, tissue damage, burns, dehydration, thyroid storm, leukemia, stress, or steroid use (George and Panos, 2005).

In this study, higher total WBC counts, neutrophil counts, and Neutrophil-to-Lymphocyte Ratio (NLCR) were observed among H. pylori-infected peptic ulcer patients and in the asymptomatic (AS) group compared to the control group. A study from Japan indicated that H. pylori eradication decreases blood neutrophil and monocyte counts (Kondo et al., 2004). The mechanism behind the elevated total WBC and neutrophil counts in H. pylori infections remains unclear. However, it is speculated that proinflammatory cytokines such as tumor necrosis factor (TNF), interleukin (IL)-1, and IL-6, which are increased in H. pylori-infected individuals (Romero-Adrian et al., 2010), may enhance the production of white blood cells from bone marrow stem cells (Hawley et al., 1991).

The present study also observed a higher NLCR among subjects infected with H. pylori, indicating an increased neutrophil count without a corresponding change in lymphocyte count.

H. pylori-infected individuals exhibit elevated levels of neutrophils. The proinflammatory cytokine IL-17A, characteristic of TH17 cells, has been demonstrated to increase neutrophil counts by inducing G-CSF (von Vietinghoff and Ley, 2009). IL-17A expression is also heightened in H. pylori-infected individuals (Jafarzadeh et al., 2009b; Kimang'a et al., 2010). Intriguingly, it has been shown that H. pylori-derived neutrophil-activating protein (HP-NAP) prolongs the lifespan of neutrophils (Cappon et al., 2010).

Our study revealed significantly higher mean total WBC count and mean neutrophil count in the asymptomatic (AS) group compared to the control group. These findings corroborate our previous observations regarding differences in CRP levels, a sensitive inflammatory marker, among AS and H. pylori-negative control groups (Jafarzadeh et al., 2009a). The elevated total WBC and neutrophil counts among the AS group may stem from subclinical microinflammatory reactions induced by H. pylori.

We also examined the association between CagA antibodies and total WBC counts and neutrophil counts among H. pylori-infected subjects. The results showed no differences in WBC or neutrophil counts between peptic ulcer (PU) and AS groups concerning cagA+ H. pylori strains. Consistent with our previous study, we found that CRP levels were not influenced by the expression of the bacterial CagA virulence factor (Jafarzadeh et al., 2009a). While cagA+ H. pylori strains are known to cause more severe gastric inflammation and are associated with a higher risk for PU disease and gastric cancer (Costa et al., 2009), some studies have failed to establish a correlation between inflammatory cytokines, such as IL-6 and TNF-α, and virulence factors like CagA (Kim et al., 2000). Polymorphisms in genes encoding cytokines such as IL-1, TNF-α, and IFN-γ have been linked to H. pylori-induced gastric adenocarcinoma and peptic ulcers (Basso and Plebani, 2004).

Considering both host and bacterial factors is crucial for understanding H. pylori-associated inflammatory responses, including elevated WBC counts. Our study found no significant differences in total WBC counts and neutrophil counts between CagA-positive and CagA-negative strains. These counts were independent of the CagA status among H. pylori strains, indicating that they are not suitable markers for determining H. pylori strains. Monitoring total WBC counts, neutrophil counts, and NLCR before, during, and after treatment of PU disease may enhance predictive or prognostic values. Further studies are warranted in this field.

Our study demonstrates higher total WBC counts and NLCR among PU and AS groups compared to controls. However, these parameters were not affected by bacterial CagA status.

while other studies appeared (Associate Professora, Yasin Sahin, M.D.a , Ozlem Gubur, M.D.b and Emine Tekingunduz, M.D.b)

More than half of the world's population remains infected with H. pylori (HP), with approximately 4.4 billion individuals reported to be infected worldwide in 2015. The prevalence of HP is particularly high in developing countries and is often associated with socioeconomic factors and hygiene conditions.

Previous studies have indicated that leukocytes and their subgroups, as well as the Neutrophil-to-Lymphocyte Ratio (NLR), serve as indicators of systemic inflammation. However, there is

limited research investigating the association between HP infection and NLR and Mean Platelet Volume (MPV).

Some studies have not found significant differences in NLR and MPV between patients with HP positivity and negativity. However, lymphocyte and thrombocyte values were within the normal range in HP-positive patients but were significantly higher than in HP-negative patients, likely due to an increase in absolute lymphocyte levels. Additionally, studies have shown no changes in MPV values in HP-positive patients.

In contrast, other studies have reported higher leukocyte, lymphocyte, and neutrophil counts in HP-positive patients compared to HP-negative patients. Higher NLR values were also detected in HP-positive patients, with higher values associated with the severity of gastritis and increased symptoms. However, some studies have shown that higher NLR values return to normal levels after successful treatment and eradication of HP, suggesting that NLR can be used in the follow-up of patients post-treatment.

While some studies have found decreases in NLR after HP eradication treatment, these differences were not statistically significant. Similarly, no significant difference was detected in NLR and MPV between HP-positive and negative patients, nor between subgroups of HP-positive patients based on the severity of infection. Additionally, NLR and MPV values did not correlate with the severity of HP infection in children in previous studies.

The lack of significant findings in some studies may be attributed to the small number of patients with severe HP infection. Further research with larger sample sizes, particularly including more patients with severe HP infection, may be necessary to elucidate these relationships.

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