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Correlation between *Helicobacter pylori* Infection and COVID-19

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Authors
Jasim Abdullah Y.*[1] *MSc,*
Hasan N.F.[2] *MSc,*
Zghair Jaber Alsaedi R.[1] *PhD*

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[1] Amara Medical Institute, Southern Technical University, Amara, Iraq
[2]Department of Radiological Technique, Health and Medical Technical College, AL_Zahraa University for Women, Iraq

Correspondence
Address: Southern Technical University, Amara Technical Institute, Amara, Iraq. Postal code: 62001
Phone: +96 (47) 702021952
Fax: -
younusjasim@stu.edu.iq

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ABSTRACT

Aims COVID-19 and Helicobacter pylori are pathogens associated with the most common viral and bacterial infections globally. The coinfection of pathogenic bacteria and COVID-19 represented a true health challenge. The current study aimed to estimate the incidence of *H. pylori* in patients with COVID-19.

Materials & Methods This experimental study was conducted in Karbalaa's COVID-19 Isolation Center from Feb. 2021 to July 2021, 130 COVID-19 patients were entered the study. A control group of 130 seemingly healthy people of similar ages and sexes was also enlisted in this research. COVID-19-infected patients were confirmed by Reverse Transcription-Polymerase Chain Reaction device. The samples were processed for total WBCs, and neutrophils were automatically computed. Data were analyzed using SPSS 21 software by independent T and Chi-square tests.

Findings COVID-19 infection was more frequent in males than females, especially between 15 and 25 years. The COVID-19 patients were detected to have increased neutrophils count ($p<0.0001$) and decreased lymphocytes compared to the healthy persons ($p<0.0001$). A significant correlation between *H. pylori* and COVID-19 was discovered, especially in females. COVID-19 infection was more frequent in males than females, especially between 15 and 25 years. The COVID-19 patients were detected to have increased neutrophils count ($p<0.0001$) and decreased lymphocytes compared to the healthy persons ($p<0.0001$). A significant correlation between *H. pylori* and COVID-19 was discovered, especially in females.

Conclusion *H. pylori*-infected patients are more susceptible to COVID-19 than other persons without H. pylori infections.

Keywords COVID-19; *Helicobacter pylori*; Correlation Study; Co-infection

CITATION LINKS

[1] Characteristics and prognostic factors of disease severity in patients with COVID-19 ... [2] Clinical features of ... [3] History is repeating itself: Probable zoonotic spillover ... [4] Impact of gastrointestinal symptoms in COVID-19: A molecular ... [5] Isolation and identification of Helicobacter pylori from drinking water in Basra ... [6] Review: Epidemiology of helicobacter ... [7] Helicobacter pylori virulence factors-mechanisms of bacterial pathogenicity ... [8] The effect of helicobacter pylori on the presentation ... [9] Sex difference in coronavirus disease ... [10] Biological attributes of age and gender variations in Indian COVID-19 cases ... [11] Male sex identified by global COVID-19 meta-analysis as a risk factor for death ... [12] Sex differences in severity and mortality from COVID-19 ... [13] Sex differences in immune ... [14] Age and sex differences in immune response following LPS treatment in ... [15] Diagnostic and prognostic utility of WBC counts and cell population data in patients ... [16] Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) ... [17] Clinical characteristics of non-ICU hospitalized ... [18] Eosinopenia and ... [19] Biomarkers associated with COVID-19 disease ... [20] COVID-19, ECMO, and lymphopenia: A word of ... [21] Susceptibility factors of stomach for SARS-CoV-2 and treatment implication of mucosal protective agent ... [22] Coinfections in people with COVID-19: A systematic review and ... [23] Bacterial and fungal coinfection in individuals with coronavirus: A rapid review to support COVID-19 ... [24] Bacterial coinfection and secondary infection in patients with COVID-19: A living rapid review ...

Introduction

The pandemic disease (COVID-19) caused by the Severe Respiratory Syndrome Coronavirus-2 (SARS-COV-2), a positive sense RNA enveloped virus, is responsible for causing the ongoing pandemic COVID-19 disease and poses a considerable challenge to global public health with extremely variable clinical outcomes ranging from a benign course to rapidly progressive disease that results in death within 2-3 weeks of symptom onset [1]. Fever, nausea, and respiratory disease are common symptoms of this viral infection, but some individuals also experience gastrointestinal symptoms, including abdominal pain, vomiting, and diarrhea. Intestinal cells have also been discovered to contain a small amount of viral nucleic acid [2]. Several proteins with distinct functions are found in the virus's lipid bilayer envelope. The spike, also known as S glycoprotein (SP), is important for invasion, adhesion, and entrance into human cells. It has two domains, S1 and S2. The main receptor for the virus on the human cell surface is angiotensin-converting enzyme-2 (ACE-2) which interacts with part of the S1protien called the receptor-binding domain. This is comparable to SARS-entry CoV's mechanism; however, the S2 domain is responsible for virus-cell membrane fusion and higher-affinity viral entrance [3]. In gastrointestinal (GI) cells, the (ACE-2) receptor is highly expressed. This means that the gastrointestinal system can be infected and serve as a replication site for COVID-19 [4].

Helicobacter pylori (HP) has been described as a gram-negative bacteria with spiral morphology and requires a microaerophilic condition. This pathogen has strongly linked to gastritis, peptic, and duodenal ulcer, as well as gastritis. It has also been linked to the onset of stomach carcinoma [5]. The transmission mode of HP is still unknown. The housefly has been identified as a possible carrier of the bacterium, particularly in places of the world where sanitation is low. Fecal–oral, iatrogenic, and oral–oral transmission pathways are also possible. Both gastrointestinal (GI) and extra-gastrointestinal (extra-GI) symptoms can be caused by HP. The pathogen's virulence actors and the immune system's corresponding response are associated with the duration and presentation of GI and extra-GI diseases caused by *H. pylori* [6]. *H. pylori* have several virulence factors that assist the colonization of the pathogen and evade the host's immune response. These virulence factors activate the host's immune system, causing elevated levels of cytokines including TNF-alpha, IL-6, IL-10, and IL-8 to be released, resulting in acute and chronic inflammation [7]. Moreover, HP has been linked to the increase in the expression of (ACE-2) receptors in the GI tract, directly linked to the infection progression and promoting immunological dysregulation through its virulent components [8].

The current study aimed to see if anti-HP IgG was present in COVID-19 individuals and associated with any clinical characteristics.

Materials and Methods

The current experimental study included COVID-19-infected patients from Karbalaa's COVID-19 Isolation Center (N=130) from 2021 Feb to 2021 Jul. A control group of (130) seemingly healthy people of similar ages and sexes. COVID-19-infected patients were confirmed by Reverse Transcription-Polymerase Chain Reaction device (Stratagene; USA).

The current study has been approved by the ethics committee of the Southern Technical University. Study procedures were supervised by the correspondence physicians of the COVID-19 isolation center in Karbala city. Venous blood samples (5mL) were obtained from the study group aseptic, then split into two portions (EDTA tubes and plane tubes). The first part from each collected blood sample was subjected to a complete blood count test, and the other part was used to estimate serum anti-HP IgG antibody test. Anti-HP IgG was diagnosed in the serum of the study groups using ELISA kits (California, USA). Biotech ELISA reader and washer (Biotech, USA) was used, and the procedure was applied, and results were calculated as indicated in the manufacturer's instructions. To estimate total counts of white blood cells (WBC), especially neutrophils, anticoagulated blood samples from both patients and the control group are run through a hematology autoanalyzer (Pentra 80, made by ABX-Horiba group, Minami-Ku Kyoto, Japan). The samples were processed by the equipment, and total WBCs and neutrophils are automatically computed.

Data were analyzed using SPSS 21 software by independent T and Chi-square tests. Statistical significance was defined as a $p \leq 0.05$.

Findings

The mean of Patients' age was 40.46±17.36 ranged from 15 to 75 years. The results of Table 1 illustrate the distribution of COVID-19 patients according to gender and age groups.

Table 1) Distribution of COVID-19 according to gender and age groups

Variable	COVID-19 (%)
Gender	
Male	57
Female	42.3
Age (year)	
15-25	30
26-35	17.7
36-45	17.7
46-55	13.8
56-65	10.8
66-75	10

Compared to the healthy control group, the mean of neutrophils was significantly increased (p<0.05), but lymphocytes were lower in patients than in control (Table 2).

Table 2) Mean±SD of total WBC counts, Lymphocytes, and neutrophils in COVID-19 patients and control group

Parameters	Patients	Control	p.
Lymphocyte (cell/ml)	$13.66\times10^3\pm4.29\times10^3$	$26.40\times10^3\pm4.79\times10^3$	0.018
Neutrophils (cell/ml)	$90.43\times10^3\pm12.40\times10^3$	$51.63\times10^3\pm5.66\times10^3$	0.000
Total WBC (cell/ml)	$10.76\times10^3\pm2.77\times10^3$	$7.9\times10^3\pm2.18\times10^3$	0.02

The correlation of *H. pylori* and COVID-19 infections was presented in Table 3. The existence of anti – *H. pylori* IgG antibodies was highly significant in COVID-19 patients than in healthy subjects (p<0.05). In all age groups listed in Table 3, anti – *H. pylori* IgG antibodies were higher in COVID-19 patients than in healthy persons. However, the highest co-occurrence of COVID-19 and *H. pylori* (29.9%) was detected in patients aged 15-25 years. The oldest patients in the current study (66-75 years) have the lowest coinfection of *H. pylori* and COVID-19. Females with COVID-19 infection were more affected by H. pylori than males, while the results were opposite in the healthy control group.

Table 3) Incidence of *H. pylori* and HP+ COVID-19 patients and control group according to the age groups and gender (n=260)

Parameters	COVID-19 patients		Control group		Total	
	N	%	N	%	N	%
***H. pylori* status**						
HP+	67	51.5	24	18.5	87	33.4
HP-	63	48.50	106	81.5	173	66.6
Age groups						
(year)	20	29.9	7	29.17	27	29.67
15-25	11	16.4	2	8.33	13	14.29
26-35	8	11.9	5	20.83	13	14.29
36-45	12	17.9	7	29.17	19	20.88
46-55	10	14.9	2	8.33	12	13.19
56-65	6	9	1	4.17	7	7.69
66-75	67	100	24	100	91	100
Total						
Gender						
Female	33	49.3	16	66.7	49	53.85
Male	34	50.7	8	33.3	42	46.15
Total	67	100	24	100	91	100

The current study also found that all lymphocytes, neutrophils, and total WBC counts were decreased in COVID-19 patients compared to COVID-19 patients with positive results to *H. pylori* serology (Table 4).

Table 4) Lymphocyte , neutrophils and total WBC counts in COVID-19 patients and HP+COVID-19 patients (Mean±SD)

Parameters	COVID-19 only Patients	COVID-19+HP Patients	p.
Lymphocyte (cell/ml)	$5.23\times10^3\pm3.14\times10^3$	$7.56\times10^3\pm3.97\times10^3$	0.032
Neutrophils (cell/ml)	$7.15\times10^3\pm6.46\times10^3$	$9.95\times10^3\pm4.25\times10^3$	0.001
Total WBC count (cell/ml)	$10.76\times10^3\pm3.87\times10^3$	$11.22\times10^3\pm4.91\times10^3$	0.062

Discussion

From the obtained results, COVID-19 was more frequent in males than females. The age rate of COVID-19 patients in this study was (40.46±17.36). The age-related differences showed that patients aged between (15-25 years) are the most influenced by the viral infection. In consistence with our results, Abate *et al.* [9] found that COVID-19 affected (55%) of males and (45%) of females, Kushwaha *et al.* [10] stated that (65%) of COVID-19 patients are men with a mean of age of (39.47±17.59) years for males and (36.85±18.51) years for females. Similar results were also found by Peckham *et al.* [11]. Immune system responses differ significantly between males and females, with females triggering higher immunity to infections. This variation in immunity could play a role in viral load, illness severity, and death.

Furthermore, because estrogen has immune-enhancing properties while testosterone has immunosuppressive properties, variations in sex-related hormone milieus could be a predictor of viral infections [12]. However, age-related differences in COVID-19 incidence could be attributable to age-related changes in adaptive immunity, which plays an important role in the immunity to viruses and falls after a certain age, leaving us exposed to different infections. Adaptive immunity differs between males and females as they get older [13]. Males have higher IgA, IgM, and Treg cells throughout the childhood or newborn stage and an equivalent number of helper/cytotoxic T-cells ratio, CD8+T cell, and B cells. Females' CD4/CD8 ratio, B cells, immunoglobulins, and T cell proliferation/activation increase as they become older (after puberty/adulthood). The outcomes may be significant and explained based on the evidence that; the male adaptive immune system weakens with increasing age compared to females [14].

Hematologic data of this study revealed that COVID-19 patients have considerably elevated numbers of WBC, especially neutrophils, and a lower number of lymphocytes than the healthy group. Several pieces of research have shown similar outcomes [15-17]. Regarding WBC counts, lymphopenia and eosinopenia were frequently seen in COVID-19 patients, and their severity correlated with illness severity. This helps identify this illness from typical viral infections, in which the counts of lymphocytes are usually higher, and eosinopenia is rare [18]. The fundamental processes of COVID-19 lymphopenia are unknown. Possible explanations include atypical hematopoiesis caused by direct infection of bone marrow progenitors, CD4 and CD8 cells, or an autoimmune reaction against blood cells [19]. The ability to replenish lymphocytes, particularly CD4, which are destroyed by the virus, may also be necessary for survival [20].

Concerning the incidence and correlation of COVID-19 with *H. pylori* infection, the current study, the

first one in Iraq, found that *the H. pylori* infection rate was higher in COVID-19 patients (p≤0.001) compared to the healthy persons. Furthermore, the coexistence of anti-*H. pylori* IgG and COVID-19 infection were higher in all age groups and females more than males. COVID-19 with positive tests for *H. pylori* have higher counts of total WBC, neutrophils, and lymphocytes than patients without *H. pylori* infection. It is hypothesized that *H. pylori* increase the expression of (ACE-2) receptors in the GI tract cell, making it another susceptible organ for the replication of COVID-19 [8, 21]. Globally, there is no data available to compare our results, but Lansbury et al. [22] found that about (7%) of the hospitalized COVID-19 patients have a bacterial coinfection *Mycoplasma pneumonia*, *Pseudomonas aeruginosa,* and *Haemophilus influenzae*. Rawson *et al.* [23] stated that COIVD-19 patients may suffering from bacterial and/or fungal coinfection such as blood stream bacteremia and urinary tract infection. On the other hand, Langford *et al.* [24], concluded that in COVID-19-infected hospitalized patients, bacterial coinfection is uncommon. The majority of these people may not need to be treated with antibacterials.

More detailed molecular studies are required to confirm the correlation between *H. pylori* and COVID-19 infections.

Conclusion

There is a correlation between *H. pylori* IgG antibodies and COVID-19, suggesting that *H. pylori*-infected patients may be more susceptible to COVID-19 infection than other people.

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Ethical Permissions: The current study has been approved by the ethics committee of the southern technical university, Amara medical institute, by ethic code 7/18/5 in 23 January 2021. Study procedures were supervised by the correspondence doctors of the COVID-19 isolation center in Karbala city.

Conflicts of Interests: All authors declare that there is no conflict of interest in the study.

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