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Clinical presentation of newly diagnosed Inflammatory bowel disease in relation to presence or absence of H. pylori infection

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ABSTRACT

Helicobacter pylori infection (H. pylori) is linked to different gastric and systemic diseases. Recent studies show that patients with inflammatory bowel disease (IBD) have a low prevalence of H. pylori infection. Several environmental factors, including diet, smoking, breastfeeding, drugs, and hygiene theory, contribute to the pathogenesis and disease activity of IBD. H. pylori is one of the environmental infections causing changes in gut microbiota and immune system dysregulation, which may affect IBD activity. The current study aimed to detect the frequency of helicobacter pylori infection among the of examined the newly diagnosed inflammatory bowel disease and compare the clinical, laboratory, and histological severity of the examined patients at time of diagnosis in relation to the presence or absence of H. pylori infection. The present study is a cross-sectional study conducted on one hundred newly diagnosed inflammatory bowel disease patients (83 ulcerative colitis patients and 17 Crohn's disease patients). Patients were recruited between January 2019 and January 2021 and tested for H. pylori by the H. pylori stool antigen. Laboratory and clinical disease activity were investigated among both positive and negative H. pylori Inflammatory bowel disease patients. Patients with positive stool antigen had a significantly lower fecal calprotectin (166.76 ± 32.81 vs. 242.95 ± 55.65 (µg/mg); P= 0.03) and Mayo score for ulcerative patients (5.18 ± 0.98 vs. 7.09 ± 2.13; P < 0.001) compared to those with negative stool antigen. Also, both groups showed a significant difference regarding histological disease activity. H. pylori-positive inflammatory bowel disease patients have less activity compared to H. pylori-negative inflammatory bowel disease patients at time of diagnosis.

1. INTRODUCTION

Helicobacter pylori (H. pylori) is a common gram-negative infection widely distributed worldwide, and it is

linked to different gastric and extra gastric diseases [1]. Despite the carcinogenic potentiality of some parts of the helicobacter pylori organism, some studies showed beneficial effects linked to the inverse relation between helicobacter pylori infection and some autoimmune diseases, bronchial asthma, and inflammatory bowel disease (IBD) [2]. This suppressing effect of H. pylori infection can be explained by the diverse immune system and changes in gut microbiota among the infected people [3], [4]. Inflammatory bowel disease is considered an emergent disease whose nature, pathogenesis, course, and even activity are not completely understood until now [5].

Inflammatory bowel disease activity may be related to genetic and environmental factors. Some studies suggest that hygiene theory can explain the geographic distribution of inflammatory bowel disease and its pathogenesis [6], [7].

There was a low prevalence of H. pylori infection among inflammatory bowel disease patients [8], [9]. Also, there was evidence of H. pylori protective effect against inflammatory bowel, which can be explained by immune diversity as dendritic cells and T helper lymphocytes cell activation causing the release of pro-inflammatory cytokines that inhibit mucosal immune response [10].

2. Patient and methods

The current study is an observational cross-sectional study conducted on one hundred newly diagnosed inflammatory bowel disease patients recruited between January 2019 to January 2021 and Sampling was done with census method.

Newly diagnosed inflammatory bowel disease was based on clinical symptoms, including bleeding per rectum, abdominal pain, and chronic diarrhea, and was confirmed by laboratory, endoscopic and histological basis.

Exclusion criteria included patients having a previous history of H. pylori eradication and patients with a recent history of antibiotics and proton pump inhibitors for the last month.

All included patients underwent the following: stool antigen for H. pylori to detect positivity or negativity of H. pylori among examined patients; laboratory tests including complete blood count, liver function tests, kidney function tests, and some markers (fecal calprotectin, C reactive protein (CRP), albumin, and Erythrocyte Sedimentation Rate (ESR); clinical assessment of disease activity among both H. pylori-positive and negative ulcerative colitis patients according to Mayo score(only for ulcerative colitis patients)

In case of the examined Crohn's diseased patients Focusing on presence of complication such as fistula and bowel stenosis histological activity determination by using biopsied colonic mucosa from patients with ulcerative colitis and ileal mucosa from patients with Crohn's disease.

2.1 Ethical consideration

All patients provided written consent, and the ethical committee of Assuit university approved the study.

2.2 Statistical analysis of the data

The collected Data was analyzed using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). Continuous data were expressed in mean ± SD or median (range), while nominal data were expressed in frequency (percentage). Chi²-test was used to compare the nominal data of the both different groups. The Student t-test compared continuous variables of the different groups. P-value was

significant if < 0.05 while the confidence level was kept at 95%.

3. Results

3.1 Characteristics of patients with IBD based on stool antigen H. pylori

Patients with positive stool antigen had a significantly higher mean age (36.06 ± 7.65 years vs. 30.69 ± 8.69 years; P < 0.001), and most of them were males (52.9% vs. 24.1%, P = 0.02). Patients with positive stool antigen tests had a significantly higher hemoglobin level (10.32 ± 0.94 mg/dl vs. 11.02 ± 0.48 mg/dl, P= 0.04), and serum albumin (28.45 ± 5.65 mg/dl vs.31.97 ± 4.44 mg/dl, P = 0.03) compared to those with negative stool antigen test.

In contrast CRP was significantly higher among patients with negative stool antigen (22.13 ± 3.33 vs. 11.34 ± 3.33 (mg/dl); *p*= 0.01).

Table 1 Characteristics of IBD patients based on stool antigen H.pylori

	Stool antigen H.pylori		
	Positive (n= 17)	Negative (n= 83)	*P* value
Age (years)	36.06 ± 7.65	30.69 ± 8.69	**< 0.001**
Sex			**0.02**
Male	9 (52.9%)	20 (24.1%)	
Female	8 (47.1%)	63 (75.9%)	
Type of IBD			0.41
Ulcerative colitis	15 (88.2%)	68 (81.9%)	
Crohn's disease	2 (11.8%)	15 (18.1%)	
Smoking	1 (5.9%)	6 (7.2%)	0.66
Diabetes mellitus	1 (5.9%)	6 (7.2%)	0.66
Hypertension	3 (17.6%)	7 (8.4%)	0.22
Chronic kidney disease	1 (5.9%)	2 (2.4%)	0.43
Hemoglobin (mg/dl)	11.02 ± 0.48	10.32 ± 0.94	**0.04**
Leucocytes (ul/10^3)	9.11 ± 1.23	8.88 ± 1.09	0.13
Platelets (ul/10^3)	290.13 ± 40.13	297.34 ± 55.09	0.98
INR	1.02 ± 0.10	1.02 ± 0.11	0.10
Bilirubin (mg/dl)	1.01 ± 0.03	1.02 ± 0.03	0.30
AST (u/l)	41.45 ± 2.45	40.01 ± 2.49	0.39
ALT (u/l)	38.45 ± 3.01	40.11 ± 4.56	0.23
Creatinine (mg/dl)	1.01 ± 0.42	1.11 ± 0.31	0.19
Serum albumin (mg/dl)	31.97 ± 4.44	28.45 ± 5.65	**0.03**
1^{st} hour ESR (ml)	37.67 ± 5.98	36.11 ± 2.9	0.45
2^{nd} hour ESR (ml)	48.35 ± 3.40	45.55 ± 4.1	0.11
C-reactive protein (mg/dl)	11.34 ± 3.33	22.13 ± 3.33	**0.01**

Data was expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05. IBD: inflammatory bowel disease

3.2 Disease activity based on H.pylori stool antigen

Patients with positive stool antigen had a significantly lower fecal calprotectin (166.76 ± 32.81 µg/mg vs. 242.95 ± 55.65 µg/mg, P = 0.03) and Mayo score (5.18 ± 0.98 vs. 7.09 ± 2.13; P < 0.001) compared to those with negative stool antigen.

Figure 1:
Mean fecal calprotectin among patients based on stool antigen of H.pylori

Also, there was a significant difference between both groups as regards the histological activity of the disease. Fifteen (88.2%) patients with positive stool antigen had mild histological disease activity. Also, 2 (11.8%) patients had moderate histological disease activity. Mild, moderate, and severe disease activity were found in 46 (55.4%), 29 (34.9%), and 8 (9.6%) patients with negative stool antigen tests, respectively.

Figure2:
Disease activity among patients based on stool antigen of H.pylori

Table 2 Disease activity based on H.pylori stool antigen

	Stool antigen H.pylori		
	Positive (n= 17)	Negative (n= 83)	*P* value
Fecal calprotectin (μg/mg)	166.76 ± 32.81	242.95 ± 55.65	**0.03**
Mayo score*	5.18 ± 0.98	7.09 ± 2.13	**< 0.001**
Histological activity			**0.03**
Mild	15 (88.2%)	46 (55.4%)	
Moderate	2 (11.8%)	29 (34.9%)	
Severe	0	8 (9.6%)	
Complicated disease			0.58
None	17 (100%)	78 (94%)	
Colonic stenosis	0	2 (2.4%)	
Fistula formation	0	3 (3.6%)	

Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05. IBD: inflammatory bowel disease. *this included only cases with UC

None of those with positive stool antigen developed complications. On the other hand, three patients with negative stool antigen developed fistula formation, and two patients developed colonic stenosis.

4. Discussion

Recently, advancements in civilization and environmental changes have altered the characteristics of inflammatory bowel disease; increasing the number of patients and the severity of the condition [11]. The variability of inflammatory bowel disease activity in different patients is poorly understood; some patients had severe symptoms while others had mild to moderate symptoms. Although genetic diversity is a major contributor to these differences, environmental risk factors such as infection with Helicobacter pylori play a role [12], [13]. The current study examined the pattern of disease activity among one hundred newly diagnosed inflammatory bowel disease patients regarding the presence and absence of H. pylori infection. These patients included 83 patients with ulcerative colitis (only 15 were positive for H. pylori) and 17 patients with Crohn's disease (only 2 were positive for H. pylori).

H. pylori-positive inflammatory bowel disease patients had a significantly higher mean age (36.06 ± 7.65 years vs. 30.69 ± 8.69 years; P < 0.001) in comparison to the H. pylori-negative ones.

Generally, no age group is immune to inflammatory bowel disease since it may affect both the young and the elderly. However, young patients are considered more susceptible to disease severity [14].

On the other hand, the older age of H. Pylori-positive inflammatory bowel disease patients may explain why their disease severity was less than that of H. pylori-negative inflammatory bwel disease patients in the present study. Two factors might explain this finding; the older age and the presence of H. pylori infection.

Although inflammatory bowel disease and helicobacter pylori infection cause anemia by different mechanisms, presence of H. pylori among the examined IBD patients was associated with higher hemoglobin levels than its absence. This finding supports the protective effect of H. pylori in inflammatory bowel disease and its role in disease activity regulation. Also, it agrees with a meta-analysis conducted by [15]. which included ten studies with 1299 IBD patients and 1817 controls. The meta-analysis demonstrated a low prevalence of H. pylori in IBD patients (24.9%) compared to controls (48.3%).

Patients with positive stool antigen had a significantly lower fecal calprotectin (166.76 ± 32.81 μg/mg vs. 242.95 ± 55.65 μg/mg; P = 0.03) lower CRP (11.34 ± 3.33 vs. 22.13 ± 3.33 (mg/dl); *p*= 0.01), and Mayo score (5.18 ± 0.98 vs. 7.09 ± 2.13; P < 0.001) compared to those with negative stool antigen in the present study.

Different microbiota patterns among both positive and negative H. pylori inflammatory bowel disease patients may explain these findings. According to [16]. gut microbiota can prevent or treat some diseases, including IBD [3]. Another explanation is the hygiene theory, in which the IBD is more common in developed rather than developing countries.

The current study showed a significant difference between positive and negative H. pylori inflammatory bowel disease patients in histological disease activity. Also, severe mucosal histological activity was not present among H. pylori-positive patients suggesting the mucosal suppressing effect of H. pylori in inflammatory bowel disease.

Although the low prevalence of positive H. pylori among inflammatory bowel disease patients supports the H. pylori protective effect, the large number of negative H. pylori inflammatory bowel patients is a limitation, as it may contribute to the variable disease activity among these patients.

Lastly In the future we need longitudinal long studies examined the effectiveness of non harmful h. pylori antigenic parts on the activity of the inflammatory bowel disease and to confirm or negate their therapeutic role.

5. Conclusions

H. pylori-positive inflammatory bowel patients have less activity compared to H. pylori-negative inflammatory bowel patients at time of diagnosis. also low frequency of helicobacter pylori among inflammatory bowel disease.

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