

## RATE OF HELICOBACTER PYLORI INFECTION AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME

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### ABSTRACT

**Background:** Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder. The association of *Helicobacter pylori* (*H. pylori*) infection with IBS still remains controversial.

**Objective:** The objective of this study is to determine the rate of *H. pylori* infection among patients with IBS through the detection of anti-*H. pylori* IgG antibody.

**Materials & Methods:** This cross-sectional study was conducted in Baquba General Teaching Hospital from August 2014 to June 2015. The study group included 134 patients with IBS, wherein their diagnosis was based on clinical and ultrasonography results. The mean age (SD) was  $45.4 \pm 14.0$  years, with a range of 15–80 years. The study group comprised 50 (37.3%) females and 84 (62.7%) males. Moreover, 50 apparently healthy individuals (25 males and 25 females) were selected as part of a control group. The mean age (SD) was  $41.7 \pm 17.7$  years, with a range of 20–74 years. From each participant, 3–5 milliliters of venous blood was aspirated. Sera were separated by centrifugation at 5,000 rpm for 5 minutes, which were used then for the detection of anti-*H. pylori* IgG antibody by enzyme-linked immunosorbent assay (Promedt Consulting GmbH, Germany). The participants' privacy was respected and informed oral consent was obtained from them. The data was analyzed using Statistical Package for Social Science (SPSS), Version 18. The results were considered significant for  $p < 0.05$ .

**Results:** The results revealed that the positivity rate of anti-*H. pylori* IgG (31.0%) was significantly higher among patients with IBS than that within the healthy control group (15.8%,  $p = 0.044$ ). The positivity rate of *H. pylori* infection was higher among female patients than that among male patients, although no significant association was observed ( $p = 0.20$ ). Moreover, the positivity rate was higher among the age group 46–60 years than that among other age groups, with no significant association ( $p = 0.29$ ).

**Conclusion:** The positivity rate of *H. pylori* infection was significantly higher in patients with IBS. However, further studies are required to elucidate the role of *H. pylori* in the pathogenesis of extragastric diseases. Furthermore, *H. pylori* infection should be considered in the clinical management of IBS.

**Keywords:** Irritable bowel syndrome, *Helicobacter pylori* infection, dyspepsia

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### INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a gram-negative, microaerophilic spiral bacterium found usually in the stomach; it causes chronic gastritis and gastric ulcers, and has been linked to the development of duodenal ulcers and stomach

cancer. According to the World Health Organization (WHO), *H. pylori* is classified as a carcinogen of class I, causing gastric cancer and gastric mucosa-associated lymphoid tissue lymphoma<sup>1</sup>. About 50% of the global population harbors *H. pylori* in the upper gastrointestinal tract, but over 80% of the individuals infected with the bacterium are asymptomatic, with just 10–20% developing clinical diseases<sup>2–4</sup>. In the past few years, some

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studies have linked *H. pylori* infection with a wide range of extragastric diseases<sup>5, 6</sup>. Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder that is characterized by abdominal pain and changes in stool habits. Several studies have described the role of various risk factors in the pathogenesis of IBS, including different infections such as *H. pylori* infection<sup>7–9</sup>. However, other studies have denied such association<sup>10–12</sup>.

The induction of typical abdominal discomfort associated with IBS occurs predominantly in *H. pylori* infected patients, indicating that *H. pylori* infection may be involved in triggering visceral hypersensitivity in patients with IBS<sup>13</sup>. Furthermore, a high *H. pylori* positivity rate was reported among patients with diarrhea-dominant IBS as the vacuolating cytotoxin A (VacA) of *H. pylori* causes *in vitro* vacuolation in colonic epithelial cells<sup>14</sup>. Moreover, in IBS patients, the presence of dyspepsia was associated with *H. pylori* infection, female gender, and perceived stress<sup>15–17</sup>. Therefore, these groups have been advised *H. pylori* eradication therapy as the first option<sup>18</sup>. In contrast, several studies have reported that there is no association between *H. pylori* infection and IBS<sup>12, 19</sup>. Hence, it has been suggested that with the exception of unexplained iron deficiency anemia and idiopathic thrombocytopenic purpura, *H. pylori* infection has no proven role in other extraintestinal diseases<sup>20, 21</sup>.

## MATERIALS & METHODS

This cross-sectional case control study was conducted in Baquba General Teaching Hospital from August 2014 to June 2015. The study group included 134 patients with IBS, wherein their diagnosis was based on clinical and ultrasonography results. The mean age (SD) was  $45.4 \pm 14.0$  years, with a range of 15–80 years. The study group consisted of 50 (37.3%) females and 84 (62.7%) males. Furthermore, 50 apparently healthy individuals (25 males and 25 females) were selected as part of a control group. The mean age (SD) was  $41.7 \pm 17.7$

years, with a range of 20–74 years. The participants provided about 3–5 milliliters of venous blood. Sera were separated by centrifugation at 5,000 rpm for 5 minutes, which were then used for the detection of anti-*H. pylori* IgG antibody by enzyme-linked immunosorbent assay (Promedt Consulting GmbH, Germany). The participants' privacy was respected and informed oral consent was obtained from them. The data was analyzed using Statistical Package for Social Science (SPSS), Version 18, and the results were considered significant for  $p < 0.05$ .

## RESULTS

Of the total patients with IBS that participated in the study, 31.0% (57 patients) were found to be positive for anti-*H. pylori* IgG antibody, significantly higher than that of the healthy control group (15.8%;  $p = 0.044$ ).

**Table 1.** *H. pylori* infection among study groups

Study groups	<i>H. pylori</i> infection		Total (%)
	Negative (%)	Positive (%)	
IBS patients	77 (41.8)	57 (31.0)	134 (72.8)
Healthy control group	21 (11.4)	29 (15.8)	50 (27.2)
Total	98 (53.3)	86 (46.7)	184 (100)

Pearson chi-square = 3.49;  $p = 0.044$

Regarding the distribution of *H. pylori* infection based on gender, the positivity rate among female patients (23.9%) was higher than that among male patients (18.7%), although there was no significant association ( $p = 0.20$ ). Moreover, males and females in the healthy control group had the same positivity rate.

The results revealed that the positivity rate of *H. pylori* infection among the age group 46–60 years was higher than that among other age groups, although there was no significant association ( $p = 0.29$ ). However, for the healthy control group, the positivity rate was higher among the age group 31–45 years ( $p = 0.79$ ).

**Table 2.** *H. pylori* infection among study groups by gender

Study groups		<i>H. pylori</i> infection		Total (%)	p value
		Negative (%)	Positive (%)		
IBS patients	Male	25 (18.7)	25 (18.7)	50 (37.3)	0.20 [NS]
	Female	52 (38.3)	32 (23.9)	84 (62.7)	
Total		77(57.5)	57 (42.5)	134 (100)	
Healthy control group	Male	8 (16.0)	17 (34.0)	25 (50.0)	0.25 [NS]
	Female	13 (26.0)	12 (34.0)	25 (50.0)	
Total		21 (42.0)	29 (38.0)	50 (100.0)	

**Table 3.** *H. pylori* infection among study groups by age

Study groups		<i>H. pylori</i> infection		Total (%)	p value
		Negative (%)	Positive (%)		
IBS patients	15–30	12 (9.0)	11 (8.2)	23 (17.2)	0.29 [NS]
	31–45	19 (14.2)	19 (14.2)	38 (28.4)	
	46–60	31 (23.1)	22 (16.4)	53 (39.6)	
	>60	15 (11.2)	5 (3.7)	20 (14.9)	
Total		77 (57.5)	57 (42.5)	134 (100)	
Healthy control group	15–30	8 (16.0)	8 (16.0)	16 (32.0)	0.79 [NS]
	31–45	4 (8.0)	9 (18.0)	13 (26.0)	
	46–60	4 (8.0)	6 (12.0)	10 (20.0)	
	>60	5 (10.0)	6 (12.0)	11 (22.0)	
Total		21 (42.0)	29 (56.0)	50 (100.0)	

## DISCUSSION

The prevalence of *H. pylori* infection among the general population varies greatly by country<sup>4</sup>. In a previous study, the seroprevalence of *H. pylori* infection among the general population in Diyala, Iraq, was 80%, with females having a significantly higher infection rate<sup>22</sup>. This high seroprevalence rate in Diyala was in line with global trend of *H. pylori* epidemiology. In the current study, we found that the seropositivity rate of *H. pylori* infection among IBS patients was significantly higher than that among the healthy control group. These results are in agreement with previous studies, which indicate that *H. pylori* infection is associated with the development of IBS<sup>9, 13, 15, 17</sup>.

The extragastric manifestations of *H. pylori* infection are still being extensively researched around the world. In fact, *H. pylori* may interfere with many biological processes, both inside and outside of the stomach, possibly influencing or determining the occurrence of many diseases

outside of the stomach. Moreover, the role of *H. pylori* in idiopathic thrombocytopenic purpura and sideropenic anemia has already been established<sup>20, 21</sup>. Recent studies suggest that *H. pylori* may increase the risk of acute coronary syndrome; contribute to insulin resistance; and may be associated with neurodegenerative, respiratory, and other miscellaneous disorders previously associated with other conditions<sup>1, 5</sup>. Such association between *H. pylori* and IBS can be partially explained by the presence of different types of *H. pylori* virulence factors, in addition to host genetic predisposition and environmental factors; moreover, the clinical outcomes are determined by the interplay of these factors<sup>21, 23–25</sup>.

Numerous studies have indicated that *H. pylori* possesses remarkable and novel virulence factors that enable the bacterium to exert its pathological effects in gastric and extragastric tissues<sup>6, 14, 26</sup>. Virulence factors, such as CagA,

VacA, DupA, IceA, OipA, and BabA, have been demonstrated to be crucial for initial colonization and subsequent predictors of severe clinical outcomes<sup>27, 28</sup>. One of the major protein toxins secreted by *H. pylori* is VacA. After its secretion from the bacteria via a type V autotransport secretion system, the VacA toxin binds to host cells and is internalized, causing severe vacuolation characterized by the accumulation of large vesicles that possess attributes of both late endosomes and early lysosomes. The development of vacuoles has been ascribed to the formation of VacA anion-selective channels in membranes<sup>29, 30</sup>. Moreover, via a type IV secretion system, *H. pylori* translocates the effector cytotoxin-associated gene A (CagA) and peptidoglycan directly into the host cytoplasm, where cancer- and inflammation-associated signal transduction pathways can be deregulated<sup>25, 28</sup>. Furthermore, *H. pylori*-associated inflammation is dependent on the host's inflammatory response, which in turn is determined by the allelic polymorphism of cytokine genes rather than the genetic characteristics of the host<sup>31</sup>. However, it is possible that additional important pathogenic genes may exist as *H. pylori* has about 1,600 genes<sup>27</sup>.

Regarding the prevalence of *H. pylori* infection based on gender, the results of our study indicated a higher positivity rate among female patients, in line with the results of other similar studies<sup>4, 9, 12, 17</sup>. The overall prevalence of IBS in females globally is 67% higher than that in males (about 1.5–3 times higher than that in males)<sup>32</sup>. The differences in reported gender-specific prevalence may reflect the differences in diagnostic criteria employed, perceived acceptability of symptoms, and ease of access to primary healthcare, which varies across healthcare systems<sup>33, 34</sup>.

## CONCLUSION

The results of our study showed that the positivity rate of *H. pylori* infection was significantly higher in patients with IBS. However, further studies are needed to elucidate the role of *H. pylori* in the

pathogenesis of extragastric diseases. Moreover, *H. pylori* infection should be considered in the clinical management of IBS.

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