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Helicobacter pylori infection and risk of salmonella infection

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Abstract

Helicobacter pylori (*H pylori*) infection is the most frequent infection worldwide and it has been postulated that it predisposes to multiple enteric pathogens and diarrheal diseases. Salmonella infection is common in tropical and under developed communities and is associated with wide range of diseases from gastroenteritis to typhoid fever. This study aimed at detecting the impact of *H pylori* infection on the incidence of salmonella infections.

The study participants were sampled from cohorts of patients in four university hospitals in different Egyptian Governorates. Their age ranged from 20 to 59 years and followed up for a rising Widal test. Case patients ($n = 109$) were subjects who visited the outpatient clinic because of diarrhea and typhoid like illness. They were either positive for *H pylori* stool antigen ($n = 53$) or negative to it ($n = 56$). All patients were subjected to thorough history taking, clinical examination, routine laboratory investigations, abdominal ultrasonography, *H pylori* stool antigen detection, and serial Widal test assay.

The proportion of salmonella-infected subjects was lower among case patients with *H pylori* infection (22.6%) than among those negative for *H pylori* (33.9%) albeit not statistically significant (adjusted odds ratio [OR], 0.57; 95% confidence interval [CI], 0.24–1.33; $P = .21$). The association persisted nonsignificant after adjusting for sociodemographic variables (adjusted OR, 0.5; 95% CI, 0.18–1.39; $P = .18$). In a multivariate analysis that adjusted for sex, dietary habits, socioeconomic status, and educational level subjects who eat outdoors were associated with a significantly greater risk of salmonella typhi infection.

Our findings suggest that there is no association between *H pylori infection* and salmonella infection in patients presented with typhoid fever or typhoid like illness.

Abbreviations: CI = confidence interval, *H pylori* = *Helicobacter pylori*, OR = odds ratio.

Keywords: *Helicobacter pylori*, salmonella, Widal test

1. Introduction

Helicobacter pylori (*H pylori*) infection is the most frequent infection worldwide and it has been postulated that it predispose to salmonella infection.[1] The stomach acidity is considered an important nonspecific barrier against the colonization of enteric pathogens into the gut,[2,3] and hypochlorhydria can predispose to increased risk of diarrheal diseases.[4] Consequently, it was

proposed that *H pylori* infection might increase the risk of diarrheal diseases and enteric infections. Furthermore, several studies have concluded an increased risk for diarrheal diseases in relation to *H pylori* infection.[5–9] A Gambian case–control study in children demonstrated greater *H pylori* seropositivity (53%) among children with chronic diarrhea compared with 26% in controls without chronic diarrhea ($P = .01$).[5]

A study in Bangladesh showed that *H pylori* infection was associated with a 1.6-fold increased risk of life-threatening cholera.[6] A follow-up study from Peru showed that *H pylori* seroconversion in children was followed by a slight but significant increase in the risk of diarrheal diseases.[7] Further studies supported these observations with shigellosis[8] and typhoid fever.[9] On the other hand, other studies could not demonstrate such relation[10,11] and several studies from Germany[12,13] and the United States[14] showed inverse association between *H pylori* infection and diarrheal diseases. Given these controversies, we designed the current cross-sectional observational study to examine the impact of *H pylori* infection on the incidence of salmonella infections.

2. Patients and methods

2.1. Study design

Cross sectional observational study.

2.2. Patients

Patients were enrolled from outpatient gastroenterology clinics of Zagazig, Kafrelsheikh, and Tanta University Hospitals, and Alexandria Medical Research Institute, Alexandria University, Egypt during the period from September 2017 to January 2018.

H pylori infection: is defined in this study when the patient was positive or negative for *H pylori* antigen in stool provided that he did not receive any PPI or antibiotics in the last 4 weeks prior to the examination.[15,16]

Salmonellosis: in this study rising Widal test over 1 week period was used to diagnose salmonella infection with titre more than 1/160 was considered significant.[14]

Diarrhea: was defined as passage of at least 3 loose stools in a 24-h period, based on the patients' self-report in the event questionnaire.

Typhoid like illness: was suspected when the patient presented with a gradual onset of a high fever over several days; weakness, abdominal pain, constipation, and headaches also commonly occur and may be diarrhea.[17]

A case patient was defined as a subject who visited the outpatient clinic with a complaint of diarrhea and/or typhoid like illness. Patients who agreed gave a written informed consent for participation in the study and for performing all labs needed. One hundred and nine patients were enrolled and were assigned into two groups according to their *H pylori* status: group I *H pylori* positive group and group II, the *H pylori* negative group.

A visit to outpatient clinic due to diarrheal episodes involved obtaining stool samples that were examined for *H pylori* antigen and blood sample for baseline Widal test.

H pylori antigen in stool (On Site H. Pylori Ag Rapid Test, CTK Biotech, San Diego, CA). It is a lateral flow chromatographic immunoassay for qualitative assessment of *H pylori* antigens depending on the use of monoclonal antibodies against *H pylori* conjugated with colloid gold. Positive cases were marked with two bands of color changes (one test band and one control band).[14]

Widal test: qualitative slide and semiquantitative tube agglutination methods were done using febrile antigen kits of *Salmonella typhi* (Chromatest Febrile Antigens Kits, Linear Chemicals, Spain).

Both infections were treated according to the current guidelines.

Sociodemographic variables information was obtained on: age, level of education, socioeconomic status, and dietary habits.

2.3. Exclusion criteria

Patients with these conditions were excluded from the study: chronic diseases, for example, diabetes, renal failure, cirrhosis, patients with malignancy, patients on PPIs, antibiotics intake within 1 month before being enrolled in the study, recent vaccination for typhoid fever, other causes of fever and other organ specific infections with localizing sign and symptoms like UTI and RTI, etc., and those who did not agree with written informed consent to participate in the study.

3. Statistical analysis

Data were checked, entered, and analyzed using SPSS version 20 for data processing and statistic. Data were expressed as number and percentage for qualitative variables. P value of $<.05$ indicates significant results. Comparison between the two groups was done using Chi square tests.

4. Ethical considerations

The study protocol was approved by the Hospital Ethics Committee. All patients gave a written informed consent for participating in the study and for performing all relevant interventions. The study protocol was adherent to practice guidelines and declaration of Helsinki.

5. Results

One hundred and nine patients were enrolled. Group I comprised 53 patients with confirmed *H pylori* infection using the readily available *H pylori* stool antigen after adequate precautions and preparation, while groups II comprised 56 patients who were negative for *H pylori* stool antigen. The proportion of salmonella-infected subjects was lower among case patients with *H pylori* infection (22.6%) than among those negative for *H pylori* (33.9%) (Fig. 1) albeit not statistically significant (odds ratio [OR], 0.57; 95% confidence interval [CI], 0.24–1.33; $P = .21$) as shown in Table 1.

The association persisted nonsignificant after adjusting for sociodemographic variables (adjusted OR, 0.5; 95% CI, 0.18–1.39; $P = .18$). In a multivariate analysis that adjusted for age, sex, dietary habits, socioeconomic status, and educational level subjects who eat outdoors were associated with a significantly greater risk of salmonella typhi infection.

6. Discussion

H pylori is the most prevalent worldwide infection mainly in developing countries. Moreover, salmonella infection is very common infection especially in tropical and subtropical communities. Both infections still bear common features beyond the prevalence including the common oral route of infection. Furthermore, both infections are good examples of persistent infections. *H pylori* inhabit the human gastric mucosa with the infection mostly acquired during childhood and persistence of the infection can be lifelong. Salmonella causes systemic infections that involve colonization of the reticuloendothelial system and some individuals become lifelong carriers of the organism.[18]

Gastric acidity is an important natural barrier against enteric infections.[19] It is known that *H pylori* infection is associated with hypochlorhydria during both acute and chronic infection. Consequently, reduced acidity and inflammatory changes in the stomach may predispose the host to an increase in the frequency of enteric infections including salmonella infection. This was the assumption that triggered the current study together with some emerging epidemiologic evidence of an association between *H pylori* infection and salmonella infection.[20]

In the current study *H pylori* prevalence in the study sample was 48.6% (53/109) which is consistent with prevalence rates reported in previous studies ranging from 30.6% to 74.4% and the infection is common in low socioeconomic status. The same class is more vulnerable to salmonella infection as shown in previous studies.[20,21]

In this study stool antigen test is used for diagnosis of *H pylori* infection because it is readily available and cheap when compared with urea breath test and it is the commonly used *H pylori* test in our daily practice. In fact the accuracy of stool antigen test for diagnosis of *H pylori* infection had been accepted among clinicians both in the local Egyptian literature and also at international level.[20,22]

However, an association between prevalence of *H pylori* and salmonella have not been confirmed in the current study. And this may reinforce some evidence that *H pylori* colonization may be protective against some infection. This has been shown in one study.[23] The authors of this study concluded that *H pylori* is
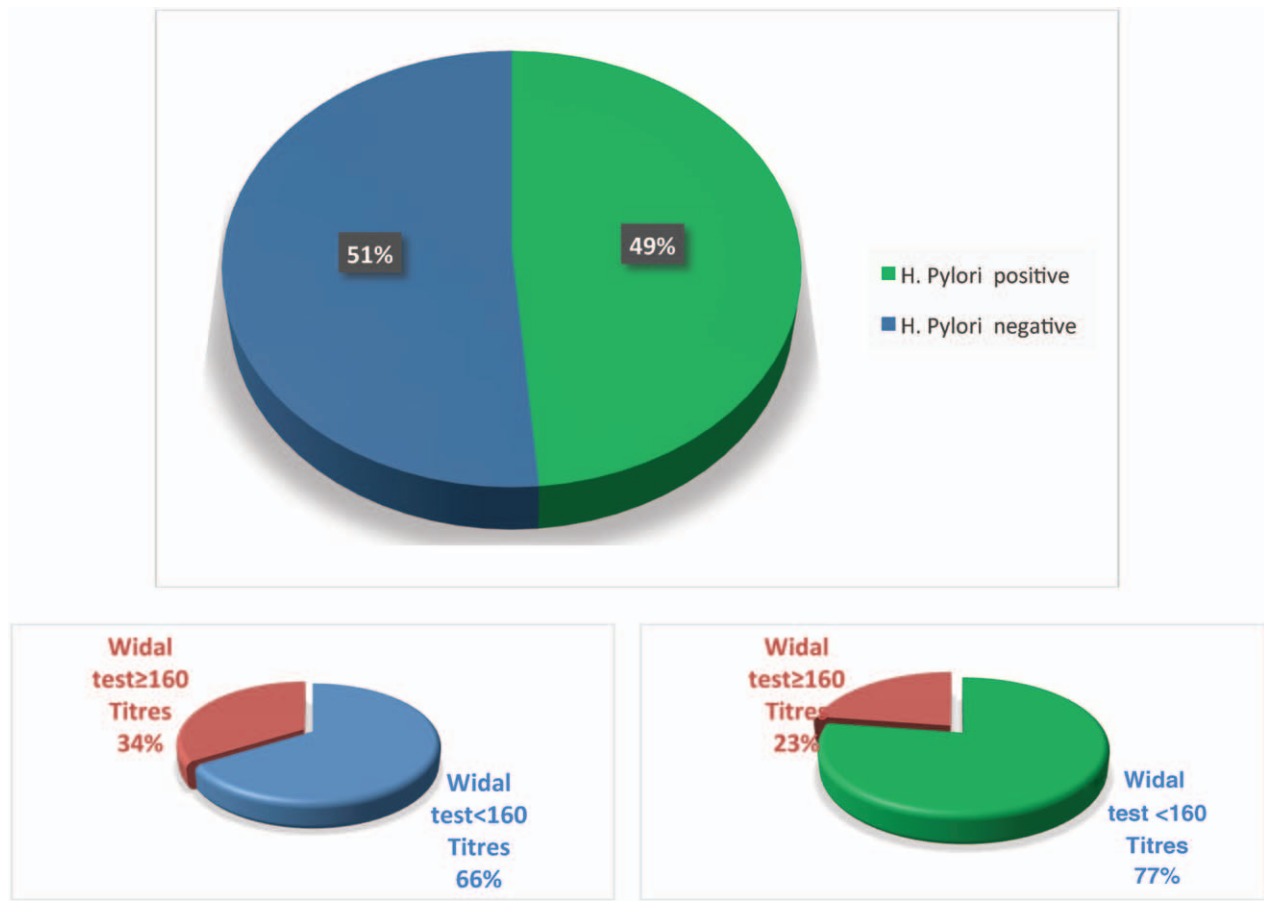
Figure 1. The proportion of salmonella-infected subjects among case patients with *H pylori* infection and those without.

protective against bacterial diarrhea in children and *H pylori* eradication should be carefully revised.

Also, another study from Indonesia suggested that a common risk of environmental exposure to both bacteria, for example,

poor hygiene, rather than a causal relationship via reduced gastric acid production is the common link in between.[24]

This study had its limitations. First, is the use of Widal test in diagnosis of salmonella infection. In fact Widal test has been

Table 1

Univariate analysis of association between *Helicobacter pylori* infection and Salmonella diseases.

	H pylori positive (*N*=53), No. (%)	*H pylori* negative (*N*=56), No. (%)	OR (95% CI)	*P*
Age				
20–39	32 (60.4)	27 (48.2)	Reference	.25
40–59	21 (39.6)	29 (51.8)	0.61 (0.28–1.3)	
Sex				
Male	37 (69.8)	43 (76.8)	Reference	.51
Female	16 (30.2)	13 (23.2)	1.43 (0.6–3.35)	
Diet				
Indoor	18 (34.0)	24 (42.9)	Reference	.43
Outdoor	35 (66.0)	32 (57.1)	1.46 (0.67–3.17)	
Socioeconomic				
Low	42 (79.2)	52 (92.9)	Reference	.05
High	11 (20.8)	4 (7.1)	3.4 (1.01–11.46)	
Education				
Low	42 (79.2)	51 (91.1)	Reference	.1
High	11 (20.8)	5 (8.9)	2.67 (0.86–8.29)	
Widal test				
<160 titres	41 (77.4)	37 (66.1)	Reference	.21
≥160 titres	12 (22.6)	19 (33.9)	0.57 (0.24–1.33)	

CI=confidence interval, OR=odds ratio.

correlated with culture results in some studies.[25] Another rationale is the lack of culture facility for every suspected case in the developing countries. In fact, Widal test examination is the real-life daily practice and its choice is a mirror image to actual circumstances practiced in the underdeveloped and poor communities. Second, is the small sample size. Third, lack of the follow up. Another study with longer follow up may answer the question, is there a difference in the natural history of both infections in the context of co-infection. Fourth, other confounders including many environmental and genetic factors were not studied and this because we intended to highlight, for the first time, in the Egyptian community, the association between both infections.

In conclusion, it seems that there is no association between *H pylori infection* and salmonella infection in patients presented with typhoid fever or typhoid like illness.

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Author contributions

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