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Case Report
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Recurrence of *Helicobacter pylori* Infection after Successful Eradication Therapy in Egyptian Patients

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Abstract

Background: *Helicobacter pylori* (*H. pylori*), a highly prevalent gastrointestinal organism, infects more than 50% of the global population. It is the most common risk factor for peptic ulcer disease, cancer stomach & gastric lymphoma.

Eradication therapy regimens for *H. pylori* are highly effective. However, bacterial resistance to antibiotics & patients non-adherence to the treatment regimens significantly increased the recurrence rates of *H. pylori* infection in the last few decades.

Study Aim: To assess the prevalence & possible risk factors of *H. pylori* recurrence in Egyptian patients after eradication therapy.

Patients and Methods: We evaluated & followed up 157 patients for one year after confirmed successful eradication of *H. pylori* infection. We investigated the patients at 3, 6, 9 & 12 months for recurrence of *H. pylori* infection using urea breathe & stool antigen tests.

Results and Conclusion: We found a one-year recurrence rate of 19% after successful eradication therapy of *H. pylori*. The education level of the patients & alcohol consumption were the most significant predictors of *H. pylori* recurrence. The one-year recurrence rate in our study is high but comparable to those reported in the developing countries most probably due to high rates of re-infection & non-adherence to the preventive measures.

Keywords: *H. pylori*; Proton pump inhibitors; Eradication therapy; Bacteria resistance; Recurrence

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Abbreviations

H. pylori: *Helicobacter pylori*; PUD: Peptic Ulcer Disease; MALT: Mucosal Associated Lymphoid Tissue Lymphoma; CagA: Cytotoxic-Associated Gene A; VacA: Vacuolating toxin A**;** BabA: Adhesin Protein**;** UBT: Urea Breath Test; PPI: Proton-Pump Inhibitors**;** PAC: PPI + Amoxicillin + Clarithromycin**;** PAL: PPI + Amoxicillin + Levofloxacin; PCL: PPI + Clarithromycin + Levofloxacin

Introduction

Helicobacter pylorus (*H. pylori*) is a gram-negative, highly-motile& spiral-shaped bacterium that infects more than 50% of the world's adult population through oro-oral or feco-oral transmission [1].

Chronic *H. pylori* infection is the most common risk factor for chronic gastritis, Peptic Ulcer Disease (PUD), stomach cancer, the second leading cause of cancer death worldwide, and Mucosal-Associated Lymphoid Tissue (MALT) lymphoma. It is also a common risk factor for esophageal cancer & idiopathic thrombocytopenic purpura [2,3].

The pathogenesis of *H. pylori* infection depends on interaction of organism virulence factors, such as Cytotoxic-Associated Gene A (CagA), Vacuolating toxin A (VacA) & adhesin protein (BabA), host factors such as cytokine genes polymorphism & environmental factors such as smoking, high salt intake, malnutrition & vitamin deficiency. The main defense mechanisms against *H. pylori* infection are gastric acidity, gastric mucus layer, gastric epithelial barrier & protective peptides produced by the gastric mucosa [4,5].

There is an inverse relationship between obesity & *H. pylori* infection. Eradication of *H. pylori* reduces gastric cancer risk. Because *H. pylori* is the most common cause of peptic ulcer, the risk of peptic ulcer recurrence is significantly reduced from 70% to less than 10% after successful eradication of *H. pylori* [6,7].

However, recurrence or re-infection isn't uncommon after successful *H. pylori* eradication therapy using triple or quadruple eradication regimens. In developed countries, the one-year recurrence rate after *H. pylori* eradications 1% to 2% [4-6], while in developing countries, the one-year recurrence rates are much higher ranging from 10% to 70% [8,9].

Recrudescence (recolonization of the same strain) that is occurring within a year after eradication therapy; rather than reinfection (colonization with a new strain) that is occurring more than a year after eradication, is responsible for most of the recurrent cases (80%) of *H. pylori* infection after successful eradication [10].

The rate of *H. pylori* recurrence after successful eradication generally depends on multiple factors including race, sex, treatment regimens, bacterial resistance and study period & method [11].

The aim of our study was to assess the recurrence rate of *H. pylori* after successful eradication and to identify the possible risk factors related to the recurrence.

Subjects and Methods

Our prospective study was carried on in Zagazig University Hospitals from March 2018 till May 2019. The study included 157 patients who were proven to be successfully treated for *H. pylori* infection. The regimens used for *H. pylori* eradication in our patients (clarithromycin-based & levofloxacin-based) and the methods used for confirmation of success of treatment or recurrence (urea breath test & stool antigen test) were in accordance with American College of Gastroenterology (ACG) guidelines 2017 [12].

The successful *H. pylori* eradication was confirmed by Urea Breath Test (UBT) 4 to 8 weeks after end of *H. pylori* eradication therapy. They included Proton-Pump Inhibitors (PPI) + Amoxicillin + Clarithromycin (PAC), PPI + Amoxicillin + Levofloxacin (PAL) and PPI + Clarithromycin + Levofloxacin (PCL). All patients signed an informed consent describing the purpose, possible risks, and benefits of the present study.

Inclusion criteria included age >18 years, both sexes, successful eradication of *H. pylori* confirmed by UBT since less than one year.

Exclusion criteria included pregnant or lactating females, patients with gastric cancer, history of with *H. pylori* treatment before 4 weeks or after one year of end of therapy.

Every patient was evaluated regarding history taking & clinical examination with emphasis on persistence or relapses of dyspeptic symptoms & signs and was investigated by urea breath test and *H. pylori* stool antigen at three, six, nine & 12 months after successful eradication therapy.

Chi-square test or Fishers' Exact test was used for qualitative variables and the Student t-test for quantitative variables. SPSS software for Windows version 18 (SPSS, Chicago, IL, USA) was then used for processing of data. A p-value of less than 0.05 was considered significant.

Results

We evaluated 157 patients, with a mean age of 36 ± 12 years, 58.6% were males and 41.4% were females. The *H. pylori* recurrence was detected in seven patients (4.5%) at 3 months, 16 patients at 6 months (10.2%), 5 patients at 9 months (3.2%) and 2 patients at 12 months (1.3%) with overall one-year recurrence rate (19.1%) of the patients observed after successful *H. pylori* eradication.

Table 1: Demographic & Clinical data of the study groups.

Patient characteristics	Patients with recurrence (N=30)	Patients without recurrence (N=127)	p. value
Age (Mean ± SD)	36 ± 12	33 ± 10	0.158
Males: Females (%)	43.3:56.6	37:63	0.518
Smokers (%)	16.7	14.2	0.729
Alcohol intake (%)	3.3	None	0.041
Eating spicy food (%)	20	22.8	0.741
Socio-economic status (%)			
Less than 1000 pounds/month	23.3	19.7	0.661
More than 1000 pounds/month	76.7	80.3	
Residence			
Rural	36.7	38.6	0.848
Urban	63.3	61.4	0.824
Education level (%)			
Illiterate	6.7	2.4	0.009
Basic education	23.3	8.7	
High education	70	88.9	
Dyspeptic symptoms (%)	63.3	51.2	0.234
Eradication regimen (%)			
PAC	73.3	68.5	0.609
PAL	20	19.7	0.97
PCL	6.7	11.8	0.42

As shown in Table 1, we found no evidence indicating a relationship between recurrence of *H. pylori* infection and either of the patient's age, sex, smoking status, residence, socio-economic status, eating habits of spicy food, recurrent dyspeptic symptoms or eradication regimens. We found a statistically significant relation between the education level & alcohol intake of our patients & recurrence of *H. pylori* after successful eradication.

Discussion

The prevalence of *H. pylori* infection in developed countries ranges from 20% to 40% with an annual incidence of 2% to 6% and a recurrence rate of 1% to 2% after successful eradication. However, in developing countries, the prevalence ranges from 70% to 90% with a recurrence rate ranging from 10% to 70% after successful eradication therapy. This higher prevalence in developing countries is mainly due to low socioeconomic conditions, overcrowding allowing spouse-to suppose, sibling-to sibling & mother- to child transmission, contaminated water & food, higher patient non-compliance in addition to the expensive cost of eradication treatment courses & repeated endoscopy [13,20].

In our study, we reported a 19% recurrence rate in our patients after 12 months of successful eradication therapy. This is comparable to the results of Morgan et al. [1] who reported one-year recurrence rates ranging from 8.6% to 18.1% in seven Latin American countries [1].

Since a genetic analysis was not performed in this study, we cannot distinguish between recrudescence and re-infection. However, we noticed that most cases of recurrence occur 6 months after the

end of eradication therapy. This may give a clue that recurrence in our patients is most probably due to re-infection rather than recrudescence. This goes in agreement with Hildebrand et al. [14] and Okimoto et al. [15] who reported that *H. pylori* isolates in patients having recurrent infection, after 6 months of successful eradication therapy, were different from the initial *H. pylori* strains before eradication therapy using DNA fingerprinting analysis [14,15].

Our study also revealed no statistically significant correlation between *H. pylori* recurrence after eradication therapy and the patients' age, sex, residence, spicy food intake, socio-economic status, smoking habits, relapsing dyspepsia or the used eradication regimen. This goes in accordance with Thong-Ngam et al. [10].

On the contrary; Benajah et al. [16] reported that low socioeconomic levels were associated with more recurrence after *H. pylori* eradication due to patients' non-compliance & increased adult-to adult transmission. Also, Cheon et al. reported that the relapse of dyspeptic symptoms was the only factor predictive of *H. pylori* recurrence [16,17].

Our results showed that *H. pylori* recurrence after eradication therapy is more common in patients who are illiterate or have low education level in comparison to patients with higher education level. This may be explained by the better adherence of educated patients to the medical instructions & preventive measures after eradication therapy.

Also, our results showed that alcohol intake may contribute to the recurrence of *H. pylori* after eradication therapy. This could be explained by the alcohol-induced gastric insults that provide proper sites for *H. pylori* re-colonization & pathogenic sequences. Additionally, alcohol consumption impairs the patients' immunity against *H. pylori* & the gastric mucosal healing from *H. pylori* infection. All these factors may predict a higher recurrence rates & re-infection after the end of eradication therapy. The literature evidence of alcohol intake effects on *H. pylori* eradication & recurrence is controversial. Zhang et al. [18] reported that although alcohol consumption increased *H. pylori* seropositivity, it had no statistically significant effect on the success rates of eradication therapy for *H. pylori* infection. Tsai et al. [19] concluded that alcohol consumption improved the outcome of eradication therapy on *H. pylori* infection by an additive value most probably by increasing gastric acidity, creating improper environment for the bacteria [18,19].

Conclusion

H. pylori recurrence after successful eradication therapy with a relatively long-term follow up period isn't uncommon. It mainly related to the lower education level & increased alcohol intake of the patients.

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