Prevalence of Helicobacter Pylori Infection in Subjects with Gastric Cancer Surgery

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Abstract

Objective: To determine the prevalence of helicobacter pylori (H. Pylori) infection in patients with gastrectomy for gastric cancer.

Material and Methods: Samples from ۹۵ (۶۹ males, ۲۶females) consecutive patients who had undergone surgery for gastric cancer were included in this study. Histologic examination of tumor obtained at the time of surgery yielded the diagnosis and then the specimens were stained with haematoxylin and eosin and Giemsa for the assessment of tumor and H.pylori infection. All patients did H.pylori immunologic and urease test.

Results: From ۹۵ patients with gastric cancer, ۸۳ patients (۸۷,۳۶٪) were positive for H. pylori infection. Histologic type of tumors was intestinal in ۶۱ patients and diffuse in ۷ patients.The prevalence of H. pylori was ۹۳,۲٪ in intestinal type carcinoma and ۲۸,۵٪ in diffuse type (P- value=۰,۰۰۰۲). No significant difference was found in sex, smoking and staging between H.pylori positive gastric cancer and H.pylori negative cases.

Conclusion: This study reconfirmed a high prevalence of H. pylori infection in patients suffering from gastric cancer and provided that evaluation for H. pylori infection might confer additional benefit in identifying the population that is at greater risk for this tumor.

Keywords:H. pylori ,gastric cancer

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Introduction

Gastric carcinoma was the most common cancer world wide in ۱۹۸۰s and is now surpassed only by lung cancer in incidence. Gastric cancer is the ۱۰th most common cancer in the United States [۱]. In Iran, it is the ۲th most common cancer in males and the ۴۰th in women. [۲] H.pylori is a spiral or helical gram negative rod with ۴ to ۶ flagella that reside in gastric-type epithelium within or beneath the mucus layer. Its shape and flagella aid its movement through the mucus layer, and it also produces a variety of enzymes that help it adapt to hostile environments. The organism is microaerophilic and the optimal temperature for isolation is ۳۵°c to ۳۷°c with growth occurring after ۲ to ۵ days. H.pylori can live only in gastric epithelium because only gastric epithelium expresses specific adherence receptors in vivo that can be recognized by the organism. Thus it can also be found in heterotopic gastric mucosa in proximal esophagus, Barrette's esophagus, gastric metaplasia in the duodenum, meckel's diverticulum's and heterotopic gastric mucosa in the rectum.

Three potential mechanisms for H.pylori induced gastrointestinal injury have been proposed including production of toxic products to cause local tissue injury; induction of a local mucosal immune response and increasing gastrin levels with a resultant increase in acid secretion [۱]. Gastric carcinogenesis involves a slow but continuous, stepwise evolution from superficial to glandular atrophy, metaplasia and finally to adenocarcinoma. In ۱۹۹۴, the international agency for research on cancer defined H.pylori as a group I carcinogen. Evidence supporting a causal association has been demonstrated by epidemiologic data as well as by experimental animal models [۳]

Helicobater pylori can be detected by multiple invasive or non invasive tests each with inherent advantages and disadvantages [۴]

Invasive tests

H.pylori can be detected at endoscopy by histology, culture or urease tests.

Histology: Although H.pylori may be recognized on sections stained with haematoxylin and eosin alone, supplementary stains (such as Giemsa, Warthin-Starry silver, Creosyl violet) are needed to

detect low levels of infection and to show the characteristic morphology of H.pylori. An important advantage of histology is that, in addition to the historical record provided, sections from biopsies or even additional sections can be examined at any time, and that gastritis, atrophy or intestinal metaplasia can also be assessed. Biopsy specimens from other parts of the stomach can be retained in formalin to be processed only if anural histology is inconclusive.

Culture: Microbiological isolation is the theoretical gold standard for identifying any bacterial infection, but culture of H.pylori can be unreliable. Risks of overgrowth or contamination make it the least sensitive method of detection and it is the least readily available test for use with endoscopy.

Urease tests: these are quick and simple tests for detecting H.pylori infection but indicate only the presence or absence of infection.

Non invasive tests

Serologic tests: H.pylori infection elicits a local mucosal and a systemic antibody response. Circulating IgG antibodies to H.pylori can be detected by enzyme ١inked immunosorbent assay (ELISA) or latex agglutination tests. These tests are generally simple, reproducible, inexpensive, and can be done on stored samples.

Urea breath test: Non-invasive detection of H.pylori by ١٣ C-urea breath test is base on the principle that a solution of urea labeled with carbon -١٣ is rapidly hydrolysed by the urease enzyme of H.pylori. It can be used as a screening test for H.pylori, to assess eradication and to detect infection in children. The simi١ar but radioactive ١٤C-urea breath test cannot be performed in primary care.

Faecal antigen test: In the stool, antigen test which is a simple sandwich ELISA can be used to detect the presence of H.pylori antigens shed in the faeces. Studies have reported sensitivities and specificities similar to those of the١٣ C-urea breath test (>٩٠٪), and the technique has the potential to be developed as a near patient test.

Material and Methods

This study was a sequential clinical trail. The series consisted of consecutive patients with gastric carcinoma diagnosed in Shohada hospital between April ٢٠٠٠ and March ٢٠٠٣.

The patients had undergone Subtotal gastrectomy or total gastrectomy and tissue samples were fixed in ١٠٪ formol- saline. Sections were stained with hematoxylin and eosin and Giemsa for the assessment of tumor type and H. pylori infection.

The patients were excluded if they had previously received anti H .pylori therapy, gastric surgery or used antibiotics or proton pump inhibitors within the last ٤ weeks.

Chi-square or fisher's test was applied to test whether differences between values were significant. P value<٠,٠٥ was considered statistically significant.

Results

A total of ٩٥ patients were studied, ٨٣ patients (٨٧,٣٦٪) were positive for H. pylori infection. Twelve patients (١٢,٦٤٪) were negative for three tests (urea's, Giemsa and Immunologic tests). Twenty six patients were woman and sixty-nine patients were males.

Mal/female ratio for gastric cancer was ٢,٦/١. Contamination with H. pylori was found in ٩٢,٣٪ of women and ٨٥,٦٪ of men.

Thirty-three patients were in stage II of gastric cancer with a prevalence of ٨٨,٤٪ for H. pylori, ٥١ patients were in stage III out of whom ٩٠,٩٪ were

Table ١: Comparative accuracy, availability, and costs of tests for H.pylori infection

Test	Sensitivity	Specificity	Availability	Cost
Invasive				
History	٨٨-٩٥٪	٩٠-٩٥٪	++++	££££
Culture	٨٠-٩٠٪	٩٥ ١٠٠٪	++	£££
Unease test	٩٠-٩٥٪	٩٠-٩٥٪	++++	£-££
Non-invasive				
١٣C-UBT	٩٠-٩٥٪	٩٠-٩٥٪	++++	£££
١٤C-UBT	٨٦-٩٥٪	٨٦-٩٥٪	+++	££
Serology				
ELISA	٨٠-٩٥٪	٨٠-٩٥٪	+++	£
NPT	٦٠-٩٠٪	٧٠-٨٥٪	++++	££
Stool antigen	٩٠-٩٥٪	٩٠-٩٥٪	++	££

UBT=urea breath test, NPT= near patient test

positive for H. pylori and ١٠ patients had metastases in whom the prevalence for H. pylori was ٧٠٪. In this study, we did not have any stage I gastric cancer cases. No relationship was seen between staging and rate of H. pylori detection. Ninety three patients had adenocarcinoma out of whom ٨١ (٨٧,٩٪ were positive for H. pylori. Two patients had lymphoma (large cell lymphoma) and both (١٠٠٪)were positive for H. pylori.

Fifty out of ٩٥ patients with gastric cancer were heavy smokers out of whom, forty three patients (٨٦٪) were positive for H. pylori while forty patients (٨٨٪) who had never smoked were positive for H. pylori, too. Statistical analysis showed no difference in detection of H. pylori and smoking.

Discussion

Helicobacter pylori infection of the human stomach is the most important risk factor for the development of gastric cancer. Gastric and duodenal ulcer, gastric adenocarcinoma and MALT lymphoma develop in a subset of infected individuals. Pathogenesis of H. pylori infection is based on the long term host to bacterial interaction and is influenced by the virulence factors of the bacterium and environmental and host factors (age, sex, blood type, etc.). Mucosal inflammation is the basic principle mechanism underlying the disease development in which tissue destruction may be initiated and maintained by both the bacterial toxins (Cag A, Vac A, LPS) and immune responses by the host (٥]. Immune evasion with bacterial modulation of host response affects the long-term host colonization which is itself affected by urease activity and or motility of the bacterium, presence of lipopoly sacchoride (LPS) and various bacterial enzymes [٥]. H. pylori colonizes the gastric mucosa of over ٥٠٪ of the world's population. All infected individuals exhibit chronic gastric inflammation, while approximately ١٪ of them develop gastric cancers, including adenocarcinoma and mucosal-associated lymphoid tissue lymphoma. Because the prevalence of gastric cancer varies among H.Pylori-infected patients in different countries and geographic areas, H.pylori-related outcomes are believed to be determined by interplays between host factors, bacterial factors and their interaction with the environment [٦] In a study, the distribution of H. Pylori vac A and cag A genotypes and their association with clinical outcomes was investigated in the Iranian population.

H. Pylori was cultured from gastric biopsy specimens obtained from ١٣٧ Iranian patients (٥٨ with duodenal ulcer, ٦١ with non ulcer dyspepsia [NUD] and ١٨ with gastric adenocarcinoma. Vac A allele was present in ١٠٧ out of ١٣٧ subjects (٧٨٪). cag A was present in ٤٤٪ of the patients. NUD

Table ٢: Demographic and socio-economics of gastric cancer cases and the prevalence of H. pylori infection

Characteristics	The patients	Positive for H.pylori	Prevalence (%) p value
Age (years)			
<٥٥٧	١٦	٩	٥٦،٥٪ (p:٠،٠٠٥)
>=٥٥	٧٩	٧٤	٩٣،٥٪
Sex			
Male	٦٩(٧٢/٦٣٪)	٥٩	٨٥،٦ (p:٠،٥)
Female	٢٦(٢٧/٣٦٪)	٢٤	٩٢،٣٪
Intestinal type	٦١	٥٧	٩٣/٤٪ (p:٠،٠٠٠٢)
Diffuse type	٧	٢	٢٨/٥٪
Smoking			
Heavy smoker	٥٠	٤٣	٨٦٪ (p:٠،٧)
Never smoked	٤٥	٤٠	٨٨٪
Socio-economic			
Low	٨٨	٨٠	٩٠،٩٪ (p:٠،٠٠٤٤)
high	٧	٣،٧	٤٢،٨٪
Antrum	٥٦	٥٤	٩٦،٤
Fundus and body	١٤	١١	٧٨،٥
Cardia	٢٠	١٣	٦٥٪
Diffuse	٨	٨	١٠٠٪

patients had a frequency of positive cag A similar to that of the overall population (٤٦٪). Cag A positive was present more frequently than cag A negative (٢٠٪ vs ٨٪ respectively) in patients with gastric carcinoma [٧]. In our study, the prevalence of contamination with H. Pylori was ٨٧,٣٦٪ in the patients with gastric cancer. In another study in china to evaluate the prevalence of H. pylori in ١٠٩ patients with gastric cancer, H. pylori was found in ٣٩,٣٪ and ٥٣,٢١٪ cases by PCR and WS, respectively. No significant differences were found in age, sex, site, histologic types and lymph node involvement in the two methods, but there was a significant difference in H. Pylori positive rate between early and advanced stages of gastric carcinomas. These results suggest that H. Pylori infection might play a certain role in the early stage of carcinogenesis of human gastric mucosa epithelia [٨]. In our study, no significant differences were found in sex, site and stage of gastric carcinoma but the histologic type was more frequently reported to be intestinal and the incidence of infection was ٨٧٪. In Italy, the prevalence of H. Pylori infection was investigated in patients who had undergone surgery for gastric cancer in which ٨٢/٣٪ of patients and ٥٦/٥٪ of controls were seropositive for anti -H. Pylori (P<٠,٠٠٠١). Anti-cag A antibody was significantly positive in the patients with gastric cancer. There was no difference between the frequency of H. Pylori in intestinal type carcinoma (٧٦/٢٪) and diffuse type cancer (٧٨/٨٪)[٩]. In a study in Germany to assess the effect of H. Pyloric on survival after curative resection for gastric adenocarcinoma, it was concluded that tumor specific immune responses might be down regulated in patients who are negative for H. Pylori and that these patients should be follow up carefully because of a poorer prognosis [١٠]. H. Pylori infection is frequent in patients with previous gastrectomy for non-neoplastic diseases. The results of the study suggest that H. Pylori infection may play a role in gastric stump cancer [١١]. Arguments in favor of the prevention of gastric carcinoma by eradicating H. Pylori are now stronger than before, given availability of simple and accurate diagnostic tests (serology)and treatment follow up (urea breath test), as well as a ٧-day treatment which is usually sufficient for eradication [١٢]

Clear indications for H. pylori treatment include patients with duodenal and gastric H. pylori associated ulcers and MALT lymphoma. There are also very clear benefits to H. pylori treatment in dyspepsia that is not investigated whereas in non-ulcer dyspepsia, the benefits are controversial. H. pylori is certainly a risk factor for gastric adenocarcinoma but eradication of this infection has not yet been shown to reduce or eliminate the risk of its development. The effect of H. pylori treatment in patients with gastroesophageal reflux disease is also unclear. There is a potential benefit in the prevention of atrophic gastritis but a potential disadvantage is the worsening of reflux disease, which has been suggested by certain studies. In addition, the interaction between H. pylori and nonsteroid anti-inflammatory drugs (NSAIDs) appears quite complicated. Although there have been several advances in the last ٢ decades regarding the treatment of H. pylori, several controversies still exist, attesting to the requirement for further research. [١٣].

In conclusion, this study revealed a high prevalence of H. Pylori in Iranian population with gastric cancer.

Because of the high prevalence of gastric cancer in Iranians, we recommend that searching for H. Pylori infection might confer additional help in identifying the population that are at greater risk for gastric cancer.

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