

## THE RELATIVE FREQUENCY OF THE HELICOBACTER PYLORI INFECTION IN PROXIMAL GASTRIC CANCERS

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Gastric cancer with the annual mortality of 700 000 is the second cause of death in the world. Iran with the annual incidence of 37 in 100 000 is among areas with high risk of gastric cancer. In Iran, Khuzestan Province with the annual incidence of 10 -15 in 100 000 is among areas with moderate risk. The role of Helicobacter pylori infection in distal gastric cancer as one of the most important risk factors of gastric ulcer has been proved but its role in proximal gastric cancer is controversial. In recent decades, the incidence of proximal cancers has increased.

**The aim of the study** was to survey the relative frequency of Helicobacter pylori infection in the people with proximal cancer and to compare it with this infection frequency in the distal cancer.

**Material and methods.** Relative frequency of Helicobacter pylori infection was surveyed by pathology tests and biopsy gastric mucosa sample staining with H&E in the patients with proximal and distal gastric ulcer whose cancers were proved by pathology method and also in the people who were healthy in terms of a gastric cancer. Data were statistically analyzed by frequency tables and chi square test.

**Results.** One hundred and seventeen people entered the study. Among 32 patients with the proximal cancer, 21 people were with the positive Helicobacter pylori (65.6%) and 11 people (34.4%) were with the negative Helicobacter pylori ( $p < 0.01$ ). Among 30 patients with the distal cancer, 26 people were with positive Helicobacter pylori (86.7%) and four people were with negative Helicobacter pylori (13.3%) ( $p < 0.01$ ); 55 people were without the cancer, which among them, 40 people were with the positive Helicobacter pylori (72.7%); and 15 people were with the negative Helicobacter pylori (37.7%) ( $p < 0.01$ ). In comparison of the frequency of Helicobacter pylori infection in the patients with the proximal cancer, a weak significant difference exists ( $p = 0.053$ ).

Comparing the frequency of Helicobacter pylori infection in the patients with the gastric cancer and people without the cancer, no significant difference existed ( $p = 0.703$ ).

**Conclusion.** A weak significant difference existed between the frequency of Helicobacter pylori infection in patients with the proximal gastric cancer and the frequency of these infections in the patients with the distal cancer. So, eradicating Helicobacter pylori infection can be effective in preventing the distal gastric cancers in addition to preventing the proximal gastric cancers.

**Key words:** distal gastric cancer, Helicobacter pylori, proximal gastric cancer

The Gastric cancer is the most prevalent malignancy in the gastrointestinal tract, the fourth reason of malignancy and the second reason for death caused by cancer in the world (1, 2). More than 930 thousand new cases of gastric are detected annually, and at least 700 thousand people die due to this disease (3). Iran, with the annual incidence rate of 37 in

100 000 is among the areas with a high risk of the gastric cancer in the world (2).

Also, the gastric cancer is the main reason of death in Iran, after accidents and cardiovascular disease (4, 5). In Iran, Ardebil with the annual incidence of 49 cases in 100 000 has the highest risk of the gastric cancer (4) Khuzestan with the annual incidence of 10-15 in

100 000 is among the areas with the moderate risk (2).

Adenocarcinoma is the most prevalent gastric malignancy and includes 95% cases of gastric cancers (6). From a histological approach, the gastric adenocarcinoma is divided into two kinds of intestinal and diffuse. Intestinal type is more prevalent and it follows gastric mucosa atrophy and intestinal metaplasia (7).

Anatomically gastric malignancies are classified as groups of the proximal and distal tumors gastroesophageal junction and tumors of cardiac region are among the proximal malignancies. Other tumors are considered as the distal malignancies. Totally, most causes of gastric adenocarcinoma occur in the distal area. But in recent decades the cancer in the proximal region is growing despite the total incidence of gastric cancer is decreasing (8). The gastric cancer is a multi-factorial disease. *Helicobacter pylori* (*H. pylori*) infection is the most important risk factor of the gastric cancer (9). This microorganism is a helical, gram negative and micro aerophilic bacteria. It enters the stomach by water and food contaminated and survives the injury of the gastric acid juice by defensive mechanism of Urease enzyme. Then, it penetrates the gastric mucosa and stays there. Toxins of the bacteria and the inflammatory response to the presence of bacteria in the gastric mucosa cause the gastritis. This infection mainly becomes chronic. Prolongation of gastric causes gradually gastric glands atrophy and changes them to intestinal cells called intestinal metaplasia. Gradually metaplasia causes dysplasia and finally gastric adenocarcinoma (10, 11, 12).

Role of *H. pylori* infection in the distal gastric cancers has been proved, and therapeutic eradication of *H. pylori* infection can prevent this disease (12). However, the role of these bacteria in the proximal cancers is controversial. In some studies a positive relation has been mentioned between *H. pylori* infection and proximal gastric cancer (13, 14), while in some others there has been a negative relationship (15, 16).

In a study conducted by Sotudeh et al., a strong correlation was found between *H. pylori* infection and gastric cancer in the cardiac region as an important pre-cancer factor In Tehran (odds ratio = 2.8) (14). In Khuz-

estan, no established study has been conducted yet.

Considering the high prevalence of *H. pylori* infection in Iran and the increase of the proximal gastric cancers in the recent decades and the effectiveness of therapeutic eradication of *H. pylori* infection in preventing the disease, the objective of this study was to survey the relative frequency of this infection in the proximal cancers and to compare that with the frequency of this infection in the people with the distal cancer and healthy people.

## MATERIAL AND METHODS

In this descriptive-epidemiologic study, patients who have referred with gastrointestinal complaints and were in the endoscopy center of the Ahvaz Imam Khomeini Hospital were surveyed. The sample volume with the confidence of 95% was calculated as 35.

Generally, variables surveyed in this study include *H. pylori* infection, proximal gastric cancer, distal gastric cancer, age, sex, and the history of gastroesophageal reflux. (According to present history, making sour and burning at the back of the sternum after heavy meal was in the description).

Among the patients that their gastric cancers were proved by the gastric mucosa biopsy sample in pathology, 35 cases were patients with the proximal cancer (patients whose tumors in the endoscopy were in the terminal 2 cm of esophagus, gastro esophageal junction and the primer 3 cm of the stomach), and 35 cases were patients with the distal gastric cancer (patients whose tumors in the endoscopy were after the primer 3 cm of the gaster). They were chosen accidentally. Furthermore, among people whose gastric biopsy samples in pathology were healthy, 70 people were selected accidentally as the control group. Three patients with the proximal cancer and five patients with the distal cancer because of diagnosis except adenocarcinoma, 15 people in the control groups because of the history of taking the medicine of proton-pump inhibitor or treatment against the *H. pylori* were during the recent two weeks excluded from the study. The *H. pylori* infection in each group was examined by staining the gastric mucosa biopsy sample (antrum, two samples of the body, and two samples of the gastro esophageal junction)

with hematoxylin and eosin stain (H&E stain) method; the results were analyzed by descriptive statistics and chi square test to compare the frequencies.

For ethical issues in this study, agreement form was prepared and was given to the patient. And the data of the patient were used with one's consent. In addition, patient data was protected and was told only to the patient. The principals of preservation and maintenance of the patient secrets were completely observed. The patients, whose test results of the *H. pylori* infection were positive, were suggested to refer to be cured.

### RESULTS AND DISCUSSION

One hundred and forty people entered the study and 23 people were excluded from the study. Frequency data of *Helicobacter pylori* infection in the three groups are shown in the tab. 1. There was a significant but weak correlation comparing the frequency of *H. pylori* infection in the patients with proximal cancer and those with the distal cancer ( $p = 0.053$ ) (fig. 1). In addition, no significant difference existed comparing the frequency of *H. pylori* infection in the patients with the gastric cancers and those without the cancer ( $p = 0.703$ ) (fig. 2).

In this study 82 men and 35 women were totally investigated. Data about the relative frequency of *H. pylori* infection was shown in the tab. 2. Among all the studied individuals, 58 people mentioned the history of gastric reflux to the esophagus in their descriptions. Overall, in this study 87 patients were with the positive *H. pylori*. The statistical parameters of their ages were presented in the tab. 3.

Totally in this study, 117 cases were examined, which among them, 55, 32, and 30 people

were without the cancer, with the proximal cancer, and with the distal cancer, respectively. Furthermore, 72.7% of those who were without the cancer, 65.6% of those with the proximal cancer and 86.7% of those with distal cancer were with the positive *H. pylori* infection ( $p$  value  $< 0.01$ ).

Given the comparison between the relative frequency of *H. pylori* infection in the patients with the proximal cancer and distal cancer by chi square test and the results obtained ( $p$  value = 0.53) and also considering that the  $p$  value obtained is a little more than 0.05; we can say that statistically, a significant weak difference exists in relative frequency of *H. pylori* infection between the proximal gastric cancer and distal gastric cancer.

In fact, the relative frequencies of the *H. pylori* infection in the proximal gastric cancer and distal gastric cancer are like each other. It seems that the *H. pylori* infection can be related to the proximal gastric cancers like the distal gastric cancers.

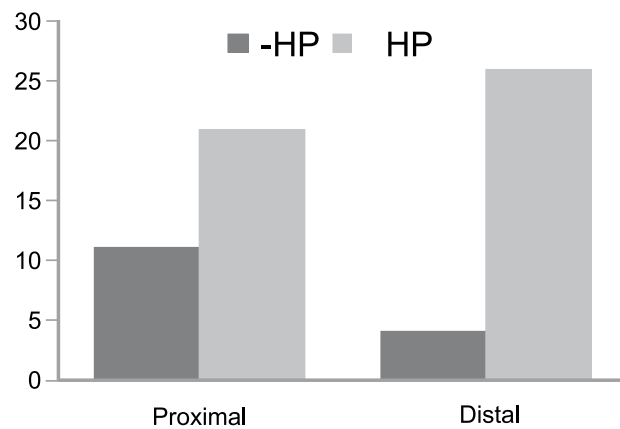


Fig. 1. Comparison of the relative frequency of *H. pylori* infection in the proximal and distal gastric cancers

Table 1. Frequency of *H. pylori* infection in the three different groups

Site		Frequency	Percent	p value
No cancer	(HP)-	15	27,3	<0,01
	(HP)+	40	72,7	
	total	55	100	
Proximal	(HP)-	11	34,4	<0,01
	(HP)+	21	65,6	
	total	32	100	
Distal	(HP)-	4	13,3	<0,01
	(HP)+	26	86,7	
	total	30	100	

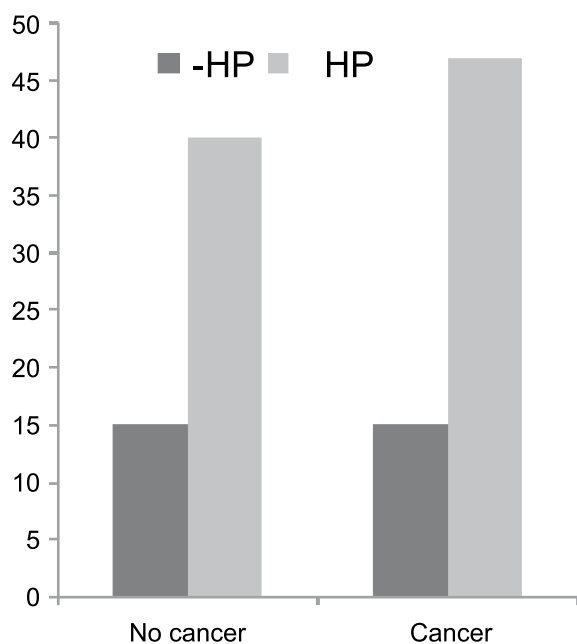


Fig. 2. Comparison of the relative frequency of the H. pylori infection in patients with the cancer and people without the cancer

area (odds ratio = 9.4). Moreover, the companionship between H. pylori infection and gastritis in the cardiac area had been remarkable (odds ratio = 2.8); this can confirm the positive relation between H. pylori infections and gastritis as a pre-cancer factor in a long period of time (14).

Also in a study conducted in Japan in the year 2010, 1503 patients with the gastric cancer were studied in terms of H. pylori infection. 82.8% of patients with cancer had H. pylori infection, but there had not been any difference between the anatomical positions of the tumor in terms of the H. pylori infection frequency (13).

Moreover, in some studies, results are different from the other studies. For example in a study conducted in Los Angeles in 2003, 87 patients with proximal and 127 patients with the distal cancer were investigated. And the serum level of the antibody of anti- H. pylori was measured by ELISA method in two

Table 2. Frequency of the H. pylori infection in the two groups

Sex		Frequency	Percent	p value
Male	valid	(HP)-	20	24,4
		(HP)+	62	75,6
		total	82	100
Female	valid	(HP)-	10	28,6
		(HP)+	25	71,4
		total	35	100

Table 3. Statistical indexes of the ages of patients with H. pylori infection

N	valid	87
	missing	0
Mean	55,0575	
Median	58,0000	
Standard deviation	16,70633	

In the previous studies, the similar results are presented; for example, the study conducted by Sotoudeh et al. in Tehran in 2010.

In this study 508 patients were examined according to the companionship of H. pylori infection with gastritis as an important factor producing gastric cancer in a long period of time. In the results achieved from this study, a strong companionship existed between H. pylori infection and gastritis in the antrum

groups; no obvious correlation has been shown between H. pylori infection and cardiac cancer (odds ratio = 0.86). (15) In addition, in a study conducted in California in 2006, 173 patients with non-cardiac cancer and 61 patients with the cardiac cancer were surveyed, and the serum level of the antibody of anti- H. pylori was measured by ELISA method, results showed a strong correlation has been reported between H. pylori infection and distal gastric cancer (Odds ratio = 7.9); however the correlation between H. pylori infection and cardiac cancer has been vice versa (odds ratio = 0.31) (16).

Considering the varieties of the results from studies conducted in the different parts of the world in this field, it seems that the correlation between the H. pylori infection and proximal gastric cancer can be dependent to the geographical distribution.

In the studies conducted in the western countries, a lesser correlation was mentioned between *H. pylori* infection and proximal cancers (15, 16).

In addition, in the studies conducted in the Asian countries, a higher positive correlation is seen between the *H. pylori* infection and proximal gastric cancer (13, 14).

Considering this point, we can mention the hypothesis that in the western countries the prevalence of reflux is high; proximal gastric cancer etiology is like esophagus cancer, and has less relation with *H. pylori* infection, this can justify the increase in the cardiac cancer incidence in the western countries in the recent decades; however, the prevalence of *H. pylori* infection has decreased. While in the Asian countries where the prevalence of reflux is less and the prevalence *H. pylori* infection is high, the etiology of the proximal gastric cancers is like the etiology of distal cancers.

In this study, the relative frequency of *H. pylori* infection in the people without the gastric cancer and the frequency of this infection in the patients with the gastric cancer (both distal & proximal) were compared by chi square Test. The  $p$  value = 0.703 was obtained from this comparison. Considering that this  $p$  value is a lot more than 0.05, no statistical variation existed between relative frequencies of this infection in these two groups. This can be due to the involvement of different factors in the gastric cancer except *H. pylori* infection.

In surveying the frequency of the *H. pylori* infection in two sex groups of male and female, 75.6% of male patients and 71.4% of female patients had *H. pylori* infection.

According to our results it seems that there is not a remarkable difference between male and female from the *H. pylori* infection frequency viewpoint.

In surveying the age distribution of individuals with *H. pylori* infection, the mean age was 55 years, the median was 58 years, and the standard deviation was 16.7.

## CONCLUSIONS

According to the results of this study and other studies, a significant but weak correlation exists between the relative frequency of the *H. pylori* infection in the proximal and distal gastric cancers. So, it can be concluded that the eradication of *H. pylori* infection can be effective in the distal cancer prevention in addition to the proximal cancer prevention.

In addition, according to the results of other studies from different parts of the world, it seems that this relation has a different geographical distribution.

In the western societies where the prevalence of the gastric reflux to the esophagus is high, the cardiac cancers have the same etiology as esophagus cancers (This can justify the increase in the incidence of proximal cancers in the recent decades, although the prevalence of *H. pylori* infection has decreased in these countries). In contrast, in the eastern societies where the prevalence of the gastric reflux to the esophagus is less but the prevalence of the *H. pylori* infection and atrophic gastric are high, the cardiac cancers have the same etiology as the distal gastric cancer. And they are more related to *H. pylori* infection.

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