Prevalence of *Helicobacter pylori* in Two Iranian Provinces with High and Low Incidence of Gastric Carcinoma

J. Mikaeli MD, R. Malekzadeh MD, B. Ziad Alizadeh MD, S. Nasseri Mogaddam MD, M. Valizadeh MD, R. Khoncheh MD, S. Massarat MD

*Digestive Diseases Research Center, Tehran University of Medical Sciences, Tehran, Iran*

**Abstract**

**Background**—Gastric cancer is significantly more prevalent in north western than central Iran. Growing evidence has related *Helicobacter pylori* (HP) to gastric cancer worldwide. We assessed the prevalence of HP infection in high (Ardebil) and low (Yazd) prevalence gastric cancer provinces of Iran.

**Methods**—Cluster sampling of healthy population aged less than 20 years was performed in Ardebil and Yazd provinces over a 2 month period. Five ml blood was drawn from each person and HP IgG was tested using ELISA (Diagnostic Corporation, sensitivity 98%, specificity 96%).

**Results**—Seven hundred and eleven individuals (358 in Ardebil and 353 in Yazd) were enrolled. One hundred and seventy individuals (47.5%) in Ardebil and 108 individuals (30.6%) in Yazd were positive for HP (P<0.0001). Logistic regression analysis showed that no other factor except for increasing age is associated with increased *H. pylori* infection in either area.

**Conclusion**—HP infection is significantly more prevalent amongst individuals less than 20 years of age in areas with high prevalence of gastric cancer in Iran. Our data suggest a relation between HP infection and gastric cancer in Iran.

**Keywords** • Gastrointestinal neoplasma • *Helicobacter pylori*

**Introduction**

*Helicobacter pylori* is a worldwide infection with a prevalence of about 30% in developed and up to 80% in developing countries.\(^1\) It becomes more frequent with aging; for example its frequency is 10% in American whites under 30 years old, but this figure is approximately equal with "age" in the over 60 age group.\(^2\)

Although, human beings are the major reservoir of *HP*, the main transmission method is not well known. Since it has been shown that members of a family are usually infected with similar strains of *HP*, person-to-person transmission may be considered. Fecal-oral and oral-oral routes of transmission have also been suggested. On the other hand, *HP* DNA has been detected in water.\(^1\) Cats have also been suggested as a reservoir of this infection.\(^1\)

Gastric cancer is the second prevalent malignancy throughout the world but its distribution varies greatly among different countries.\(^3\) It’s prevalence varies according to geographical and ethnic differences, (e. g. higher frequency among American blacks as compared to whites).\(^4\)

Recent studies have suggested that gastric cancer is more frequent in areas where higher *HP* infection rate prevails.\(^5\)

It has been found that adenocarcinoma of the body and antrum as well as lymphoma and maltona of stomach appear to have some correlations with *HP* infection but not with adenocarcinoma of gastric cardia.\(^6\)

Gastric cancer has been already shown to be more frequent in northwestern Iran compared to the
central areas. Regarding the suggested correlation between Helicobacter Pylori (HP) infection and gastric cancer, we aimed to assess the prevalence of HP infection in two Iranian provinces with high (Ardebil) and low (Yazd) frequency of gastric cancer.

Materials and Methods

Ardebil and Yazd have been shown as provinces of high and low frequency of gastric cancer, respectively. Healthy 6 to 20 year old individuals in these provinces were enrolled by cluster sampling (since it had been shown that acquiring HP infection at younger ages could be a predisposing factor of gastric cancer at senility). Blood (5ml) was obtained from each subject. Sera were separated and stored and finally transferred to our central laboratory in Tehran. From September to October 1997, 711 persons were sampled in these two provinces (358 from Ardebil, 353 from Yazd).

Sera were tested by ELISA for HP IgG antibody using kits produced by Diagnostics Co. with a sensitivity of 98% and a specificity of 96%. All subjects were interviewed and personal, environmental and geographical data were obtained as follows:

1. Age: subjects were categorized into three groups: 6-10 yrs, 11-15 yrs and 16-20 yrs.
2. Gender
3. Socioeconomic status (poor, intermediate and high, based on economic, social and cultural characteristics).
4. Number of family members categorized into three groups: under 5, between 5 and 8, and over 8 years old.
5. Living area; Home area divided by number of family members, three categories; under 10 m², between 10 and 20 m² and above 20 m² per capita.
6. Parents’ educational level: Five groups; Illiterate, elementary, secondary school, high school and college education.

We analysed the interview data and serologic tests by statistical package of WIN SPSS 6. and t-test, X² test and logistic regression analysis were used as appropriate.

Results

Blood specimens from 711 subjects were collected (358 in Ardebil and 353 in Yazd). One hundred and seventy persons in Ardebil and 108 in Yazd were HP seropositive.

Infection prevalence was 47.5% (CI95% = 42.3 - 52.7) and 30.6% (CI95% = 25.8 – 35.4) in Ardebil and Yazd respectively. HP infection rate was significantly higher in Ardebil than in Yazd (P<0.0001). Table 1 presents the distribution of HP infection according to age.

Age was the only predicting factor of infection in the two areas (P<0.0001) ( The higher the age, the higher the infection rate). Other factors such as socioeconomic status, number of family members, gender, father’s literacy, mother’s literacy, and size of living area did not have any correlation with prevalence of HP infection.

Discussion

Recent studies have shown a strong correlation between the prevalence of HP infection and gastric cancer. Many authors have found higher frequency of HP infection in patients with gastric cancer. Kohmoto found 88.4% HP infection rate in young patients with gastric cancer compared to 26.9% in the control groups.
The prevalence of *HP* infection amongst children and teenagers differs in different countries; for example this rate has been shown to be 80% in India \(^9\) and 25.7% in Hungary. \(^10\)

The prevalence also varies amongst different ethnic groups in a given geographic area as shown in the Giessen area, West Germany where the prevalence was 15.9% among Germans versus 45% among Turkish immigrants. \(^11\)

The age of patients at the onset of infection may predict the pattern of involvement of the stomach. *HP* infection in lower age groups, which is often seen in developing countries, usually presents as pangastritis followed by gradual mucosal atrophy, intestinal metaplasia, dysplasia and gastric cancer. In addition, this infection can cause some changes in vitamin C content of gastric juice, reactive oxygen metabolites and epithelial cell proliferation, each of which individually predisposes to gastric cancer by itself. \(^5\)

A four-fold increase in the incidence of gastric cancer has been reported following *HP* infection. \(^12\) Infection in higher age groups (as often seen in developed countries), usually presents as antral predominant gastritis and duodenal ulcers. \(^1\)

In our study, it has been confirmed that *HP* infection rate is meaningfully higher in an area with higher prevalence of gastric cancer (Ardebil) than in an area with lower prevalence (Yazd). This difference in young individuals may reflect the role of early *HP* infection in subsequent gastric cancer development.

The disparity between the two regions may be due to special dietary and behavioral habits, life style or environmental factors.

The point that gastric cancer prevalence varies in different populations with the same *HP* infection rate, reflects involvement of other factors in the pathogenesis of cancer. \(^13\)

Of the 60 million *HP* infected individuals, only 0.4% were involved by gastric cancer \(^14\). Other factors like dietary and behavioral habits, onset of infection, virulence of different strains and genetic susceptibility, affect the process of carcinogenesis in the stomach.

Environmental factors probably start their effect early in life and it has been shown that immigration to areas with less frequency of gastric carcinoma reduces the risk of cancer in the offspring of immigrants. \(^3\)

It seems that dietary factors such as long term consumption of smoked or salted food and alcohol as well as smoking makes an individual more prone to gastric cancer. \(^3\) It has also been shown that spoiled foods, that are often used by indigent families, play a role in converting nitrate compounds to nitrates which in turn produces carcinogenic elements by bacteria. *HP* may also affect this process.

It seems that some strains of *HP* are more effective in subsequent development of gastric cancer. *HP* strains containing cag A cytoxin have been shown to increase the risk of gastric cancer 5.8 fold compared to the control group. \(^15\)

It has been shown that inflammatory processes and atrophic gastritis are more frequent in cag A positive *HP* infection. Rudi et al showed that *HP* infection with vac A\(^+\) or cag A\(^+\) strains, especially in younger ages increases the susceptibility to gastric cancer. \(^16\)

In our study, like previous ones \(^2,17,18\), *HP* infection seroprevalence was higher among older
teenagers. Some studies showed that a low socioeconomic status increases the risk of involvement.\textsuperscript{17}

In this study, variables such as socioeconomic level, residence area, number of family members, educational state of parents and condition of drinking water, have not been shown to affect the susceptibility to \textit{HP} infection. Age and living in two different provinces were the only effective factors predicting the \textit{HP} infection rate.

Some studies have proposed that \textit{HP} eradication be carried out in the infected family members of patients with gastric cancer.\textsuperscript{9} Some others believe that \textit{HP} eradication is necessary in premalignant states such as mucosal atrophy, intestinal metaplasia, dysplasia, adenomatous polyposis and hypo or achlorhydria (idiopathic or drug-induced), immunocompromised patients, susceptible ethnic groups and upon patients’ request.\textsuperscript{20} An effective vaccine to prevent \textit{HP} infection and associated complications is needed.

Some studies are evaluating the role of \textit{HP} eradication in the prevention of gastric cancer. If this proves to be useful, mass screening of young individuals in high prevalence areas may be considered to decrease the prevalence of gastric cancer.

References
