

## Seroepidemiology of *Helicobacter pylori* infection in elderly people in the Beijing region, China

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### Abstract

**AIM:** To investigate seroepidemiology of cagA<sup>+</sup> and vacA<sup>+</sup> strains of *Helicobacter pylori* (*H. pylori*) in an elderly population in Beijing and to determine risk factors for seropositivity.

**METHODS:** A total of 2006 elderly persons (> 60 years) were selected using a random cluster sampling method in different parts of the Beijing area (urban, suburban and mountainous districts). Structured questionnaires were completed during home visits, including history of *H. pylori* infection, history of gastrointestinal diseases, diet types, hygiene habits, occupation and economic status. Blood samples (2 mL) were collected from each participant, and serum IgG antibodies to cagA, vacA and *H. pylori* urease antigens were measured by immunodetection.

**RESULTS:** The prevalence of *H. pylori* infection in elderly subjects was 83.4% and the type I *H. pylori* strain infection rate was 56%. The seroprevalence for type I *H. pylori* strain infection in urban and suburban

districts was higher than that in the mountainous areas ( $P < 0.001$ ). Elderly subjects who had previously performed manual labor or were in the young-old age group (age < 75 years) had a higher seroprevalence of *H. pylori* infection than those who had previously performed mental labor or were in the oldest-old age group (age  $\geq 75$  year) ( $P < 0.05$ ). The type I *H. pylori* strain infection rate in the elderly with vegetarian diets was higher than in those eating high-protein foods ( $P < 0.001$ ). There was no significant difference in the prevalence of *H. pylori* strains between male and female elderly participants ( $P > 0.05$ ).

**CONCLUSION:** Type I *H. pylori* seroprevalence is higher in elderly people. The distribution of strains of *H. pylori* is significantly affected by age, area and dietary habits.

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**Key words:** Elderly; Epidemiology; *Helicobacter pylori*; Virulence factors; Immunoblotting

**Core tip:** As society ages, a considerable proportion of the elderly population will suffer from digestive diseases combined with *Helicobacter pylori* (*H. pylori*) infection. In Beijing, there are no data regarding the pattern of *H. pylori* genotypes in the elderly. Our study investigated the seroepidemiology of the cytotoxin-associated gene product cagA<sup>+</sup> and vacuolating cytotoxin vacA<sup>+</sup> strains of *H. pylori* in elderly people in Beijing, and risk factors for seropositivity. Interesting associations between *H. pylori* seropositivity and subjects' habits were found in this population. This is the first prospective study conducted in China to investigate the genotype profiles of *H. pylori*.

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## INTRODUCTION

Evidence shows that *Helicobacter pylori* (*H. pylori*) infection is associated with chronic gastritis, peptic ulcers, gastric mucosa-associated lymphoid tissue lymphoma and gastric cancer<sup>[1-5]</sup>. It has been estimated that half of the world's population is infected by *H. pylori*<sup>[6,7]</sup>, but with different clinical outcomes. The role of *H. pylori* as an obligate pathogen remains questionable. One of the challenges of *H. pylori* research is to ascertain why so many people carry it (approximately 50%), but only approximately 20% of those become sick. Recent research has shown that *H. pylori* virulence factors, the cytotoxin-associated gene product A (cagA) and vacuolating cytotoxin A (vacA), in addition to host and environmental factors, may be very important<sup>[8,9]</sup>. It is clear that there is a paucity of well-designed studies of asymptomatic populations. With an aging society, elderly people suffering from digestive diseases combined with *H. pylori* infection account for a considerable proportion. In Beijing, there are no data regarding the pattern of *H. pylori* genotypes in elderly people; therefore, this is the first prospective study conducted in our country to investigate the genotype profiles (vacA and cagA) of *H. pylori*. Until we can obtain a better understanding of the nature of *H. pylori* and its relation to the human host in asymptomatic individuals, indiscriminate eradication of this infection may likely do more harm than good at the community level, and may represent a waste of medical and economic resources. To ascertain the prevalence of type I *H. pylori* strain infection in the elderly population in the Beijing area, we chose elderly persons in the general community in different parts of Beijing (urban, suburban and mountainous districts), to study the seroepidemiology of the type I *H. pylori* strain and risk factors for its seropositivity.

## MATERIALS AND METHODS

### Research subjects

The cluster sampling was based on a random sample of the elderly population of three Beijing districts [Xuanwu (urban), Daxing (suburban) and Huairou (mountainous)], stratified by living conditions, education and age in 2010. A total of 2006 elderly persons aged more than 60 years were randomly selected. Their average age was 70.9 years. Of these, 1005 (50.1%) were male and 1001 (49.9%) female, with 966 (48.2%), 522 (26.0%) and 518 (25.8%) from urban, suburban and mountainous areas, respectively.

### Methods

The survey was comprised questionnaires that were pro-

vided to the residents. Contents of the survey included history of *H. pylori* infection, occupation and diet types, hygiene habits, economic status and history of gastrointestinal diseases. A blood sample (2 mL) was collected after the survey. The specimen was centrifuged to separate the serum, which was then stored at low temperature (-20 °C) for later analysis. An immunodetection method was used to test for *H. pylori* IgG antibodies (*H. pylori*-blot kit 1.0 reagent; Shenzhen Blot Biotech, Shenzhen, China).

### Study protocol

An immunodetection method was used to test *H. pylori* IgG antibodies as reported previously<sup>[10]</sup>. *H. pylori* antigen was put into the reaction wells of a microtiter plate and inactivated sample serum was added. *H. pylori* antibody recognition of protein cagA (116 kDa), protein vacA (87 kDa) and urine enzyme subunit (66 kDa) was measured using a plate reader (Special Assay Kit for Helicobacter Pylori Tester, Shenzhen Blot Biotech, Shenzhen, China). Positive, negative and blank controls were included in each test.

### Result criteria

If the samples were seropositive for cagA and/or vacA (*i.e.*, vacA<sup>+</sup>cagA<sup>+</sup>, vacA<sup>+</sup>cagA<sup>-</sup> or vacA<sup>-</sup>cagA<sup>+</sup>) it was considered as a type I *H. pylori* strain infection. If antibodies only positive for urease and negative for cagA and vacA (*i.e.*, vacA<sup>-</sup>cagA<sup>-</sup>) were present, the sample was considered as type II *H. pylori* strain infection. Negativity for all three antibodies was considered as no *H. pylori* infection.

### Statistical analysis

The  $\chi^2$  test was used to analyze the data.  $P < 0.05$  was considered statistically significant. All calculations were carried out with SPSS ver. 13.0 statistical software (SPSS, Chicago, IL, United States).

## RESULTS

### Prevalence of different strains of *H. pylori* infection and distribution characteristics of the *H. pylori* strains with respect to sex

Of the 2006 elderly persons, 1673 (83.4%) were seropositive for *H. pylori* infection: 1124 (56%) were seropositive for the type I *H. pylori* strain, and 549 (27.4%) were seropositive for type II *H. pylori* strain infection. Of the 1673 patients seropositive for *H. pylori* infection, 67% were seropositive for the type I *H. pylori* strain and 33% were seropositive for the type II *H. pylori* strain. Overall, 851 (84.7%) of male persons were seropositive and 822 (82.1%) of females were seropositive for *H. pylori* infection. There was no significant difference in the prevalence of *H. pylori* strains between male and female participants (Table 1).

### Characteristics and distribution of *H. pylori* strains in elderly people of different ages

*H. pylori* infection rates were not different among differ-

**Table 1 Seropositivity for *Helicobacter pylori* strains affected by age, sex and area *n* (%)**

	<i>n</i>	<i>H. pylori</i> infection rate	<i>H. pylori</i> strains	
			I	II
Sex				
Male	1005	851 (84.7)	578 (57.5)	273 (27.2)
Female	1001	822 (82.1)	546 (54.5)	276 (27.6)
Age				
< 75 yr	1368	1140 (83.3)	792 (57.9)	348 (25.4)
≥ 75 yr	638	533 (83.5)	332 (52.0) <sup>a</sup>	201 (31.5) <sup>b</sup>
Area				
Mountainous (huairou)	518	472 (91.1)	258 (49.8)	214 (41.3)
Suburban (daxing)	522	403 (77.2) <sup>d</sup>	303 (58) <sup>d</sup>	100 (19.2) <sup>d</sup>
Urban (xuanwu)	966	798 (82.6) <sup>d</sup>	563 (58.3) <sup>d</sup>	235 (24.3) <sup>d</sup>
Total	2006	1673 (83.4)	1124 (56)	549 (27.4)

<sup>a</sup>*P* < 0.05, <sup>b</sup>*P* < 0.01 vs young-old persons. <sup>d</sup>*P* < 0.01 vs among urban, suburban and mountainous areas. *H. pylori*: *Helicobacter pylori*.

**Table 2 Seropositivity of *Helicobacter pylori* strains affected by age**

Age (yr)	<i>n</i>	<i>H. pylori</i> infection rate	
		<i>H. pylori</i> cases	%
60-64	395	343	86.8
65-69	497	389	78.3
70-74	476	408	85.7
75-79	384	322	83.9
≥ 80	254	211	83.1
Total	2006	1673	83.4

*H. pylori*: *Helicobacter pylori*.

ent ages. However, young-old persons had a significantly higher seropositivity for the type I *H. pylori* strain than older-old persons in the selected group (Tables 1 and 2).

**Distribution of *H. pylori* strains in different areas**

The overall *H. pylori* infection rate was significantly higher in the mountainous district than in the urban and suburban districts, while type I *H. pylori* strain seropositivity was the reverse (Table 1).

**Prevalence of *H. pylori* strains in different occupations**

Of the 2006 elderly persons, 1575 persons reported a definite occupation, among whom 1302 persons were seropositive, with a corresponding *H. pylori* infection rate of 82.7%. There was a significant difference in the total *H. pylori* infection rate between subjects who had been mental and manual workers; however, no difference of type I *H. pylori* strain infection rate was found between them (Table 3).

**Prevalence of *H. pylori* strains affected by different diet types**

According to the structured questionnaire, a diet containing protein (*e.g.*, chicken, duck, fish, meat, egg) more than 3 d a week for at least 1-5 years was considered a high-

**Table 3 Prevalence of *Helicobacter pylori* strains affected by previous occupation *n* (%)**

	<i>n</i>	<i>H. pylori</i> infection rate	<i>H. pylori</i> strains	
			I	II
Mental work	647	514 (79.5)	351 (54.3)	163 (25.2)
Manual work	928	788 (84.9) <sup>b</sup>	519 (55.9)	269 (29.0)
Total	1575	1302 (82.7)	870 (55.2)	432 (27.4)

<sup>b</sup>*P* < 0.01 vs mental workers in the total *Helicobacter pylori* infection rate. *H. pylori*: *Helicobacter pylori*.

**Table 4 *Helicobacter pylori* infection rate affected by diets *n* (%)**

	<i>n</i>	<i>H. pylori</i> infection rate	<i>H. pylori</i> strains	
			I	II
Vegetarian diet	593	524 (88.4)	345 (58.2)	179 (30.2)
High-protein diet	1413	1149 (81.3) <sup>b</sup>	779 (55.1) <sup>b</sup>	370 (26.2)
Total	2006	1673 (83.4)	1124 (56)	549 (27.4)

<sup>b</sup>*P* < 0.01 vs elderly persons on a vegetarian diet. *H. pylori*: *Helicobacter pylori*.

protein diet; a diet containing vegetables everyday and meat occasionally for at least 1-5 years was considered a vegetarian diet. The prevalence of *H. pylori* infection and type I *H. pylori* strain infection was higher in elderly persons on a vegetarian diet than those on a high-protein diet (Table 4).

**DISCUSSION**

Studies have shown that the virulence of CagA and VacA protein is immuno-independent, but they are strongly associated with each other in terms of pathogenicity. The molecule size of VacA is 87 kDa<sup>[11]</sup>. VacA is the major virulence factor of *H. pylori*. It is encoded by the *vacA* gene, and regulates the virulence of the vacuolating cell, inducing epithelial cell vacuolating proliferation. The molecule size of CagA is 128 kDa, and it is encoded by the *cagA* gene<sup>[12]</sup>. There are two main virulent strains of *H. pylori*<sup>[13]</sup>: the type I strain *H. pylori* expressing both the CagA and VacA proteins, and the type II strain expressing neither of them. The type I strain of *H. pylori* shows higher pathogenicity than the type II strain, which was closely correlated to gastric cancer and peptic ulceration<sup>[14-16]</sup>. There have been many epidemiological reports on *H. pylori* infection. Some reports indicate that the Beijing area adult infection rate was approximately 40%-50%<sup>[17]</sup>; however, there have been fewer investigations concerning the elderly generation. As the elderly population is increasing globally, we should pay more attention to geriatric infection rates. Therefore, we conducted a seroepidemiological study of type I *H. pylori* strain infection in elderly persons in different parts of the Beijing area. The results showed that 83.4% of the elderly people were seropositive for *H. pylori* infection (56% for type I *H. pylori* strain and 27.4% for the type

II strain). In *H. pylori* seropositive persons, type I *H. pylori* strain infection had higher prevalence (67%) than the type II strain. There was no significant difference in the prevalence of *H. pylori* infection and no difference in the distribution of *H. pylori* strains between men and women, which was consistent with reports from other countries<sup>[18]</sup>. The type I *H. pylori* strain infection rate was 60%-80% in Western countries<sup>[19,20]</sup>, and more than 90% in Asian countries<sup>[21]</sup>, indicating that the infection rate differed between populations and areas<sup>[22]</sup>. Our study aimed to investigate the elderly group in different parts of the Beijing area [Xuanwu (urban), Daxing (suburban) and Huairou (mountainous)]. The results showed that the *H. pylori* infection rate of the mountainous district was the highest (91.1%) and that the type I *H. pylori* infection rate was 49.8% overall, representing 54.6% of the infected persons. The prevalence of *H. pylori* infection was relatively lower in the suburban area (77.2%) and its type I strain *H. pylori* infection rate was 58% overall, representing 75.1% among *H. pylori*-infected persons. These results indicated that the type I *H. pylori* strain infection rate was significantly higher in the suburban area compared with the mountainous area. This suggested that in different parts of a country or in different geographical areas of one province, the *H. pylori* infection rate may be different. Although the suburban population had a lower *H. pylori* infection rate than the mountainous area, its major infected strain of *H. pylori* was type I. Whether this phenomenon was related to host factors, environmental factors or others, or if this correlated with some high occurrence of diseases, requires further epidemiological studies. On the other hand, in the study group, persons in the young-old group had a higher type I *H. pylori* strain infection rate. *H. pylori* infection also varied for different occupations among the elderly population. Those who performed manual or technical labor had a higher infection rate than those with other non-manual occupations; however, there was no significant difference when comparing the sub-strains between these two groups. The type I *H. pylori* infection rate was significantly higher in those with a mainly vegetarian diet than those whose diet was higher in protein. Studies have shown an association of *H. pylori* seropositivity with a low frequency of eating meat<sup>[23]</sup>. Other studies have shown that food antioxidant factors inhibit *H. pylori* infection<sup>[24-26]</sup>. Some scholars have reported that eating soy foods may reduce male *H. pylori* risk of infection (especially beans containing the antioxidant factors, isoflavones). This requires further study. There have been published reports that *H. pylori* infection was positively correlated with age, according to the statistics displayed in age groups. In the elderly population, the total infection rate of *H. pylori* was not significantly different in the elderly of different ages, while the *H. pylori* subtype (cagA, vacA) infection rate in the younger elderly and elderly was different. The World Health Organization and the Chinese Committee on Aging define the younger elderly as persons under the age of 75 years, and oldest-old as persons aged 75 year and older. The type I *H.*

*pylori* infection rate was also significantly lower among the oldest portion of the elderly population compared to the youngest. The decline may be related to social activity, with social factors reducing the influence of *H. pylori* infection.

## CONCLUSION

The prevalence of *H. pylori* infection was higher in the elderly population in the Beijing area, and the type I *H. pylori* strain was the major infection sub-strain. The type I *H. pylori* strain infection rate was different by area, age and diet. Whether we can decrease the type I *H. pylori* strain infection rate by changing some of the factors mentioned, so as to decrease the incidence of the correlated digestive diseases, still requires further research.

## COMMENTS

### Background

With the ageing of society, more elderly people will suffer from digestive diseases combined with *Helicobacter pylori* (*H. pylori*). In Beijing, there are no data regarding the pattern of *H. pylori* genotypes in elderly people.

### Research frontiers

Recent studies have shown that *H. pylori* virulence factors, the cytotoxin-associated gene product A (cagA) and vacuolating cytotoxin A (vacA), in addition to host and environmental factors, may be very important.

### Innovations and breakthroughs

This study investigated the seroepidemiology of the cytotoxin-associated gene product cagA<sup>+</sup> and vacuolating cytotoxin vacA<sup>+</sup> strains of *H. pylori* in elderly people in Beijing, and assessed risk factors for seropositivity. This is the first prospective study conducted in China to investigate the genotype profiles of *H. pylori*.

### Peer review

In this epidemiologic study entitled "Seroepidemiology of *Helicobacter pylori* infection in elderly people in the Beijing region, China", the authors considered a large elderly population and reported interesting associations between *H. pylori* seropositivity and subjects' habits.

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