

Comparison of precancerous conditions: atrophy and intestinal metaplasia in *Helicobacter pylori* gastritis among Chinese and Dutch patients

X-Y Chen, R W M van der Hulst, Y Shi, S-D Xiao, G N J Tytgat, F J W Ten Kate

Abstract

Aim—Atrophy and intestinal metaplasia (IM) as precancerous conditions consistently begin in the antrum and are most severe along the lesser curvature. The aim of this study was to investigate discrepancies in the prevalence, the severity of atrophy, and IM in antral mucosa of *Helicobacter pylori* infected gastritis and difference in age of onset among Chinese and Dutch patients.

Methods—Two hundred and sixty five Chinese patients and 261 Dutch patients with *H pylori* infection were enrolled. The degrees of atrophy and IM were graded according to the updated Sydney system.

Results—The overall prevalences of atrophy and IM were lower in Dutch patients (42% and 26%, respectively) than in Chinese patients (52% and 32%, respectively). Only the difference in atrophy reached significance ($p = 0.028$). However, in both Chinese and Dutch patients, the degrees of atrophy and IM were low and severe degrees were rare. The mean ages of Chinese and Dutch patients with atrophy and IM were higher than those without atrophy and IM (with atrophy (Chinese patients): mean, 42.12; SD, 9.80; with IM (Chinese patients): mean, 42.56; SD, 9.96; with atrophy (Dutch patients): mean, 55.16; SD, 12.20; with IM (Dutch patients): mean, 57.79; SD, 11.13; without atrophy (Chinese patients): mean, 39.71; SD, 10.16; without IM (Chinese patients): mean, 40.19; SD, 9.99; without atrophy (Dutch patients): mean, 45.70; SD, 12.44; without IM (Dutch patients): mean, 46.89; SD, 12.68). Atrophy and IM occurred earlier and were more severe in Chinese patients, with both reaching a peak value in patients over 60 years.

Conclusions—There are geographical differences in the prevalence and severity of *H pylori* infected gastritis, in particular with respect to atrophy and IM, which suggests that infection with *H pylori* occurs earlier in life and has a higher prevalence in China.

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Keywords: *Helicobacter pylori* infected; gastritis; atrophy; intestinal metaplasia; discrepancy/prevalence; China; the Netherlands; age groups

Helicobacter pylori infection is frequent worldwide and is closely associated with chronic gastritis, peptic ulcer disease, and gastric malignancy. The pathological changes, atrophy and

intestinal metaplasia (IM), which have been accepted as precancerous conditions, are serious consequences of *H pylori* associated infection.¹⁻⁴ Geographical variations in the incidence and severity of these pathological lesions have been related to differences in the incidence of gastric cancer.⁵⁻⁷ However, there is disagreement on the understanding and interpretation of grading of atrophy and IM among pathologists worldwide, and the data are not usually comparable. In our study, the degree of atrophy and IM in 265 Chinese and 261 Dutch patients with *H pylori* infection were graded according to the updated Sydney scoring system and the sections were examined by the same pathologist. To find out whether there were geographical variations in *H pylori* gastritis, our study was designed to compare the prevalence and severity of atrophy and IM in the antral mucosa among Chinese and Dutch dyspeptic patients infected with *H pylori*.

Materials and methods

STUDY POPULATION

All patients were included in multinational follow up studies ("Dutchigas Hp studies") on *H pylori* eradication treatment in China and the Netherlands. Those patients infected with *H pylori* underwent endoscopic examination because of the presence of upper gastrointestinal symptoms in the Shanghai institute of digestive disease of the Shanghai Second Medical University and the academic medical centre of the University of Amsterdam.

A total of 265 untreated Chinese patients (135 duodenal ulcer, 11 gastric ulcer, 19 peptic ulcer, and 100 chronic gastritis confirmed by endoscopy) and 261 Dutch patients (93 duodenal ulcer, 23 gastric ulcer, 11 peptic ulcer, and 134 chronic gastritis confirmed by endoscopy) were enrolled into our study. Chinese patients, comprising 151 men and 114 women, age range 18 to 73 years (mean age, 40.95; SD, 10.03), Dutch patients, comprising 152 men and 109 women age range 19 to 75 years (mean age, 49.68; SD, 13.18) were subdivided into five different age groups. Table 1 shows the mean age and sex of the five groups of patients. Owing to the small numbers involved in the various age groups, statistical analysis could not be performed and a statistical analysis of age was only performed for the overall group ($p = 0.121$). There were no significant differences in the age and sex distribution ($p = 0.771$ and $p = 0.121$, respectively) between Chinese patients and Dutch patients.

We excluded those less than 18 or greater than 75 years of age, and those with a history of

Department of Pathology, Renji Hospital, Shanghai Second Medical University, Shanghai Institute of Digestive Disease, Shanghai (200001), China
X-Yu Chen
Y Shi

Department of Gastroenterology, Renji Hospital
S-D Xiao

Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
R W M van der Hulst
G N J Tytgat
F J W Ten Kate

Correspondence to:
Dr Chen, Department of Pathology, Shanghai Institute of Digestive Disease, Shanghai Second Medical University, 145 Shan-Dong Road, Shanghai, 200001, The People's Republic of China
xiaoyu64@public7.sta.net.cn

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Table 1 General data of all patients according to age and nationality

	No. of patients (%)			Mean age (SD)			No. of men (%)		
	Chinese	Netherlanders	p Value	Chinese	Netherlanders	p Value	Chinese	Netherlanders	p Value
Total	265	261		40.95 (10.03)	49.68 (13.18)	<0.001	151 (57)	152 (58)	0.771
Age									
-18	25 (9)	14 (5)	0.075	26.44 (2.93)	26.44 (2.32)		11 (44)	11 (79)	
-30	124 (47)	54 (21)	<0.001	36.47 (2.66)	35.62 (2.74)		78 (63)	38 (70)	
-40	74 (28)	72 (28)	0.931	44.88 (2.55)	44.82 (3.13)		38 (51)	39 (53)	
-50	27 (10)	57 (22)	<0.001	53.90 (7.00)	54.86 (3.14)		15 (56)	30 (53)	
-60	15 (6)	64 (24)	<0.001	66.40 (3.68)	67.54 (6.08)		9 (60)	35 (55)	
Age standardised	26.76	22.34	0.121						

gastrectomy, active upper gastrointestinal bleeding or perforation, and severe gastro-oesophageal reflux disease.

ENDOSCOPY AND BIOPSY SAMPLINGS

All 526 patients underwent upper gastrointestinal endoscopy before *H pylori* eradication treatment in Shanghai or Amsterdam. According to the mapping principle of our study, during endoscopic examination, at least four biopsy specimens were taken from the antrum within 2–3 cm from the pylorus, two from the distal lesser curvature, and two from the distal greater curvature. Additional biopsy specimens were taken from any lesional areas when necessary. Two biopsy specimens were used for microbiological assessment (rapid urease test and culture), the others were used for histopathological examination. For optimal histological evaluation, all gastric biopsy specimens included surface epithelium and muscularis mucosae, and small pinch biopsies were excluded from our study.

HISTOPATHOLOGY

All biopsy specimens for histological examination were fixed in 10% formalin, embedded in paraffin wax on the oriented edge, and cut into 5 µm thick sequential sections. All tissue sections were routinely stained with haematoxylin and eosin for histological examination. When there was doubt about the presence of *H pylori*, an additional Genta stain was performed. Atrophy and IM were graded independently on a four point scale (absent or normal, mild, moderate, and severe abnormality), according to the updated Sydney classification for the histological grading of gastritis.⁸ All sections were examined by the same pathologist or, when a definite diagnosis was difficult to achieve, discussed by two pathologists. Atrophy was defined as the loss of inherent glandular tissue, with or without replacement by intestinal-type epithelium. IM was diagnosed when gastric foveolar and glandular tissues were focally or diffusely replaced by intestinal-type epithelium.

Table 2 The differences in the degree of atrophy and intestinal metaplasia (IM) in antral mucosa in both Chinese and Dutch patients

	Chinese (N = 265)				Netherlanders (N = 261)			
	N	Mild	Moderate	Severe	N	Mild	Moderate	Severe
Atrophy	137 (52)*	73 (28)	53 (20)	11 (4)	110 (42)*	57 (22)	40 (15)	13 (5)
IM	85 (32)**	43 (16)	31 (12)	11 (4)	67 (26)**	30 (11)	23 (9)	14 (5)

Values are number (%).
*p = 0.028; **p = 0.105.

HELICOBACTER PYLORI ASSESSMENT

Helicobacter pylori assessment was performed by the rapid urease test, culture, and histopathology in the initial antral biopsies. Results were positive when *H pylori* was detected by at least two of the three methods.

STATISTICAL ANALYSIS

Statistical analysis was performed using a statistical program package (SAS) and the χ^2 test, Fisher's exact test, Student's *t* test, and the u test. Significance was set at $p < 0.05$.

Results

MEAN AGE OF CHINESE AND DUTCH PATIENTS INFECTED WITH *H PYLORI*

Atrophy and IM occurred nearly 10 years earlier in Chinese than in Dutch patients. The mean age in Chinese patients was 40.95 years (SD, 10.03) compared with 49.68 (SD, 13.18) in the Dutch patients. There was a significant difference ($p < 0.001$) between the two populations.

PREVALENCE OF ATROPHY AND IM IN THE ANTRUM IN CHINESE AND DUTCH PATIENTS

In general, the prevalences of atrophy and IM were lower in Dutch patients (42% and 26%, respectively) than in Chinese patients (52% and 32%, respectively). For atrophy, the difference reached significance ($p = 0.028$; table 2). In both Chinese and Dutch patients, low degrees of atrophy and IM were common and high degrees of atrophy and IM were rare: 11 of 265 (4%) and 11 of 265 (4%), respectively, among Chinese, and 13 of 261 (5%) and 14 of 261 (5%), respectively, among the Netherlanders.

AGE OF ONSET OF ATROPHY AND IM IN CHINESE AND DUTCH PATIENTS

For both nationalities, those patients with atrophy and IM had higher mean ages than those without atrophy and IM; this was particularly true for the Dutch patients ($p < 0.0001$; table 3). When the prevalence and severity of atrophy and IM were analysed in five different age groups (~ 18, ~ 30, ~ 40, ~ 50, ~ 60 years), there was a striking difference between the two population groups (fig 1). Atrophy and IM occurred earlier in life and more frequently in Chinese patients than in Dutch patients. In patients less than 30 years of age, the prevalence of atrophy and IM was 36% and 20%, respectively, among the Chinese, but only 7% and 0%, respectively, in the Dutch patients. The prevalence of atrophy and IM in both

Table 3 Relation between the age distribution of patients with and without antral atrophy and intestinal metaplasia (IM) among Chinese and Dutch patients

Patient group	Mean age (SD)		p Value	Mean age (SD)		p Value
	With atrophy	Without atrophy		With IM	Without IM	
Chinese	42.12 (9.80)	39.71 (10.16)	0.05	42.56 (9.96)	40.19 (9.99)	>0.05
Dutch	55.16 (12.20)	45.70 (12.44)	<0.0001	57.79 (11.13)	46.89 (12.68)	<0.0001

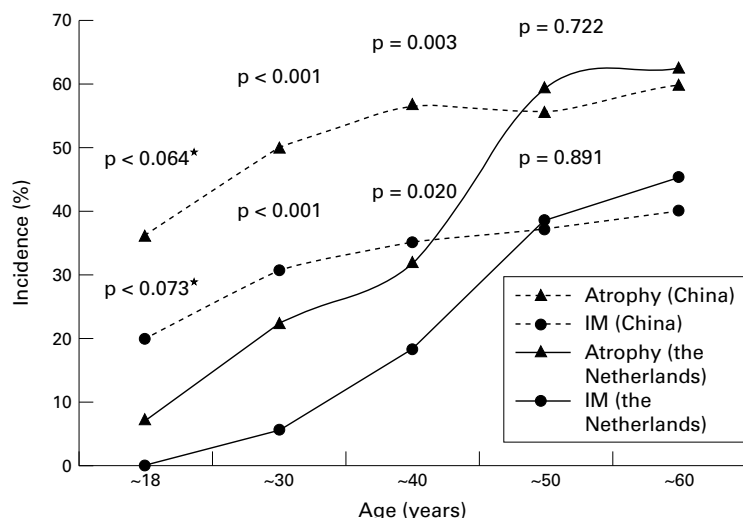


Figure 1 Incidence of antral atrophy and intestinal metaplasia (IM) in patients of different age groups within the two nationalities.

Chinese and Dutch patients increased with age, being nearly equal in patients over 50 years and highest in patients over 60 years—63% v 60% for atrophy, and 45% v 40% for IM, respectively.

Discussion

The pathological changes of *H pylori* infected gastritis, especially regarding the precancerous conditions, have been studied extensively in recent years.^{9,10} However, very few data are available concerning gastric mucosa from different countries using the same grading criteria and with the samples being assessed by the same pathologist. To compare differences between Chinese and Dutch patients with respect to prevalence and severity of atrophy and IM in *H pylori* infected gastritis, we selected two distinct populations from China and the Netherlands. The former had a higher incidence of gastric cancer (Shanghai) and the latter a relatively lower incidence of gastric cancer (Amsterdam) and we hoped to identify other factors that might affect the “*H pylori* infection→gastric cancer” process.

The age distribution revealed a close correlation between the prevalence and severity of atrophy, IM, and age, both in China and the Netherlands. The prevalence of atrophy and IM reached peak values in patients over 60 years in both the Chinese and Dutch patients: 60% v 63% (atrophy) and 40% v 45% (IM), respectively. We also found that the degree of atrophy and IM was low in most cases, both in Chinese and Dutch patients, and higher degrees were rare (4–5%).

Differences in the prevalence and severity of atrophy and IM in *H pylori* infected antral mucosa in different geographical populations

have been studied previously and considerable differences have been found. In Colombia and the United Arab Republic (high incidence of gastric cancer), the prevalence of atrophy was 45% and 26%, respectively, and IM was 54% and 11%, respectively; whereas in Germany (relatively low incidence of gastric cancer) the prevalence of antral IM was only 22.9%.^{2,10,11}

These studies also found considerable variation between rates in different parts of the same country. In a previous study, the prevalences of atrophy and IM were 60% and 38%, respectively, in northern central China-Lanzhou (high incidence of gastric cancer), but only 38% and 28%, respectively, in southern China-Guangzhou (low incidence of gastric cancer).⁵ Our study showed that the overall prevalence of atrophy was higher in Shanghai than in Amsterdam in patients with *H pylori* infected gastritis (52% v 42%; p = 0.028). We also found that the onset of atrophy and IM among Chinese patients was nearly 10 years earlier (p < 0.001). Among the younger age group (< 30 years), the prevalence of atrophy and IM were 36% and 20%, respectively, in Chinese patients. The incidence of gastric carcinoma also varied greatly in different regions of the world.¹² It is well known that the incidence of gastric cancer and infection with *H pylori* are positively correlated and that morbidity and mortality from gastric carcinoma are high in the Chinese population. In China, about 40% of children acquire *H pylori* infection early in life and the prevalence increases with age to about 70% in adults. In the Netherlands (relatively low incidence of gastric cancer), however, the prevalence of *H pylori* infection increases slowly with age to about 53% by the age of 50. It has been reported that the incidence of gastric cancer is low in the Netherlands (men, 27.5/100 000; women, 9.5/100 000), compared with 55.7/100 000 (men) and 21.0/100 000 (women) in China.¹³ Early acquisition and long duration of infection could be important factors predisposing to gastric carcinoma. The peak incidence of gastric cancer was found in patients older than 50 years; however, our results also showed that the prevalence of atrophy and IM was also higher in patients over 50 (both Chinese and Dutch) (fig 1). Why was the incidence of gastric cancer in China twice as high as in the Netherlands? Other factors such as differences in race, dietary factors, climate, social economy, and other unknown variables might also play a role in its development. Clearly, *H pylori* infection is a predisposing factor.

Overall, our data indicate that there are geographical differences in the prevalence and severity of *H pylori* infected gastritis, especially for atrophy and IM. Atrophy and IM were more prevalent and began earlier in life in Chinese patients, which is possibly related to the younger age and higher prevalence of *H pylori* infection among these patients.

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