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AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 642 experts in gastroenterology and hepatology from 59 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

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ORIGINAL ARTICLE

Retrospective Study

Serum anti-*Helicobacter pylori* antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study

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Abstract

AIM

To clarify the role of serum anti-*Helicobacter pylori* (*H. pylori*) antibody titers in gastric cancer.

METHODS

In this cross-sectional study, the effect of patients' baseline characteristics and endoscopic findings on their serum antibody titers were assessed. We evaluated consecutive patients who underwent esophagogastroduodenoscopy and their first evaluation for *H. pylori* infection using a serum antibody test. We excluded patients with a history of eradication therapy. The participants were divided into four groups according to their E-plate serum antibody titer. Patients with serum antibody titers < 3, 3-9.9, 10-49.9, and ⩾ 50 U/mL were classified into groups A, B, C, and D, respectively.

RESULTS

In total, 874 participants were analyzed with 70%, 16%, 8.7%, and 5.1% of them in the groups A, B, C, and D, respectively. Patients in group C were older than patients in groups A and B. Gastric open-type atrophy, intestinal metaplasia, enlarged folds, diffuse redness, and duodenal ulcers were associated with a high titer. Regular arrangements of collecting venules, fundic gland polyps, superficial gastritis, and gastroesophageal reflux disease were related to a low titer. Multivariate analysis revealed that nodularity (P = 0.0094), atrophy (P = 0.0076), and age 40-59 years (*vs* age ⩾ 60 years, P = 0.0090) were correlated with a high serum antibody titer in *H. pylori*-infected patients. Intestinal metaplasia and atrophy were related to age ⩾ 60 years in group C and D.

CONCLUSION

Serum antibody titer changes with age, reflects gastric mucosal inflammation, and is useful in predicting the risk of gastric cancer.

Key words: Antibody; *Helicobacter pylori*; Gastritis; Gastric cancer; Endoscopy

Core tip: A positive-low serum anti-*Helicobacter pylori* (*H. pylori*) antibody titer (E-plate Eiken) (10-49.9 U/mL) and a negative-high titer (3-9.9 U/mL) are associated with intestinal-type gastric cancer. A positive-high titer (⩾ 50 U/mL) correlates with diffuse-type gastric cancer. Few studies have reported on the relationship between the serum antibody titer and endoscopic findings. In *H. pylori*-infected patients, a high titer of serum antibody was associated with gastric nodularity and atrophy. In *H. pylori*-infected patients, the antibody titer decreased in patients aged 60 years. Intestinal metaplasia and gastric atrophy were related to age ⩾ 60 years in patients with positive titers.

Toyoshima O, Nishizawa T, Sakitani K, Yamakawa T, Takahashi Y, Yamamichi N, Hata K, Seto Y, Koike K, Watanabe H, Suzuki H. Serum anti-*Helicobacter pylori* antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study. *World J Gastroenterol* 2018; 24(35): 4061-4068 Available from: URL: http://www.wjgnet.com/1007-9327/full/v24/i35/4061.htm DOI: http://dx.doi.org/10.3748/wjg.v24.i35.4061

INTRODUCTION

Helicobacter pylori (*H. pylori*) infection is the main carcinogenic entity in the stomach, and eradicating it reduces the incidence of gastric cancer[1-5]. The ^{13}C-urea breath test (UBT), serum immunoglobulin G anti-*H. pylori* antibodies, stool antigen test, esophagogastroduodenoscopy (EGD), rapid urease test, culture, and pathology are used in routine practice to diagnose *H. pylori* infection. UBT is the gold standard for diagnosing *H. pylori* infection because its accuracy is the best of all these tests[2,6]. However, UBT requires the patients to stop using proton pump inhibitors or antibiotics.

Other than UBT, measuring the serum antibody titer is useful because serum antibody testing is easy, inexpensive, and hardly affected by changes in the stomach[7]. Some serological tests are of high-quality, and measuring the antibody titer once in adults makes it possible to observe subsequent changes in it with time and diagnose *H. pylori* infection[8-11]. Serum antibody titer is useful to evaluate both new-onset and successful eradication of the disease[12]. Furthermore, serum antibody titer is associated with the risk of gastric cancer. For example, a high titer correlates with diffuse-type of gastric cancer according to Lauren's classification. A positive-low titer and negative-high titer are associated with intestinal-type cancer[10,13-15]. An E-plate (Eiken Chemical, Tokyo, Japan) is frequently used for commercial serological examination in routine clinical practice in Japan. The E-plate is a direct enzyme immunoassay test designed to identify the Japanese strain of *H. pylori* and has been widely applied in large-scale studies in Japanese participants[14,16]. The manufacturer defined the cutoff E-plate titer as 10 U/mL and reported that its accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 94.0%, 95.2%, 92.6%, 93.8%, and 94.3%, respectively[17].

EGD is another diagnostic tool for *H. pylori* infection because it is able to not only accurately diagnose gastric malignancies, but also stratify the risk of gastric cancer by evaluating gastritis[3,18]. In Japan, EGD is performed to diagnose *H. pylori* infection in routine clinical practice. We previously reported that the endoscopic Kyoto classification of gastritis is associated not only with gastric cancer, but also with *H. pylori* infection[11].

Few studies have described the relationship between the serum anti-*H. pylori* antibody titers and endoscopic findings. We conducted this cross-sectional study to investigate the association between patients' baseline characteristics and endoscopic findings, and the serum antibody titer; subsequently, we determined the role of

serum antibody titers in these patients.

MATERIALS AND METHODS

Ethics

This retrospective study was approved by the ethical review committee of Hattori Clinic on September 7, 2017. Written informed consent was obtained from the participants. All clinical investigations were conducted according to the ethical guidelines of the Declaration of Helsinki.

Patients

We enrolled consecutive patients who underwent EGD and serum antibody testing at Toyoshima Endoscopy Clinic, which is an endoscopy specialty clinic, between September 2016 and August 2017. We included patients who were evaluated for *H. pylori* infection for the first time. The indications for EGD were the symptoms, abnormal findings on upper gastrointestinal radiography, screening, or surveillance for upper gastrointestinal diseases. The serum antibody titer was measured at the time of EGD. We excluded patients with a history of *H. pylori* eradication therapy, gastric cancer, or gastrectomy.

We grouped the subjects based on their serum antibody titers. Data on the patients' baseline characteristics, including age, sex, and indication for EGD, were collected.

The serum anti-H. pylori antibody

The serum antibody titer was measured using the following enzyme-linked immunoassay kit using antigens derived from Japanese individuals: E-plate Eiken H. pylori antibody Ⅱ kit (Eiken Chemical, Tokyo, Japan). The measurable titers were ≥ 3 U/mL and < 100 U/mL. The manufacturer recommended a cut-off value of 10 U/mL for *H. pylori* positivity. We previously reported that a titer of 3-9.9 U/mL had a lower negative predictive value than a total titer of < 10 U/mL did (83.1% *vs* 94.3%)[11]. A titer of 3-9.9 U/mL was also reported to indicate the risk of intestinal gastric cancer[15]. The previous study set the cut-off point as 50 U/mL to differentiate the low and high serum antibody titer groups, ensuring that the ratio of patients in both groups was approximately half of all *H. pylori*-seropositive subjects. A titer of 10-49.9 U/mL was reported to indicate the risk of intestinal gastric cancer, and a titer ≥ 50 U/mL was considered to indicate the risk of diffuse cancer[10].

In the present study, we divided the subjects into four groups according to their serum antibody titer as follows: group A: Titer < 3 U/mL (negative-low), group B: 3-9.9 U/mL (negative-high), Group C: 10-49.9 U/mL (positive-low), and group D: ≥ 50 U/mL (positive-high).

EGD

EGD was performed using the Olympus Evis Lucera Elite system with GIF-HQ290 or GIF-H290Z endoscope (Olympus Corporation, Tokyo, Japan) by expert physicians who jointly met and discussed the endoscopic images before this study. We performed EGD with the patient under conscious sedation with midazolam and/or pethidine hydrochloride. Other expert physicians retrospectively reviewed the EGD images. Discrepancies in diagnoses between the two sets of physicians were resolved through a discussion between them.

We evaluated the Kyoto classification of gastritis score[19]. The Kyoto classification of gastritis is based on the sum of the scores of the following five endoscopic findings, which are scored on a scale from 0-8: Atrophy, intestinal metaplasia (IM), enlarged folds, nodularity, and redness. A high score represents an increased risk of gastric cancer[15,20]. Gastric atrophy was classified according to the extent of mucosal atrophy, as described by Kimura and Takemoto[21]. Classifications of C-Ⅱ and C-Ⅲ were scored as 1, while those of O-Ⅰ to O-Ⅲ were scored as 2. IM is typically observed as grayish-white and slightly opalescent patches. IM within the antrum was scored as 1 and IM extending into the corpus was scored as 2. Enlarged folds greater than 5 mm were scored as 1. Nodularity is characterized by the appearance of multiple whitish elevated lesions, mainly in the pyloric gland mucosa. Nodularity was scored as 1. Diffuse redness refers to uniform redness involving the entire fundic gland mucosa. Redness with regular arrangements of collecting venules (RAC) was scored as 1 and that without RAC was scored as 2.

We also investigated gastric and duodenal ulcers. Ulcer scars were considered positive findings. RAC, fundic gland polyps, superficial gastritis, gastroesophageal reflux disease (GERD), Barrett's esophagus (BE), and hiatal hernia were considered *H. pylori* infection-negative endoscopic findings[19]. We defined the three endoscopic findings of hematin (bleeding spots), red streaks (linear erythema), and raised erosion as superficial gastritis. We defined grade A (one or more mucosal breaks of ≤ 5 mm in length) or worse of the Los Angeles classification of GERD as positive. Short-segment BE was classified as BE.

Statistical analysis

First, we evaluated the association between the serum antibody titer and age, sex, indication, and endoscopic findings using Kruskal-Wallis test for continuous variables and Cochran-Armitage test, chi-squared test, or polytomous logistic regression analysis for categorical variables in the four groups. Simultaneously, in comparisons between two groups, Steel-Dwass test was used for continuous variables. Second, we compared patients with *H. pylori* infection (groups C and D) based on age (< 40 years, 40-59 years, and ≥ 60 years) using the Cochran-Armitage test. Subsequently, we conducted a subgroup analysis of *H. pylori*-infected patients (groups C and D). We evaluated the effect of age, sex, indication, and endoscopic findings on the serum antibody titer in univariate analysis using the Mann-Whitney *U* test

Table 1 Characteristics and endoscopic findings of the serum antibody titers of the 874 study participants *n* (%)

Group	Total	A	B	C	D	*P* value
Serum antibody titer (U/mL)		< 3	3-9.9	10-49.9	⩾ 50	
Number	874	612 (70.0)	141 (16.1)	76 (8.7)	45 (5.1)	
Male	336 (38.4)	241 (39.4)	48 (34.0)	33 (43.4)	14 (31.1)	0.36
Age (yr), continuous, mean ± SD	48.3 ± 13.8	47.8 ± 13.1	47.1 ± 14.9	52.5 ± 15.8	50.9 ± 14.3	0.010
Age, categorical						0.002
< 40 yr	233	167 (71.7)	43 (18.5)	15 (6.4)	8 (3.4)	
40-59 yr	473	342 (72.3)	70 (14.8)	33 (7.0)	28 (5.9)	
⩾ 60 yr	168	103 (61.3)	28 (16.7)	28 (16.7)	9 (5.4)	
Indication						0.52
Symptoms	415	295	65	36	19	
Abnormal upper gastrointestinal radiography findings	93	60	14	12	7	
Screening	227	165	39	14	9	
Surveillance for upper gastrointestinal diseases	139	92	23	14	10	
Kyoto classification score, mean ± SD	0.43 ± 1.09	0.11 ± 0.57	0.43 ± 0.95	1.92 ± 1.70	2.33 ± 1.45	< 0.001
Open-type atrophy	65 (7.4)	11 (1.8)	11 (7.8)	21 (27.6)	22 (48.9)	< 0.001
Intestinal metaplasia	46 (5.3)	8 (1.3)	7 (5.0)	19 (25.0)	12 (26.7)	< 0.001
Enlarged folds	25 (2.9)	6 (1.0)	1 (0.7)	12 (15.8)	6 (13.3)	< 0.001
Nodularity	15 (1.7)	1 (0.2)	1 (0.7)	3 (3.9)	10 (22.2)	< 0.001
Diffuse redness	31 (3.5)	4 (0.7)	3 (2.1)	15 (19.7)	9 (20.0)	< 0.001
Gastric ulcer	14 (1.6)	9 (1.5)	0 (0)	5 (6.6)	0 (0.0)	0.43
Duodenal ulcer	19 (2.2)	3 (0.5)	2 (1.4)	10 (13.2)	4 (8.9)	< 0.001
Regular arrangement of collecting venules	470 (53.8)	376 (61.4)	75 (53.2)	16 (21.1)	3 (6.7)	< 0.001
Fundic gland polyps	311 (35.6)	259 (42.3)	48 (34.0)	4 (5.3)	0 (0.0)	< 0.001
Superficial gastritis	390 (44.6)	314 (51.3)	53 (37.6)	16 (21.1)	7 (15.6)	< 0.001
Gastroesophageal reflux disease	108 (12.4)	84 (13.7)	16 (11.3)	3 (3.9)	5 (11.1)	0.047
Barrett's esophagus	250 (28.6)	175(28.6)	41 (29.1)	23 (30.3)	11 (24.4)	0.95
Hiatal hernia	105 (12.0)	75 (12.3)	17 (12.1)	10 (13.2)	3 (6.7)	0.66

P-values were calculated by comparing groups A, B, C, and D using the Kruskal-Wallis test, Cochran-Armitage test, chi-squared test, or a polytomous logistic regression analysis, as appropriate. The Kyoto classification of gastritis score was estimated based on gastric atrophy, intestinal metaplasia, enlarged folds, nodularity, and redness[19]. SD: Standard deviation.

for continuous variables and Fisher's exact test or a binominal logistic regression analysis for categorical variables. We considered age 40-59 years as the reference. Finally, we performed multivariate analysis to identify the factors that were independently associated with the serum antibody titer using a binominal logistic regression analysis of the variables with a *P*-value less than 0.1 in the univariate analysis. A two-sided *P*-value less than 0.05 was considered statistically significant. The data were analyzed using Ekuseru-Toukei 2015 software (Social Survey Research Information, Tokyo, Japan).

RESULTS

A total of 919 patients were enrolled. We excluded 37 patients with a history of eradication therapy, four with a history of gastric cancer, and four with a history of gastrectomy. Finally, 874 patients were analyzed. The age of the study participants ranged between 16-95 years (mean: 48.3, standard deviation: 13.8). Thirty-eight percent of the patients were men. The mean Kyoto classification score was 0.43 (standard deviation: 1.09). There were 612 (70%), 141 (16%), 76 (8.7%), and 45 (5.1%) patients in groups A, B, C, and D, respectively (Table 1).

In our analysis of the association between serum antibody titer and baseline characteristics and endoscopic findings in all participants, we found that those in group C were significantly older than those in groups A and B (P = 0.018 and 0.025, respectively, Table 1). There was no difference in sex and indication between the patients in the four groups. We found that the Kyoto classification of gastritis score in group B was higher than that in group A, and those in groups C and D were higher than that in group B (mean score of groups A, B, C, and D: 0.11, 0.43, 1.92, and 2.33, respectively; group A *vs* B, group B *vs* C, and group B *vs* D: $P < 0.001$; group C *vs* D: $P = 0.32$, Table 1). Open-type atrophy (according to the Kimura-Takemoto classification), IM, enlarged folds, nodularity, diffuse redness, and duodenal ulcers occurred more frequently in patients with a higher titer than in those with a lower titer. However, the frequencies of RAC, fundic gland polyps, superficial gastritis, and GERD were lower in patients with a higher titer (Table 1). Representative endoscopic images are shown in Figure 1A-F. The proportion of patients in group C and D who were *H. pylori*-infected increased with age (< 40 years: 9.9%; 40-59 years: 12.9%; ⩾ 60 years: 22.0%; $P <$ 0.001, Figure 2A).

We conducted a sub-analysis of groups C and D to determine the difference between low-positive and high-positive serum antibody titers in *H. pylori*-infected patients. We compared the proportion of patients in groups C and D, stratified by age, as shown in Figure 2B. The proportion of patients in group D among those aged ⩾ 60 years was lower than that in patients aged 40-59

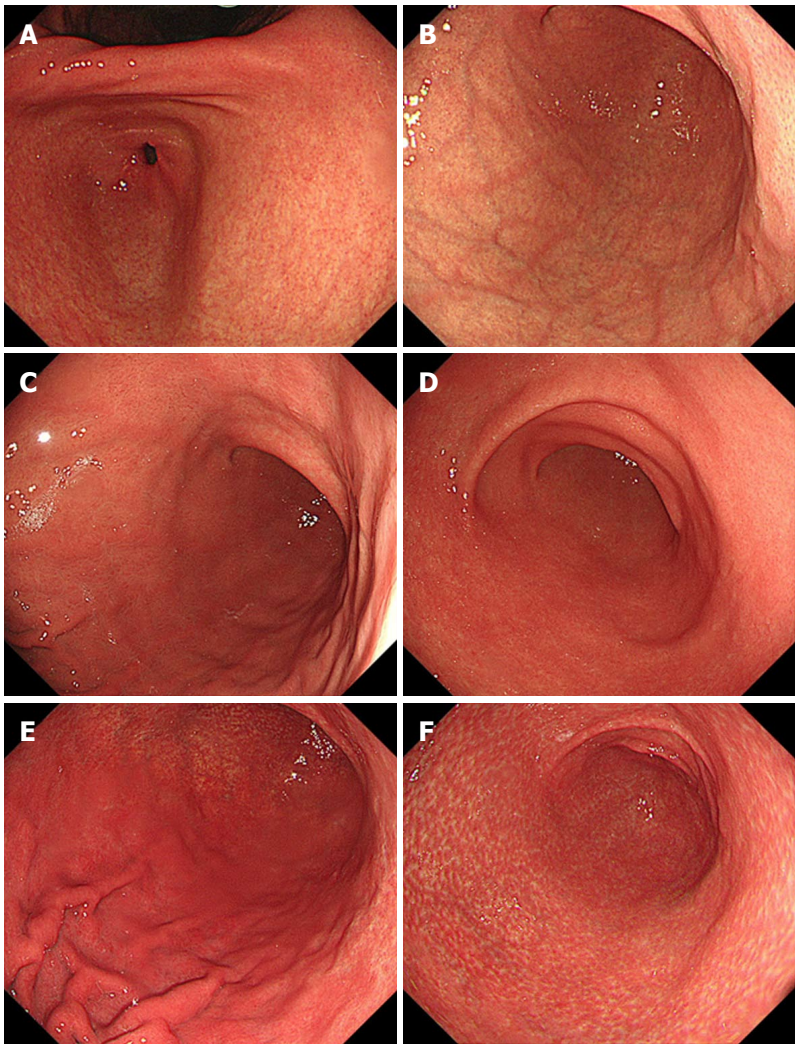

Figure 1 Representative endoscopic images of patients in each of the groups. A and B: Group A (serum antibody titer < 3 U/mL). A 20-year-old woman with a serum antibody titer < 3 U/mL and Kyoto classification score of 0. Atrophy was absent and RAC and superficial gastritis were present; C and D: Group C (serum antibody titer of 10-49.9 U/mL). A 36-year-old woman with a serum antibody titer of 25.5 U/mL and Kyoto classification score of 1. Closed-type atrophy was present and enlarged folds, nodularity, diffuse redness, and RAC were absent; E and F: Group D (serum antibody titer ⩾ 50 U/mL). A 50-year-old woman with a serum antibody titer ⩾ 100 U/mL and Kyoto classification score of 7. Open-type atrophy, enlarged folds, nodularity, and diffuse redness were present, and RAC was absent. RAC: Regular arrangement of collecting venules.

years [odds ratio (OR): 0.38, 95% confidence interval (CI): 0.15-0.94, P = 0.035]. There was no difference between patients aged < 40 and those between 40-59 years in terms of the proportion of patients in group D (OR: 0.63, 95%CI: 0.23-1.7, P = 0.36). In our comparison of the endoscopic findings of patients in groups C and D, we found that the frequencies of nodularity (P = 0.0042) and open-type atrophy (P = 0.018) were higher in group D than those in group C. The frequency of RAC was lower in group D than that in group C (P = 0.040). We evaluated the effect of patients' baseline characteristics and endoscopic findings on the serum antibody titer using multivariate analysis. Age ⩾ 60 years (OR: 0.24, 95%CI: 0.083-0.70, P = 0.0090), nodularity (OR: 7.1, 95%CI: 1.6-31, P = 0.0094), and open-type atrophy (OR: 3.9, 95%CI: 1.4-10, P = 0.0076) were independently associated with the serum antibody titer in *H. pylori*-infected patients (Table 2).

We compared the endoscopic findings of *H. pylori*-infected patients aged < 60 years and those ⩾ 60 years, as shown in Table 3. Intestinal metaplasia and gastric atrophy were related to age ⩾ 60 years in group C and D.

DISCUSSION

In this study, we investigated the association between patients' baseline characteristics and endoscopic findings and the serum antibody titer, and we clarified the role of serum antibody titers in patients with *H. pylori* infection. We found that nodularity and endoscopic open-type atrophy correlated with a high serum antibody titer in *H. pylori*-infected patients. In patients aged > 60 years, the serum antibody titer tended to decrease and IM tended to be more prevalent. Higher bacterial counts induce intense immune responses, resulting in higher

Table 2 Multivariate analysis of the effect of patients' characteristics and endoscopic findings on the serum antibody titer in *Helicobacter pylori*-infected patients

	Odds ratio	95%CI	*P*-value
Age < 40 yr[1]	0.69	0.21-2.2	0.54
Age ⩾ 60 yr[1]	0.24	0.083-0.70	0.0090
Open-type atrophy	3.9	1.4-10	0.0076
Nodularity	7.1	1.6-31	0.0094
Regular arrangement of collecting venules	0.36	0.088-1.5	0.16

[1]The odds ratios were calculated by considering age 40-59 years as reference. *P*-values were calculated using a binominal logistic regression analysis. CI: Confidence interval.

Table 3 Comparison of the endoscopic findings of *Helicobacter pylori*-infected patients aged < 60 years and those ⩾ 60 years

	Group C		*P* value	Group D		*P* value
	Age < 60 yr	Age ⩾ 60 yr		Age < 60 yr	Age ⩾ 60 yr	
Number	48	28		36	9	
Kyoto classification score, mean ± SD	1.52 ± 1.56	2.61 ± 1.75	0.0068	2.19 ± 1.53	2.89 ± 0.928	0.084
Open-type atrophy	7	14	0.0014	14	8	0.0098
Intestinal metaplasia	4	15	< 0.001	6	6	0.0062
Enlarged folds	8	4	1.0	3	3	0.084
Nodularity	2	1	1.0	10	0	0.17
Diffuse redness	9	6	0.77	9	0	0.17
Gastric ulcer	3	2	1.0	0	0	1.0
Duodenal ulcer	4	6	0.16	4	0	0.57
Regular arrangement of collecting venules	12	4	0.38	3	0	1.0
Fundic gland polyps	4	0	0.29	0	0	1.0
Superficial gastritis	11	5	0.77	7	0	0.31
Gastroesophageal reflux disease	2	1	1.0	3	2	0.26
Barrett's esophagus	13	10	0.45	9	2	1.0
Hiatal hernia	5	5	0.48	3	0	1.0

P-values were calculated with Mann-Whitney *U* test or Fisher's exact test, as appropriate. SD: Standard deviation.

serum antibody titers, while genetic differences among human hosts may affect the antibody levels in response to pathogens[4,22]. Tatemichi *et al*[14,23] demonstrated that a low-positive serum antibody titer was associated with intestinal-type gastric cancer and a high-positive titer was considered to indicate a high risk of diffuse-type cancer. The intestinal type of cancer develops through a sequence in which atrophy progresses and IM appears as a person ages, while the diffuse type of cancer is associated with high mucosal inflammation, particularly in young patients and those with nodularity[2,4,6,24-26]. In this study, we elucidated that the natural history of *H. pylori* infection is as follows: 40-59-year-old *H. pylori*-infected patients develop high inflammatory gastritis, frequently with nodularity and a high serum antibody titer, and they have a higher risk of developing diffuse-type gastric cancer. Subsequently, some *H. pylori*-infected patients older than 60 years of age have less gastric mucosal inflammation, progression of gastric atrophy, IM, decreased serum antibody titers, and the risk of developing intestinal-type gastric cancer.

In our investigation of all subjects, endoscopic findings indicating *H. pylori* infection were associated not only with positive or negative serum antibodies, but also with the serum antibody value. Regardless of whether they have an *H. pylori* infection, patients with a high serum antibody titer are more likely to have *H. pylori* infection-related endoscopic findings and are less likely to have *H. pylori* infection-negative endoscopic findings than are those with a lower serum antibody titer. Endoscopic findings are related to the risk of gastric cancer; therefore, these results confirmed that the serum antibody titer is associated with the risk of gastric cancer[2,6].

The *H. pylori* infection rate is declining in Japan; however, our study indicated that a large number of people have negative antibodies, but high titers. Since some previous studies have demonstrated that patients with negative-high serum antibody titers, especially those with *H. pylori* infection, were at a risk of developing intestinal gastric cancer, these results should be considered in clinical practice[10,11,14,15].

We previously reported that the *H. pylori* infection rate was 17% in group B[11]. The infection rate at the time serum antibodies were measured was 13% in people < 40 years old, 15% for those aged 40-59 years, and 25% for those ⩾ 60 years. Ueda *et al*[27] described that the prevalence of *H. pylori* infection in Japan was the highest in patients born between 1940-1949 and then decreased in those born in the ensuing years. Our results were concordant with those of their reports and might indicate the current infection rate in urban areas in Japan.

This study has some limitations. The subjects

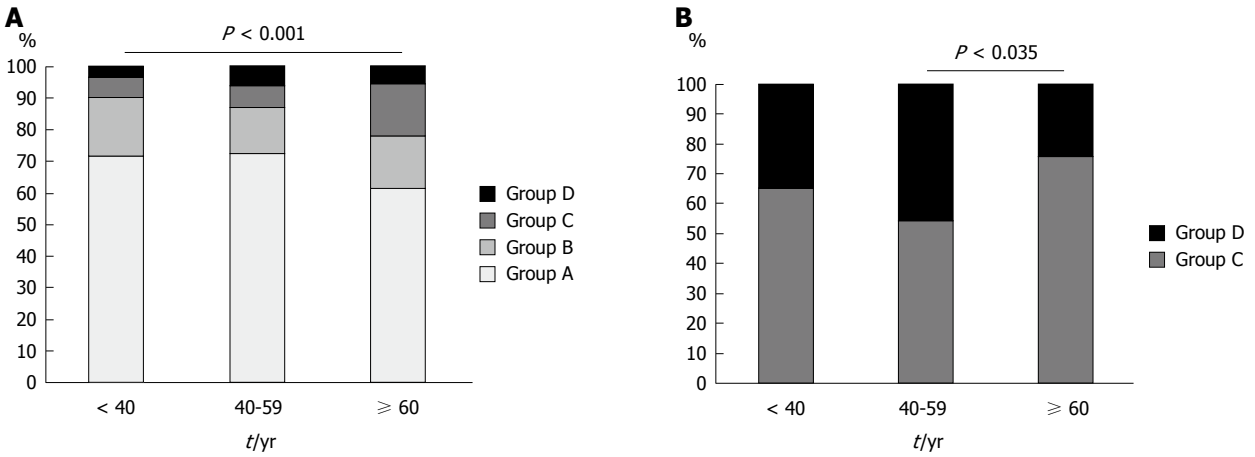

Figure 2 Proportion of *Helicobacter pylori*-infected patients. A: The proportion of patients in each of the groups, stratified by age. B: The proportion of patients in groups C and D, stratified by age.

included in the study were limited to outpatients. In the future, population-based research is expected. We did not diagnose *H. pylori* infection accurately because this study based on serum antibodies for diagnostic method. Investigating *H. pylori* infection with UBT is needed to determine the fluctuations in serum antibody titers in a time series in *H. pylori*-infected patients. Cytotoxin-associated gene A (CagA), which is a virulent form of *H. pylori,* was also not evaluated because 95% of Japanese patients with *H. pylori* infection have East Asian-type CagA[28]. Further investigations in those who do not have East Asian-type CagA-positive *H. pylori* infection is necessary.

In *H. pylori*-infected patients, high titers of serum anti-*H. pylori* antibodies were associated with gastric nodularity and atrophy, and the serum antibody titer tended to decrease in 60-year-old patients. Serum antibody titer reflects gastric mucosal inflammation; therefore, patient with high antibody titer may be at risk for diffuse gastric cancer and should be carefully screened in clinical practice.

ARTICLE HIGHLIGHTS

Research background

Serum anti-*Helicobacter pylori* (*H. pylori*) antibody titer and endoscopic findings are associated with the risk of gastric cancer.

Research motivation

Few studies have reported on the relationship between the serum antibody titer and endoscopic findings.

Research objectives

To clarify the role of serum anti-*H. pylori* antibody titers in gastric cancer.

Research methods

A cross-sectional study was conducted to investigate the effect of patients' baseline characteristics and endoscopic findings on their serum antibody titers. We excluded patients with a history of eradication therapy.

Research results

Gastric nodularity, atrophy, and age 40-59 years (*vs* age ⩾ 60 years) were correlated with a high serum antibody titer in *H. pylori*-infected patients.

Research conclusions

Serum antibody titer reflects gastric mucosal inflammation

Research perspective

In the future, population-based research is expected.

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