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ORIGINAL ARTICLE

Retrospective Cohort Study

Does the antibody production ability affect the serum anti-*Helicobacter pylori* IgG titer?

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Abstract

AIM: To investigate the relationship between serum titers of anti-*Helicobacter pylori* (*H. pylori*) immunoglobulin G (IgG) and hepatitis B virus surface antibody (HBsAb).

METHODS: Korean adults were included whose samples had positive Giemsa staining on endoscopic biopsy and were studied in the hepatitis B virus surface antigen (HBsAg)/HBsAb serologic assay, pepsinogen (PG) assay, and *H. pylori* serologic test on the same day. Subjects were excluded if they were positive for HBsAg, had a recent history of medication, or had other medical condition(s). We analyzed the effects of the following factors on serum titers of HBsAb and the anti-*H. pylori* IgG: Age, density of *H. pylori* infiltration in biopsy samples,

serum concentrations of PG Ⅰ and PG Ⅱ, PG Ⅰ/Ⅱ ratio, and white blood cell count.

RESULTS: Of 111 included subjects, 74 (66.7%) exhibited a positive HBsAb finding. The serum anti-*H. pylori* IgG titer did not correlate with the serum HBsAb titer (P = 0.185); however, it correlated with the degree of *H. pylori* infiltration on gastric biopsy (P < 0.001) and serum PG Ⅱ concentration (P = 0.042). According to the density of *H. pylori* infiltration on gastric biopsy, subjects could be subdivided into those with a marked (median: 3.95, range 0.82-4.00) (P = 0.458), moderate (median: 3.37, range 1.86-4.00), and mild *H. pylori* infiltrations (median: 2.39, range 0.36-4.00) (P < 0.001). Subjects with a marked *H. pylori* infiltration on gastric biopsy had the highest serological titer, whereas in subjects with moderate and mild *H. pylori* infiltrations titers were correspondingly lower (P < 0.001). After the successful eradication, significant decreases of the degree of *H. pylori* infiltration (P < 0.001), serum anti-*H. pylori* IgG titer (P < 0.001), and serum concentrations of PG I (P = 0.028) and PG Ⅱ (P = 0.028) were observed.

CONCLUSION: The anti-*H. pylori* IgG assay can be used to estimate the burden of bacteria in immunocompetent hosts with *H. pylori* infection, regardless of the HBsAb titer after HBV vaccination.

Key words: Antibody; *Helicobacter pylori*; Hepatitis B; Immunoglobulin G; Pepsinogen

Core tip: Koreans receive a routine childhood immunization program, including hepatitis B vaccinations, but serum hepatitis B virus (HBV) surface antibody responses are variable. It is unclear whether the beneficial functional immune aspects inherent in vaccine responders can be translated into a robust immune response after *Helicobacter pylori* (*H. pylori*) infection. In this study, the serum anti-*H. pylori* immunoglobulin G (IgG) titer appears to be significantly linked to the bacterial load of the stomach, regardless of the ability of antibody production after HBV vaccination. The serum anti-*H. pylori* IgG assay can be used to estimate the burden of bacteria in immunocompetent hosts with *H. pylori* infection.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) infection triggers inflammatory and immune responses[1,2]. The serum anti-*H. pylori* immunoglobulin G (IgG) titer is affected by various factors, including bacterial colonization, persistence, virulence, and host immune responses[3,4]. However, the persistence of *H. pylori* over decades in infected individuals suggests that the anti-*H. pylori* IgG does not play a role in the host immune response.

Serum antibody titers depend on the ability of individuals to produce antibodies. It is known that in Koreans, serum titers of the surface antibody against the hepatitis B virus (HBsAb) vary after hepatitis B virus (HBV) vaccinations[5]. Approximately 10% of Koreans do not develop an adequate immune response after they have received a vaccination series, and the rate of non-responsiveness correlates with older age, smoking, male gender, and the presence of chronic diseases[6,7]. Similarly, variable anti-*H. pylori* IgG titers may reflect different immune statuses in individuals with a similar *H. pylori* burden. Taken together with an established link between the HBV vaccine response and immune constitution[8,9], these findings suggest that the evaluation of the HBsAb response in HBV-vaccinated individuals could provide useful information regarding their immune states.

The immune response *via* the activation of helper T cells may stimulate production of both the *H. pylori* IgG and HBsAb[2,8], although the theoretical background underlying this mechanism remains uncertain. Little is known about the serum anti-*H. pylori* IgG titer as a parameter of the immune response to *H. pylori* infection because the knowledge of the *H. pylori* immunopathogenesis is limited. In addition, it is unclear whether the beneficial functional immune aspects inherent in vaccine responders can be translated into a robust immune response after *H. pylori* infection.

In the present study, gastric biopsy samples were analyzed to determine whether there is a correlation between the serum titers of the anti-*H. pylori* IgG and HBsAb in conditions with a similar *H. pylori* burden. In addition, variables that significantly correlated with the serum titers of the anti-*H. pylori* IgG and HBsAb were analyzed.

MATERIALS AND METHODS

Study population

In this cross-sectional study, Korean adults who underwent upper esophagogastroduodenoscopy (EGD) with gastric biopsies for pathology and Giemsa staining, serum pepsinogen (PG) assay, serum anti-*H. pylori* IgG assay and serum HBV surface antigen (HBsAg)/HBsAb assay on the same day at our center were included (Figure 1). The subjects were excluded in following conditions: (1) negative Giemsa staining; (2) positive HBsAg finding; (3) recent medication; (4) history of *H. pylori* eradication; (5) serum anti-*H. pylori* IgG testing other than the Vidas assay; or (6) the presence of disease(s) including any condition related to immunosuppressed state. This study was registered at ClinicalTrials.gov ID: KCT0001302 (https://cris.nih.go.kr) after the approval

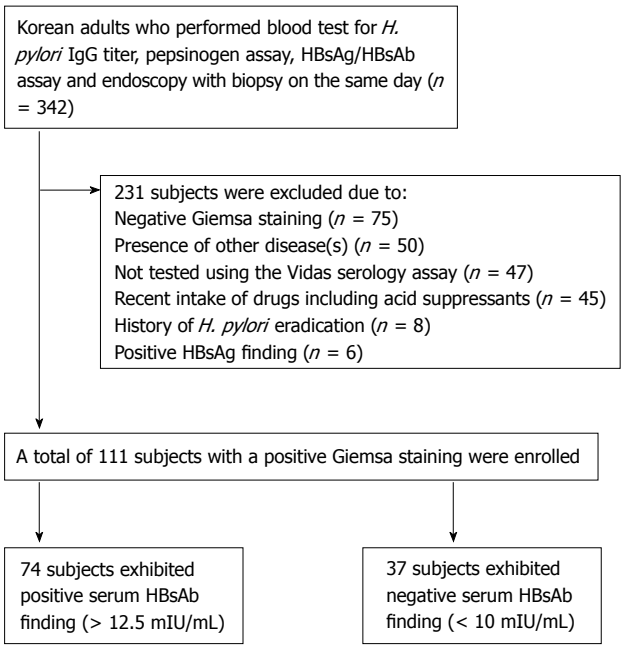

Figure 1 Flow of this study. Of the 342 Korean adults, only the subjects with a positive Giemsa staining were included in the study. *H. pylori*: *Helicobacter pylori*; HBsAg: Hepatitis B surface antigen; HBsAb: Hepatitis B surface antibody.

by the institutional review board of the Konkuk University School of Medicine (KUH1010625).

Serum anti-H. pylori IgG assay

Venous blood was sampled after 12 h of fasting for serum anti-*H. pylori* IgG assay, serum PG assay and serum HBsAg/HBsAb assay. The *H. pylori* serology titer was measured using the Vidas *H. pylori* IgG assay (BioMérieux, Marcy-l' Etoile, France) according to the manufacturer's instruction. Based on the Vidas *H. pylori* IgG assay package insert, positive finding was defined as a serum IgG titer equal or over 1.00 with sensitivity of 98.1% and specificity of 90.8%.

Serum PG assay

For serum PG Ⅰ and PG Ⅱ concentrations, the fasting blood samples were centrifuged and measured using the latex-enhanced turbidimetic immunoassay (HBi Co., Anyang, South Korea)[10]. Gastric corpus atrophy was diagnosed if the serum PG Ⅰ/Ⅱ ratio was less than 3.0 and the serum PG Ⅰ concentration was less than 70 ng/mL.

Serum HBsAg and HBsAb assay

Fasting blood sample was analyzed for the serum HBsAg and HBsAb levels using the ADVIA Centaur system (Siemens Healthcare Diagnostics Inc., Deerfield, IL, United States) as described in the previous study[11]. According to the manufacturer's instructions, negative findings were provided if the index value of HBsAg was of < 1.0 and if HBsAb was of < 7.5 mIU/mL on this chemiluminescent immunoassay. For HBsAg, equivocal findings were provided if the index value was equal to 1.0, while positive findings were provided if it was of > 1.0. For HBsAb, equivocal findings were provided if the index value was between 7.5 and 12.5 mIU/mL, while positive findings were provided if it was of > 12.5 mIU/mL.

Upper gastrointestinal endoscopy and gastric biopsy

Each participant underwent EGD on the same day of blood sampling at our center using GIF-H260 (Olympus, Tokyo, Japan) endoscope. During EGD, gastric biopsy was performed for pathology, histologic assay of *H. pylori* density and Giemsa staining. The biopsied specimens were fixed in 95% ethanol and embedded in paraffin blocks. Thereafter, the samples were sectioned and stained with hematoxylin and eosin (HE) and Giemsa. Histologic assay of *H. pylori* density were graded as mild, moderate and marked infiltration. If the density differed according to the biopsied site, the highest density and location were collected for the statistical analysis. Based on the Updated Sydney System, the grades were scored as either none (0), mild (1), moderate (2), or marked (3) for activity (the intensity of acute polymorphonuclear cell infiltrates), inflammation (the intensity of chronic mononuclear cell infiltrates), atrophy, and intestinal metaplasia.

H. pylori eradication and follow-up tests

A first-line therapy was performed with amoxicillin 1 g, clarithromycin 500 mg, and a proton pump inhibitor 20 mg twice daily to the subjects who agreed on *H. pylori* eradication. Four weeks after the eradication, a urease breath test was carried out. If it was positive, a second-line therapy was performed with tetracycline 500 mg, bismuth 300 mg four times a day, metronidazole 500 mg and a proton pump inhibitor twice a day. Follow-up tests for EGD and serum assays were performed as the initial tests described above.

Statistical analysis

For the statistical analysis, SPSS version 19.0 (SPSS Inc., Chicago, IL, United States) were used. A *P*-value less than 0.05 was considered statistically significant. Continuous variables were summarized as mean ± SD using the Student's *t*-test, while categorical variables were summarized as frequency (%) using the χ^2 test. The differences between the groups were compared using the ANOVA test for continuous variables.

The strength of correlation between the serum anti-*H. pylori* IgG titer and variables were estimated by correlation analysis. For continuous variables that were found to be related to severe *H. pylori* infiltration on gastric biopsy, a receiver operating characteristic (ROC) curve was constructed by plotting sensitivity (true-positive rate) against 1-specificity (false-positive rate). Accuracies of the significant variables were measured based on the area under the ROC curve (AUC) analysis with a 95%CI and standard error (SE) values.

Follow-up data were analyzed to compare the changes between the subjects with successful eradication

Table 1 Baseline characteristics of the included subjects *n* (%)

Variables	Subjects (*n* = 111)
Age (years old, mean ± SD)	55.3 ± 9.7
Gender (male:female)	66:45
Serum anti-*H. pylori* IgG titer (AU/mL, mean ± SD)	3.26 ± 0.97
Serum PG Ⅰ level (ng/mL, mean ± SD)	72.0 ± 28.8
Serum PG Ⅱ level (ng/mL, mean ± SD)	22.0 ± 9.2
Serum PG ratio (mean ± SD)	3.5 ± 1.2
Presence of corpus gastric atrophy as reflected by serum PG assay	23 (20.7)
Degree of *H. pylori* infiltration on biopsy	
Mild	14 (12.6)
Moderate	23 (20.7)
Marked	74 (66.7)
Scores based on Updated Sydney system	
Activity (mean ± SD)	1.92 ± 0.69
Chronic inflammation (mean ± SD)	2.04 ± 0.38
Atrophy (median with ranges)	0.97 (0-3)
Intestinal metaplasia (median with ranges)	0.64 (0-3)
Biopsied site	
Antrum	69 (62.2)
Body or angle	36 (32.4)
Fundus or cardia	6 (5.4)
Serum HBsAb titer (mIU/mL, median with ranges)	102.19 (1-1000)
Positive HBsAb assay	78 (70.3)
Platelet (× 10^3/μL, mean ± SD)	235.3 ± 48.2
White blood cell count (× 10^3/μL, mean ± SD)	5853.8 ± 1595.9
Neutrophil (%)	56.0 ± 9.3
Lymphocyte (%)	36.4 ± 8.7
Monocyte (%)	4.7 ± 1.6
Eosinophil (%)	1.84 (0-13)
Basophil (%)	0.41 (0-5)

HBsAb: Hepatitis B surface antibody; PG: Pepsinogen; *H. pylori*: *Helicobacter pylori*.

and those with persistent *H. pylori* infection. For the eradicated subjects, differences between pre- and post-eradication were analyzed using the Wilcoxon signed rank test. In similar, differences between initial and follow-up data were analyzed using the Wilcoxon signed-rank test in the subjects with persistent *H. pylori* infection.

RESULTS

Characteristics of the subjects

A total of 111 Korean adults were tested with the Vidas assay, and 74 (66.7%) subjects exhibited a positive HBsAb finding. The degrees of *H. pylori* infiltration on gastric biopsy were mild in 14 subjects, moderate in 23 subjects, and marked in 74 subjects (Table 1). The serum HBsAb findings did not differ between the groups (Table 2). Of all variables, marked degree of *H. pylori* infiltration showed the highest serum anti-*H. pylori* IgG titer ($P < 0.001$) and serum PG Ⅱ concentration ($P = 0.021$).

Variables correlated with serum HBsAb titer

There was no significant correlation between serum anti-*H. pylori* IgG titer and serum HBsAb titer ($P = 0.557$). The serum HBsAb titer was not related to any of the tested variables including the counts of platelet and white blood cell (Table 3).

Variables correlated with serum anti-H. pylori IgG titer

The serum anti-*H. pylori* IgG titer was positively correlated with the density of *H. pylori* infiltration on gastric biopsy ($P < 0.001$) and the serum PG Ⅱ concentrations ($P = 0.042$) using the correlation analysis. However, it was neither related to the positive HBsAb finding ($P = 0.905$) nor the serum HBsAb titer ($P = 0.557$). Distribution of serum anti-*H. pylori* IgG titers according to the *H. pylori* infiltration are shown in Figure 2.

Significant variables for *H. pylori* infiltration were analyzed using the ROC curve analysis (Figure 3). The cut-off value of serum anti-*H. pylori* IgG titer for correlating with severe density of *H. pylori* infiltration was 2.9 AU/mL with sensitivity and specificity values 81.1% and 51.4% (AUC = 0.659, 95%CI: 0.548-0.770, SE = 0.057, $P = 0.007$). However, serum PG Ⅱ concentration showed no statistical significance (AUC = 0.593, 95%CI: 0.481-0.705, SE = 0.057, $P = 0.111$) on the ROC analysis.

Subgroup analysis of the followed-up subjects

Of 111 included subjects, 41 were followed up for EGD and serum assays. Of these 41 followed-up subjects, 29 underwent *H. pylori* eradication therapy, and 4 failed on eradication. Therefore, a comparison was made between 25 subjects with successful eradication and 16 subjects with persistent infection (including 4 who failed on eradication). There was no difference on the initial test findings between the eradicated and persistent groups (Table 4).

After *H. pylori* eradication, significant decreases were noticed on the degree of *H. pylori* infiltration ($P < 0.001$), serum PG Ⅰ concentration ($P = 0.028$) and serum PG Ⅱ concentration ($P = 0.028$). As a consequence, the serum PG Ⅰ/Ⅱ ratio was significantly increased after eradication ($P = 0.028$). On the contrary, there was no significant differences between the initial and follow-up data on *H. pylori* infiltration ($P = 0.335$) and serum PG Ⅰ/Ⅱ ratio ($P = 0.395$) in the subjects with persistent *H. pylori* infection.

DISCUSSION

A significant link has been found between the serum anti-*H. pylori* IgG titer and the bacterial load of the stomach, regardless of the antibody producing capability of the host. Furthermore, significant decreases of the degree of *H. pylori* infiltration, serum anti-*H. pylori* IgG titer, and serum concentrations of PG Ⅰ and PG Ⅱ in the subjects with successfully eradicated *H. pylori* infection were observed. At the same time, such changes were not observed in the subjects with persistent *H. pylori* infection. Based on these results, the serum anti-*H. pylori* IgG titer could be considered an indicator of the

Table 2 Characteristics of the subjects according to the degree of *H. pylori* infiltration on gastric biopsy *n* (%)

Variables	Mild *H. pylori* infiltration (*n* = 14)	Moderate *H. pylori* infiltration (*n* = 23)	Marked *H. pylori* infiltration (*n* = 74)	*P* value
Age (yr, mean ± SD)	54.7 ± 8.4	57.7 ± 12.0	54.7 ± 9.0	0.428
Gender (male)	6 (42.9)	16 (69.6)	44 (59.5)	0.276
Serum anti-*H. pylori* IgG titer (AU/mL)[1]	2.39 (0.36-4.00)	3.37 (1.86-4.00)	3.95 (0.82-4.00)	< 0.001
Serum PG Ⅰ level (ng/mL, mean ± SD)	58.0 ± 19.3	75.5 ± 32.6	73.6 ± 28.7	0.146
Serum PG Ⅱ level (ng/mL, mean ± SD)	15.6 ± 6.3	22.9 ± 9.5	22.9 ± 9.2	0.021
Serum PG Ⅰ / Ⅱ ratio (mean ± SD)	4.1 ± 1.7	3.4 ± 1.0	3.4 ± 1.1	0.118
Presence of corpus gastric atrophy as reflected by PG assay	3 (21.4)	5 (21.7)	15 (20.3)	0.986
Biopsied site (antrum:body or angle:fundus or cardia)	1:3:0	15:7:1	43:26:5	0.625
Scores based on Updated Sydney system				
Activity (mean ± SD)	1.5 ± 0.7	1.9 ± 0.5	2.0 ± 0.7	0.034
Inflammation (mean ± SD)	1.9 ± 0.5	2.0 ± 0.2	2.1 ± 0.4	0.052
Atrophy (median with ranges)	0.8 (0-3)	1.3 (0-3)	0.9 (0-3)	0.589
Intestinal metaplasia (median with ranges)	0.6 (0-3)	0.9 (0-3)	0.6 (0-3)	0.771
Positive HBsAb finding	9 (64.3)	17 (73.9)	52 (70.3)	0.824
HBsAb titer (mIU/mL)[1]	174.9 (1-1000)	120.7 (1-1000)	86.8 (1-1000)	0.601
Platelet (× 10^3/μL, mean ± SD)	252.2 ± 41.9	231.9 ± 51.9	233.2 ± 48.1	0.375
White blood cell count (× 10^3/μL, mean ± SD)	5688.6 ± 1552.3	5780.0 ± 1390.9	5908.0 ± 1678.0	0.869
Neutrophil (%)	55.1 ± 9.3	54.9 ± 10.3	45.5 ± 9.1	0.702
Lymphocyte (%)	36.8 ± 8.7	37.0 ± 9.8	36.2 ± 8.4	0.919
Monocyte (%)	4.9 ± 1.6	4.9 ± 2.1	4.6 ± 1.5	0.732
Eosinophil (%)	2.4 (0-6)	2.0 (0-1)	1.8 (0-1)	0.819
Basophil (%)	0.4 (0-1)	0.5 (0-1)	0.4 (0-5)	0.771

[1]Values are shown as median with ranges due to asymmetrical distribution. HBsAb: Hepatitis B surface antibody; PG: Pepsinogen; *H. pylori*: *Helicobacter pylori*.

Table 3 Correlation analysis for the serum anti-*H. pylori* IgG titer and serum HBsAb titer

Variables	Correlation coefficient	*P* value
Serum anti-*H. pylori* IgG titer		
Old age	-0.009	0.924
Increased density of *H. pylori* infiltration	0.389	< 0.001
Increased serum PG Ⅰ level	0.116	0.224
Increased serum PG Ⅱ level	0.194	0.042
Increased serum PG Ⅰ / Ⅱ ratio	-0.18	0.059
Higher degree of activity	0.272	0.004
Higher degree of inflammation	0.125	0.192
Higher degree of atrophy	0.021	0.826
Higher degree of intestinal metaplasia	-0.047	0.624
Presence of gastric corpus atrophy as reflected by PG assay	-0.015	0.876
Increased HBsAb titer	-0.056	0.557
Increased platelet count	-0.061	0.522
Increased white blood cell count	-0.078	0.417
Serum HBsAb titer		
Old age	-0.088	0.358
Increased density of *H. pylori* infiltration	-0.07	0.466
Increased serum PG Ⅰ level	0.046	0.634
Increased serum PG Ⅱ level	-0.054	0.572
Increased serum PG Ⅰ / Ⅱ ratio	0.136	0.154
Higher degree of activity	0.077	0.42
Higher degree of inflammation	-0.112	0.24
Higher degree of atrophy	0.036	0.706
Higher degree of intestinal metaplasia	0.054	0.573
Presence of gastric corpus atrophy as reflected by PG assay	-0.164	0.086
Increased platelet count	0.008	0.935
Increased white blood cell count	-0.069	0.473

HBsAb: Hepatitis B surface antibody; PG: Pepsinogen; *H. pylori*: *Helicobacter pylori*.

bacterial burden in infected subjects. This finding may lead to novel opportunities toward enhancing *H. pylori* eradication.

H. pylori has the ability to persist despite a vast array of host immune responses, which appear to differ between infected subjects[12]. The present findings

Table 4 Findings of the followed-up subjects *n* (%)

	Successful *H. pylori* eradication (*n* = 25)	Persistent *H. pylori* infection (*n* = 16)	*P* value	Before eradication	After eradication	*P* value (Z[1])	Initial	Follow-up	*P* value
Initial test findings									
Age (yr, mean ± SD)	52.3 ± 7.9	55.3 ± 12.7	0.351						
Gender (male:female)	15:10	9:07	1						
Degree of *H. pylori* infiltration on biopsy (mild:moderate: marked)	4:05:16	2:04:10	0.907						
Anti-*H. pylori* IgG titer (AU/mL, mean ± SD)	3.00 ± 1.17	3.17 ± 0.92	0.632						
PG Ⅰ level (ng/mL, mean ± SD)	79.3 ± 31.7	64.9 ± 23.4	0.126						
PG Ⅱ level (ng/mL, mean ± SD)	23.4 ± 8.5	18.9 ± 9.1	0.117						
PG ratio (mean ± SD)	3.5 ± 1.1	3.9 ± 1.5	0.419						
Presence of corpus gastric atrophy as reflected by serum PG assay	4 (16.0)	2 (12.5)	0.566						
HBsAb titer (mIU/mL, median with ranges)	72.2 (3.1-1000)	170.3 (3.1-1000)	0.632						
Positive HBsAb assay	16 (64)	12 (75)	0.513						
Duration of the follow-up period (months, median with ranges)	18.1 (2-61)	20.2 (6-41)	0.887						
Subjects with successful *H. pylori* eradication (*n* = 25)									
Follow-up test findings									
Degree of *H. pylori* infiltration on biopsy (none:mild:moderate: marked)				0:4:5:16	25:0:0:0	< 0.001 (-4.520)			
Anti-*H. pylori* IgG assay (negative:lowest:middle:highest quartiles)[2]				3:2:14:6	20:4:1:0	< 0.001 (-4.171)			
PG Ⅰ level (ng/mL, mean ± SD)				79.3 ± 31.7	54.2 ± 14.5	0.028 (-2.201)			
PG Ⅱ level (ng/mL, mean ± SD)				23.4 ± 8.5	7.0 ± 1.7	0.028 (-2.201)			
PG ratio (mean ± SD)				3.5 ± 1.1	7.8 ± 1.6	0.028 (-2.200)			
HBsAb titer (mIU/mL, median with ranges)				72.5 (3.1-1000)	18.4 (3.1-1000)	0.308			
Subjects with persistent *H. pylori* infection (*n* = 16)									
Follow-up test findings									
Degree of *H. pylori* infiltration on biopsy (none:mild:moderate: marked)							0:2:4:10	1:3:2:10	0.335
Anti-*H. pylori* IgG assay (negative:lowest:middle:highest quartiles)[2]							1:0:8:7	0:2:7:7	1.18
PG Ⅰ level (ng/mL, mean ± SD)							64.9 ± 23.4	71.8 ± 35.2	1
PG Ⅱ level (ng/mL, mean ± SD)							18.9 ± 9.1	21.4 ± 10.3	0.779
PG ratio (mean ± SD)							3.9 ± 1.5	3.6 ± 0.8	0.395
HBsAb titer (mIU/mL, median with ranges)							170.3 (3.1-1000)	202.1 (3.1-1000)	0.314

[1]Z values are shown for the significant variables using Wilcoxon signed rank test; [2]The serum anti-*H. pylori* IgG titer was compared using the quartiles because it was measured using the Vidas *H. pylori* IgG assay until 2012, and using the Chorus *H. pylori* IgG assay thereafter. SD: Standard deviation; HBsAb: Hepatitis B surface antibody; PG: Pepsinogen; *H. pylori*: *Helicobacter pylori*.

suggest that the serum anti-*H. pylori* IgG titer is related to the burden of *H. pylori* antigens, because lymphocytes are sensitized to the *H. pylori* antigens and IgG is produced by B cells against a variety of *H. pylori* surface (flagellar) proteins and bacterial toxins. Furthermore, the development of the positive HBV vaccine antibody response involves not only the T cell functions, but also other functional pathways, including B cell activity and antigen presentation of the peptide-based vaccine[6,7,13]. These findings suggest that the amount of IgG production *via* the host immune response upon *H. pylori* infection is more closely related to the burden of *H. pylori* antigens than to the ability of the host to produce antibodies, which is gauged by the serum HBsAb titer.

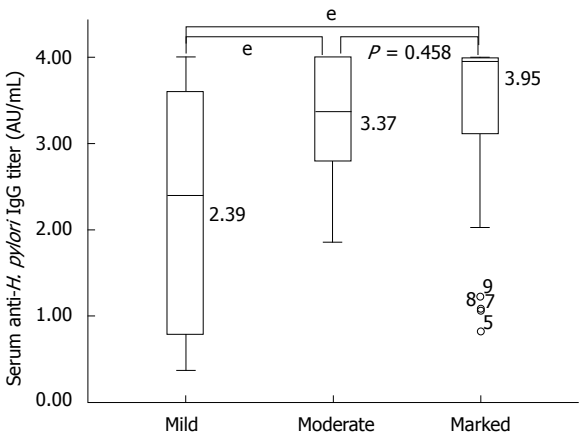

Figure 2 The serum anti-*H. pylori* IgG titer according to the degree of *H. pylori* infiltration on gastric biopsy. Subjects with marked *H. pylori* infiltration showed the highest serology titer followed by those with moderate and mild infiltrations.

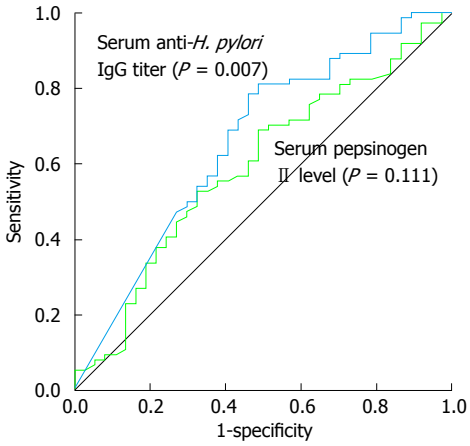

Figure 3 Receiver operating characteristic curves for correlating with the density of *H. pylori* infiltration. The cut-off value of the serum anti-*H. pylori* IgG titer for correlating with severe density of *H. pylori* infiltration was 2.9 AU/ml (AUC = 0.659, 95%CI: 0.548-0.770, SE = 0.057, *P* = 0.007). There was no significant finding with regard to the serum PG Ⅱ concentration (AUC = 0.593, 95%CI: 0.481-0.705, SE = 0.057, *P* = 0.111).

In the present study, it was found that the serum anti-*H. pylori* IgG titer positively correlated with the degree of *H. pylori* infiltration on the biopsied specimen, regardless of the biopsied site of the stomach. This finding is consistent with the results of previous studies, in which the significance of the serum anti-*H. pylori* IgG titer was demonstrated, and indirectly indicates the relationship between the severity of histological changes and mucosal bacterial density[14-16]. Evaluation of the serum anti-*H. pylori* IgG titer can detect *H. pylori* infection in patients with marked atrophic gastritis and metaplastic gastritis, even in the event of negative biopsy specimens, and provide an indicator of the efficacy of *H. pylori* eradication[17-20].

Serum PG assays are widely used for the measurements of gastric inflammation[21,22] and in combination with the serum anti-*H. pylori* IgG assay during gastric cancer screening[10,23]. The link between the immune response and *H. pylori* infection-induced gastric inflammation, as measured by the serum PG assay, has been established[24]. In that study, the *Salmonella typhi* (*S. typhi*) IgG seroconversion was more common in the subjects with the *H. pylori* infection than in those without it after anti-*S. typhi* vaccination. In the present study, the serum anti-*H. pylori* IgG titer positively correlated with the serum PG levels and *H. pylori* infiltration in biopsy samples, regardless of the HBsAb titer. This suggests that the bacterial burden directly correlates with the degree of gastric inflammation, despite the differential development and recruitment of specifically committed cells that occurred after the *H. pylori* infection in the subjects.

The limitation of this study is that only 41 subjects underwent the follow-up tests. Furthermore, the serum anti-*H. pylori* IgG titer was followed up using the Chorus *H. pylori* IgG assay (DIESSE Diagnostica Senese, Siena, Italy) because the initially used Vidas *H. pylori* IgG assay was not available after 2012. Despite these limitations, significant differences in the follow-up findings of serum assays and *H. pylori* infiltration were found only in the subjects in whom *H. pylori* eradication was successfully achieved. In support of these observations, a recent study described a high rate of concurrence and similar diagnostic accuracy between the Vidas *H. pylori* IgG assay and the Chorus *H. pylori* IgG assay[25].

In conclusion, the findings of this study show that the serum anti-*H. pylori* IgG titer is significantly associated with the bacterial load of the stomach, regardless of the antibody producing capability of the host. Although the anti-*H. pylori* IgG response requires preserved function of several immune pathways, it appears that the serum anti-*H. pylori* IgG titer correlates with the intragastric bacterial load rather than with the HBsAb titer. The serum anti-*H. pylori* IgG titer is therefore useful for estimating the bacterial burden of *H. pylori* infection.

COMMENTS

Background

Serum antibody titers depend on the ability of individuals to produce antibodies. It is unclear whether the beneficial functional immune aspects inherent in hepatitis B virus vaccine responders can be translated into a robust immune response after *Helicobacter pylori* (*H. pylori*) infection.

Research frontiers

In this cross-sectional study, consecutive Korean adults were included whose samples had positive Giemsa staining on endoscopic biopsy and were studied in the hepatitis B virus surface antigen (HBsAg)/HBsAb serologic assay, pepsinogen (PG) assay, and anti-*H. pylori* immunoglobulin G (IgG) assay on the same day. This approach allows the authors to demonstrate correlation between serum HBsAb titer and anti-*H. pylori* IgG titer.

Innovations and breakthrough

In this study the authors demonstrated that the serum anti-*H. pylori* IgG titer correlates with the intragastric bacterial load rather than with the HBsAb titer.

Applications

The serum anti-*H. pylori* IgG titer is therefore useful for estimating the bacterial

burden of *H. pylori* infection.

Terminology

Serologic testing for IgG antibodies to *H. pylori* is commonly used noninvasive method to diagnose *H. pylori* infection. The IgG antibody titer is indicative of the severity of gastritis and the presence of *H. pylori*.

Peer-review

This is a novel look at a very interesting topic. In the clinical finding presented in this manuscript, the authors showed that the serum anti-*H. pylori* IgG assay can be used to estimate the burden of bacteria in immunocompetent hosts with *H. pylori* infection.

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