Risk Factors for Helicobacter pylori Infection and Endoscopic Reflux Esophagitis in Healthy Young Japanese Volunteers

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Abstract:
Objective  The aim of this study was to determine the prevalence and risk factors of reflux esophagitis and Helicobacter pylori (H. pylori) infection and their interrelationship in healthy young Japanese volunteers.
Methods  Between 2010 and 2016, 550 fifth-year medical students at Saga Medical School, aged 22 to 30 years, underwent upper gastrointestinal endoscopy and completed a questionnaire (frequency scale for symptoms of gastroesophageal reflux disease). H. pylori infection was determined by detecting urinary immunoglobulin G antibodies.
Results  H. pylori antibodies were detected in 45 of the 550 subjects (8.2%). Endoscopic reflux esophagitis was detected in 38 out of 550 (6.9%): grade A in 37 subjects (97.3%) and grade B in 1. Most subjects with reflux esophagitis were H. pylori-negative (35/37). Nodular gastritis was observed in 33.3% (15/45) of H. pylori-positive subjects. The risk factors for H. pylori infection were drinking well water in childhood, nodular gastritis, and duodenal ulcer scars. The risk factors for endoscopic reflux esophagitis were male gender and obesity (body mass index ≥25).
Conclusion  This study describes the risk factors for H. pylori infection and reflux esophagitis in healthy young Japanese subjects. The prevalence of reflux esophagitis was relatively high, and the infection rate of H. pylori was low compared with the aged Japanese population.

Key words: endoscopy, dyspepsia, gastroesophageal reflux, nodular gastritis, F scale

Introduction

A recent study in Japan indicated that the Helicobacter pylori (H. pylori) infection rate increased with age by around 1% per year, whereas the population-wide infection rate decreased in a time-dependent manner (1). Several diseases, such as peptic ulcers, mucosa-associated lymphoid tissue lymphoma, gastric cancers and chronic gastritis, are induced by H. pylori infection (2, 3). Chronic gastritis, including nodular gastritis, has been recognized in relatively young adults (4, 5), but the prevalence of nodular gastritis in young Japanese adults is still unclear.

Several studies in Japan have shown that the eradication of H. pylori induced endoscopic reflux esophagitis, suggesting that H. pylori infection prevented endoscopic reflux esophagitis by decreasing gastric acid secretion (6-10). Several studies in Western countries also suggested that the eradication of H. pylori induced reflux esophagitis (11, 12). However, the precise relationship between H. pylori infection and endoscopic reflux esophagitis is not clear, and a direct relationship between H. pylori infection and reflux
esophagitis in young adults has not been clearly demonstrated.

The infection route of H. pylori in Japan is still unknown, but several studies have suggested that transmission between family members is an important route (5, 13). The drinking of well water might also be a major infection route in developing countries (6, 14).

Several studies in Japan have indicated risk factors for endoscopic reflux esopahgitis (gender, obesity, hiatus herniation, smoking, alcohol consumption), but few studies have focused on risk factors for young adults (15). The aim of the present study was to determine i) the prevalence of reflux esophagitis and H. pylori infection in healthy young Japanese adults and ii) the risk factors for H. pylori infection and endoscopic reflux esophagitis.

### Materials and Methods

The present study included 550 fifth-year medical students (men/women: 315/235) in Saga Medical School who provided their informed consent to participate between 2010 and 2016. The mean age of the students was 22.5±1.8 years, and the mean body mass index (BMI) was 21.0±3.1 kg/m². Among the 550 subjects, 38 (6.9%) had endoscopic esophagitis (grade A: 37, grade B: 1), and 173 (31.5%) had hiatus herniation. The frequency of short-segmented Barrett’s esophagus was relatively high (10.5%, n=58), whereas no subjects had long-segmented Barrett’s esophagus. The frequency of positive H. pylori infection was 8.2% (45/550). No subjects received eradication therapy for H. pylori infection, and none had taken gastric acid secretion inhibitors. A duodenal ulcer scar was detected in 7 subjects (1.3%), including 3 H. pylori-positive subjects. Nodular gastritis was detected in 16 subjects (7 men, 9 women) (2.9%), including 15 H. pylori-positive subjects, by gastrointestinal endoscopy.

Table 2 shows the risk factors for H. pylori infection in these subjects evaluated by a multivariate analysis. Gender and body weight were not markedly different between the H. pylori-positive and H. pylori-negative subjects. The smoking rate in both the positive and negative groups was very low, and the difference was not significant. The frequency of alcohol consumption tended to be higher in the positive subjects than in the negative ones, but not significantly so. The rates of hiatus herniation and Barrett’s esophagus were not markedly different between the two positivity groups. The frequency of drinking well water in

Table 1. Characteristics of Healthy Young Adult Volunteers Who Underwent Upper Gastrointestinal Endoscopy in Japan (n=550).

| Characteristic                      | Frequency  |
|------------------------------------|------------|
| Age (years)                        | 22.5 ± 1.8 |
| Gender (men/women)                 | 315/235    |
| Body mass index (kg/m²)            | 21.0 ± 3.1 |
| Endoscopic esophagitis (Los Angeles classification) |           |
| Grade 0                            | 512 (93.0%)|
| Grade A                            | 37 (6.7%)  |
| Grade B                            | 1 (0.2%)   |
| Grade C                            | 0          |
| Grade D                            | 0          |
| Hiatus herniation                  | 173 (31.5%)|
| Barrett’s esophagus                |            |
| Short segment                       | 58 (10.5%) |
| Long segment                       | 0          |
| Duodenal ulcers scar               | 7 (1.3%)   |
| Nodular gastritis                  | 16 (2.9%)  |
| Helicobacter pylori infection      | 45 (8.2%)  |

#### Table 2. Results

Table 1 shows the characteristics of the 550 subjects (315 men, 235 women) in the present study. The mean age of the subjects was 22.5±1.8 years, and the mean body mass index (BMI) was 21.0±3.1 kg/m². Among the 550 subjects, 38 (6.9%) had endoscopic esophagitis (grade A: 37, grade B: 1), and 173 (31.5%) had hiatus herniation. The frequency of short-segmented Barrett’s esophagus was relatively high (10.5%, n=58), whereas no subjects had long-segmented Barrett’s esophagus. The frequency of positive H. pylori infection was 8.2% (45/550). No subjects received eradication therapy for H. pylori infection, and none had taken gastric acid secretion inhibitors. A duodenal ulcer scar was detected in 7 subjects (1.3%), including 3 H. pylori-positive subjects. Nodular gastritis was detected in 16 subjects (7 men, 9 women) (2.9%), including 15 H. pylori-positive subjects, by gastrointestinal endoscopy.

#### Results

Table 2 shows the risk factors for H. pylori infection in these subjects evaluated by a multivariate analysis. Gender and body weight were not markedly different between the H. pylori-positive and H. pylori-negative subjects. The smoking rate in both the positive and negative groups was very low, and the difference was not significant. The frequency of alcohol consumption tended to be higher in the positive subjects than in the negative ones, but not significantly so. The rates of hiatus herniation and Barrett’s esophagus were not markedly different between the two positivity groups. The frequency of drinking well water in
might not be effective for detecting reflux esophagitis in that a symptomatic diagnosis with the FSSG questionnaire markedly different for any question. These results suggest non-reflux groups. The rate of positive symptoms was not scores were not markedly different between the reflux and reflux esophagitis symptoms are shown in Table 4. The FSSG questionnaire, were not risk factors for reflux esophagitis. High BMI was a risk factor for endoscopic reflux esophagitis. Other factors, including smoking, alcohol consumption, hiatus herniation, Barrett’s esophagus and H. pylori infection, were not risk factors for reflux esophagitis.

The results of the FSSG questionnaire for endoscopic reflux esophagitis were more frequently seen in men than in women. Specifically, 34 out of 315 men (10.8%) but only 4 out of 235 women (1.7%) suffered from reflux esophagitis. High BMI was a risk factor for endoscopic reflux esophagitis. Other factors, including smoking, alcohol consumption, hiatus herniation, Barrett’s esophagus and H. pylori infection, were not risk factors for reflux esophagitis.

The results of the FSSG questionnaire for endoscopic reflux esophagitis symptoms are shown in Table 4. The FSSG scores were not markedly different between the reflux and non-reflux groups. The rate of positive symptoms was not markedly different for any question. These results suggest that a symptomatic diagnosis with the FSSG questionnaire might not be effective for detecting reflux esophagitis in young adults.

### Discussion

The present study revealed that the H. pylori infection rate was less than 10% in young adults in Japan, which was consistent with previous results (1). This study also indicated that the risk factors for H. pylori infection in young adults were drinking well water in childhood, nodular gastritis and duodenal ulcer scars shown by upper gastrointestinal endoscopy. Previous studies in Japan have suggested that a major infection route is transmission between family members-i.e. to a child from siblings, parents or grandparents (13, 20, 21). The results of this study suggested that drinking well water in childhood might be another infection route for H. pylori in Japan, as observed in developing countries (14).

The prevalence of endoscopic esophagitis was not affected by H. pylori infection in young adults in the present study. Several previous studies in Japan showed that the prevalence of reflux esophagitis was lower in H. pylori-positive subjects than in H. pylori-negative subjects (6-10). The low infection rate in young adults as indicated in this study might be one of the reasons why H. pylori infection showed no influence on endoscopic esophagitis.

Previous studies have reported that nodular gastritis was diagnosed in relatively young women (4, 5). The present study demonstrated that the prevalence of nodular gastritis was 33% in H. pylori positive adults in their 20s in Japan, and the prevalence was not markedly different between men and women. Regarding atrophic gastritis, the present study

### Table 2. Risk Factors For Helicobacter Pylori infection as Evaluated by a Multivariate Analysis.

| Factors                  | H. pylori (+) | H. pylori (-) | Odds ratio | 95% CI  | p value |
|--------------------------|--------------|---------------|------------|---------|---------|
| Gender (men:women)       | 28:17        | 287:218       | 0.81       | 0.42-1.55 | 0.52    |
| BMI (>25)                | 4 (8.9%)     | 23 (4.6%)     | 2.91       | 0.88-9.64 | 0.08    |
| Smoking                  | 1 (2.2%)     | 44 (8.7%)     | 0.43       | 0.54-3.33 | 0.42    |
| Alcohol                  | 42 (93.3%)   | 438 (79.6%)   | 2.58       | 0.75-8.94 | 0.14    |
| Herniation               | 12 (26.7%)   | 161 (31.9%)   | 0.69       | 0.34-1.43 | 0.32    |
| Barrett’s esophagus      | 3 (6.7%)     | 55 (10.9%)    | 0.62       | 0.18-2.15 | 0.45    |
| Drinking well water      | 21 (46.7%)   | 82 (16.2%)    | 4.96       | 2.59-9.50 | <0.01   |

The age is presented as the mean ± standard deviation. H. pylori: Helicobacter pylori, BMI: body mass index (kg/m²), DU: duodenal ulcer, 95% CI: confidence interval.

### Table 3. Risk Factors for Endoscopic Reflux Esophagitis as Evaluated by a Multivariate Analysis.

| Factors                  | Esophagitis (+) | Esophagitis (-) | Odds ratio | 95% CI  | p value |
|--------------------------|-----------------|-----------------|------------|---------|---------|
| Gender (men:women)       | 34:4            | 281:231         | 0.14       | 0.05-0.43 | <0.01   |
| BMI (>25)                | 6 (15.8%)       | 21 (4.1%)       | 5.23       | 1.76-15.52 | <0.01   |
| Smoking                  | 1 (2.6%)        | 25 (4.9%)       | 0.37       | 0.05-3.02 | 0.36    |
| Alcohol consumption      | 33 (89.5%)      | 447 (86.9%)     | 1.39       | 0.48-4.05 | 0.54    |
| Herniation               | 17 (44.7%)      | 156 (30.3%)     | 1.35       | 0.66-2.75 | 0.41    |
| Barrett’s esophagus      | 5 (13.2%)       | 53 (10.2%)      | 1.39       | 0.49-4.00 | 0.54    |
| H. pylori                | 3 (7.9%)        | 42 (8.2%)       | 0.66       | 0.15-2.90 | 0.58    |

The age is presented as the mean ± standard deviation. BMI: body mass index (kg/m²), 95% CI: confidence interval, DU: duodenal ulcer, H. pylori: Helicobacter pylori.
did not evaluate the presence of atrophic gastritis with the upper gastrointestinal endoscopy.

The risk factors for endoscopic reflux esophagitis were male gender and obesity (BMI > 25). Our previous study indicated that obesity was a risk factor for reflux esophagitis in men in their 30s and 40s (22, 23), and several studies in Japan have shown that obesity exacerbates endoscopic reflux esophagitis (24, 25). These data are compatible with the present results for endoscopic reflux esophagitis in adults in their 20s. Why the prevalence of reflux esophagitis was high in men in the present study was not clear, although obesity and alcohol drinking are more popular in men than in women in Japan. However, in the present study, endoscopic esophagitis was not affected by alcohol consumption, smoking or hiatus herniation. In addition, the smoking rate was very low in the present study (4.7%) compared with the Japanese average rate (19.3%), possibly due to that the subjects in the present study were medical students and therefore more conscientious of the effects of smoking. Alcohol consumption was evaluated based on the frequency of drinking, not by the quantity consumed. The rate of hiatus hernia was also low in the present study.

Clinical symptoms were evaluated by the FSSG questionnaire (17, 26-29) before the endoscopic examination. Regarding the scores for the 12 evaluated symptoms, there were no marked differences between the normal subjects and those with endoscopic esophagitis. All of the subjects with reflux esophagitis in the present study had mild symptoms of grade A or B under the Los Angeles classification, which might be one of reasons why they did not complain of clinical symptoms.

*H. pylori* infection was only detected by the presence of urinary IgG antibodies with immunochromatography and not evaluated by other methods, such as the rapid urease test or the urea breath test. The sensitivity of the immunochromatography method is lower than with other methods, which might be one reason why there were several *H. pylori*-negative subjects among those with duodenal ulcer scars or nodular gastritis. This observation warrants further explanation.

In summary, the present study of healthy young adult volunteers who received upper gastrointestinal endoscopy revealed the following: i) the infection rate of *H. pylori* was 8.2%, ii) the prevalence of endoscopic reflux esophagitis was 6.9%, iii) *H. pylori* infection had no influence on the prevalence of endoscopic reflux esophagitis, iv) nodular gastritis accounted for 33.3% of *H. pylori* infection, v) the risk factors for *H. pylori* infection were drinking well water in childhood, nodular gastritis and duodenal ulcer scars and vi) the risk factors for endoscopic reflux esophagitis were male gender and obesity (BMI > 25).

The authors state that they have no Conflict of Interest (COI).

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