The Association between Metaplasia and Gastric Malignancy with Helicobacter pylori Infection

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ABSTRACT

Background: Helicobacter pylori (H. pylori) infection is the main cause of peptic ulcer disease, gastric mucosa metaplasia, and gastric malignancy. The hypothesis of this study is whether there’s an association between metaplasia and gastric malignancy with H. pylori infection.

Method: We conducted a retrospective study on 1,127 dyspepsia subjects who performed endoscopy between 2001 to 2011 at a hospital in North Jakarta. Data is obtained based on endoscopy and histopathology data. Investigation of H. pylori in this study using histopathology examination.

Results: Of the 1,127 dyspepsia subjects who performed endoscopy and biopsy, there were 130 (11.54%) H. pylori-positive subjects. Gender proportion was composed of 55.37% men and 44.63% women, with median age was 47 years. On the histopathology examination, we obtained 45 metaplasia subjects with median age of 45 years and 7 malignancy subjects with median age of 64 years. Metaplasia was found in 33 of 997 (3.31%) H. pylori-negative subjects and 12 of 130 (9.23%) H. pylori-positive subjects. All gastric malignancy subjects had H. pylori-negative results.

Conclusion: There was an association between metaplasia and H. pylori infection, but no association between gastric malignancy and H. pylori infection.

Keywords: metaplasia, gastric malignancy, H. pylori infection, retrospective study

ABSTRAK


Hasil: Dari 1.127 subyek dyspepsia yang dilakukan endoskopi dan biopsi, terdapat 130 (11,54%) subyek positif H. pylori. Proporsi jenis kelamin didapatkan 53,37% laki-laki dan 44,63% perempuan dengan median usia 47 tahun. Pada pemeriksaan histopatologi, kami mendapatkan 45 subyek dengan gambaran metaplasia dengan median usia 45 tahun dan 7 subyek mengalami keganasan lambung dengan median usia 64 tahun. Metaplasia didapatkan pada 33 dari 997 (3,31%) subyek negatif H. pylori dan 12 dari 130 (9,23%) subyek positif H. pylori. Semua subyek keganasan lambung memberikan hasil H. pylori yang negatif.
**INTRODUCTION**

*H. pylori* is one of the most common infections in human. This infection is associated with a number of important conditions in the upper gastrointestinal tract, such as chronic gastritis, peptic ulcer disease (PUD), and gastric malignancy. The prevalence of *H. pylori* tends to be related to socioeconomic conditions, therefore the infection is more prevalent in developing countries. The prevalence of *H. pylori* in developed countries is generally below 40% and this number is dominated by adults and elderly. In Asia, the prevalence of *H. pylori* infection ranges from 54% to 76%. Each year, about 990,000 individuals in the world are diagnosed with gastric malignancy, and 738,000 of them die. This causes gastric malignancy is in the fourth position as the most common cancer, and the second position as most common cause of cancer death.

Gastric malignancy usually develops due to mucosal changes from non-atrophic gastritis to atrophic gastritis, intestinal metaplasia and dysplasia, and adenocarcinoma. Atrophic gastritis and intestinal metaplasia may be considered as a pre-neoplastic gastric lesion. *H. pylori* infection is the first step in the presence of gastric carcinogenesis cascade. Several studies hypothesize that treatment of *H. pylori* may prevent the development of intestinal metaplasia into gastric adenocarcinoma. There is no definitive population data suggesting that *H. pylori* eradication can decrease the incidence of gastric adenocarcinoma. The hypothesis of this study is whether there is an association between metaplasia and gastric malignancy with *H. pylori* infection.

**METHOD**

This retrospective study was conducted in hospitals at North Jakarta between 2001-2011. A total of 1,127 subjects, who underwent endoscopy, with complaints of dyspepsia, defined as pain or discomfort centered in the upper abdomen and lasting for one month or more, were included in the study. Subjects with a history of gastrointestinal surgery were excluded. Informed consent is obtained from subjects who will undergo endoscopic examination. All endoscopic examinations are performed by endoscopic expert. Endoscopic findings are evaluated, such as macroscopic changes, i.e. erythema, erosion, mucosal defects, absence of rugae, or bleeding spots.

The data taken are endoscopic and histopathology data from research subjects. In this study, *H. pylori* examination used histopathological examination. The biopsy sample was examined in anatomical pathology department. Data were entered and analyzed using statistical package for social science (SPSS) for windows version 16.0. The analysis was done using Chi-square test to determine the association between metaplasia and gastric malignancy, and *H. pylori* infection. A statistically significant level was defined as p < 0.05.

**RESULTS**

Total of 1,127 of dyspepsia subjects were enrolled in the study and the median age of the subjects was 47 years old. The proportion of gender was 55.37% (n = 624) men and 44.63% (n = 503) women. Out of 1,127 subjects, 130 (11.54%) were positive and 997 (88.46%) were negative for *H. pylori* infection. Table 1 describes the characteristics among subjects enrolled in the study.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Total</th>
<th><em>H. pylori</em>-positive</th>
<th><em>H. pylori</em>-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Men</td>
<td>624</td>
<td>78 (12.5)</td>
<td>546 (87.5)</td>
</tr>
<tr>
<td>Women</td>
<td>503</td>
<td>52 (10.34)</td>
<td>451 (89.66)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>394</td>
<td>44 (11.17)</td>
<td>350 (88.83)</td>
</tr>
<tr>
<td>40-59</td>
<td>436</td>
<td>53 (12.16)</td>
<td>383 (87.84)</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>297</td>
<td>33 (11.11)</td>
<td>264 (88.89)</td>
</tr>
<tr>
<td>Total</td>
<td>1,127</td>
<td>130 (11.94)</td>
<td>997 (88.46)</td>
</tr>
</tbody>
</table>

A comparison of histologic findings between two groups is explained in Table 2. A significant association was observed between *H. pylori*-positive infection and the intestinal metaplasia findings (p < 0.05). We obtained 45 subjects have metaplasia with a median age of 45 years and 7 subjects have gastric malignancy with a median age of 64 years. Metaplasia was found in 33 of 997 (3.31%) *H. pylori*-negative subjects and 12 of 130 (9.23%) *H. pylori*-positive subjects. All subjects of gastric malignancy were found have negative *H. pylori* infection. We found that there were no association between gastric malignancy and *H. pylori* infection (p > 0.05).
Subjects with metaplasia and gastric malignancy were dominated by men, i.e. 57.8% and 57.1%. Intestinal metaplasia and gastric malignancy are more common in elderly subjects, i.e. 51.1% and 71.4% (Table 3). A strongly significant positive association was noted between histologic findings (intestinal metaplasia and gastric malignancy) and elderly (p < 0.05).

Table 3. Histologic findings of patients based on gender and age

<table>
<thead>
<tr>
<th>Metaplasia</th>
<th>Gastric malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>26 (57.8)</td>
</tr>
<tr>
<td>Women</td>
<td>19 (42.2)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>9 (20)</td>
</tr>
<tr>
<td>40-59</td>
<td>13 (28.9)</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>23 (51.1)</td>
</tr>
<tr>
<td>Total</td>
<td>45 (100)</td>
</tr>
</tbody>
</table>

DISCUSSION

Colonization of H. pylori is not a stand-alone disorder, but it is a condition that causes a relative risk to the development of various clinical disorders that vary from upper gastrointestinal tract to hepatobiliary tract. The incidence of H. pylori infection varies in different countries of the world. Study about H. pylori also conducted in Yogyakarta that involved 92 subjects. There were 22.8% of subjects with H. pylori infection.

Our study found that the prevalence of subjects with H. pylori infection dominated by men, i.e. 60% (n = 78). This finding agreed with previous reports. Based on 18 large studies, De Martel et al concluded that H. pylori infection are more common in men than women. Another study by Sasidharan et al also explained that prevalence rate of H. pylori infection on Malaysian patients was higher in men (51.9%).

We found an association between H. pylori infection with an intestinal metaplasia in our study subjects (p < 0.05). Previous study conducted in Korea evidence a higher prevalence of intestinal metaplasia in subjects with H. pylori infection (44.3%).

Intestinal metaplasia is more common in our elderly subjects (51.1%). Intestinal metaplasia appears to be caused by either aging, process and result of H. pylori infection, or both of them. Progression H. pylori infection to intestinal metaplasia usually occurs in the elderly due to long periods of H. pylori infection.

Previous study reported that H. pylori infection rates increase with age, i.e. 51.6% at age around 30 years and 70% at age above 60 years. Ohkuma et al explained that the prevalence of intestinal metaplasia increased significantly in elderly (OR = 5.5) with H. pylori infection.

Geographical data affect the prevalence of H. pylori and incidence of gastric malignancy. H. pylori colonization is estimated to increase the risk of gastric malignancy by tenfold. The development of gastric malignancy consists of several stages, i.e. inflammation of gastric mucosa associated with H. pylori infection, atrophic gastritis, intestinal metaplasia, dysplasia, and intestinal type gastric malignancy. The histologic developmental mechanisms remain unknown. Intestinal metaplasia is defined as the replacement of gastric columnar epithelial cells into intestinal morphological cells, which is characterized by goblet cells, Paneth cells, and absorptive cells. Point of no return can occur in the histological cascade of chronic gastritis to adenocarcinoma, where H. pylori eradication can’t prevent gastric malignancy occurring in this condition. A meta-analysis of 12 studies conducted on 2,658 patients concluded that H. pylori eradication had an impact on improvements in gastric corpus atrophy, but did not have any effect on intestinal metaplasia. However, H. pylori elimination is still a promising strategy for reducing the incidence of gastric malignancy. Leung et al concluded that H. pylori eradication has a protective effect in progression to a pre-neoplastic gastric lesion in Chinese populations. Study that involved 1,526 Japanese populations provide evidence that H. pylori infection significantly increases the risk of gastric malignancy. Uemura et al reported that gastric malignancy can develop in about 3% of subjects infected with H. pylori, compared with uninfected subjects. H. pylori eradication may significantly reduce the risk of gastric malignancy in infected subjects, with no gastric pre-neoplastic lesions. Diagnosis of gastric pre-neoplastic lesions, such as atrophic gastritis and intestinal metaplasia, of endoscopy results are helpful for individuals at high risk of gastric malignancy. Health check-up endoscopy is a well-known screening test for gastric malignancy.

In our study, there was a gastric malignancy of the subjects with a negative H. pylori infection. Some studies described about H. pylori-negative gastric cancers (HpNGC) cases, and the prevalence was about 0.42-5.4% of the gastric malignancy total incidence. The prevalence of HpNGC is found to be very low in the Japanese population (0.66%), with pathological...
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characteristics distinct from gastric malignancy in general. Kato et al reports that a small proportion of patients with gastric malignancy indicates a multifactorial carcinogen without H. pylori infection. This indicates that gastric malignancy can still exist without H. pylori infection, with an incidence of 2-10.6%. Diagnostic criteria for HpNGC vary greatly among case reports, and have not been definitively defined. Etiology of gastric malignancy, in addition to H. pylori infection, is usually associated with several factors, such as lifestyle, viral infections, autoimmune diseases, and germline mutations. Nevertheless, the main factor causing HpNGC remains unclear.

This study also has limitations. The location of endoscopy and severity has not been classified. In additional, patients with metaplasia and H. pylori-negative infection have either had a previous H. pylori infection or currently have an ongoing infection, even though no bacteria were found in the histologic analyses. The large amount of analytical experience from endoscopic experts can also help increase the rate of detection of intestinal metaplasia in future studies.

CONCLUSION

There was an association between metaplasia and H. pylori infection, but no association between gastric malignancy and H. pylori infection. Further research with a larger sample or case series that includes subjects with gastric malignancy is needed to provide evidence regarding the association between these two things.

REFERENCES