RESEARCH ARTICLE

Prevalence and Risk Factors for *Helicobacter Pylori* Infection among Healthy Inhabitants in Northern Jakarta, Indonesia

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Abstract

Background: The prevalence of *Helicobacter pylori (H. pylori*) infection in Indonesia has been reported to be exceedingly low. The purpose of our study was to confirm whether this is the case in Northern Jakarta using a sensitive 13C-urea breath test (UBT), and to examine any associations with lifestyle/environment factors and potential routes of transmission. **Methods:** We recruited a total of 196 subjects from a low-income community in Northern Jakarta, Indonesia, data from 193 who completed a questionnaire about their lifestyle/environment and had UBT being included as the final. Odds ratios (ORs) adjusted for sex and age with 95% confidence intervals (CIs) were calculated using a logistic regression model. **Results:** The overall *H. pylori* infection rate was 15.0% (95%CI, 10.3-20.9), with variation among Javanese (9.1%, total=77), Buginese (40.0%, 35), Betawi (9.1%, 33), Sundanese (3.7%, 27), and Batak (40.0%, 5). On multivariate analysis, the ORs for intake of soybean milk, cucumber more than once a week, infrequent hand washing practice before meals, and alcohol consumption were 0.10 (95%CI: 0.01-0.97), 6.61 (95%CI: 1.87-23.3), 4.10 (95%CI: 1.15-14.6), and 61.9 (95%CI: 1.67-2300.8), respectively. Rates for Buginese (OR=7.84; 95%CI: 1.82-33.8) and Batak (OR=20.1; 95%CI: 1.90-213.2) were significantly higher than for Javanese. **Conclusions:** The *H. pylori* infection rate in this study was relatively low, in line with previous studies. Regarding ethnicity factors, Buginese and Batak reported eating food using fingers more frequently than Javanese, Betawi, and Sundanese. Our study indicated that person-person transmission is possible in this low prevalence area. The low infection rates for *H. pylori* among Javanese, Betawi, and Sundanese ethnics could be partly due to their sanitary practices.

Keywords: *H. pylori*- infection- Indonesia

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Introduction

Helicobacter pylori (H. pylori) is a pathogen of gastritis, and peptic ulcer, gastric cancer and mucosa-associated lymphoid tissue lymphoma (Peek et al,. 2002). The prevalence is higher in developing countries than developed countries (Go., 2002). *H. pylori* can be transmitted via fecal-oral or oral-oral route, depending on lifestyle/environment factors such as hygiene, water supply, and living conditions (Abebaw et al., 2014; Goh et al, 2011; Laszewicz et al., 2014; Miftahussurur et al., 2014; Salah et al., 2009). For example, in Japan the infrastructure before World War was not well established. Most of Japanese at the time were under unsanitary condition. That is why *H. pylori* infection rate is reported to be so high in Japan, although the rate has been declining recently due to improvement in the infrastructure (Asaka et al., 1992; Hirayama et al., 2014; Watanabe et al., 2015).

In Indonesia, the prevalence of *H. pylori* infection is expected to be high, because *H. pylori* infection is related to sanitary condition, and the economic status (Malaty et al., 1992), and the infrastructure of Indonesia is still developing. However, the reported prevalence of *H. pylori* infection in Mataram was 11.2% (Zhao et al., 2012), in Purwokerto was 36.5%, (Arinton, 2011), in Yogyakarta was 30.6% (Syam et al., 2006), and in Jakarta was 8% (Syam et al., 2006) and 9.5% (Syam et al., 2005). These unexpected results could be due to the sensitivity and specificity of the test used to detect *H. pylori* and due to the different study populations (Miftahussurur et al., 2015).

The purpose of this study was to evaluate the prevalence of *H. pylori* infection in Northern Jakarta by using 13C-urea breath test (UBT), a noninvasive test for detecting *H. pylori* infection (Bilal et al., 2007; Bruden et al., 2011; Patel et al., 2014; Redeen et al., 2011) and to examine possible associations of lifestyle/environment factors with *H. pylori* infection in order to reveal routes of transmission.

Materials and Methods

Study subjects

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We recruited 196 healthy subjects aged 14 to 80 years attending the primary health care center in a low-income community in the suburbs of Northern Jakarta, Indonesia. This study was conducted from April to December, 2015. Exclusion criteria included subjects who had a history of gastric surgery, or in 2 weeks prior to UBT, had *H. pylori* eradication therapy, antibiotics, bismuth-containing compounds, H2-receptor blockers or proton pump inhibitors.

13C-urea breath test (UBT)

UBT was performed at the point-of-contact after an overnight fast according to the manufacture's instruction. Those with ≥ 2.5‰ value were defined as being infected with *H. pylori*. Of 196 subjects, one had breakfast and could not be tested, and two could not be measured due to a low CO2 concentration.

Questionnaire about lifestyle/environment

The questionnaire included items on demographic characteristics, marital status, living condition, personal hygiene, monthly income, education level, smoking, alcohol, source of drinking water, dietary habit, medical history and medications. Questions on hand wash practice before meal and after toilet use, and the use of fingers to consume food (sanitary practices) had four categories namely always, most of my meal time, sometimes, never. Questions on food intake frequency had 6 categories namely never, less than 1 times/week, 1-2 times/week, 3-4 times/week, 5-6 times/week and everyday, and the ones on food intake quantity had 7 categories namely never, 1-2 pieces (plates)/week, 3-4 pieces (plates)/week, 5-6 pieces (plates)/week, 1-2 pieces (plates)/day, 3-4 pieces (plates)/day and ≥5 pieces (plates)/day. The information was obtained through face-to-face interview lasting approximately 15 minutes by two internists (N.D and F.H).

This study was approved by the ethics committees at Dr. Cipto Mangunkusumo Teaching Hospital (Jakarta, Indonesia) and Kyoritu Hospital (Nagoya, Japan). All subjects were enrolled after informed consent was obtained.

Statistical Analysis

Frequencies were compared by a χ^2 test or a Fisher's exact probability test. The 95% confidence intervals (CIs) of the percentage were calculated under the assumption of a binominal distribution. Odds ratios (ORs) adjusted for sex and age (a continuous variable) with 95% CIs were calculated using a logistic regression model. In the model, we grouped the 4 categories for the sanitary practices into 2 categories namely always and less frequent. Similarly, we grouped 6 categories for food intake frequency into 2 categories namely<1 time/week and ≥1 times/week and 7 categories for food intake quantity into 2 categories namely <3 pieces (plates)/week and ≥3 pieces (plates)/week. Education level was grouped into three categories namely low (elementary school or less), medium (junior or senior high school), high (university or above).

After univariate analysis, the lifestyle and environment factors with p<0.10 were entered to a multivariate logistic regression analysis. These calculations were performed by computer program STATA Version 13 (STATA Corp, College Station, TX).

Results

Of 196 subjects, 3 subjects failed to complete UBT. So, 193 subjected were included in this study. Of them, one subject did not know his age. The overall *H. pylori* infection rate was 15.0% (95%CI, 10.3-20.9): 10.6% (95%CI, 3.6-23.1) among men and 16.4% (95%CI, 10.8-23.5) among women. The *H. pylori* infection rates according to the characteristic are shown in Table 1. The prevalence of *H. pylori* increased slightly with age without significance. Among occupations, housewives tended to be infected more frequently. There was a statistically significant difference in *H. pylori* infection rates among ethnics.

The association between environment factors and *H. pylori* infection is presented in Table 2. The prevalence of *H. pylori* infection did not significantly differ by the number of persons per household, per room, and per bed, education level, annual income, and marital status. Infrequent use of fingers to eat food prevented *H. pylori* infection significantly (OR=0.28, 95% CI, 0.12-0.67). Infrequent hand wash practice before meal increased risk of *H. pylori* infection with marginal significance (OR=2.45, 95% CI, 0.99-6.06). Infrequent hand wash practice after toilet was not significantly associated with risk of *H. pylori* infection.

Table 3 shows the association between *H. pylori* infection and lifestyle factors. The statistically significant risk factors for *H. pylori* infection were intake of cucumber more than one time a week (OR=4.23, 95%CI, 1.69-10.6). Intake of chicken (OR=2.45, 95% CI, 0.97-6.20), green vegetable (OR=6.99, 95% CI, 0.91-53.6), carrot (OR= 2.55, 95% CI, 0.97-6.72) and alcohol (OR=6.68 for former drinker, 95% CI, 0.86-52.0) increased the risk of *H. pylori* infection and drinking soybean milk (OR=0.15, 95% CI, 0.02-1.18) decreased it with marginal significance. There was no association between *H. pylori* infection and, the source of drinking water (data not shown) and smoking, although we could collect the information on source of drinking water from 96 subjects.

The significant and marginally significant environment and lifestyle factors we identified in univariate analysis, as well as sex, age, and ethnic, were analyzed by a multivariate logistic regression model (Table 4). The infrequent use of fingers to eat food decreased significantly the risk of *H. pylori* infection in model 1 which excluded ethnic, but not in model 2 which included ethnic. Drinking soybean milk more than one time a week decreased the risk of *H. pylori* infection (OR=0.1, 95% CI, 0.01-0.97). The infrequent hand wash before meal (OR=4.10, 95% CI, 1.15-14.6) and intake of cucumber more than one time a week (OR=6.61, 95% CI, 1.87-23.3), and drinking alcohol (OR=61.9 for former drinker, 95% CI, 1.67-2300.8) were significantly associated with the risk of *H. pylori* infection. The OR for the intake of green vegetable more than one time a week was 10.6 (95% CI, 0.96-117.3). Moreover, Buginese (OR=7.84, 95% CI, 1.82-33.8) and Batak (OR=20.1, 95% CI, 1.90-213.2) were more likely than

Table 1. Characteristics of Study Subjects

	Total	n (infected)	*Hp*+[1]% (95%%)	p value[2]
Sex				
Male	47	5	10.6 (3.6-23.1)	0.48
Female	146	24	16.4 (10.8-23.5)	
Age				
≤19	9	0	0.0 (0.0-33.6)	0.49
20-39	27	4	14.8 (4.2-33.7)	
30-39	43	5	11.6 (3.9-25.1)	
40-49	49	7	14.3 (5.9-27.2)	
50-59	35	5	14.3 (4.8-30.3)	
60-69	24	6	25.0 (9.8-46.7)	
≥70	6	2	33.3 (4.3-77.7)	
Occupation				
Housewife	86	18	20.9 (12.9-31.0)	0.09
Labor	24	1	4.2 (0.1-21.1)	
Unemployed	20	4	20.0 (5.7-43.7)	
Others	63	6	9.5 (3.6-19.6)	
Ethnic				
Javanese	77	7	9.1 (3.7-17.8)	<0.001
Buginese	35	14	40.0 (23.9-57.9)	
Betawi	33	3	9.1 (1.9-24.3)	
Sundanese	27	1	3.7 (0.1-19.0)	
Batak	5	2	40.0 (5.3-85.3)	
Others3	16	2	12.5 (1.6-38.3)	

[1]Helicobacter pylori positve; [2]p value was calculated by a χ^2 test or a Fisher's exact probability test ; [3]Malay (2); Minangkabau (2); Maduranese (2); Tolaki (of 2, 1 positive); Chinese (1); Baliness (1); Kendari (of 1, 1 positive); Jambi (1); Manado (1); Palembang (1); Riau (1); Timor (1)

Javanese to be infected with *H. pylori.*

Discussion

We observed a low infection rate in Northern Jakarta, Indonesia. This result was similar to the previous studies in Jakarta (Saragih et al., 2007; Syam et al., 2005; Syam et al., 2006), which used histological examination and rapid urease test. However, the sensitivity and specificity of these tests are not high. Conversely, UBT is often considered as gold standard due to the high accuracy (Bilal et al., 2007; Bruden et al., 2011; Patel et al., 2014; Redeen et al., 2011). Therefore, we had to evaluate whether *H. pylori* infection rate is low in Jakarta, Indonesia by using UBT.

It has been reported that the source of drinking water is an important factor. Syam AF et al and other studies have reported that the use of river/well as drinking water is risk of *H. pylori* infection (Brown et al., 2002; Ozaydin et al., 2013; Syam et al., 2015). In addition, Japanese were supposed to drink water from well before World War. It could explain why the prevalence rate of *H. pylori* is high in Japan (Karita et al., 2003; Iso et al., 2005; Yang et al., 1999). But this study did not confirm the association

Table 2. Age-Sex Adjusted Odds Ratios (ORs) and 95% Confidence Intervals of Environment Factors for *Helicobacter Pylori* Infection

	n (infected)/N (Total)	OR	95%CI
Education			
Low	15/90	1.0	Reference
Medium	13/89	1.3	0.54-3.32
High	1/14	0.7	0.08-6.34
Income per month			
<Rp. 2,500,000	23/134	1.0	Reference
≥Rp. 2,500,000	6/59	0.7	0.6-1.95
Marital status			
Married	28/188	1.0	Reference
Single	1/5	3.5	0.32-38.1
Persons household			
≤3	8/76	1.0	Reference
≥4	21/117	2.0	0.82-4.84
Persons per room			
≤1	9/55	1.0	Reference
≥2	20/138	0.9	0.40-2.29
Persons per a bed			
≤1	5/22	1.0	Reference
≥2	24/171	0.7	0.23-2.21
Sharing tooth-brush			
Yes	8/163	1.0	Reference
No	1/30	0.2	0.03-1.66
Using fingers to eat food			
Always	12/37	1.0	Reference
Less frequent	17/156	0.3	0.12-0.67
Hand washing before meal			
Always	8/79	1.0	Reference
Less frequent	21/114	2.4	0.99-6.06
Hand washing after toilet			
Always	15/112	1.0	Reference
Less frequent	14/80	1.6	0.71-3.74

(data not shown), because only 3.1% (3/96) drunk river/well water. It has been reported that drinking well water in childhood is risk for *H. pylori* infection (Karita et al., 2003; Yang et al., 1999). We also collected information on the source of water from 62 subjects, which they drunk while their childhood. Of them, 35.5% (22/62) drunk river/well water, but it was not associated with the risk of *H. pylori* infection, neither. Moreover, 75.8% always boiled water before drinking, irrespective of the source of drinking water. It is conceivable that boiling water could prevent them from *H. pylori* infection, resulting in null association between *H. pylori* infection and the source of drinking water. In fact, the infrequency of boiling water increased the risk of *H. pylori* infection without significance (OR adjusted for age=2.86, 95% CI, 0.39-20.8).

Table 3. Age-Sex Adjusted Odds Ratios (ORs) and 95% Confidence Intervals of Lifestyle Factors for *Helicobacter Pylori* Infection

	n (infected)/N (Total)	OR	95%CI
Smoking			
Never	24/157	1	Reference
Former	3/14	2.4	0.4-14.4
Current	2/22	1.3	0.2-9.3
Drinking Alcohol			
Never	26/184	1	Reference
Former	2/6	6.7	0.9-52.0
Current	1/3	3.4	0.2-47.8
Red meat			
<1 time/week	27/174	1.0	Reference
≥1 times/week	2/19	0.9	0.2-4.1
Raw vegetable			
<1 time/week	2/140	1.0	Reference
≥1 times/week	7/53	0.9	0.3-2.3
Fresh fruits			
<1 time/week	12/82	1.0	Reference
≥1 times/week	17/111	1.2	0.5-2.6
Chicken			
<1 time/week	7/72	1.0	Reference
≥1 times/week	22/121	2.4	0.9-6.2
Green vegetable			
<1 time/week	1.38	1.0	Reference
≥1 times/week	28-155	7.0	0.9-53.6
Carrot			
<1 time/week	6/78	1.0	Reference
≥1 times/week	3/115	2.5	0.9-6.7
Garlic			
<1 time/week	2/37	1.0	Reference
≥1 times/week	27/156	2.8	0.6-12.9
Onion			
<1 time/week	2/31	1.0	Reference
≥1 times/week	27/162	2.0	0.4-9.2
Tomatoes			
<1 time/week	5/62	1.0	Reference
≥1 times/week	24/131	2.0	0.7-5.7
Cucumber			
<1 time/week	7/102	1.0	Reference
≥1 times/week	22/91	4.2	1.7-10.6
Cabbage			
<1 time/week	20/17	1.0	Reference
≥1 times/week	9/66	0.9	0.4-2.2
Fired rice			
<3 plates/week	27/166	1.0	Reference
≥3 plates/week	2/27	0.5	0.1-2.3
Tofu			
<3 pieces/week	9/60	1	Reference
≥3 pieces/week	20/133	0.9	0.4-2.1
Soybean cake			
<3 pieces	9/49	1.0	Reference
≥3 pieces/week	20/144	0.7	0.3-1.7
Coffee			
<1 time/week	23/153	1.0	Reference
≥1 times/week	6/40	1.2	0.4-3.4
Soybean milk			
<1 time/week	18/162	1.0	Reference
≥1 times/week	1/31	0.1	0.02-1.2
Milk			
<1 time/week	19/127	1.0	Reference
≥1 times/week	10/66	1.3	0.53-3.06
Tea			
<1 time/week	4/37	1.0	Reference
≥1 times/week	25/156	1.4	0.5-4.4

This study showed intake of cucumber increased the risk for *H. pylori* infection after a multivariate analysis. There are no studies about the association between the intake of cucumber and *H. pylori* infection as long as we searched for it on PubMed using the key words as following; cucumber, and/or *H. pylori*, and/or infection, and/or foodborne, and/or lifestyle. This association we found in this study might be a chance association. However, it has been reported that the intake of cucumber, which caused the outbreak of Salmonella, was a possible reservoir for Salmonella (Angelo et al., 2015). We could not deny the possibility that cucumber was a reservoir for *H. pylori.* The OR for intake of green vegetable more than one time a week was 10.6, which was higher than the OR for cucumber. But the association with *H. pylori* infection risk was marginal significance probably due to lack of statistical power. Fresh leafy green vegetables carry the potential risk of microbiological contamination because of usage of untreated irrigation water, inappropriate organic fertilizers, wildlife or other sources (Mercanoglu et al., 2011). Green vegetable also could be the reservoir for *H. pylori.* These associations remain to be further investigated.

Batak and Buginese ethnics were infected more frequently than Javanese, Betawi and Sundanese ethnics. This result was compatible as the previous reports (Miftahussurur et al., 2014; Miftahussurur et al., 2015; Syam et al., 2015; Tokudome et al., 2005; Tokudome et al., 2005). Although it is unclear why there was difference in *H. pylori* infection among ethnics in Indonesia, host genetic factors and/or environmental factors could explain the difference. In our study, there was another suggestion that the factor of ethnic was correlated with unsanitary practice, considering the comparison of model 1 with model 2 (Table 4). It was possible that the high prevalence of *H. pylori* infection among Buginese and Batak was caused by the frequent use of fingers to eat food. The percentages of the use of fingers every time eating food among Buginese and Batak were 45.7% and

Table 4. Multivariate Analysis for Risks of *Helicobacter Pylori* Infection

	Model 1[1]		Model 2[2]	
	OR	95%CI	OR	95%CI
Using fingers to eat food (compared with always)				
Less frequent	0.2	0.1-0.6	0.3	0.1-1.2
Hand washing before meal (compared with always)				
Less frequent	3.6	1.1-11.0	4.1	1.1-14.6
Chicken (compared with <1 time/week)				
≥1 times/week	1.9	0.6-5.6	1.4	0.4-4.6
Green vegetable (compared with <1 time/week)				
≥1 times/week	11.9	0.9-154.8	10.6	0.9-117.3
Carrot (compared with <1 time/week)				
≥1 times/week	2.7	0.9-8.7	2.6	0.7-9.0
Cucumber (compared with <1 time/week)				
≥1 times/week	4.3	1.5-12.3	6.6	1.9-23.3
Soybean milk (compared with <1 time/week)				
≥1 times/week	0.1	0.01-0.9	0.1	0.01-0.9
Drinking Alcohol (compared with never)				
Former	44.5	1.8-1102.1	61.9	1.7-2300.8
Current	7.2	0.2-228.7	21.5	0.4-1160.4
Ethnic (compared writh Javanese)				
Buginese			7.8	1.8-33.8
Betawi			1.2	0.2-6.2
Sundanese			0.8	0.1-8.8
Batak			20.1	1.9-213.2
Others[3]			1.6	0.2-13.4

Model 1, contained all variables except ethnicity above; Mode 2, contained all variables above; Malay (2); Minangkabau (2); Maduranese (2);Tolaki (of 2, 1 positive); Chinese (1); Baliness (1); Kendari (of 1, 1 positive); Jambi (1); Manado (1); Palembang (1); Riau (1); Timor (1)

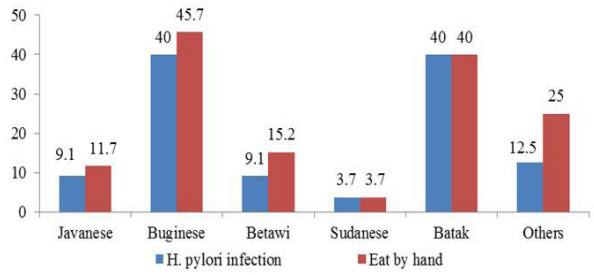

Figure 1. The Percentage of *Helicobacter Pylori* Infection and the Use of Fingers Every Time They Consume Food by Ethnics

40.0%, respectively, whereas the percentages among Javansese, Betawi and Sundanese were 11.7%, 15.2% and 3.70%, respectively (Figure1). In addition, the infrequent hand wash practice before meal increased the risk for *H. pylori* infection, which was consistent with the previous studies (Abebaw et al., 2014; Brown et al., 2002). Unsanitary practices were thought to be important factors in transmission of *H. pylori*. Moreover, the more number of persons per household tended to increase the risk of *H. pylori* infection as the past studies have reported (Laszewicz et al., 2014; Salah et al., 2009; Webb et al., 1994). These results indicated person-to-person transmission was plausible even in this low prevalence area, and avoidance of using fingers to eat food might keep Javansese, Betawi and Sundanese away from the risk of *H. pylori* infection.

Considering the previous study, which have reported that the consumption of soybean curd was negatively related to *H. pylori* infection (Shinchi et al., 1997), it was indicated that drinking soybean milk was a protective factor against *H. pylori* infection. In addition, other foods from soybean such as tofu and soybean cake showed negative relationship with infection insignificantly. However, this could not explain the reason why *H. pylori* infection rate is low in Indonesia, because the number of those who drinking soybean milk was small.

Regarding smoking and alcohol intake, these associations are controversial (Abebaw et al., 2014; Brown et al., 2002; Camargo et al., 2004; Ito et al., 2001; Liu et al., 2015; Moges et al., 2006; Zhu et al., 2014). In this study, we could find the relation between alcohol and *H. pylori* infection. As for alcohol, we assumed the reason for the various results might be explained by the types of alcoholic beverages consumed and the lifetime history of alcohol consumption. We found no relation between smoking and *H. pylori* infection.

There were some limitations in this study. The infection is established during childhood. Our study could examine the factors for continuation of the infected state. But considering that lifestyle and diet habit hardly change without intervention (Penalvo et al., 2012), we believe the environment and lifestyle factors we collected from

the subjects also could be the risk for *H. pylori* infection. We collected the subjects in the restricted area, where the sanitary condition and infrastructure were worse, and this study could not reflect all Indonesians. The number of subjects in this study was relatively small. Especially, the number of subjects who provided the information on the source of drinking water was small. Therefore, we could not investigate the association between *H. pylori* infection and source of drinking water with enough statistical power.

In conclusion, we found *H. pylori* infection rate was as low as the previous studies have reported (Arinton, 2011; Miftahussurur et al., 2014; Miftahussurur et al., 2015; Syam et al., 2005; Syam et al., 2006; Syam et al., 2015; Tokudome et al., 2005; Tokudome et al., 2005; Zhao et al., 2012). Batak and Buginese ethnics were infected with *H. pylori* more frequently. The intake of cucumber, and drinking alcohol increased the risk of *H. pylori* infection. The intake of soybean milk prevented infection with *H. pylori*, but most of our study subjects did not drink it. After we scrutinized the factor of ethnic, Buginese and Batak ethnics eat using fingers more frequently. Moreover, infrequent hand wash practice before meal increased the risk of *H. pylori* infection. Therefore, person-to-person route was indicated as transmission of *H. pylori* infection even in this low prevalence area. The lower infection rates among Javansese, Betawi and Sundanese ethnics could be due to sanitary practices namely avoidance of using fingers to eat food. Furthermore studies are needed to confirm our results

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