

## RESEARCH ARTICLE

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

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### Abstract

Indonesia is a developing country, in most of which the infection rates of *Helicobacter pylori* (*H. pylori*) have been reported to be high. However, the prevalence of *H. pylori* infection in Indonesia has been unexpectedly reported to be low. The purpose of our study was to confirm whether the prevalence of *H. pylori* infection is low among healthy inhabitants in Northern Jakarta by 13C-urea breath test (UBT), and to examine the association of their lifestyle/environmental factors with *H. pylori* infection and to identify potential routes of transmission. We recruited a total of 196 subjects from a low-income community in Northern Jakarta, Indonesia. Of them, 193 subjects who completed a questionnaire about their lifestyle/environment and had UBT were included in this study. Odds ratios (ORs) adjusted for sex and age with 95% confidence intervals (CIs) were calculated using logistic regression model. The overall *H. pylori* infection rate was 15.0%. There was difference in *H. pylori* infection rates among Buginese (40.0%), Betawi (9.1%), Sundanese (3.7%), and Batak (9.1%). After multivariate analysis, the ORs of intake of soybean milk, cucumber more than one time a week, infrequent hand washing 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 for former drinkers (95% CI: 1.67-2300.8), respectively. Buginese (OR=7.84; 95% CI: 1.82-33.8) and Batak ethnic groups (OR=20.1; 95% CI: 1.90-213.2) were infected more frequently, compared with Javanese. The *H. pylori* infection rate in this study was low, as reported previously. After we scrutinized the factors, Buginese and Batak ethnic groups eat food using fingers more frequently than Javanese, Betawi, and Sundanese. In addition, infrequent hand wash practice before meal increased the risk. Our study indicated that person-person transmission was possible in this low prevalence area. The low infection rates of *H. pylori* among those of Javanese, Betawi, and Sundanese ethnicity could be partly due to sanitary practice.

**Keywords:** *H. pylori* - infection - Indonesia - ethnic variation

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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 (Salah et al., 2009; Goh et al, 2011; Abebaw et al., 2014; Laszewicz et al., 2014; Miftahussurur et al., 2014). For example, in Japan the infrastructure before World War II was not well established. Most of Japanese at the time were under unsanitary condition. That is why *H. pylori* infection rate had been 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 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

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detecting *H. pylori* infection (Bilal et al., 2007; Bruden et al., 2011; Redeen et al., 2011; Patel et al., 2014) and to examine possible association of lifestyle/environment factors with *H. pylori* infection in order to reveal routes of transmission.

## Materials and Methods

### Study subjects

We recruited 196 healthy subjects aged 14 to 80 years attending 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  $\geq 2.5\%$  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 CO<sub>2</sub> concentration.

### *Questionnaire about lifestyle/environment*

The questionnaire included items on demographic characteristics, marital status, housing, living condition, personal hygiene, monthly income, smoking, alcohol, source of 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  $\geq 5$  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  $\chi^2$  test or a Fisher’s exact probability test. Odds ratios (ORs) adjusted for sex and age (a continuous variable) with 95% confidence intervals (CIs) were calculated using 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  $\geq 1$  times/week and 7 categories for food intake

quantity into 2 categories namely  $<3$  pieces (plates)/week and  $\geq 3$  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 socioeconomic, lifestyle and dietary factors with  $p < 0.10$  were entered to 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%; 10.6% among men and 16.4% 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 statistically significant difference in *H. pylori* infection rates among ethnics.

The association between socioeconomic 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, per bed, and education level, annual income, and marital status. The infrequent use of fingers to eat food prevented *H. pylori*

**Table 1. Characteristics of Study Subjects**

	Total	n (infected)	Hp <sup>a</sup> positive (%)	p value <sup>b</sup>
Sex				
Male	47	5	10.6	0.48
Female	146	24	16.4	
Age				
$\leq 19$	9	0	0	0.49
20-39	27	4	14.8	
30-39	43	5	11.6	
40-49	49	7	14.3	
50-59	35	5	14.3	
60-69	24	6	25.0	
$\geq 70$	6	2	33.3	
	Total	n (infected)	Hp <sup>1</sup> positive (%)	p value <sup>2</sup>
Occupation				
Housewife	86	18	20.9	0.09
Labor	24	1	4.2	
Unemployed	20	4	20.0	
Others	63	6	9.5	
Ethnic				
Javanese	77	7	9.1	<0.0001
Buginese	35	14	40.0	
Betawi	33	3	9.1	
Sundanese	27	1	3.7	
Batak	5	2	40.0	
Othersc	16	2	12.5	

<sup>a</sup>Helicobacter pylori, <sup>b</sup>p value was calculated by a  $\chi^2$  test or a Fisher’s exact probability test, <sup>c</sup>Malay (2), Minangkabau (2), Maduranese (2), Tolaki (of 2, 1 positive), Chinese (1), Balinese (1), Kendari (of 1, 1 positive), Jambi (1), Manado (1), Palembang (1), Riau (1), Timor (1)

**Table 2. Age-sex Adjusted Odds Ratios (ORs) and 95% Confidence Intervals of Socioeconomic Factors for *Helicobacter pylori* Infection**

	n (infected)/N (Total)	OR	95%CI
Education			
Low	15/90	1	Reference
Medium	13/89	1.34	0.54-3.32
High	1/14	0.71	0.08-6.34
Income per month			
<Rp. 2500000	23/134	1	Reference
≥Rp. 2500000	6/59	0.72	0.26-1.95
Marital status			
Married	28/188	1	Reference
Single	1/5	3.47	0.32-38.1
Persons per household			
≤3	8/76	1	Reference
≥4	21/117	1.99	0.82-4.84
Persons per room			
≤1	9/55	1	Reference
≥2	20/138	0.95	0.40-2.29
Persons per a bed			
≤1	5/22	1	Reference
≥2	24/171	0.72	0.23-2.21
Sharing toothbrush			
Yes	28/163	1	Reference
No	1/30	0.21	0.03-1.66
Using fingers to eat food			
Always	12/37	1	Reference
Less frequent	17/156	0.28	0.12-0.67
Hand washing before meal			
Always	8/79	1	Reference
Less frequent	21/114	2.45	0.99-6.06
Hand washing after toilet			
Always	15/112	1	Reference
Less frequent	14/80	1.63	0.71-3.74

**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	2.36	0.39-14.4
Current	2/22	1.30	0.18-9.32
Drinking Alcohol			
Never	26/184	1	Reference
Former	2/6	6.68	0.86-52.0
Current	1/3	3.37	0.24-47.8
Red meat			
<1 time/week	27/174	1	Reference
Raw vegetable			
<1 time/week	22/140	1	Reference
≥1 times/week	7/53	0.90	0.35-2.28
Fresh fruits			
<1 time/week	12/82	1	Reference
≥1 times/week	17/111	1.16	0.51-2.64
Chicken			
<1 time/week	7/72	1	Reference
≥1 times/week	22/121	2.45	0.97-6.20
Green vegetable			
<1 time/week	1/38	1	Reference
≥1 times/week	28/155	6.99	0.91-53.6

**Table 3 (Continued) Age-sex Adjusted Odds Ratios (ORs) and 95% confidence Intervals of Lifestyle Factors for *Helicobacter pylori* Infection**

Carrot			
<1 time/week	6/78	1	Reference
≥1 times/week	23/115	2.55	0.97-6.72
Garlic			
<1 time/week	2/37	1	Reference
≥1 times/week	27/156	2.80	0.61-12.9
Onion			
<1 time/week	2/31	1	Reference
≥1 times/week	27/162	1.98	0.42-9.21
Tomatoes			
<1 time/week	5/62	1	Reference
≥1 times/week	24/131	2.00	0.70-5.68
Cucumber			
<1 time/week	7/102	1	Reference
≥1 times/week	22/91	4.23	1.69-10.6
Cabbage			
<1 time/week	20/127	1	Reference
≥1 times/week	9/66	0.92	0.38-2.18
Fired rice			
<3 plates/week	27/166	1	Reference
≥3 plates/week	2/27	0.50	0.11-2.31
Tofu			
<3 pieces/week	9/60	1	Reference
≥3 pieces/week	20/133	0.89	0.37-2.12
Soybean cake			
<3 pieces/week	9/49	1	Reference
≥3 pieces/week	20/144	0.71	0.30-1.72
Coffee			
<1 time/week	23/153	1	Reference
≥1 times/week	6/40	1.24	0.45-3.41
Soybean milk			
<1 time/week	28/162	1	Reference
≥1 times/week	1/31	0.15	0.02-1.18
Milk			
<1 time/week	19/127	1	Reference
≥1 times/week	10/66	1.28	0.53-3.06
Tea			
<1 time/week	4/37	1	Reference
≥1 times/week	25/156	1.42	0.46-4.44
Source of drinking water			
Tap water	2/17	-	-
Well	0/2	-	-
River	0/1	-	-
Mineral	10/76	-	-

\*The information is collected from 96 subjects.  $p=1.00$  for 2 by 4 table using a Fisher's exact probability test

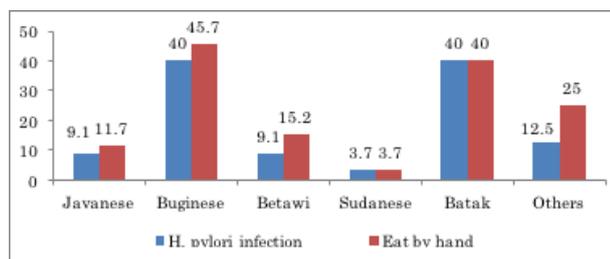
infection significantly (OR=0.28, 95% CI, 0.12-0.67). The infrequent hand wash practice before meal increased risk of *H. pylori* infection with marginal significance (OR=2.45, 95% CI, 0.99-6.06). The infrequent hand wash practice after toilet was not significantly associated with risk of *H. pylori* infection.

Table 3 shows the association between *H. pylori* infection and lifestyle factors. 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 risk of *H. pylori* infection and drinking soybean milk (OR=0.15, 95% CI,

**Table 4. Multivariate analysis for risks of *Helicobacter pylori* infection**

	Model 1 <sup>a</sup>		Model 2 <sup>b</sup>	
	OR	95%CI	OR	95%CI
Using fingers to eat food (compared with always)				
Less frequent	0.18	0.06-0.56	0.34	0.10-1.22
Hand washing before meal (compared with always)				
Less frequent	3.62	1.15-11.4	4.10	1.15-14.6
Chicken (compared with <1 time/week)				
≥1 times/week	1.90	0.64-5.63	1.40	0.43-4.56
Green vegetable (compared with <1 time/week)				
≥1 times/week	11.9	0.91-154.8	10.6	0.96-117.3
Carrot (compared with <1 time/week)				
≥1 times/week	2.74	0.86-8.75	2.58	0.74-9.03
		Model 1 <sup>1</sup>		Model 2 <sup>1</sup>
	OR	95%CI	OR	95%CI
Cucumber (compared with <1 time/week)				
≥1 times/week	4.29	1.50-12.3	6.61	1.87-23.3
Soybean milk (compared with <1 time/week)				
≥1 times/week	0.09	0.01-0.88	0.10	0.01-0.97
Drinking Alcohol (compared with never)				
Former	44.5	1.80-1102.1	61.9	1.67-2300.8
Current	7.23	0.23-228.7	21.5	0.40-1160.4
Ethnic (compared with Javanese)				
Buginese			7.84	1.82-33.8
Betawi			1.18	0.23-6.19
Sundanese			0.81	0.08-8.75
Batak			20.1	1.90-213.2
Others <sup>c</sup>			1.64	0.20-13.4

<sup>a</sup>Model 1 contained all variables except ethnicity above; <sup>b</sup>Model 2 contained all variables above; <sup>c</sup>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 Consume Food.** It was possible that Buginese and Batak were infected more frequently because of the frequent use of fingers to consume food

0.02-1.18) decreased it with marginal significance. There was no association between *H. pylori* infection and, the source of drinking water or smoking, although we could collect information on source of drinking water from 96 subjects.

The significant and marginally significant socioeconomic 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=0.10, 95% CI, 0.01-0.97). 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 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 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 II. It could explain why the prevalence rate of *H. pylori* is high in Japan (Yang et al., 1999; Karita et al., 2003; Iso et al., 2005). But this study did not confirm the association, because only 3.13% (3/96) drunk river/well water. It has been reported that drinking well water in childhood is the 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 *H. pylori* infection risk without significance (OR adjusted for age=2.86, 95% CI, 0.39-20.8).

This study showed intake of cucumber increased the risk of *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 of intake of green vegetable more than one time a week was 10.6, which was higher than the OR of 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 the 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 (Tokudome et al., 2005; Tokudome et al., 2005; Miftahussurur et al., 2014; Miftahussurur et al., 2015; Syam et al., 2015). 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. The percentages of the use of fingers every time eat food among Buginese and Batak were 45.7% and 40.0%, respectively, whereas the percentages among Javanese, Betawi and Sundanese were 11.7%, 15.2% and 3.70%, respectively (Figure 1). In addition, infrequent hand wash practice before meal increased risk of *H. pylori* infection, which was consistent with the previous studies (Brown et al., 2002; Abebaw et al., 2014). Unsanitary practices were thought to be important factors in transmission. 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 the use of fingers might keep Javanese, 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 low.

Regarding smoking and alcohol intake, these associations are controversial (Ito et al., 2001; Brown et al., 2002; Camargo et al., 2004; Moges et al., 2006; Abebaw et al., 2014; Zhu et al., 2014; Liu et al., 2015). 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 socioeconomic 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 low. 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 (Tokudome et al., 2005; Syam et al., 2005; Syam et al., 2006; Arinton, 2011; Zhao et al., 2012; Miftahussurur et al., 2014; Miftahussurur et al., 2015; Syam et al., 2015). 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 Javanese, Betawi and Sundanese ethnics could be due to sanitary practices namely avoidance of the use of fingers to eat food. Furthermore studies are now needed to confirm our results for the different ethnic groups and lifestyle factors.

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