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Ethnicity is a strong predictor for *Helicobacter pylori* infection in young women in a multi-ethnic European city

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Abstract

BACKGROUND AND AIM—At the same time that *H. pylori* prevalence is declining in Western countries, immigrants from developing countries with high *H. pylori* prevalence have settled in Western urban areas. Actual epidemiologic data on *H. pylori* in a migrant community may help in realizing a more selective approach to assess *H. pylori*-related diseases. We aimed to define *H. pylori* prevalence as well as risk groups for *H. pylori* in a cohort of young women living in a multi-ethnic European city.

METHODS—We measured IgG anti-*H. pylori* and CagA-antibodies in serum of pregnant women included in a population-based prospective cohort study. Information on demographics, and socioeconomic status was collected by questionnaires. Chi-square and logistic regression were used.

RESULTS—In total, 3146 (46%) of the 6837 tested women (mean age 29.7 ± 5.3) were *H. pylori*-positive and 1110 (35%) of them were CagA-positive. The *H. pylori* prevalence in Dutch women was 24%, which was significantly lower than in non-Dutch women (64%; p<0.001). In particular, *H. pylori* positivity was found in 92% of Moroccan (OR 19.2; 95% CI 11.8-32.0), 80% of Cape Verdean (7.6; 5.0-11.5), 81% of Turkish (9.0; 6.7-12.1), 60% of Dutch Antillean (3.3; 2.3-4.7), and 58% of Surinamese women (3.0; 2.3-3.8). Among *H. pylori*-positive Dutch subjects, 19% were CagA-positive compared with 40% of the non-Dutch subjects (p<0.001).

CONCLUSIONS—Despite a general trend of declining prevalence in Western countries, *H. pylori* remains highly prevalent in migrant communities, which may constitute target groups for screening and eradication to prevent *H. pylori*-related diseases.

Keywords

Helicobacter pylori; cagA protein; epidemiology

INTRODUCTION

Isolation and identification of *Helicobacter pylori* in 1982 led to better understanding of gastric pathophysiology. This Gram-negative bacterium is an important risk factor for peptic ulcer disease, gastric adenocarcinoma and MALT-lymphoma¹. The prevalence of *H. pylori* widely varies geographically, and is highest in developing countries. In Western countries, however, prevalences have declined over recent decades to below 40%, in part as a result of improved hygiene and sanitation as well as the active elimination by antibiotics¹. In parallel to the declining *H. pylori* prevalence, incidences of certain *H. pylori*-related diseases are decreasing as well^{2,3}.

These trends in Western populations call for risk group identification, as test-and-treat strategies for *H. pylori* both on population as well as individual level are unlikely to be cost-effective in low prevalence countries⁴. Knowledge about specific risk groups may permit assessment of disease risk, and will offer opportunities for targeted interventions. The *H. pylori* colonization rate is associated with factors such as age, socioeconomic status, childhood crowding, and non-western ethnicity⁵. During past decades, many immigrants from developing countries with high *H. pylori* prevalence have settled in Western urban areas. In Rotterdam, a large Western city, more than 50% of the urban population is originating from outside The Netherlands. The largest non-Dutch ethnic groups consist of people from Morocco, Turkey, Suriname, Dutch Antilles, and Cape Verde. Previous studies indicated that *H. pylori* colonization rates in immigrants are higher compared to native western populations⁶⁻⁸. Some of these migrant communities have a high risk of gastric cancer^{9,10}, in which *H. pylori* is involved as the major causative agent. Especially CagA-positive *H. pylori* strains are known to be more interactive with higher risk of peptic ulcer disease, atrophic gastritis, and gastric cancer^{11,12}, and lower risk of gastro esophageal reflux disease, Barrett's esophagus, adenocarcinoma of the gastric-esophageal junction, and childhood-onset asthma^{13,14}. In this study, we aimed to obtain actual epidemiologic data on *H. pylori* prevalence in different ethnic groups living in a Western urban area. Moreover, we also measured anti-CagA-antibodies. As mothers are considered to be a source for transmission to their children, this study was performed in a cohort of pregnant women living in Rotterdam, a multi-ethnic European city.

METHODS

Setting and participants

This study was embedded in the Generation R Study, a population-based cohort study from fetal life until young adulthood in Rotterdam, with a multiethnic community, and the second largest city in the Netherlands. The background, design and aims of this study have been reported in detail¹⁵.

Briefly, 8880 pregnant women were enrolled in the study between April 2002 and January 2006. Medical data were collected by physical examination, and by questionnaires, and information on age, ethnicity, educational level, life style, and household income was obtained by questionnaires¹⁵.

The Generation R Study was approved by the Medical Ethical Committee of the Erasmus University Medical Center. All participants gave written informed consent.

Socio-demographic determinants

The cohort comprises various ethnic groups, reflecting the urban population of Rotterdam. The largest ethnic groups consist of Dutch, Surinamese, Turkish, Moroccan, Dutch-Antilles and Cape Verdean mothers. Ethnicity was determined by country of birth of the pregnant

mother and her parents. A participating mother was considered of non-Dutch ethnic origin if one of her parents was born abroad (according to the definition of Statistics Netherlands)¹⁶. If both parents were born in different countries other than the Netherlands, the country of the mother prevailed. Subjects of non-Dutch origin and born abroad were defined as first-generation immigrants. A participant of non-Dutch origin but born in the Netherlands was defined as a second-generation immigrant. People of Dutch origin were considered as the native population. According to the definitions of Statistics Netherlands¹⁶ participants with other ethnic background as mentioned above were grouped as 'other western' for European (n=493), North American (n=24), Oceanian (n=9), Japanese (n=7) and Indonesian (n=194), and as 'other non-western' for African (n=123), Asia (n=189) and South- and Central American (n=91). The division into 'western' and 'non-western' is based on differences in socioeconomic and cultural situation. Participants from Indonesian were classified as 'western', since they are originating from former Dutch-East Indies. Educational level was classified into four educational levels on the basis of the highest completed education: high (university or higher vocational training), high-secondary (general secondary school or intermediate vocational training), low-secondary (intermediate general school or lower vocational training), and low (primary school or no education). Educational level served as proxy for the socio-economic status. Household income, defined by the total net monthly income of the family, was categorized as < €1200, €1200-2000, and > €2000. Data on possible confounders like age, smoking habits, and alcohol use were obtained from the questionnaires.

Serologic determinants

Mid-pregnancy serum samples of 7185 mothers were available for analysis (**Figure 1**). Mothers included more than once (due to more than one pregnancy within inclusion period) were excluded (n=348), which left a total study population of 6837 pregnant women. Procedures for collection and storage of the sera samples have been described in detail previously¹⁷. Samples were examined for *H. pylori* IgG antibody levels by enzyme-linked immunosorbent assay (ELISA), using whole cell antigens¹⁸. A separate ELISA was performed to determine serum IgG antibodies against a specific recombinant truncated CagA protein, as described¹⁹. All samples were measured in duplicate. For each sample, the optical density ratio (ODR) was calculated by dividing the optical density (OD) by the mean OD of the positive controls. *H. pylori* positivity was defined as either an ODR ≥ 1 or CagA positivity. The cut-off for CagA positivity was an ODR value ≥ 0.35. Both ELISAs were validated locally.

Statistical analysis

Chi-square tests (categorical variables) and t-tests (continuous variables) were used to compare different variables in relation to *H. pylori* status. Univariate analysis was performed to assess determinants associated with the presence of *H. pylori*. To study the individual effect of each potential determinant, each was separately tested, followed by a multivariate analysis corrected for all other determinants. In addition, a stratified analysis according to ethnicity was performed. Subjects with missing data on any of above-mentioned covariates were excluded from the multivariate analysis; this left a total of 4605 evaluable subjects.

A two sided p-value <0.05 was considered to be statistically significant. All analyses were performed using PASW Statistics 20.0 (SPSS, IBM, New York, United States).

RESULTS

Presence of *H. pylori*

In total, the serum samples of 6837 women were analyzed. Their mean age was 29.7 ($\pm$ 5.3) years. Subjects of Dutch origin were older (mean age 31.4 years) than non-Dutch participants (mean age 28.4 years) ($p < 0.001$). **Table 1** shows the general characteristics and *H. pylori* status: 3146 (46%) subjects were *H. pylori*-positive and 3691 (54%) subjects *H. pylori*-negative. Data on ethnicity were available for 6389 women: 3166 (50%) subjects were of Dutch ethnicity, 597 (9%) of Turkish, 577 (9%) of Surinamese, 408 (6%) of Moroccan, 275 (4%) of Cape Verdean, 237 (4%) of Dutch Antilles, 726 (11%) of other western and 403 (6%) of other non-western origin. The *H. pylori* positivity rate was highest among Moroccan women (92%), followed by Cape Verdian (80%), Turkish (81%), Dutch Antillean (60%), and Surinamese subjects (58%) (**Figure 2**). In contrast, the prevalence in women of Dutch origin was 24% ($p < 0.001$).

The overall CagA-prevalence rate was 16.2%. Among *H. pylori*-positives, 1110 women (35.2%) were colonized with a CagA-positive strain, which however varied widely between ethnicities (**Figure 2**). Only 64 subjects were CagA-positive but *H. pylori*-negative (6%). Colonization with a CagA-positive *H. pylori* strain was most common in Surinamese (56%) mothers, followed by subjects of other non-western (46%), Dutch Antillean (46%), Turkish (39%), Cape Verdean (34%), Moroccan (34%), other western (29%), and Dutch (19%) origin ($p < 0.001$).

Determinants of *H. pylori* colonization

Univariate logistic regression revealed that non-Dutch ethnicity was an independent risk factor for *H. pylori* positivity (**Table 1**). Furthermore, lower educational level, first generation immigrant, and lower household income were significantly associated with *H. pylori* infection. However, alcohol use was inversely associated with *H. pylori* presence.

The following variables were entered into the multivariate logistic regression model: age, ethnicity, education level, household income, smoking, and alcohol use. This analysis continued to reveal ethnicity as the most important independent risk factor for *H. pylori* (**Figure 3**). Compared to Dutch ethnicity, highest risk was found for Moroccan women (odds ratio 19.4; 95% confidence interval 11.8-32.0), followed by Turkish (9.0; 6.7-12.1), Cape Verdean (7.6; 5.0-11.5), other non-western (3.4; 2.6-4.5), Dutch Antillean (3.3; 2.3-4.7), Surinamese (3.0; 2.3-3.8), and other western (1.7; 1.4-2.0) subjects. In addition to ethnicity, the following independent risk factors were found: low education level compared with high education level (1.9; 1.4-2.5), and low income compared with high income (1.5; 1.2-1.9).

After stratification by ethnicity, multivariate analysis showed within all non-Dutch ethnicities that subjects born abroad (first generation immigrants) had a significantly higher risk to be colonized with *H. pylori* compared with second-generation immigrants ($p < 0.05$ for Turkish, Surinamese, Moroccan, Cape Verdean, and Dutch Antillean subjects) (**Table 2**). Within the different ethnicities, age, smoking, and alcohol use were not associated with *H. pylori* colonization. Except for the Turkish and Cape Verdean subjects, low socio-economic status was an independent risk factor for *H. pylori* colonization. Dividing the whole population into either western or non-western showed in both groups first generation immigrants, subjects with low education level, and low household income to be more at risk for *H. pylori* colonization (**Table 3**).

DISCUSSION

This population-based study demonstrates that *H. pylori* colonization is still common in a Western society, in particular in migrant communities. Among women of non-Dutch ethnicity, first generation immigrants were more at risk for *H. pylori* colonization than second-generation immigrants. Although others have focused on risk group identification as well, both the cohort size and design of this study are unique, and results reflect the actual epidemiologic data on *H. pylori* colonization in a Western urban area.

The relatively high prevalence of *H. pylori* and CagA-positive strains found in ethnic minority groups indicates that the health risks imposed by *H. pylori* remain a significant concern. Studies comparing first and second-generation immigrants with the native population have demonstrated a higher risk for non-cardia gastric cancer in first-generation immigrants^{20, 21}. Childhood colonization with *H. pylori* could be a possible cause^{22, 23}. Our results support this explanation, since *H. pylori* colonization among second-generation immigrants was significantly lower compared to first-generation immigrants, but still higher than in the native population.

Based on estimates of the incidence of gastric cancer in different regions all around the world, study participants originating from Surinam, Caribbean, and Turkey are expected to have a higher gastric cancer risk compared with subjects from Western Europe²⁴. Indeed, studies from Sweden have indicated a higher gastric cancer incidence ratio in immigrants born in high risk countries and living in Sweden²⁰. Hence, those migrant communities could be an appropriate focus for considering the health advantages of *H. pylori* eradication. The latter is found effective for gastric cancer prevention in patients without precancerous lesions^{25, 26}.

We tested for *H. pylori* antibodies in pregnant women, about to give birth. Close family members like mothers and siblings are considered to be the major transmission sources for *H. pylori* acquisition during the first years of life¹. Hence, a high prevalence in mothers may be considered predictive for a high colonization rate in their children.

Moreover, via day care attendance these children may also be a source for transmission to other children^{27, 28}. Our finding indicates that *H. pylori* will remain to be prevalent for the coming decades, even in Western societies.

The observed *H. pylori* colonization rate in the Dutch study subjects was consistent with a previous study in subjects of the same age²⁹. Studies evaluating *H. pylori* colonization in immigrant groups all showed higher infection prevalence than in native populations^{8, 29-33}. A previous study of 288 adults in Rotterdam showed nearly similar positivity rates among different immigrant groups, however higher prevalence in subjects of Dutch origin (46%) than we observed⁸. This may have been due to both the relative higher age and the small number of Dutch patients in that study.

The geographical variance of *H. pylori* strains was confirmed by this study. *H. pylori* strains colonizing Western subjects were least often CagA-positive³⁴. In a Finnish population, CagA-positive *H. pylori* strains declined faster than CagA-negative *H. pylori* strains, especially among subjects less than 45 years old³⁵. The low CagA prevalence among Dutch and other Western subjects is consistent with those observations. Nevertheless, overall prevalence of CagA-positive strains was lower than expected, especially in subjects born abroad.

This study is limited by the inclusion of young women in a limited age range which restricted the possibility of extrapolating our finding to older age cohorts. Owing to the well

described birth cohort effect for *H. pylori*²⁷, we expect *H. pylori* to be more prevalent in older age cohort. However, whether this is true for all various ethnic groups remain unclear. Second, the population in our study may not have been reflective of the general population of Rotterdam owing to overrepresentation of more highly educated women in this cohort³⁶.

In conclusion, in a multi-ethnic population, ethnicity is the strongest predictor of *H. pylori* colonization in young women. In particular, migrant communities constitute target groups for screening of *H. pylori* to minimize *H. pylori*-related diseases. Additional knowledge of *H. pylori* biological cost, and details on implementation require further research.

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Figure 1.
Flowchart of the study.

Figure 2.
Proportion of CagA-positive and *H. pylori*-positive subjects.

Figure 3. Multivariate analysis of determinants associated with *H. pylori* colonization in one model. Odds ratios (ORs) and 95% confidence intervals are adjusted for age.

Table 1Baseline characteristics of study population, distribution by *H. pylori* status, and univariate analysis

	Study population (n)	<i>H. pylori</i> – (n=3,691)	<i>H. pylori</i> + (n=3,146)	OR Univariate	95% CI
Age, mean (SD)	6,837 (100)	30.7 (4.9)	28.7 (5.4)	0.93	0.92-0.94
Dutch population (%)	3,166 (46)	31.5 (4.4)	31.0 (4.9)	0.98	0.96-1.0
Non-Dutch	3,223 (47)	29.2 (5.5)	27.9 (5.4)	0.96	0.94-0.97
Parity (%)					
Nulli parity	3,746 (55)	2,173 (58)	1,573 (42)	1.0	
Multi parity	3,025 (45)	1,496 (50)	1,529 (51)	1.4	1.3-1.6
Missing	66 (1)				
Ethnicity (%)					
Dutch	3,166 (50)	2,415 (76)	751 (24)	1.0	
Other western	726 (11)	467 (64)	259 (36)	1.8	1.5-2.1
Turkish	597 (9)	116 (19)	481 (81)	13.3	10.7-16.6
Surinamese	577 (9)	244 (42)	333 (58)	4.3	3.7-5.3
Moroccan	408 (6)	32 (8)	376 (92)	37.8	26.0-54.7
Cape Verdean	275 (4)	54 (20)	221 (80)	13.2	9.7-17.9
Dutch Antilles	237 (4)	94 (40)	143 (60)	4.9	3.7-6.4
Other non-western	403 (6)	154 (38)	249 (62)	5.2	4.2-6.5
Missing	448 (7)				
Dutch + Western	3,892 (61)	2,882 (74)	1,010 (26)	1.0	
Non Western	2,497 (39)	694 (28)	1,803 (72)	7.4	6.6-8.3
Immigrant generation (%)					
Native	3,115 (49)	2,376 (76)	739 (24)	1.0	
1st generation	2,225 (35)	688 (31)	1,537 (69)	7.2	6.4-8.1
2nd generation	1,046 (16)	510 (49)	536 (51)	3.4	2.9-3.9
Missing	451 (7)				
Education (%)					
Low	719 (11)	199 (28)	520 (72)	6.6	5.5-8.0
Low secondary	980 (16)	451 (46)	529 (54)	3.0	2.6-3.5
High secondary	1,971 (31)	1,026 (52)	945 (48)	2.3	2.1-2.6
High	2,613 (42)	1,873 (72)	740 (28)	1.0	
Missing	554 (8)				
Household income (%)					
<1200 Euro	1,101 (21)	354 (32)	747 (68)	5.2	4.5-6.0
1200-2000 Euro	992 (19)	489 (49)	503 (51)	2.5	2.2-2.9
>2000	3,182 (60)	2,264 (71)	918 (29)	1.0	
Missing	1,562 (23)				
Alcohol (%)					
Yes	3,005 (51)	2,027 (68)	978 (32)	0.4	0.3-0.4
No	2,948 (49)	1,296 (44)	1,652 (56)	1.0	
Missing	884 (13)				

	Study population (n)	<i>H. pylori</i> – (n=3,691)	<i>H. pylori</i> + (n=3,146)	OR Univariate	95% CI
Smoking (%)					
Yes	1,688 (28)	930 (55)	758 (45)	1.0	0.9-1.2
No	4,348 (72)	2,430 (56)	1,918 (44)	1.0	
<i>Missing</i>	<i>801 (12)</i>				

Table 2

Multivariate analysis of *H. pylori* stratified to ethnicity

	Dutch n=2,545	Other western n=574	Turkish n=376	Surinamese n=355	Moroccan n=196	Cape Verdean n=149	Dutch Antillean n=154	Other non-western n=254
Age	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (0.9-1.0)	1.0 (1.0-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.0 (1.0-1.1)
Education								
Low	2.0 (1.1-3.4)	2.2 (0.9-5.3)	0.5 (0.2-1.4)	1.4 (0.6-3.6)	3.7 (0.5-24.7)	--	1.7 (0.4-6.9)	10.3 (2.7-38.6)
Low secondary	1.4 (1.0-1.9)	1.5 (0.7-3.2)	0.8 (0.3-2.3)	1.7 (0.8-3.7)	3.1 (0.5-17.7)	--	3.0 (0.8-10.8)	2.0 (0.7-5.7)
High secondary	1.2 (0.9-1.5)	1.5 (1.0-2.1)	1.0 (0.4-2.4)	1.5 (0.8-2.8)	1.1 (0.3-5.0)	--	1.2 (0.4-3.4)	1.6 (0.8-3.0)
High	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Generation								
Native	1.0	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
1st generation	N.A.	1.4 (1.0-2.1)	2.9 (1.6-5.3)	1.8 (1.1-3.0)	4.3 (1.4-13.3)	4.6 (1.6-13.4)	4.9 (1.9-12.7)	1.8 (0.8-3.8)
2nd generation	N.A.	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Household income								
<1200 Euro	1.7 (1.2-2.5)	1.6 (0.9-3.1)	1.3 (0.6-2.8)	2.0 (1.1-3.7)	0.8 (0.2-2.7)	0.3 (0.1-1.8)	0.7 (0.2-1.8)	1.6 (0.8-3.3)
1200-2000 Euro	1.0 (0.8-1.4)	1.4 (0.9-2.2)	1.0 (0.5-2.1)	1.6 (0.9-2.8)	3.1 (0.7-15.1)	0.1 (0.0-0.8)	0.4 (0.1-1.3)	1.4 (0.6-3.1)
>2000	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Alcohol								
Yes	0.9 (0.7-1.1)	0.7 (0.5-1.1)	0.7 (0.3-1.5)	1.0 (0.6-1.6)	3.6 (0.3-43.7)	1.2 (0.5-2.9)	0.8 (0.4-1.7)	0.9 (0.5-1.7)
No	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Smoking								
Yes	1.1 (0.9-1.3)	1.0 (0.6-1.5)	0.8 (0.4-1.3)	0.6 (0.4-1.1)	0.6 (0.1-3.0)	0.5 (0.2-1.3)	1.0 (0.5-2.4)	1.0 (0.4-2.1)
No	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0

Numbers are displayed as Odds Ratio (95% Confidence Interval). Reference categories are put as 1.0.

All listed variables were entered into the multivariate analysis.

N.A. = Not applicable.

-- No output due to too small numbers

Table 3

Multivariate analysis stratified to ethnicity (western vs non-western)

	All Western n=3,119	All non-Western n=1,484
Age	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Education		
Low	2.0 (1.3-3.2)	2.1 (1.4-3.2)
Low secondary	1.4 (1.1-1.9)	2.0 (1.4-3.0)
High secondary	1.2 (1.0-1.5)	1.4 (1.0-1.9)
High	1.0	1.0
Generation		
Native	1.0	N.A.
1st generation	1.8 (1.4-2.3)	2.0 (1.5-2.6)
2nd generation	1.4 (1.1-1.8)	1.0
Household income		
<1200 Euro	1.7 (1.2-2.4)	1.4 (1.1-2.0)
1200-2000 Euro	1.1 (0.9-1.4)	1.4 (1.0-1.9)
>2000	1.0	1.0
Alcohol		
Yes	0.9 (0.7-1.0)	0.6 (0.5-0.8)
No	1.0	1.0
Smoking		
Yes	1.0 (0.8-1.3)	0.8 (0.6-1.1)
No	1.0	1.0

Numbers are displayed as Odds Ratio (95% Confidence Interval). Reference categories are put as 1.0.

All listed variables were entered into the multivariate analysis.

N.A. = Not applicable.