Prevalence of and risk factors for *H. pylori* infection in healthy children and young adults in Belgium anno 2010/2011

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Abstract

Objective : **Estimation of prevalence and risk factors for *Helicobacter pylori* (*H. pylori*) infection in children and young adults in Belgium.**

Study design : **Five hundred and sixteen schoolchildren between 12 and 25 years old were tested for *H. pylori* infection using ^{13}C-UBT in different regions in Belgium. A questionnaire was used to evaluate risk factors.**

Results : **Fifty six (11%) tested positive. In children born in Belgium, with parents from Belgium, 13 (3,2%) tested positive. In children born in a foreign country, 20 (60%) tested positive ; if born in Belgium but 1 or 2 parents were from a foreign country, 15 (30%) tested positive. Differences were significant ($p < 0.001$). In the multivariate analyses, significant risk factors were staying in a day nursery, a birthplace of child or father outside Belgium, and lower education levels of mother.**

Conclusion : **In this cohort of Belgian asymptomatic children and young adults, the prevalence of *H. pylori* infection is 11%, ranging from 3,2% in Belgian born children with Belgian parents to 60% in children born in high prevalence countries from foreign parents. The most significant risk factor found in this study was origin.** (Acta gastroenterol. belg., **2013**, 76, **381-385**).

Key words : *Helicobacter pylori*, prevalence, Belgium, risk factors, transmission.

Introduction

Helicobacter pylori (H. pylori) is a common pathogen with about 50% of the world population infected. This infection is more prevalent in developing countries, and it has been associated with poverty and social deprivation. Different risk factors include overcrowded households, institutionalization, low education of the father, poor sanitation and poor water supply but positive and negative studies have been published around these issues (1). The infection has been associated with peptic ulcer disease, dyspepsia, idiopathic thrombocytopenic purpura (ITP), investigated iron deficiency anaemia, MALT lymphoma and non-cardiac gastric cancer. Although usually acquired before the age of 10 years, *H. pylori*-related diseases are rare during childhood and asymptomatic in most adults (2). Gastric cancer develops in 1-5% of infected individuals and is the most deadly and therefore the most feared complication. Trials investigating the effect of eradication on gastric cancer prevention remain contradictory but there is growing evidence that early eradication can be efficient and cost effective in the prevention of gastric cancer, especially in high risk populations (3,4-6). This means that prevention of gastric cancer needs to target the younger population. However, the prevalence of *H. pylori* infection is very diverse and there are large differences between and in countries (1,7,8). Furthermore, few studies followed the changes of prevalence in time (8,9).

We conducted a study to estimate the prevalence of *H. pylori* infection in children and young adults in Belgium and to define risk factors for *H. pylori* infection. To include different population groups and economical groups, tests were performed in different areas of Belgium. These included people living in rural and non-rural areas ; multicultural metropolises like Brussels and Antwerp ; more isolated areas without immigrants ; areas with late and recent immigration ; and different kind of schools. To estimate the economic situation, information on household composition and educational level of parents was collected through a questionnaire.

Patients and methods

Study population

Between September 2010 and October 2011, 516 schoolchildren between the age of 12 and 25 years old were tested in 8 different schools in Belgium (colleges, vocational schools, universities and boarding schools) and in different regions (Antwerp, Brussels, Aalst, Genk and Ciney). Informed consent was signed by the parents or by the student if older than 18. The study was performed according to the declaration of Helsinki and was approved by the local ethical committee.

Assessment of primary outcome event

H. pylori infection status was tested by ^{13}C-UBT (infrared spectrometer) after an overnight fast or after at least 4 hours of fasting. The exclusion criteria included : intake of antibiotics in the 4 weeks or proton pump inhibitors in the 2 weeks preceding the test and children

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with a history of eradication of *H. pylori* infection. ^{13}C-UBT was performed and results were interpreted using the method and cut-off levels based on previous studies in our centre (10,11). Briefly, we used 75 mg of ^{13}C-urea with citric acid. A breath sample was collected before and 10 minutes after ingestion of ^{13}C-ureum. Values above > 5,0 DOB ‰ are positive results and < 4,0 are negative result. Results between 4 and 5 are in the grey zone and not interpretable.

Risk factors for H. pylori

A questionnaire was filled out by the children and their parents. Information was gathered about age (years), gender, number of siblings, stay in day nursery (before age of 3) (yes/no), birth place of child, mother, and father (country), and education level of father and mother (age when getting final degree). Countries labelled as foreign are Africa (14 children), far and middle east (5 children), east Europe (10 children), other (2 children) (Caribbean, south America), Australia (2 children), Western-Europe (20 children). Australia and Western countries (The Netherlands, France, Germany) were not considered high prevalence countries.

Statistical analyses

The initial analyses of our data were exploratory and descriptive, with categorical data presented as numbers of patients and percentages and continuous data presented as median and means with standard deviation (SD). Patient characteristics and risk factors for *H. pylori* were then recoded into binary categorical variables : age (15 years or less *versus* 16 years or more), number of people in the household (4 or less *versus* 5 or more), stay in day nursery (yes *versus* no), birth place of child, mother, and father (Belgium versus foreign country), and education level of father and mother (estimates according to schooling < 19 years or > 19).

As a second step, the group of patients who were *H. pylori* positive and the group of patients without *H. pylori* infection were compared using Fisher's exact test. In all cases, an unadjusted (crude) odds ratio (OR) was calculated using univariate logistic regression. In addition, ORs simultaneously adjusted for the factors that were found to be statistically significant in univariate analyses were calculated using multivariate regression analysis. Each OR is presented with its 95% confidence interval. All computational procedures were performed using Excel 2003 (Microsoft® Office Excel 2003) and IBM® SPSS® Statistics, version 20 (IBM Corporation, 2011).

Results

Study population

Of the 516 tests performed, 4 results were in the grey zone and 3 tests failed, leaving 509 tests (98.6%) for further evaluation. Study population characteristics and number of children with available information, i.e., with correctly filled out questionnaires, are shown in Table 1. Median and mean age were 15.0 years and 16.3 years, respectively (SD for mean age : 2.3 years ; 95% confidence interval for mean age : 16.1 to 16.5). There were slightly more girls, slightly more children with 4 or more household members, and slightly more children not staying in a day nursery. Four hundred and ninety-five children (93.3%) and respectively 379 (87.5%) and 384 (88.1%) fathers and mothers (433 total answers) were born in Belgium. Fifty children were born in Belgium with 1 or 2 parents from foreign origin. All children born outside Belgium came to Belgium after the age of 6. Likewise, a vast majority of parents were highly educated (> 80%), with both father and mother graduating at least from senior high school.

Prevalence of H. pylori

Among the 509 tests (children) available for further evaluation, 56 tests were positive for *H. pylori* infection. The mean DOB in the children with a negative test was 0.64 ‰ (range 0-2.8) and 23.59 ‰ (range 5.2-74) in children with a positive test . Thus, the overall prevalence of being infected with *H. pylori* was 11.0%. We found a very low infection prevalence of 3.2% in children born in Belgium from Belgian born parents, compared with 30.0% in children with parents born in high prevalence countries, and 60.6% in children born in high prevalence countries.

The prevalence of *H. pylori* infection according to study population characteristics is shown in Table 1. Prevalence of *H. pylori* did not differ according to gender, age category, and number of household members. By contrast, not staying in a day nursery, a birthplace of child, mother, or father outside Belgium, and lower education levels of both father and mother, were all associated with higher prevalence of *H. pylori*.

Risk factors for H. pylori

Table 2 shows the results univariate (i.e. considering the effect of each characteristic separately ; left panel) and multivariate analyses (i.e considering the simultaneous effect of several characteristics ; right column).

Statistically significant risk factors for *H. pylori* infection were staying in a day nursery, a birthplace of child or father outside Belgium, and lower education levels of mother in multivariate analyses (i.e. considering the simultaneous effect of staying in a day nursery, birthplace of child, mother, or father, and education levels of both father and mother). We found no relationship between *H. pylori* infection and birthplace of mother and education level of father (Table 2, right column).

Discussion

Multiple studies have been conducted on all aspects of *H. pylori* infection since the discovery in 1983 and since

Table 1. — **Prevalence of *H. pylori* infection according to study population characteristics**

		H. pylori positive		
Characteristic	Number*	Number	Percentage (95% CI)**	P value***
All participants	509	56	11.0% (8.4 to 14.1)	
Gender				
Female	289/508 (56.7%)	38	13.2% (9.5 to 17.7)	0.086
Male	220/508 (43.3%)	18	8.2% (4.9 to 12.6)	
Age				
15 years or less	228/448 (50.9%)	21	9.2% (5.8 to 13.7)	0.751
16 years or more	220/448 (49.1%)	23	10.5% (6.7 to 15.3)	
Number of household members				
4 or less	119/487 (24.4%)	11	9.2% (4.7 to 15.9)	0.613
5 or more	368/487 (75.6%)	41	11.1% (8.1 to 14.8)	
Stay in day nursery				
No	272/485 (56.1%)	37	13.6% (9.8 to 18.3)	**0.040**
Yes	213/485 (43.9%)	16	7.5% (4.3 to 11.9)	
Place of birth child				
Belgium	459/492 (93.3%)	34	7.4% (5.2 to 10.2)	**< 0.001**
Other country	33/492 (6.7%)	20	60.6% (42.1 to 77.1)	
Place of birth father				
Belgium	379/433 (87.5%)	12	3.2% (1.6 to 5.4)	**< 0.001**
Other country	54/433 (12.5%)	25	46.3% (32.6 to 60.4)	
Place of birth mother				
Belgium	384/436 (88.1%)	18	4.7% (2.8 to 7.3)	**< 0.001**
Other country	52/436 (11.9%)	19	36.5% (23.6 to 51.0)	
Education father				
School ≤ age 19	70/440 (15.9%)	12	17.1% (9.2 to 28.1)	**0.047**
School > age 19	370/440 (84.1%)	32	8.6% (5.9 to 12.0)	
Education mother				
School ≤ age 19	49/424 (11.63%)	9	18.4% (8.8 to 32.0)	**0.012**
School > age 19	375/424 (88.4%)	26	6.9% (4.6 to 9.9)	

* number of children against available information, i.e., with correctly filled out questionnaires.
** denotes 95% exact binomial confidence interval for proportion of *H. pylori* positive.
*** denotes P value for Fisher's exact test; P values of less than 0.05 are printed in bold.

1994 updated guidelines are published on the management of the infection, for adults as well as for children (12,13). There is no doubt anymore about the role of *H. pylori* infection in diseases like gastric ulcer and gastric cancer and the beneficial effect of eradication (1-5,14). In the prevention of ulcer disease timing of eradication is probably less important since the disease is rarely fatal and eradication prevents recurrence although early eradication will prevent the morbidity and mortality associated with complicated ulcers, decrease hospitalizations and the need for interventions of the physician. The timing of eradication in the prevention of gastric cancer however is a more difficult discussion since there is probably no benefit anymore in eradication once certain changes have taken place. When exactly this "point of no return" is reached remains largely unknown. In developing countries incidence of gastric cancer stays high and strategies are being developed to reduce the prevalence of the infection or eradicate infected persons before premalignant lesions are present (3-5). In the meantime, the prevalence of *H. pylori* infection seems to be decreasing in industrialized countries in younger age groups (15,16). However, results range from 7% infected children in the Czech republic, 19% in Latvia, up to 50% in Portugal (age group 11 to 14) (17-19) and there are also large differences within countries (7,8). Results of prevalence of *H. pylori* infection in the Belgium population are scarce or come from studies in symptomatic patients (20). A small study was conducted in 2010 which compared prevalence of *H. pylori* infection between sewerage workers and a control group. In the control group the prevalence was as low as 15% (21). An older study from 2007 comparing staff members of institutions for people with intellectual disability with controls showed prevalence's of 40% and 29% (controls) (22).

The aim of our study was to determine the prevalence of *H. pylori* infection in children and young adults, and to determine risk factors for infection. We presumed that these results would give an estimation of the evolution of *H. pylori* associated disease in the future since re-infection is rare in industrialized countries (23). We found that the general infection rate was only slightly lower than results compared to a 1993 study which also including asymptomatic but younger children between 8 and 14 years in Belgium, and used serology (11.0% in our study versus 13.4% in 1993) (24). However we found a

Table 2. — **Risk factors for *H. pylori* infection**

Characteristic	Unadjusted OR (95% CI) *	Adjusted OR (95% CI) **
Gender		
Female (reference)	–	–
Male	0.59 (0.33 to 1.06)	–
Age		
15 years or less (reference)	–	–
16 or more	1.51 (0.62 to 2.15)	–
Number of household members		
4 or less (reference)	–	–
5 or more	1.23 (0.61 to 2.48)	–
Stay in day nursery		
No (reference)	–	–
Yes	**0.52 (0.28 to 0.96)**	**3.39 (1.10 to 10.44)**
Place of birth child		
Belgium (reference)	–	–
Other country	**19.23 (8.81 to 41.98)**	**4.81 (1.19 to 19.40)**
Place of birth father		
Belgium (reference)	–	–
Other country	**26.37 (12.02 to 57.82)**	**38.45 (8.72 to 169.50)**
Place of birth mother		
Belgium (reference)	–	–
Other country	**11.71 (5.61 to 24.45)**	0.67 (0.15 to 2.93)
Education father		
School ≤ age 19 (reference)	–	–
School > age 19	**0.46 (0.22 to 0.94)**	0.93 (0.30 to 2.91)
Education mother		
School ≤ age 19	–	–
School > age 19	**0.33 (1.15 to 0.76)**	**0.26 (0.08 to 0.86)**

* Crude odds ratio (OR), 95% confidence interval (CI), calculated using univariate logistic regression (i.e. considering the effect of each characteristic separately).

** OR simultaneously adjusted for the factors that were found to be statistically significant in univariate analyses (i.e. the current adjusted, multivariate analysis considers the effect of stay in day nursery, place of birth child, place of birth father, place of birth mother, education father, and education mother simultaneously).

ORs not including unity (value of no effect) are printed in bold.

very low infection rate of 3,2% in children, born in Belgium from Belgian born parents (6% in 1993) compared with 30% in children with parents born in high prevalence countries (20% in 1993) and 60% in children born in high prevalence countries.

In the current study, we found in multivariate analyses that staying in a day nursery, a birthplace of child or father outside Belgium, and lower education levels of mother were statistically significant risk factors for *H. pylori* infection. Known risk factors like lower economic status (taking education level of father as a surrogate marker), and crowded families were not associated with infection in our study.

A significant risk factor for *H. pylori* infection was origin, as documented by birthplace of child and birthplace of father. These results also suggest that infection in Belgium takes place within the family since the infection risk is also very high in children born in Belgium but with parents who came from regions with high prevalence. It must be mentioned that we found a striking discrepancy between unadjusted and adjusted ORs concerning place of birth of the mother, which is most likely due to missing and low number of the infected population. A similar study from Germany, conducted in 1998 in children between 5 and 8 years old, found already a very low infection rate of 4,8% in children from Germany, and born in Germany and infection rates from 60% in children born in high prevalence countries but growing up in Germany (25).

Results from asymptomatic children in non-industrialized countries range from 7 to 80% (1,26). Low prevalence was noted in the Czech Republic (7%) but high prevalence in Poland (children < 4 years) and Latvia (17,18,27). In our study infection rate in the small and heterogeneous group of east European countries was 60%. In the children born in Africa (mainly sub-Saharan Africa) the prevalence was 93%. Of course, comparison between all these studies is difficult since age differs between 2 and 20 years and often serology is used.

Our large Belgian study, examining prevalence in a representative population sample of children and young adults, showed that prevalence of *H. pylori* infection in

the native Belgian children and young adults is as low as 3.2% and halved in the last 20 years. Infection risk stays very high and seems to change little in children whose parents have their origin in countries with high prevalence. These results are important for decisions concerning public health measurements (screening).

The study also supports the available evidence that spread of infection is from person-to person, particularly within families.

Conclusion

In this cohort of Belgian asymptomatic children and young adults, the prevalence of *Helicobacter pylori* infection is very diverse. The general prevalence is 11%. In Belgian born children with Belgian parents infection risk was as low as 3,2%. The risk of infection increased significantly to 30% if one or two parents where from high prevalence countries and rose to 60% in children born in high prevalence countries. The most significant risk factor found in this study was origin.

In multivariate analyses staying in a day nursery, a birthplace of child or father outside Belgium, and lower education levels of mother were statistically significant risk factors for *H. pylori* infection. Known risk factors like lower economic status (taking education level of father as a surrogate marker), and crowded families were not associated with infection in our study.

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On behalf of all authors, the corresponding author states that there is no conflict of interest.

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