DECREASE IN PREVALENCE OF *HELICOBACTER PYLORI* INFECTION DURING A 10-YEAR PERIOD IN BRAZILIAN CHILDREN

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ABSTRACT – ***Background*** - Decreasing prevalence of *H pylori* infection has been reported in some countries. ***Aim*** - To evaluate the prevalence of *Helicobacter pylori* infection in a 10-year period in children submitted to upper digestive endoscopy. ***Methods*** - It was a retrospective observational study. The records of 1,165 endoscopies performed during a 10-year period in a public hospital of the City of São Paulo, SP, Brazil, in patients up to 18-year-old. Only the first endoscopy was considered. *Helicobacter pylori* infection was defined by the rapid urease test, performed with one fragment of antral mucosa. Chi-square for trend has been estimated to compare *Helicobacter pylori* prevalence across the period. ***Results*** - The main indication for endoscopy was epigastric pain (47.4%). There were 392 patients with *H pylori* infection (33.6%), 12.8% being infants, 19.4% toddlers, 28.8% schoolchildren and 46.3% adolescents. Prevalence was 60.47% in the first year of the study and 30.43% in the last. Among the less than 6-year-old patients there was a decrease in infection prevalence from 25% for the 1993-6 period to 14.3% in the 2000-02 period, while among the over 12-year-old patients the decrease was from 55.5% in the first period to 39.6% in the latter. The decrease in *H pylori* infection prevalence was more intense within patients with epigastric pain, in which prevalence has decreased from 48.2% (92/191) in 1993-6, to 41.9% (65/155) in 1997-9 and 27.7% (57/206) in 2000-02. ***Conclusion*** - The study suggests a significant decrease in the prevalence of *H pylori* infection regarding the studied patients. The trend was mainly observed in the younger age group and in patients with epigastric pain.

HEADINGS – Helicobacter infection, epidemiology. Urease. Child.

INTRODUCTION

Adult individuals who live in precarious conditions during childhood constitute the population at the highest risk for morbidity due to *Helicobacter pylori* infection. The recent increase in life expectancy in most of these countries allows foreseeing an increase of its morbidity in the next years, particularly due to peptic ulcers and gastric cancer.

Study of the epidemiology of *H pylori* infection in childhood allows to visualize morbidity in adult life, since it is at this age that most patients acquire the infection, even in developed countries[18]. On the other hand, incidence in childhood is related to prevalence in adults, since the child is more exposed to the bacterium by contagion within the family, particularly the infected mother[4]. Presently it is believed that the infection is acquired during childhood, mainly in populations at high risk. Studies show a 2.2%-3.3% incidence among children of developing countries or groups at high risk in developed countries[7, 9, 11], although most of these studies are based on serology, a test of less accuracy in smaller children[2, 15].

In developed countries, the past high prevalence of the infection was surpassed by improvement in environmental conditions, since its prevalence is closely related to socioeconomic factors. Some recent studies suggest that infection incidence in high-risk groups in developed countries, particularly immigrants, is declining, similarly to developing countries, as a consequence of better access to health, unintentional use of medications (antibiotics and antisecretory drugs) and improvement in environmental conditions[13, 17, 20].

In our country, documented improvement of infantile mortality and increase in life expectancy occurred in the last decades, attributed to improvement in basic sanitation and access to the public health system[10]. We may experience a silent decrease in the prevalence of *H pylori* infection.

The objective of this study was to verify differences in *H pylori* infection based on a retrospective analysis of a data bank of an endoscopy service of a public university hospital in the city of São Paulo, Brazil.

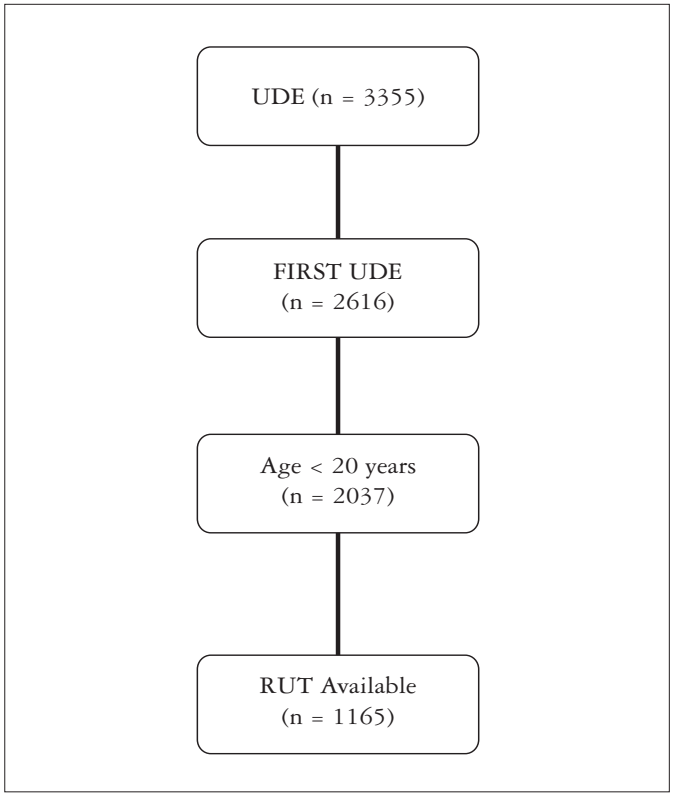
This study was conducted on Pediatric Gastroenterology Division of "Universidade Federal de São Paulo / Escola Paulista de Medicina", São Paulo, SP, Brazil. Correspondence: Dr. Rodrigo Strehl Machado – Pediatric Gastroenterology Division – Rua Pedro de Toledo, 441 – 04039-031 – São Paulo, SP, Brazil. E-mail: rodrigo@gastroped.epm.br

METHODS

A retrospective study where the records of upper digestive endoscopy performed from 1993 to 2002 at the Digestive Endoscopy Sector of the Pediatric Gastroenterology Division, "Universidade Federal de São Paulo – Escola Paulista de Medicina" – UNIFESP/EPM, São Paulo, SP, Brazil, were reviewed. The attended patients are from the public health system, generally from low-income families, referred from Health Units or from the outpatient clinic of Pediatric Gastroenterology, UNIFESP/EPM. Records of 2003 to 2004 were not included because in those years part of the services were transferred to other sectors.

Patients

Only the first upper digestive endoscopies of less than 20-year-old patients performed in the studied period using the rapid urease test were analyzed (Figure 1). One thousand one hundred sixty-five patients, aged from 1 month to 19 years and 8 months were included (M/F 563:602, mean 8.82 years, standard deviation 4.31 years). These cases originated from several research protocols on diagnosis and treatment of infection with *H pylori* during the studied decade. Usually the rapid urease breath test was performed in all patients, except for those in use of antibiotics, antisecretory drugs or bismuth salts in the last months for non-digestive diseases and with a therapeutic purpose.



UDE:upper digestive endoscopy
rut:rapid urease test

FIGURE 1. Selection of endoscopy records participating in the study

Endoscopy

It was performed after an 8-hour fast under conscious sedation with midazolam and meperidine (over 10-year-old patients) or under deep sedation administered by an anesthetist (the other patients).

Rapid urease test (RUT)

A non-commercial solution, prepared in the endoscopy room was used. This solution contains 100 mg urea in 1 mL distilled water, with a drop of phenol red. RUT is evaluated within 1 hour after immersion of two gastric antrum fragments, and was previously validated in our service, with 100% sensitivity and 84.2% specificity[12].

Statistics

The quantitative variables were summarized by estimation of mean and standard deviation, while the qualitative by proportion. Pearson's chi-square test was used for comparison between treatment groups in 2x2 tables. Significance of trend to variation of positive results for RUT was evaluated by chi-square for trend, with a significance level of 0.05[1].

RESULTS

In the studied period most indication for endoscopy of the 1,165 cases was epigastric pain with 47.4%, followed by gastroesophageal reflux with 16.5% (Table 1). Indication for the test presented a significant variation during the period, significant trend to lower proportion of patients with epigastric pain and higher proportion of patients with malabsorption syndrome in the series of the more recent years (Table 2).

There was a higher proportion of patients less than 6 years old in the more recent years (16.3% in 1993, 36.6% in 2002, $\chi^2_{trend} = 33.68$, $P = 0.0001$). Correspondently there was a significant decrease in the proportion of patients with age equal to or more than 12 years (27.9% in 1933, 15.5% in 2002, $\chi^2_{trend} = 11.97$, $P = 0.0005$), as well as patients with age between 6 years and 12 years (55.8% in 1993, 47.8% in 2002, $\chi^2_{trend} = 4.76$, $P = 0.0291$).

General prevalence of *H pylori* infection was 33.6% (392/1165) in the studied period. There was no difference between male and female gender regarding prevalence (216/602F and 176/563M, $P = 0.107$), except for over 12-year-old patients, where a higher infection prevalence occurred in females (58.5%, vs 39.8%, $P = 0.002$). Infection was significantly associated with the endoscopic diagnoses of duodenal ulcer and nodular antrum gastritis, and inversely associated with a normal examination (Table 3). A direct and significant relationship between prevalence and the patient's age was observed, with 12.8% (11/86) infected among those less

TABLE 1. Indication for endoscopic examination in 1,165 patients

Indication	n	%
Epigastric abdominal pain	552	47.4%
Gastroesophageal reflux	192	16.5%
Abdominal pain – other localizations	169	14.5%
Malabsorption syndrome	158	13.6%
Upper digestive hemorrhage	41	3.5%
Other indications	53	4.5%

TABLE 2. Indication for endoscopies according to year

Year	Epigastric pain*	Gastroesophageal reflux†	Abdominal pain‡	Malabsorption syndrome§	Total
1993	24 (55.8%)	6 (13.9%)	11 (25.6%)	0 (0%)	43
1994	59 (54.6%)	11 (10.2%)	13 (12%)	7 (6.4%)	108
1995	63 (54.3%)	11 (9.5%)	19 (16.3%)	11 (9.5%)	116
1996	45 (44.5%)	17 (16.8%)	26 (25.7%)	7 (6.9%)	101
1997	35 (44.3%)	27 (34.1%)	9 (11.4%)	5 (6.3%)	79
1998	41 (56.9%)	11 (15.3%)	9 (12.5%)	3 (4.2%)	72
1999	79 (62.7%)	21 (16.7%)	8 (6.3%)	9 (7.1%)	126
2000	85 (45%)	37 (20.1%)	14 (7.4%)	33 (17.5%)	189
2001	77 (45.3%)	24 (14.1%)	18 (10.6%)	41 (24.1%)	170
2002	44 (27.3%)	26 (16.1%)	42 (26.1%)	42 (26.1%)	161

* $\chi^2_{trend} = 16.59$, $P < 0.0001$
† $\chi^2_{trend} = 1.29$, $P = 0.256$
‡ $\chi^2_{trend} = 0.44$, $P = 0.507$
§ $\chi^2_{trend} = 50.89$, $P < 0.0001$

TABLE 3. Endoscopic diagnosis and its relationship with *H pylori* infection (each patient may have more than one diagnosis)

Endoscopy result	n	%	*H pylori (%)*	Chi-square	*P*
Normal	617	53	20.1	95.36	*P* <0.0000001
Antrum nodularity	164	14.1	87.8	250.74	*P* <0.0000001
Gastric mucosal enanthema	116	10	35.3	0.17	*P* = 0.68
Esophagitis	114	9.8	27.1	2.36	*P* = 0.12
Non erosive duodenitis	73	6.3	34.2	0.01	*P* = 0.91
Duodenal ulcer	65	5.6	63.1	26.7	*P = 0.0000002*
Erosive gastritis	34	2.9	35.3	0.04	*P* = 0.84
Gastric ulcer	13	1.1	46.2	0.92	*P* = 0.34
Total	1165	100%	33.6%		

than 2 years old, 19.4% (46/273) among preschool children, 28.8% (90/313) among patients with age between 6 and 10 years and 46.3% (245/529) among the patients over ten years old (χ^2_{trend} = 165.69, $P = 0.0001$).

During the studied period there occurred significant prevalence of infection reduction from 39.1% in the 1993-1994 biennium to 28.4% in the 2001-2002 biennium (Figure 2, $\chi^2_{trend} = 14.84$, $P = 0.0001$). In the analysis according to age range, the interval was divided into three periods (1993-6, 1997-9, 2000-2). Among the patients with age less than 6 years, there was a reduction in prevalence from 25% (18/72) in the first period to 19.3% (12/62) in the second period and finally 14.3% (27/189) in the last period ($\chi^2_{trend} = 4.27$, $P = 0.038$). In the patients aged 12 years or more the percents were respectively 55.5% (61/110), 57.3% (47/82) and 39.6% (42/106) ($\chi^2_{trend} = 5.34$, $P = 0.021$). In the intermediary age range infection prevalence did not present variation (37.1%, 31.6% and 32.9%, $\chi^2_{trend} = 0.75$, $P = 0.386$) (Figure 3).

The decrease in *H pylori* infection prevalence was more intense within patients with epigastric pain, in which prevalence has decreased from 48.2% (92/191) in 1993-6, to 41.9% (65/155) in 1997-9 and 27.7% (57/206) in 2000-02 ($\chi^2_{trend} = 17.66$, $P = 0.00003$), but it was not significant in patients with malabsorption, in which prevalence was 28% (7/25) in 1993-6, to 29.4% (5/17) in 1997-9 and 19.8% (23/116) in 2000-02 ($\chi^2_{trend} = 1.125$, $P = 0.29$).

DISCUSSION

The study showed decrease in *H pylori* prevalence during a 10-year period, with a 39.1% reduction in the 1993 to 1994 biennium to 28.4% in the 2003-2004 biennium. Despite the increase during the period in the number of examinations performed in younger patients, we could show that decrease in prevalence was significant in two age ranges: less than 6-year-old patients and adolescents. A more detailed analysis of the variation according to age range is difficult because of the small number of patients. However, reduction in infection prevalence in children less than 6 years old constitutes a strong evidence of the current change in the epidemiology among us. Recently, ROWLAND et al.[18] evaluated prospectively the incidence of *H pylori* infection during 4 consecutive years using the ^{13}C-urea breath test in 227 Irish children aged 2 to 4 years. The authors observed that infection rate for 100 individuals/year was higher between 2 and 3 years (5.05; CI 95%: 1.64-11.78); 47/48 infected children acquired the infection before the age of 5 years and only one, after the age of 5. This study shows that even in a developed country, the first infection occurred early. In Germany, in children of Turkish descent, incidence in those less than 4 years old was 7%, being higher during the second year of life[16]. The importance of childhood in the epidemiology of the infection is similar in the different situations and not dependent on the socioeconomic condition[19].

Retrospective evaluation imposes restrictions: population-based prospective design is undoubtedly more consistent for the study of the epidemiology of the pathogen in a historical series. However, the different research protocols of *H pylori* infection in children in the studied period led to the natural exclusion of patients where the urease test was less accurate, since routinely the patient or representative is asked about medications in use. Finally,

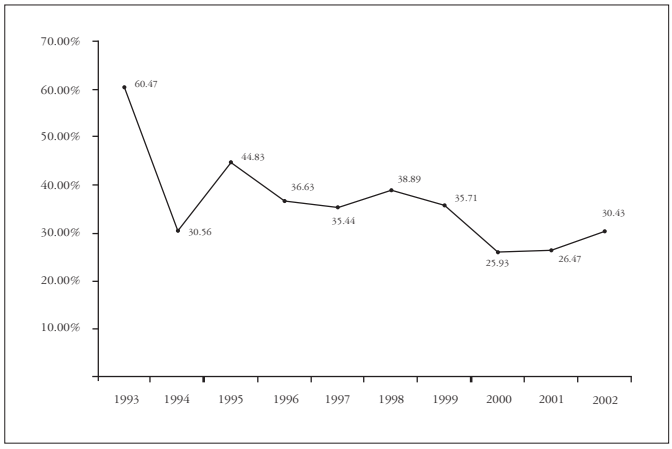


FIGURE 2. Prevalence of *H pylori* infection along 10 years among 1165 children and adolescents

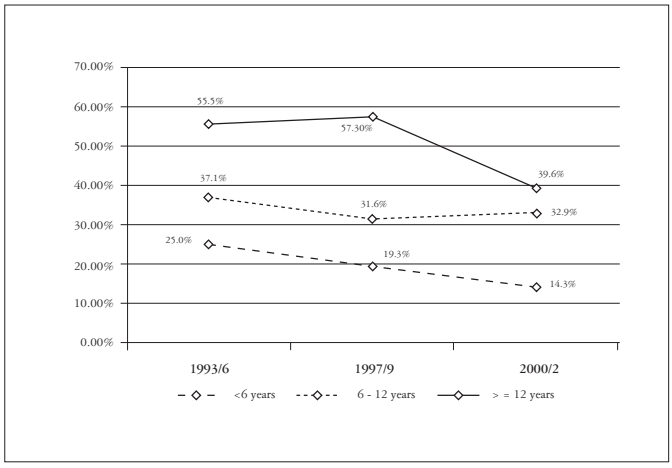


FIGURE 3. Prevalence of the infection along 10 years according to age group

inclusion of only the first endoscopy performed in the service contributes to a greater safety regarding quality of data.

In the study only 63.1% of the patients with duodenal ulcer had a positive urease test. This figure is surprising, since we recently reported a series of duodenal ulcer cases with 95.3% of the patients with *H pylori*[5]. However, other ulcer cases have to be taken into account, such as use of anti-inflammatory drugs and non-*H pylori* related ulcer disease[3].

Change in the profile of patients who attend the service may be reflected in the found result. The "Hospital São Paulo" linked to UNIFESP/EPM attends patient of the Public Health System and of private health insurance companies. However, the studied data base included only patients from the Public Health System, since the data bank does not encompass patients of the private health insurance companies. During the period there was no alteration in the reference system and the patients were usually referred by the Pediatric Gastroenterology outpatient clinic of the institution. Thus, we think that alterations in the attended socioeconomic profile would only reflect alterations in the socioeconomic profile of the population as a whole, without relation to access to the health service. From 2003 on there were changes in agenda organization criteria, which was the reason for excluding the years of 2003 and 2004 from the analysis. Clinical features of patients have changed during the study period, and the change has attenuated the decrease of *H pylori* prevalence. There was a decline of proportion of patients with epigastric pain, but the decline of prevalence in these patients was sharper than in the whole group. On the other hand, it has been increased proportion of endoscopies to evaluate malabsorption. This group of patients has not varied the infection prevalence, which was already low since the beginning of the period. It is common in our country treat patients with failure to thrive with anti-parasite medicines before further evaluation, and metronidazol is a very popular drug in this context.

Reduction in the prevalence of *H pylori* gastritis and its consequences is a phenomenon recognized in developed countries, where the analysis of historical series allows foreseeing the natural eradication of the infection in the next centuries[19]. In Holland, a retrospective study of 14,909 endoscopies performed during 10 years (1993 to 2002) showed a trend towards decrease in infection prevalence in patients less than 50 years old, pointing to a lower than 10% prevalence in this age group in 2009 and global prevalence less than 10% in 2027[8]. In Spain there was a reduction in prevalence from 1990 to 2000 (adults) among users of an endoscopy service from 76.3% to 69.3% with a parallel decrease in duodenal ulcer incidence (130.8 per 100,000 inhabitants in 1985 to 86.1 in 2000) and its complications (109.1 per 100,000 inhabitants in 1990 to 81.4 in 2000)[14]. In the period, in spite of the slight increase in anti-inflammatory drug use, there was a great increase in the prescription of proton pump inhibitors. Even in high prevalence population groups in developed countries, the infection is on the decline, particularly in childhood. In only one year, a group identified a 9% to 4% prevalence decrease in children of Turkish immigrants in Germany, in their first year of life[17]. In developing countries there is already increasing evidence of decrease in prevalence of infection and its consequences. In Estonia, adjusted seroprevalence of infection among hospitalized children decreased from 42.2% to 28.1% in 1991 to 2002, with a more intense decrease in the group aged less than 5 years[13]. In the Philippines, from 1996 to 2002 there was a reduction of duodenal ulcer prevalence from 15.83% to 7.02% in adults, from 20.05% to 14.7% for gastric ulcer among patients with endoscopy while, among patients with peptic ulcer the proportion of infected patients decreased from 71.9% to 34.6%[20]. A study from Hong Kong reached similar results, but with the additional factor of less consumption of anti-inflammatory drugs in the period[21]. A seroprevalence study in Taiwan did not reproduce the trend on comparing its data with another study of 1989. However, the study was conducted with a population of low infection prevalence (0.9% between 1 and 3 years of age to 19.4%, between 9 and 12 years, in 1989) and the two studies used different serology tests[6].

The present study detected reduction in the prevalence of *H pylori* infection in an endoscopy data bank of patients attended at a public hospital in the city of São Paulo, particularly those at a higher risk to acquire the infection. Prospective studies on the epidemiology of the infection among us are needed to better establish goals to fight it.

Kawakami E, Machado RS, Ogata SK, Langner M. Diminuição na prevalência da infecção por *Helicobacter pylori* em crianças brasileiras num período de 10 anos. Arq Gastroenterol. 2008;45(2):147-51.

RESUMO – ***Racional*** - Redução da prevalência de infecção por *Helicobacter pylori* tem sido relatada em alguns países. ***Objetivo*** – Avaliar, em crianças, a prevalência de infecção por *H pylori* em um período de 10 anos, realizando endoscopia digestiva alta. ***Métodos*** - Estudo retrospectivo observacional. Os relatórios de 1.165 endoscopias digestivas altas realizadas em 10 anos em um hospital público da cidade de São Paulo, SP, foram revisados, sendo incluídas as primeiras endoscopias de pacientes com idade inferior a 18 anos. A infecção por *H pylori* foi definida pelo teste rápido da urease, com um fragmento de mucosa antral. ***Resultados*** - A principal indicação de endoscopia foi dor epigástrica (47,4%). A prevalência de infecção foi 33,6% (12,8% em lactentes, 19,4% em pré-escolares, 28,8% em escolares e 46,3% em adolescentes). No primeiro ano de estudo foi 60,47%, e 30,43% no último. Entre os pacientes menores de 6 anos, houve diminuição na prevalência de 25% (1993-6) para 14.3% (2000-02), enquanto entre os pacientes maiores de 12 anos a diminuição foi de 55,5% (1993-6) para 39,6% (2000-02). A diminuição da prevalência foi significativa nos pacientes com dor epigástrica, nos quais passou de 48,2% (92/191) em 1993-6, para 41,9% (65/155) em 1997-9 e 27,7% (57/206) em 2000-02. ***Conclusão*** - O estudo sugere que houve diminuição significativa na prevalência da infecção por *H pylori* nos pacientes estudados. A tendência foi principalmente observada no grupo etário mais jovem e nos pacientes com dor epigástrica.

DESCRITORES – Infecções por Helicobacter, epidemiologia. Urease. Criança.

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