Helicobacter pylori infection in Turkish preschool and school children: role of socioeconomic factors and breast feeding

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It has been shown that Helicobacter pylori (H. pylori) infection is rare among children in developed countries. In Turkey, the prevalence of H. pylori infection among adults is about 80-85%, which is close to the ratios reported in developing countries. There is limited knowledge, however, on the prevalence, determinants and associations of this infection, such as short stature, familial history of dyspepsia and abdominal pain, in children. The aims of this study were to estimate the prevalence, determinants and associations of H. pylori infection in a group of healthy school children using ^{13}C-urea breath test (^{13}C-UBT).

The study subjects were selected from a kindergarten and an elementary school. The H. pylori status was determined by ^{13}C-UBT. Standard questionnaires ascertaining sociodemographic data were completed for each child by questioning the mothers. Three hundred twenty-seven children aged 3-12 years participated in the study. Overall, 162 children (49.5%) were infected with H. pylori, and the prevalence increased with age: 18.2% under 4 years, 41% at 4-6 years, 48.6% at 6-8 years, 50% at 8-10 years, and 63% at 11-12 years of age. No association was determined between H. pylori infection and height and weight percentiles, history of abdominal pain or family history of dyspepsia in the study group. Investigation of the prevalence of H. pylori infection in our study group in relation to socioeconomic data in a logistic regression model revealed that low income, high household density of children, use of stove for heating, and no breast feeding were important risk factors for H. pylori infection.

This study was done in a group of healthy Turkish children to estimate the age-related prevalence of H. pylori infection and to determine the factors predisposing to H. pylori infection during childhood. It was found that 1/5 of healthy Turkish children were infected with H. pylori before four years of age, and that every one child out of two under 11 years of age was infected with H. pylori. Low socioeconomic status, poor household living conditions and no breast feeding were determined as independent risk factors of H.

Helicobacter (H. pylori) related diseases are responsible for morbidity and mortality in both developed and developing countries[1,2]. H. pylori infection is an important risk factor for gastroduodenal diseases and gastric cancer[1,3-7]. The association between H. pylori infection and malnutrition, short stature and diarrhea have also been demonstrated in children[2,8-10]. There are conflicting data on the association between H. pylori and abdominal pain and family history of dyspepsia[11-14].

H. pylori infection is usually acquired during the early years of life and persists for several years. The prevalence of H. pylori infection has been reported to increase with age[15-19]. There seems to be an association between the prevalence of H. pylori in adults and the risk of acquisition of H. pylori infection during childhood[18-22]. It has been noted that the prevalence of H. pylori infection differs among developing and developed countries[17-20,23]. Among children, the prevalence of H. pylori infection is not more than 10% in developed countries, whereas it may reach up to 75-80% in developing countries[17,18,20,23]. It has been reported that the variation in the prevalence of H. pylori infection in different populations might be associated with socioeconomic factors and some habitual living and housing conditions[20,24,25].

Studies have demonstrated that children who belong to a population originating from a high prevalence country have high prevalence of H. pylori. Living conditions and socioeconomic factors, secondary to immigration, may play a role in acquisition of H. pylori infection. There have been several studies done in Turkish children whose families migrated to Germany before or after their birth, investigating the prevalence and associated risk factors for H. pylori infection[26-28]. The prevalence of H. pylori infection is very high among adults in Turkey. There are data on the prevalence of H. pylori infection in children of Turkish immigrants living in different parts of Europe, however, there is limited knowledge on the prevalence, determinants and associations of H. pylori infection among healthy Turkish children living in their native country[19,20,26].

The aim of this study was to find out the prevalence, determinants and associations of H. pylori infection in a population of pre-school and school-aged healthy children using ^{13}C-urea breath test (^{13}C-UBT).

Material and Methods

Three hundred twenty-seven healthy children, 169 boys and 158 girls, with a mean age of 8.2±2.1 years (range, 3-12 years) were studied. Children who received oral or parenteral antibiotics four weeks prior to the investigation were excluded from the study. The current height and weight of each child were measured on the day of the ^{13}C-UBT. Standard weight and height scales were used, weighing the body with a sensitivity of at least 100 g and measuring the height with a sensitivity of at least 0.5 cm. Informed consent forms from parents were obtained for each child. The study was approved by the Ethical Board of the Marmara University School of Medicine.

Data Collection

Infection status was determined by ^{13}C-UBT, which shows active infection with H. pylori, and for this purpose INFAI ^{13}C-urea breath test (Institut for Biomedizinische, Bochum, Germany) kits were used. Fasting children were asked to drink 100-200 ml of orange juice (pH 2.3-2.5) to avoid premature gastric emptying. Two baseline breath samples were collected directly into 10 ml vacutainer tubes via a straw. The tubes were recapped immediately after breath collection. Then 75 mg non-radioactive ^{13}C labelled urea was dissolved in 15 ml orange juice which the children were asked to drink. Two additional breath samples were collected 30 minutes later.

^{13}C abundance was determined by the isotope ratio mass spectrometry (AP 2003 Analytical Precision, Manchester, UK) on breath samples. Isotope enrichment was expressed as corrected delta per mil (δ‰) relative to the Pee Dee belemnite limestone (PDB) international standard. A change in the δ ^{13}C value over baseline of more than 5‰ was considered positive.

Questionnaire

Mothers were asked to answer each question in a standardized questionnaire. The same physician was responsible for filling in the questionnaires. The questionnaire was designed to obtain information about family demographics such as the education level of parents, occupation, family income, and housing and living conditions (residence, number of rooms in the house the number of household members, the heating source, type of drinking water, the presence of a pet within the house), and association with height, weight, recurrent vomiting, defecation pattern, history of abdominal pain and family history of dyspepsia. Growth was determined using centile values of height and weight, which were calculated by using standard weight and height charts for Turkish children. Recurrent abdominal pain was defined as the presence of unexplained abdominal pain, occurring at least three times during the last three months and severe enough to interfere with daily activity. Vomiting was assessed by asking the presence of voimiting episodes during the last three months and occurring at least once a day.

Methods of Analysis

H. pylori infection was defined as a positive ^{13}C-UBT result. Categorization of socioeconomic class was based on the combination of occupation and education, with income[29]. Four education levels (elementary school, secondary school, high school, university), five occupational categories (major professionals, minor professionals and administrators, clerks-sales-technicians, skilled workers, semi-skilled or unskilled workers), and three income levels were used to identify social classes. Five social classes were identified ranging from the highest (I) to the lowest (V) (Table I).

Table I. Socioeconomic Classes

Social class	Education	Occupation	Income
I	University	Major professionals	High
II	High school (college)	Minor professionals and administrators	Moderate to high
III	High school	Clerks, sales, and technicians	Middle
IV	Secondary school	Skilled workers	Middle to low

Statistical Analysis

Univariate analyses were carried out to examine the associations between study variables with ^{13}C-UBT positivity for H. pylori using chi-square test (X^2 test). Five social classes were analysed as three categories by combining II and III as "middle", and IV and V as "low". Multiple logistic regression with ^{13}C-UBT positivity for H. pylori as the dependent variable was used to determine independent predictors. Variables associated univariately were included in the multiple regression models (forward stepwise selection). The improvement of the model was evaluated with the low-likelihood ratio test using X^2 distribution of significance (>95%).

Results

Three hundred twenty-seven children were included in the study; 158 (48.3%) were girls and 169 (51.7%) were boys. Forty-four of 327 (13.4%) were below 6 years of age, 107 (32.7%) were between 6-8 years of age, 106 (32.4%) of them were between 8.1-10 years of age, and the remaining 70 children (21.4%) were older than 10 years of age.

Overall, 162 of 327 children (49.5%) had positive ^{13}C-UBT for H. pylori. The prevalences were 18.2% under 4 years, 41% for 4-6 years,

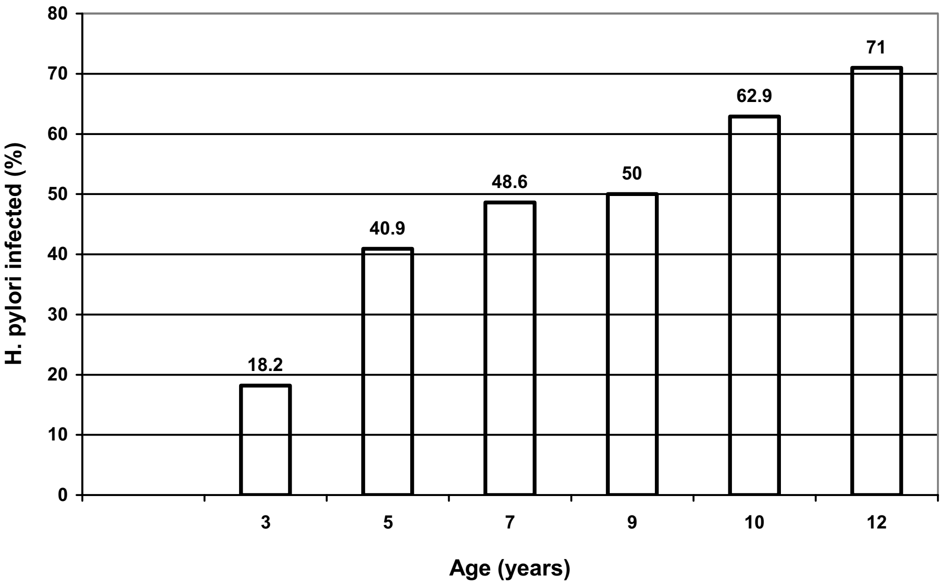

Fig. 1. Age-specific distribution of H. pylori infection.

48.6% at 6-8 years, 50% at 8-10 years, and 63% at 10-12 years of age (Fig. 1). It was seen that the prevalence of H. pylori infection increased with age and the highest prevalence was found in children older than 10 years of age ($p<0.01$). There was not a significant sex difference for the prevalence of H. pylori infection in the study population ($p=0.702$).

Table II shows the determinants of H. pylori infection and the prevalence of H. pylori infection according to family demographics, living and housing conditions and socioeconomic status. As the study group was unequally distributed into five socioeconomic classes, social classes were combined into three categories: I (high), II and III (middle), IV and V (low). There was an inverse relation between socioeconomic status and prevalence of H. pylori infection ($p=0.0002$). When the high socioeconomic class was taken as reference category, it was seen that the risk of H. pylori infection increased in the middle and low categories, with odds ratios of 2.15 and 1.83, respectively (Table III). Although

Table II. Prevalence of H. pylori Infection According to Family Demographics, Education of Parents and Breast Feeding

	H. pylori positive cases		
	n	%	p*
Socioeconomic class			
low (IV and V)	49/84	58.3	
middle (II and III)	68/113	60.2	0.0002
high (I)	45/130	34.6	
Household density			
≤1 person/room	39/104	37.5	
1.1-2 persons/room	106/198	53.5	0.01
≥2 persons/room	17/25	68.0	
Number of sibling			
None	18/60	30.0	
1	79/166	47.6	0.0001
2	65/101	64.4	
Heating system			
Coal-stove	123/211	58.3	
<0.0001			
Central heating	39/116	33.6	
Drinking water source			
city water	44/69	63.8	
well-artesian well	12/21	57.1	0.01
bottled water	106/237	44.7	
Education of mother			
None	19/27	70.4	
≤5 years	105/189	55.6	
<0.0001			
6-11 years	33/84	39.3	
university	5/27	18.5	
Education of father			
≤5 years	90/156	57.7	
6-11 years	63/128	49.2	0.0001
university	9/43	20.9	
Breast feeding			
not breast-fed	12/23	52.2	
≤1 months	44/81	54.3	0.02
2-3 months	25/64	39.1	
4-5 months	37/89	41.6	
6-24 months	44/70	62.9	

Table III. Logistic Regression Analysis of Risk Factors and Their Association with H. pylori Infection in the Study Group

Variable	Total number (% positive)	OR	95% CI	p
Socioeconomic class				
high	45 (34.6)	1*		
middle	68 (60.2)	2.15	1.20-3.86	0.01
low	49 (58.3)	1.83	0.96-3.49	0.07
Number of siblings				
none	18 (30)	1*		
1	79 (47.6)	1.94	1.20-3.86	0.01
≥2	65 (64.4)	3.30	0.96-3.49	0.07
Heating system				
central heating	39 (33.6)	1*		
coal-stove	99 (55.3)	2.14	1.25-3.68	0.006
Breast feeding				
breast-fed	154 (48.7)	1*		
not breast-fed	8 (72.7)	4.45	1.04-19.1	0.04

1* Reference category, adjusted for all other variables listed in table and age, percentile values for weight and height, household density, education of parents.

OR: odds ratio; CI: confidence interval.

being the owner of the house seemed to be a protective factor from H. pylori infection in children in the univariate analysis, it was not an important factor for acquisition of H. pylori in the multivariate analysis. Being the owner of house might be related to the socioeconomic status of the family but not to the hygienic conditions in which the family lived. Residential crowding was related to the prevalence of H. pylori infection. The highest proportions of infected children were found in houses in which two or more persons were sharing the same room ($p=0.01$). There was a significant association between H. pylori infection and increased number of siblings in the study group ($p=0.001$). The risk for H. pylori infection was doubled in children having more than two siblings when compared to children having no siblings at all (64.4% versus 30%, respectively). This variable remained as an independent risk factor for prevalence of H. pylori infection in the multivariate analysis (Table III). In our study, it was found that a central heating system was a protective factor for H. pylori infection in children ($p<0.0001$). When the central heating was taken as reference category, the risk of H. pylori infection was doubled in coal-stove heated houses ($p=0.006$, Table III). Prevalence of the infection was inversely related to the education level of both parents ($p=0.0001$). The water source seemed to be a significant predictor of H. pylori infection. Although most of the children in our study group were drinking bottled water from water stations, the prevalence of H. pylori infection was the highest among children who were drinking city water ($p=0.01$). Although both parental education and drinking water source were important risk factors for acquisition of H. pylori infection in the univariate analysis, neither factor contributed significantly to the prediction of infection status in logistic regression analysis. There was no significant increase in the prevalence of H. pylori infection in children who had a pet in their house, on the contrary there was a lower prevalence of infection when compared with those who had no pet (41.6% versus 52%). The explanation for this disparity could be that presence of a pet in the house in our country may indicate a better socioeconomic status.

There was a significant negative association between H. pylori infection and breastfeeding ($p<0.05$). To analyze the role of breastfeeding, the groups were adjusted for socio-economic classes and it was found that the protective role of breastfeeding was only present in the low socioeconomic class ($p=0.007$). Breastfeeding was also identified as an independent risk factor for H. pylori infection in multivariate analysis ($p=0.04$, Table III).

It has been found that the taller or heavier the child, the lower the prevalence of H.

pylori infection (53.1% for short vs. 39% for tall children, and 55.1% for heavy vs. 39.3% for thin children). The shortest and the thinnest children showed the highest rates of H. pylori infection (53.1% and 55.1%, respectively). Neither vomiting nor diarrhea seemed to be associated with H. pylori infection in our study. Almost one-third of the study group was suffering from chronic recurrent abdominal pain, which was a rather common complaint even in healthy school children, but there was no statistically significant difference in frequency of H. pylori infection between children who did or did not suffer from abdominal pain (53.6% versus 46.4% respectively). The family history of dyspepsia was present in 75.5% of the family members in the study group but there was no statistically significant difference in H. pylori prevalence between children whose family members did or did not have dyspeptic complaints.

Discussion

The prevalence of H. pylori infection differs in different parts of the world. The infection is rare in developed countries when compared to developing or eastern European countries[17-20,23]. Studies in adults have suggested that the difference in the prevalence of H. pylori among developing and developed countries reflects differences in socioeconomic status and cultural habits during childhood[15,20,26].

It has been suggested that in developing countries the infection is usually acquired before five years of age[16,24]. Rothenbacher et al.[28] studied a group of Turkish children living in Germany and found that H. pylori infection was acquired mainly between the first and second years of life. In our study group the frequency of H. pylori infection was 18.2% under 4 years of age and increased to 41% between 4-6 years, 48.6% at 6-8 years, 50% at 8-10 years, and 63% at 10-12 years of age. Our findings also suggested that the infection might be acquired during the first few years of life in countries where the prevalence of H. pylori infection is high in the adult population. A study conducted in France in children undergoing upper gastrointestinal endoscopy demonstrated a prevalence of 5% in children younger than 6 years of age, and of 15% in the 6-8 years of age group[30]. A sero-prevalence study from Nothern Ireland showed that 21.4% of children under 6 years of age and 29.6% of children aged 6-8 years were sero-positive for H. pylori[24]. Furthermore, sero-prevalence studies from Belgium and Finland revealed that the prevalence of H. pylori infection was 8%, in children aged 6-10 years and 10% in children aged 3-18 years, respectively[17,18]. In contrast to developed countries, studies from North Africa and Colombia Andes have demonstrated that the prevalence of H. pylori infection among children younger than 10 years varies between 36 and 82%[1,21,31]. In Turkey, the sero-prevalence of H. pylori among adults reaches 80-85% but there is limited knowledge about children[19,20,26]. Doppl et al.[26] found that the sero-prevalence of H. pylori in Turkish children younger than 5 years of age living in Turkey was 28.4%, and increased to 44% between 5-10 years of age. The huge difference of H. pylori infection in childhood between the developing and developed world suggests the possibility of an environmental pool of H. pylori to which children are exposed in developing countries. A study done by Rothenbacher et al.[27] using ^{13}C-urea breath test in a group of healthy preschool German and Turkish children living in the south of Germany supported this suggestion. They demonstrated a large variation in the prevalence of H. pylori infection according to the nationality of children living in the same geographical area[27]. They concluded that children who belonged to a population originating from a high prevalence country had a particularly high prevalence of H. pylori infection.

The acquisition of H. pylori infection varies remarkably between and within populations[2,17,32]. The age-specific prevalence of H. pylori is higher in developing countries, particularly in those of lower socioeconomic status whether assessed by income, housing, education or ethnic group[20]. In our study, we found a rather high overall frequency for H. pylori infection in children between 3-12 years of age. The frequency was 18.2% under 4 years of age but it increased to 41% in preschool children, which was similar to the serological results found by Doppl et al.[26]. Another serological study from Turkey which included children who came to the hospital with any kind of complaint without gastrointestinal symptoms revealed a 15.5% prevalence of H. pylori in children aged 1-4 years[19]. Since sick children were included in this study, and serological tests, which might indicate either active or past infection, were used for the investigation, it was not possible to make a conclusion for general healthy Turkish children with these results.

Several invasive and non-invasie diagnostic methods have been developed to detect H. pylori, and different methods have been used to determine the infection status in various studies[28,33-38]. Non-invasive tests are important not only in epidemiological studies but also for follow-up of patients after treatment. The serological tests, especially quick tests, are not as reliable in children as in adults, and most of the commercial kits have not been validated in children[34,39]. They also do not allow a distinction between current or past infection. Furthermore, serological tests are unreliable indicators of H. pylori status particularly in children who have frequently received antibiotics for other reasons. ^{13}C-UBT was used instead of serological test to detect H. pylori status of healthy children in our study group. UBTs are reliable and validated non-invasive tests in children[40-44]. The diagnostic accuracy of ^{13}C-UBT is well established in adults and in children older than two years[40,41,45,46].

When the determinants of H. pylori infection in our study group were investigated in multivariate analyses, socioeconomic status, household density of siblings, heating source of the house and breastfeeding were determined as independent predictors for H. pylori infection in children. The association between lower socioeconomic status and increased risk of H. pylori infection is well established[16,18,20,22,24,27,31,47]. The explanation for this might be the household crowding and lower standards of living conditions in families with low income. In our study group, rather than household density, the number of siblings sharing the same house was an independent risk factor for acquisition of the infection. There might be an alternative source of infection for these children, presumably outside the house. The heating source (coal stove or central heating) of the house was determined as an important risk factor, which was not dependent on the socioeconomic status of the family. There is no such data for this parameter, but it can be suggested that the hygienic conditions in families which heat their houses with coal stoves might be sub-optimal when compared with the families using central heating.

There are some studies investigating the possible protective role of breastfeeding against H. pylori infection[24,48,49]. Anti-H. pylori IgA in human breast milk has been shown to protect against early acquisition of H. pylori infection in developing countries[48]. Malaty et al.[49] found that breastfeeding had a significant protective effect against acquiring the infection in children. On the other hand, McCallion et al.[24] were not able to show the protective role of breastfeeding against H. pylori infection, but they concluded that breastfeeding might reduce the risk of infection. In our study group, being not breast-fed during the first year of life was an important risk factor for H. pylori infection, and this factor remained as an independent predictor for the infection in multivariate analysis. The children who were not breast-fed had an almost 4.5 fold-increased risk for acquiring H. pylori infection.

The effect of H. pylori infection on growth was investigated in several studies, which suggested that children and adults infected with H. pylori are shorter than uninfected counterparts[10,25,50-52]. The mechanism by which H. pylori infection might lead to growth delay is not clearly known. One possible explanation for this might be dyspeptic symptoms resulting in low energy intake and malnutrition in the long term. Another suggestion is based on the assumption that long-standing infection induces a low-grade chronic inflammation in the stomach and the release of some inflammatory cytokines, which would affect growth[10]. Patel et al.[25] identified an effect of H. pylori infection on growth in prepubertal girls but not in boys. Perri et al.[10] similarly found that H. pylori infection was associated with short stature in older children. On the other hand, Oderda et al.[50] and Malaty et al.[51] reported that H. pylori was not a risk factor for short stature in children. In our study group it was found that H. pylori infection was associated with both weight and height percentiles. But, when the H. pylori status was taken as the dependent variable in a logistic regression analysis, the centile values were not important risk factors for H. pylori infection.

There are many studies investigating the relationship between H. pylori infection in childhood and symptoms of abdominal pain in selected and unselected populations[11-14].

These studies showed that H. pylori infection childhood was mostly asymptomatic and not associated with specific gastrointestinal symptoms[11-13]. In our study group, healthy children were asked about the presence of any gastrointestinal complaint, particularly recurrent abdominal pain, and it was found that the frequency of H. pylori was not different in children who had abdominal pain when compared with those children who did not.

Drumm et al.[53] investigated the family members of 34 children who were diagnosed to have H. pylori gastritis by upper gastrointestinal endoscopy. They found that the sero-prevalence of H. pylori was 73.5% in family members of the study group. This study showed that intra-familial clustering of H. pylori infection might be an important risk factor for the spread of infection to the children. When the association between H. pylori infection and the family history of dyspepsia was investigated in our study group, neither maternal nor paternal history of dyspepsia was associated with H. pylori infection in children. Since this conclusion was derived from parental dyspeptic complaints in the questionnaire, the presence or absence of dyspeptic complaints does not exclude or include H. pylori infection in parents. A possible explanation for this finding might be a rather high (35-40%) rate of dyspeptic complaints among parents in the study group.

This study is not a population-based study. Rather, a healthy group of children were studied with a sensitive and non-invasive method, and age-dependent frequency of H. pylori infection and possible risk factors applicable for our country were determined. In order to determine the origin of infection and risk factors predisposing to H. pylori infection, it would be interesting to compare the prevalence of H. pylori infection in children who are living in their native countries with that of children who immigrated abroad at different ages.

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