Evaluation of association between hepatitis A and *Helicobacter pylori* infections and routes of transmission

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SUMMARY: Egemen A, Yılmaz Ö, Akil İ, Altuğlu İ. Evaluation of association between hepatitis A and *Helicobacter pylori* infections and routes of transmission. Turk J Pediatr 2006; 48: 135-139.

Previous research about coexistence of *Helicobacter pylori* (HP) and hepatitis A virus (HAV) infections and the factors that increase their prevalence has suggested that the route of transmission of HP infection includes oral-oral and water-foods as well as the fecal-oral route. The aim of this study was to evaluate the routes of transmission of HP by comparing the seroprevalences of HP and HAV in children. One hundred and two children aged 1-18 years living in rural and urban regions of İzmir were included in this study. Anti-HP IgG and anti-HAV IgG antibodies were measured via enzyme immunoassay method. Seropositivities for HP and HAV were 56.8% and 51.9%, respectively. Seroprevalence for both infections increased with increasing age. However, a significant difference could not be detected between rural and urban areas. Sex did not have a significant effect. There was no infection in 22.1% of children, while 30.8% had both of the infections. 21.1% were positive only for HAV while 26% were positive only for HP. No significant correlation between seroprevalences of HP and HAV was detected.

This study suggests the existence of various other routes of transmission of HP apart from the fecal-oral route.

Key words: Helicobacter pylori, hepatitis A virus, seroprevalence, transmission.

Helicobacter pylori (HP), which lives within the mucous layers and affects the lining of the human stomach, is now established as the major etiologic agent of chronic gastritis and peptic ulcer and a predisposing factor in gastric cancer and lymphoma of the mucosa-associated lymphoid tissue[1]. Although it is assumed that oral-oral, fecal-oral and gastro-oral routes of transmission are used, the precise mode of transmission of HP remains unclear[2]. There exists a view supporting that transmission of HP is mainly via person-to-person contact[3,4]. Hepatitis A virus (HAV) is an endemic infectious disease that is usually asymptomatic in children, leading to underdiagnosis or missed diagnosis in young children. This virus, which has a seropositivity of 71.3% in Turkey, is commonly used as a predictor of fecal-oral route of transmission[5-9].

The aim of this study was to evaluate the association between HAV and HP infections and routes of transmission.

Material and Methods

The study consisted of 104 asymptomatic children (52 boys and 52 girls aged 1-18 years). A cluster sample design developed by the EPI/WHO for immunization was carried out for selection of the study population in the Izmir region of Turkey. Age and sex of the study population as well as the number of the individuals sharing the same household with them were recorded.

Blood sample was collected from each subject and serum specimens were kept at -20°C until laboratory evaluation.

Immunoglobulin G antibodies to HP were determined quantitatively by a commercial enzyme linked immunoabsorbent assay (Zeus Scientific Inc, USA). Anti-HAV IgG antibodies were measured quantitatively using Dade-Behring micro-ELISA kits (Dade Behring Marburgh, Germany).

Logistic regression analysis was used for comparison of HAV and HP seropositivities. Relationship of HP and HAV seropositivity with age was evaluated statistically by linear association. Relationship of HP and HAV seropositivity with sex, study area and number of household contacts of the study population was determined by Pearson's chi-square test.

Results

Seropositivities for both HAV and HP increased significantly with age (Table I and Fig. 1). However, seropositivities for both HAV and HP were not significantly related to number of household contacts, sex and study area (Table I).

Seropositivity for HP was found in 59 of 104 (56.8%), while seropositivity for HAV was detected in 54 of 104 (51.9%) children included in the study population (Fig. 2). The association between seropositivity of anti-HP and anti-HAV was not statistically significant even after adjustment for age, sex, study area and number of household contacts. Logistic regression analysis demonstrated that age was the only factor influencing the seroprevalence of HP significantly (Tables II and III).

Discussion

Helicobacter pylori, which commonly resides in the human stomach, is usually acquired during childhood and remains asymptomatic

Table I. Seroprevalence of Anti-HP and Anti-HAV Antibodies According to Some Characteristics

Characteristic		HAV IgG (+)		HP IgG (+)		Total n
		n	%	n	%	
Age (year)	1-4	4	33.3	4	33.3	12
	5-9	13	46.4	12	42.9	28
	10-14	18	45.0	26	65.0	44
	15-18	19	79.2	17	70.8	20
		p=0.009*		p=0.007*		
Gender	Male	29	55.8	30	57.7	52
	Female	25	48.1	29	55.8	52
		p=0.432**		p=0.843**		
Region	Urban	37	53.6	36	52.2	69
	Rural	17	48.6	23	65.7	35
		p=0.626**		p=0.188**		
Households	2-4	40	47.6	45	53.6	84
	≥5	14	70	14	70.0	20
		p=0.072**		p=0.183**		

* Using linear association.
** Using chi-square test.
HP: Helicobacter pylori. HAV: Hepatitis A virus.

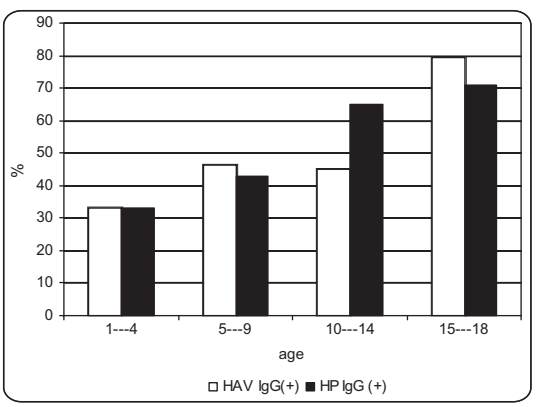

Fig. 1. *Helicobacter pylori* (HP) and hepatitis A virus (HAV) seroprevalence in different age groups.

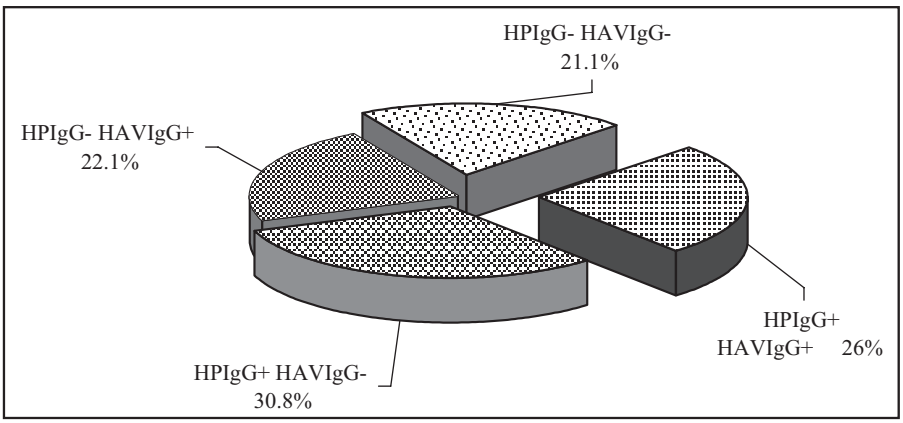

Fig. 2. Hepatitis A virus (HAV) and *Helicobacter pylori* (HP) seroprevalence in the study population.

Table II. Logistic Regression Analysis of *Helicobacter pylori* Cases

	β	p	OR	95% CI
Number of household contacts	0.545	0.330	1.73	0.58-5.17
Region	0.581	0.197	1.79	0.74-4.32
Age	0.108	0.023	1.11	1.02-1.22
Hepatitis A virus	-0.055	0.899	0.95	0.40-2.21
Gender	0.048	0.909	1.05	0.46-2.38
Constant	-1.739	0.099	0.17	

OR: Odds ratio. 95% CI: 95% Confidence interval.

Table III. Logistic Regression Analysis of Hepatitis A Virus Cases

	β	p	OR	95% CI
Number of household contacts	0.892	0.109	2.44	0.82-7.27
Region	-0.295	0.505	0.75	0.31-1.77
Age	0.99	0.036	1.104	1.00-1.21
Hepatitis A virus	-0.302	0.466	0.74	0.38-1.67
Gender	-0.049	0.910	0.95	0.41-2.22
Constant	-1.438	0.162		

OR: Odds ratio. 95% CI: 95% Confidence interval.

in most individuals[10,11]. However, in a small proportion of infected individuals it is associated with gastritis, peptic ulcer disease, gastric adenocarcinoma, and malignant lymphoma of mucosa-associated lymphoid tissue[11]. More than half of the world's population is infected, but its prevalence varies according to geographic area, age, race and socioeconomic status[11].

Possible routes of transmission include person-to-person contact, and waterborne and iatrogenic spread through contaminated medical equipment[2-4, 11].

In this study including children aged 1-18 years, prevalence of seropositivity for both HAV and HP demonstrated a trend of increase with age. This increase was equally significant for both HAV and HP (p=0.009 and 0.007, respectively). This is not surprising when expected routes of transmission for both are considered. Hepatitis A seroprevalence is a commonly used predictor of fecal-oral route of transmission[5-8]. HP and HAV, as indicated by a similar pattern of increase in seropositivity with age, may share a common mode of transmission, but

changes in environmental conditions make this very difficult if not impossible to prove with seroepidemiological data[12].

The pattern of HP infection was similar to HAV infection and the age-specific seroprevalence of HP and HAV infection tended to overlap in previous studies[13,14]. However, some contradictory findings were reported against associations[15,16]. Comparison of seropositivity rates for HP with that of HAV by multivariate analysis in our study revealed that these two were not significantly related. This may be attributed to a route of transmission of HP which is different from the fecal-oral route of transmission of HAV. As has been postulated before, transmission of HP is person-to-person and that transmission may not be the fecal-oral route[3]. Person-to-person contact is supported by the fact that intrafamilial factors were shown to be more important than community factors for HP infection[17]. Similarly, a study carried out on 11-14-year-old children living in two islands of Taiwan was inadequate to conclude that HP and HAV infection share the same fecal-oral transmission pattern[18]. The seroprevalence of HAV infection failed to correlate with that of HP infection on both islands because of 1) the lack of age-specific progression phenomenon and 2) the striking difference of HAV seroprevalence between the two islands (5.5% vs 90.6%) despite a significant but less prominent difference between HP seroprevalence on both (82.4% vs 71%). These two islands, though they share similar meteorologic and geographic characteristics, differed in the composition of residents; one rich in residents who migrated from Taiwan, the other rich in native people. The highly prevalent HAV infection on one island indicated that the infection of HAV should be earlier than the infection of HP. The authors suggested that inappropriate waste water management may explain the universal early HAV infection in children on the island with native residents. The difference of HP infection on the two islands may be due to either racial cohort phenomenon or way of life on the island with native residents, which may be due to high intrafamilial transmission[18]. Furuta et al.[7] has stated that infection rate of HAV in younger individuals in Japan was very rare; however, infection rates of HP ranging from 10-20% were observed, which also supports that transmission of HP is different from that of HAV. As a different approach, he postulated that HAV may not be a suitable marker of fecal-oral transmission since it is detected in shellfish and its infection sometimes occurs via such food. Additionally, he proposed that detection of a live HP in feces would support the possibility of fecal-oral transmission of HP[19].

A different perspective on the natural history of HP is the presence of transient infection in young children. Redlinger et al.[20] detected HP seropositivity in 21% of 365 children with a significant monotonic decrease in seroprevalence by one year age intervals. Given that HP antibodies diminish after infection clears, this trend suggests that transient infection may be common in young children[20]. In contrast to this point of view, in this study, HP seropositivity demonstrated an increasing trend with age similar but not related significantly to HAV. Though use of antimicrobials may contribute to a reversal of seropositivity in children, the results obtained in this study did not support this.

In conclusion, a person-to-person transmission obviously exists for HP as indicated by the increase in seropositivity with age. However, if HAV is taken as a predictor of fecal-oral route, HP lacks evidence for the presence of this route of transmission in children living in the Izmir region of Western Anatolia.

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