

A Study is Proven that Transmission of *Helicobacter pylori* is Not Fecal-Oral Route in Children Living in A Rural Part of Turkey

TÜRKİYE'NİN KIRSAL BİR BÖLGESİNDE YAŞAYAN ÇOCUKLARDA HELİKOBAKTER PYLORİ'NİN BULAŞ YOLUNUN FEKAL-ORAL OLMADIĞINI DESTEKLEYEN BİR ÇALIŞMA

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Abstract

Objective: The aim of this study is to determine the seropositivities of *Helicobacter pylori* (*H. pylori*), Hepatitis E and Hepatitis A virus (HEV and HAV) infections in childhood and to investigate whether a common mode of transmission could be shared between these microorganisms.

Material and Methods: A total of 301 children (151 male, 150 female) who were ranging from 1 to 16 years old were included. Subjects were separated into the three groups according to age: Group 1 (1-5 years), Group 2 (6-10 years), and Group 3 (11-16 years). Blood samples were obtained from all patients for detection of immunoglobulin G antibody levels against *helicobacter pylori*, hepatitis E and hepatitis A.

Results: Overall seropositivity rates were found to be 19.6% (59/301), 11.6% (35/301) and 1.3% (4/301) for *H. pylori*, HAV and HEV, respectively. The seropositivity rates for *H. pylori* increased significantly with age. The HAV seropositivity rates in males was higher than females. Of the 301 cases, 8 cases were seropositive for both *H. pylori* and HAV infections. None of the children was seropositive for both HEV and *H. pylori* or HEV and HAV infections.

Conclusion: We could not demonstrate a correlation between *H. pylori* and HAV seroprevalance rates with respect to increasing age. Our study supports the theory against the fecal-oral transmission of *H. pylori* infections.

Key Words: *Helicobacter pylori*, hepatitis A, virus, hepatitis E virus, transmission, child

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Özet

Amaç: Bu çalışmanın amacı çocukluk çağında *Helicobacter pylori*, (*H.pylori*) hepatit A ve hepatit E seropositivitesini belirlemek ve bu mikroorganizmalar arasında ortak bir bulaş yolu olup olmadığını araştırmaktır.

Gereç ve Yöntemler: Yaşları 1 ile 16 yıl arasında değişen toplam 301 olgu (151 erkek, 150 kız) çalışmaya alınmıştır. Olgular yaşlarına göre Grup 1 (1-5 yıl), Grup 2 (6-10 yıl), Grup 3 (11-16 yıl) olarak gruplara ayrılmıştır. Tüm hastalardan *Helicobacter pylori*, hepatit A ve hepatit E'ye karşı oluşmuş serum immunglobulin G'lerin tespiti için kan örnekleri alınmıştır.

Bulgular: Seropositivite oranları; *H. pylori* için %19.6 (59/301), hepatit A için %11.6 (35/301) ve hepatit E için %1.3 (4/301) bulunmuştur. *H. pylori* seropositivitesinin yaşla birlikte arttığı saptanmıştır. Hepatit A seroprevalansı erkeklerde kızlara oranla daha yüksek olarak bulunmuştur. 301 olgudan 8'inde *Helicobacter pylori* ve hepatit A birlikteliği gösterilirken, *Helicobacter pylori* ve hepatit E'nin ve hepatit A ile E'nin birlikteliği gösterilememiştir.

Sonuç: Çalışmamız sonucunda *helicobacter pylori* seroprevalansı ile hepatit A ve hepatit E seroprevalansı oranları arasında anlamlı bir ilişki bulunamamıştır. Bu çalışma; çocukluk çağı *Helicobacter pylori* enfeksiyonunda fekal-oral bulaşa karşı olan teoriyi desteklemektedir.

Anahtar Kelimeler: *Helicobacter pylori*; Hepatit A virüsü; hepatit E virüsü; bulaş, çocuk

Helicobacter pylori (*H. pylori*) infection is probably the most common chronic bacterial infection, mainly acquired in

early childhood, particularly in developing countries.^{1,2} Several modes of transmission for *H. pylori* have been proposed including fecal-oral and oral-oral route.³⁻⁶ However; the precise mode of transmission of *H. pylori* is still unclear.

Hepatitis A and E viruses (HAV and HEV) are non-enveloped RNA viruses that share fecal-oral route of transmission.⁷ There is seroepidemiological evidence both for and against the fecal-oral

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route in the transmission of *H. pylori*, as shown by studies comparing the seroprevalance of *H. pylori* with known fecal-oral spreading pathogens such as HAV.⁸⁻¹² As far as we know from the English literature, there is no seroepidemiological study either in adults or in children that investigated *H. pylori* and HEV co-existence.

The aim of this study is to determine the seropositivities of *H. pylori*, HEV and HAV infections in childhood and to investigate whether a common mode of transmission could be shared between these microorganisms.

Material and Methods

A total of 301 children (151 male and 150 female), who were ranging in age from 1 to 16 years included to study. Informed consents were taken from all subjects and this study was organized appropriately to the rules of Helsinki Declaration policy. The study was also approved by the local Ethics Committee of Zonguldak Karaelmas University School of Medicine. Patients who had a chronic disease, immune dysfunction, active infections and those who had already been vaccinated against HAV and had a history of blood transfusion were excluded from the study. Subjects were separated into the three groups according to age: Group 1 (1-5 years), Group 2 (6-10 years), and Group 3 (11-16 years). Blood samples were obtained from all patients and after centrifuged at 4000x g for 10 minutes stored at -20 C until tested.

Serum Hepatitis A antibodies were analyzed by means of a commercially available enzyme immunoassay kits (Beckman Coulter Access, USA). Anti-*H. pylori* immunoglobulin G antibody was detected by means of *H. pylori*-specific en-

zyme-linked immunosorbent assay (ELISA). (Euroimmuno, Germany). Serum samples were also screened by commercial anti-HEV Ig G by ELISA (Dia Pro Diagnostics, Italy).

The statistical significance of seropositivity rates for HAV, HEV and *H. pylori* were assessed by means of Fisher's exact test. The Chi-square test was used to examine the relationship of the three infections with respect to age and sex. The correlation among the seropositivity rates for *H. pylori* -HAV, *H. pylori*-HEV and HAV-HEV were evaluated by correlation analysis. P value less than 0.05 was considered statistically significant.

Results

A total of 301 children aged from 1 to 16 years were selected to determine the seropositivities of Hepatitis A, Hepatitis E and *H. pylori* infections. Distribution of the study population by age and sex was showed in Table 1. Overall seropositivity was found 19.6 % (59/301) of the cases for *H. pylori*, 11.6% (35/301) for HAV and 1.3% (4/301) for HEV. The seropositivity rates for *H. pylori*, Hepatitis A, Hepatitis E viruses according to age groups were showed in Table 2, Figure 1. The seropositivity rate for *H. pylori* increased significantly with age (p= 0.001) but it remained unchanged for HAV

Table 1. Distribution of the study population by age and sex.

Age range (yıl)	Number	Male (%)	Female (%)
1-5	168	94 (55.9)	74 (44.1)
6-10	82	29 (35.3)	53 (64.7)
11-16	51	28 (54.9)	23 (45.1)
Total	301	151	150

Table 2. The seropositivity rates for *H. pylori*, Hepatitis A, Hepatitis E viruses according to age groups.

Age range (yıl)	No tested	<i>H. pylori</i>		HAV		HEV	
		Seropositive no	%	Seropositive no	%	Seropositive no	%
1-5	168	19	11.3	17	10.1	2	1.2
6-10	82	21	25.6	10	12	1	1.2
11-16	51	19	37.2	8	15.7	1	1.9
Total	301	59	19.6	35	11.6	4	1.3

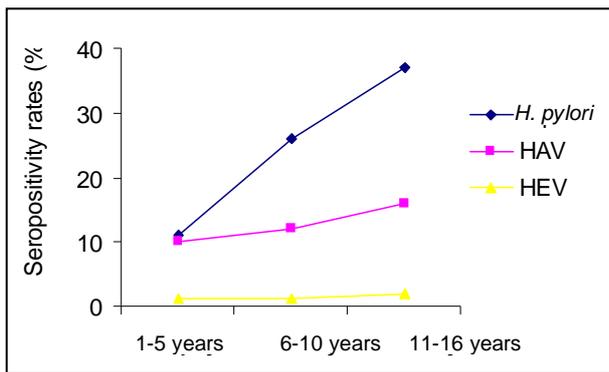


Figure 1. Seropositivity rates for *H. pylori*, Hepatitis A, Hepatitis E viruses according to age groups.

and HEV. The HAV seropositivity in males was higher than females ($p=0.017$). The sex was not an important factor affecting seropositivity rates for *H. pylori* and HEV. Of the 301 cases, 8 cases were seropositive for both *H. pylori* and HAV infections. There weren't any cases which were seropositive for both HEV and *H. pylori* or HEV and HAV infections.

The correlation among the seropositivity rates for *H. pylori*-HAV, *H. pylori*-HEV and HAV-HEV by correlation analysis was not statistically significant ($p>0.05$).

Discussion

Evidence suggests that initial acquisition of *H. pylori* occurs primarily during childhood.¹ The major issue is quandaries about its route of transmission. Although *H. pylori* is one of the most common human bacterial infections worldwide, universal public health measures for the prevention and control of this infection have not been yet established in most countries including ours. Therefore, understanding the transmission routes of *H. pylori* is essential to prevent children from being infected with this microorganism.

Turkey as a developing country is a well-known endemic region for enteric infectious organisms such as *H. pylori*, HAV and so on. Our locoregional properties in this study represent a rural area in Turkey. *H. pylori* and HAV seroprevalance rates in our study group were lower than expected: 19.6% and 11.6% respectively. Overall; our loco-

regional *H. pylori* and HAV seroprevalances in the childhood period was different to data from other geographic regions in Turkey ranging from 27.9 to 50.8% and 29.5 to 50% respectively.¹³⁻¹⁶ We could not demonstrate a correlation between *H. pylori* and HAV seroprevalances with increasing age. Thus; our study supports the theory against the fecal-oral transmission of *H. pylori* infection. HEV infection is a very rare problem in the childhood period, which is a classical knowledge.¹⁷ Our region represented mild HEV endemicity when compared with the data from other geographic areas in Turkey.^{17,18} As an example, anti HEV seropositivity rate was reported to be around 0.89% in Antalya region in Turkey.¹⁷ So; we could not use HEV as a marker for fecal oral transmission of enteric organisms.

Iatrogenic transmission of *H. pylori* following endoscopy is the only proven mode.¹ For the general population, the most likely mode of transmission is from person to person, by either the oral route (through vomitus or possibly saliva) or perhaps the fecal-oral route.¹⁹ Knowledge of the epidemiology and mode of transmission of *H. pylori* is important to prevent its spread and may be useful in identifying high-risk populations, especially in areas that have high rates of gastric lymphoma, gastric cancer and gastric ulcer.

There are lots of contradictory reports about the fecal-oral transmission route of *H. pylori* microorganisms in childhood period and adult life. Most of the relevant reports from Turkey, Taiwan, Italy and Australia could not indicate an increase in serum anti-HAV antibodies in *H. pylori* infected children.^{5,8,20-23} These authors connoted that the *H. pylori* microorganism may not preserve its viability after passage through the gastrointestinal tract. Thus; they alluded that fecal-oral transmission of *H. pylori* is unattainable. On the other hand; some reports showed that *H. pylori* DNA can be amplified from feces samples of infected patients. This evidence suggests us a potential fecal-oral route of transmission of *H. pylori*. This belief was advocated by the other reports from South Africa, Kazakhstan, Japan and India, which indicated fecal oral spread of *H. pylori* like HAV in childhood period.²⁴⁻²⁷

We believe that fecal-oral transmission of *H. pylori* is an unresolved issue. There are contradictory reports in such a consequential subject. We need more studies and also meta-analysis in this theme to uncover a fundamental gap in our knowledge about *H. pylori* infection in childhood. We also believe that if we can be sure about its transmission through fecal-oral pathway, we can take relevant precautions to break its spread during early childhood. Thus; we can be able to prevent long term chronic infection with *H. pylori* and its consistent bad sequels in the gastrointestinal tract.

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