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## Observational Study

Epidemiologic characteristics of *Helicobacter pylori* infection in southeast Hungary

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## Abstract

## BACKGROUND

Epidemiologic studies have revealed a decrease in the prevalence of *Helicobacter pylori* (*H. pylori*) infection in Western Europe.

## AIM

To obtain data regarding the prevalence of *H. pylori* in Csongrád and Békés Counties in Hungary, evaluate the differences in its prevalence between urban and rural areas, and establish factors associated with positive seroprevalence.

## METHODS

One-thousand and one healthy blood donors [male/female: 501/500, mean age: 40 (19–65) years] were enrolled in this study. Subjects were tested for *H. pylori* IgG antibody positivity *via* enzyme-linked immunosorbent assay. Subgroup analysis by age, gender, smoking habits, alcohol consumption, and urban *vs* non-urban residence was also performed.

## RESULTS

The overall seropositivity of *H. pylori* was 32%. It was higher in males (34.93% *vs* 29.2%,  $P = 0.0521$ ) and in rural areas (36.2% *vs* 27.94%,  $P = 0.0051$ ). Agricultural/industrial workers were more likely to be positive for infection than office workers (38.35% *vs* 30.11%,  $P = 0.0095$ ) and rural subjects in Békés County than those in Csongrád County (43.36% *vs* 33.33%,  $P = 0.0015$ ).

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## CONCLUSION

Although the prevalence of *H. pylori* infection decreased in recent decades in Southeast Hungary, it remains high in middle-aged rural populations. Generally accepted risk factors for *H. pylori* positivity appeared to be valid for the studied population.

**Key words:** *Helicobacter pylori*; Epidemiology; Prevalence; Central Europe; Healthy volunteers; Enzyme-linked immunosorbent assay; Differences in urban and rural population

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**Core tip:** Whereas a decrease in the prevalence of *Helicobacter pylori* (*H. pylori*) has been confirmed in Western Europe, its prevalence in Central Europe, which has a substantial rural population, is unclear. Therefore, this study analyzed the prevalence of *H. pylori* among healthy volunteers in two Hungarian counties. The results of the study illustrated that the seropositivity of *H. pylori* in this area was 32%. The prevalence was higher in males, among people living in rural areas. Agricultural/industrial workers were more likely to be positive for infection than office workers. Meanwhile, rural subjects in Békés County had higher prevalence than those in Csongrád County.

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## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) infection is one of the most common chronic human bacterial infections worldwide, affecting up to half of the world's population. It is the main cause of gastritis, gastroduodenal ulcer, gastric adenocarcinoma, and mucosa-associated tissue lymphoma. Its prevalence is variable in relation to geography, ethnicity, age, and socioeconomic factors<sup>[1,2,3]</sup>.

The prevalence of *H. pylori* has declined worldwide, although wide variation has been observed.

According to a 2017 and a 2018 meta-analysis, the countries with the lowest *H. pylori* prevalence were Switzerland (13.1%-24.7%), Denmark (17.8%-26.5%), New Zealand (21.4%-26.5%), Australia (17.2%-32.1%), and Sweden (18.3%-34.1%) in the former meta-analysis, Indonesia (10.0%), Belgium (11.0%), Ghana (14.2%), and Sweden (15.0) in the latter, whereas those with the highest prevalence were Nigeria (83.1%-92.2%), Portugal (84.9%-87.9%), Estonia (75.1%-90.0%), Kazakhstan (74.9%-84.2%), and Pakistan (75.6%-86.4%) in the former study, Serbia (88.3%), South Africa (86.8%), Nicaragua (83.3%), and Colombia (83.1%) in the latter. The former study used two periods to analyze the prevalence trend over time. The *H. pylori* prevalence after 2000 was lower than that before 2000 in Europe (48.8 vs 39.8), North America (42.7% vs 26.6%), and Oceania (26.6% vs 18.7%)<sup>[4,5]</sup>.

The major risk factors for *H. pylori* infection include socioeconomic status and the household hygiene of the patient and family during childhood. A previous Hungarian study revealed greater seropositivity among undereducated subjects, in persons living without sewers, those living in crowded homes or having three or more brothers and sisters, and those with high alcohol consumption, and they observed significant differences in prevalence between industrial and office workers. A Russian study reported that 88% of the Moscow working population is infected with *H. pylori*, 78% in people younger than 30 years, 97% in individuals older than 60 years. Recent epidemiologic studies revealed decreases in the prevalence of *H. pylori* in Western Europe and the United States. Conversely, little is known regarding the prevalence of *H. pylori* in Central Europe, in which a substantial population resides in rural areas<sup>[6,7,8,9,10]</sup>.

The aims of this study were to obtain data regarding *H. pylori* prevalence in Csongrád and Békés Counties in Hungary, evaluate differences in prevalence

between urban and rural areas, and establish factors associated with positive seroprevalence.

## MATERIALS AND METHODS

One-thousand and one healthy blood donors [male/female: 501/500, mean age: 40 (18–65) years] were consecutively enrolled in Csongrád and Békés Counties. Detailed demographic data are shown in [Figure 1](#)<sup>[11,12,13]</sup>.

In Hungary, blood donation is allowed for individuals weighing more than 50 kg and aged 18–65 years. Data collection was performed using an anonymous questionnaire including 26 questions associated with demographic parameters (gender, age, place of birth, childhood residence, marital status, current residence, crowding in family, and educational status) and medical status (symptoms associated with *H. pylori* infection and gastroduodenal ulcer disease, smoking habits, alcohol consumption, and family history of *H. pylori* infection, gastroduodenal ulcer disease, and gastric malignancy).

On the basis of the childhood residence of the subjects, the following four groups of 250 subjects were established: Urban males, urban females, rural males, and rural females. Groups were matched by age. Subgroup analysis was performed according to living circumstances, residence in Békés or Csongrád County, smoking habits, alcohol and coffee consumption, occupation, intermittent agricultural work, pet or domestic animal rearing, gastrointestinal complaints, and family history of *H. pylori* infection, gastric ulcer, and gastric cancer.

All subjects were tested for *H. pylori* IgG antibody positivity using a Platelia *H. pylori* IgG enzyme-linked immunosorbent assay, which reportedly has 100% sensitivity and 90% specificity according to the manufacturer. These values were 95.6% and 85.1% in the validation study of Burucoa *et al.*<sup>[14]</sup> respectively (Bio-Rad).

For the statistical analysis of different variables related to *H. pylori* infection, the chi-squared test or two-sample *t*-test was applied. The association between *H. pylori* infection and potential risk factors was established *via* univariate analysis, and odds ratios and 95% confidence intervals were calculated. In addition, a stratified analysis according to age (18–35, 35–50, and 50–65 years) was performed. The final model was developed using a generalized linear regression model *via* stepwise regression, with inclusion and exclusion criteria set at significance levels of 0.05 and 0.10, respectively. A two-sided *P* value < 0.05 was considered statistically significant. All statistical analyses were performed using MATLAB (Mathworks, Natwick, MA, United States).

## RESULTS

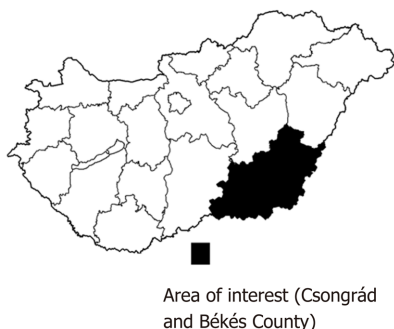
The overall seropositivity of *H. pylori* was 32% in the studied healthy subjects. There was no statistically significant difference in prevalence between males and females (*P* = 0.0521) in our study. According to residence, the prevalence of *H. pylori* was significantly higher in rural areas than in urban areas (*P* = 0.0051). Furthermore, residence in rural areas for at least one year was associated with a significantly higher *H. pylori* prevalence than continuous urban residency (*P* = 0.0003). Parameters related to occupation were also associated with *H. pylori* infection. A higher prevalence was established for industrial workers and agricultural workers than for office workers and non-agricultural workers, respectively. Coffee consumption and pet or domesticated animal rearing were associated with *H. pylori* infection, whereas the rate of *H. pylori* positivity was similar for the remaining parameters. Detailed data are shown in [Table 1-3](#).

A significant positive association was observed between age and *H. pylori* positivity ([Table 1](#)). To rule out this strong effect of age, three age groups were formed for further analysis. In the youngest group, the presence of epigastric pain was an independent risk factor for *H. pylori* positivity. By contrast, animal rearing was a risk factor for the middle age group, and male sex and living in rural areas for at least one year were risk factors in the oldest age group ([Table 4](#)).

## DISCUSSION

This prospective study proved that the Hungarian prevalence of *H. pylori* infection has followed international trends, falling to 32% over the last two decades. The prevalence between 1990 and 2000 was similar throughout the country (58.6%–63.3%) excluding the capital, in which the prevalence was only 47.3% ([Table 5](#)). Although the

Local demographics



	Hungary	Csongrád County	Békés County
Population			
Total	9,909,000 (Male/Female: 4,716,000/5,193,000)	410,000 (Male/Female: 193,000/216,000)	359,000 (Male/Female: 172,000/188,000)
Urban	6,936,000 (70%)	307,000 (75%)	270,000 (75%)
Rural	2,972,700 (30%)	102,000 (25%)	89,000 (25%)
Population density	106/km <sup>2</sup>	96/km <sup>2</sup>	63/km <sup>2</sup>
Work			
Employment rate	58.4%	50.3%	48.8%
Unemployment rate	10.3%	12.3%	11.1%
Physical work	-	55%	61%
Intellectual work	-	45%	39%

Figure 1 Csongrád and Békés Counties and detailed demographic data regarding Csongrád and Békés Counties.

Southeastern region of the country was not studied prospectively before this study, the *H. pylori* Workgroup of our institute conducted a retrospective analysis in 2005 and 2010 among patients with dyspepsia and gastroduodenal ulcer disease. The rate of seropositivity decreased from 46% to 38%. The 2017 meta-analysis used two periods to analyze the changes of prevalence trend. The *H. pylori* prevalence after 2000 was lower than that before 2000 in Europe (48.8 vs 39.8), North America (42.7% vs 26.6%), and Oceania (26.6% vs 18.7%). In the surrounding Central European countries, such as the Czech Republic and Slovakia, the prevalence of *H. pylori* infection followed the trends of our region, decreasing from 42% to 23% after 10 years in the former from 62% to 35% after 15 years in the latter<sup>[4,6,15-21]</sup>.

Having examined the potential factors associated with a higher *H. pylori* prevalence, our results were in concordance with previous observations revealing a positive linear association with age. Furthermore, our study supported findings that rural subjects are more likely to be *H. pylori*-positive than urban residents. Although we could not establish a significant effect of gender on the seroprevalence, it is impressive that older rural males have an approximately sixfold higher risk of *H. pylori* positivity than young urban females (61.29% vs 11.11% *P* < 0.0001). Such results are most commonly explained by differences in socioeconomic status and household hygiene of the family during childhood. Furthermore, a new original finding is that people who lived in rural conditions for at least one year also had an increased risk for *H. pylori* seropositivity. An evaluation of the occupations of the subjects provided further proof that socioeconomic factors can influence *H. pylori* infection risk. Meanwhile, the lack of difference in risk between urban and rural residence can be explained by the general improvement of living standards in our country over the last two decades, as most rural people currently have access to water supply and sanitation<sup>[6-8,16,20-23]</sup>.

The link between epigastric pain and *H. pylori* seropositivity among young subjects supports the currently accepted, Rome IV diagnostic protocol for functional dyspepsia, which states the excluding *H. pylori* infection (known as “*H. pylori*-associated dyspepsia”) should be the first step in the presence of such symptoms. Conversely, improved household hygiene in recent decades likely explains the lack of a relationship between socioeconomic status and *H. pylori* prevalence in this group. The findings further supported the hypothesis that hygiene differences between urban and rural areas were more significant at their childhood than nowadays. In addition, young males had poorer hygiene, than young females at that during childhood<sup>[24]</sup>.

This study has a limitation. In Hungary, blood donors are unpaid, healthy, and conscious volunteers; therefore, they may not completely represent all segments of the population of Southeast Hungary.

In conclusion, we proved that in line with the worldwide trends, the prevalence of *H. pylori* infection has decreased in Southeast Hungary with changes of society, including improvements in socioeconomic status and living standards, during recent decades. Meanwhile, the prevalence remains high in the middle-aged and older rural populations. Generally accepted risk factors for *H. pylori* positivity appeared valid for the studied population, whereas the presence of dyspeptic symptoms was identified as an independent risk factor in the young population.

**Table 1** Sociodemographic factors associated with *Helicobacter pylori* prevalence

Socio-demographic factors	<i>H. pylori</i> positive		<i>H. pylori</i> negative		Total	P value	Odds ratio (univariate)	95%CI
	n	%	n	%				
Sex						0.0521		
Female	146	29,2	354	70,8	500		1.0	
Male	175	34,9	326	65,1	501		1.3016	[0.9973, 1.6987]
Age						0.000		
	44.5638	10.7693	37.3599	11.9457			0.9484	[0.9363, 0.9606]
18-25	25	14,9	143	85,1	168			
25-35	32	16,9	157	83,1	189			
35-45	97	34,4	185	65,6	282			
45-55	106	43,6	137	56,4	243			
55 +	61	51,3	58	48,7	119			
Residence						0.0809		
Urban	185	30,0	431	70,0	616		1.0	
Rural	136	35,3	249	64,7	385		1.2725	[0.9706, 1.6683]
Childhood						0.0051		
Urban	140	27,9	361	72,1	501		1.0	
Rural	181	36,2	319	63,8	500		1.4631	[1.1201, 1.9110]
Min. one year in rural environment						0.0003		
Negative	104	25,6	303	74,4	407		1.0	
Positive	217	36,5	377	63,5	594		1.6770	[1.2695, 2.2153]

*H. pylori*: *Helicobacter pylori*; CI: Confidence interval.

**Table 2** Socioeconomic and lifestyle factors associated with *Helicobacter pylori* prevalence

Socio-economic + lifestyle factors	<i>H. pylori</i> positive		<i>H. pylori</i> negative		Total	P value	Odds ratio (univariate)	95%CI
	n	%	n	%				
Smoking						0.1121		
Non-smoker	169	29,5	403	70,5	572		1.0	
Smoker	91	34,2	175	65,8	266		1.2400	[0.9090, 1.6915]
Former smoker	61	37,4	102	62,6	163		1.4261	[0.9904, 2.0534]
Alcohol consumption						0.1420		
Never	95	36,0	169	64,0	264		1.0	
Occasional	216	30,3	497	69,7	713		0.7731	[0.5740, 1.0413]
Regular	10	41,7	14	58,3	24		1.2707	[0.5434, 2.9715]
Coffee						0.0390		
Never	82	26,7	225	73,3	307		1.0	
1	94	36,3	165	63,7	259		1.5632	[1.0929, 2.2358]
More than 1	145	33,3	290	66,7	435		1.3720	[0.9943, 1.8931]
Household population						0.1649		
Alone	51	39,2	79	60,8	130		1.0	
Adults only	135	31,5	294	68,5	429		0.7113	[0.4736, 1.0683]
Adults and children	135	30,5	307	69,5	442		0.6812	[0.4538, 1.0224]
Work						0.0000		
Industrial	186	38,4	299	61,6	485		1.0	
Office	135	26,2	381	73,8	516		0.5696	[0.4355, 0.7450]
Agricultural work						0.0012		
No	140	27,4	371	72,6	511		1.0	



Yes	181	36,9	309	63,1	490		1.5523	[1.1882, 2.0279]
Domestic animals						0.0015		
No	54	23,5	176	76,5	230		1.0	
Yes	267	34,6	504	65,4	771		1.7266	[1.2301, 2.4236]

*H. pylori*: *Helicobacter pylori*; CI: Confidence interval.

**Table 3** Factors in patient history associated with *Helicobacter pylori* prevalence

Patient history	<i>H. pylori</i> positive		<i>H. pylori</i> negative		Total	P value	Odds ratio (univariate)	95%CI
	n	%	n	%				
Family history of <i>H. pylori</i>						0.8829		
Negative	161	32,5	335	67,5	496		1.0	
Positive	18	31,0	40	69,0	58		0.9363	[0.5205, 1.6844]
NA	142	31,8	305	68,2	447			
Family history of GI ulcer						0.3810		
Negative	217	33,3	435	66,7	652		1.0	
Positive	57	29,7	135	70,3	192		0.8464	[0.5965, 1.2009]
NA	47	29,9	110	70,1	157			
Family history of GI cancer						0.0014		
Negative	277	32,1	587	67,9	864		1.0	
Positive	17	63,0	10	37,0	27		3.6025	[1.6284, 7.9701]
NA	27	33,8	53	66,3	80			
Abdominal pain						0.8108		
Negative	264	32,2	555	67,8	819		1.0	
Positive	57	31,3	125	68,7	182		0.9586	[0.6784, 1.3547]
Epigastric pain						0.1105		
Negative	214	30,5	487	69,5	701		1.0	
Positive	107	35,7	193	64,3	300		1.2617	[0.9481, 1.6789]

*H. pylori*: *Helicobacter pylori*; CI: Confidence interval; NA: Not applicable; GI: Gastrointestinal.

**Table 4** Independent risk factors associated with *Helicobacter pylori* prevalence

	Age 18-35	Age 35-50	Age 50-65
Male sex	Not significant	Not significant	<i>P</i> = 0.0389; OR = 0.5847; CI: [0.0753, 1.0940]
Rural residence in childhood	Not significant	Not significant	<i>P</i> = 0.0246; OR = 1.8537; CI: [1.3154, 2.3920]
Animal rearing	Not significant	<i>P</i> = 0.0036; OR = 2.0855; CI: [1.5897, 2.5812]	Not significant
Epigastric pain complaint	<i>P</i> = 0.0026; OR = 2.5514; CI: [1.9422, 3.1606]	Not significant	Not significant

OR: Odds ratio; CI: Confidence interval.

Table 5 The prevalence between 1990 and 2000 throughout the country

Date	1993	1999	2000	1998-2000
Region	Tolna	Vas	Szabolcs-Szatmár-Bereg	Pest
Authors	Tamássy <i>et al</i> <sup>[15]</sup>	Lakner <i>et al</i> <sup>[6]</sup>	Iszlai <i>et al</i> <sup>[16]</sup>	Prónai <i>et al</i> <sup>[19]</sup>
Method	Serology	Serology	Serology	13C-UBT
Population	Blood donors	Blood donors	Healthy volunteers	Symptomatic patients
n =	400	533	756	1027
Prevalence of <i>H. pylori</i> (%)	63, 3	62, 3	58, 6	47, 3

*H. pylori*: *Helicobacter pylori*.

## ARTICLE HIGHLIGHTS

### Research background

Epidemiologic studies have revealed a decrease in the prevalence of *Helicobacter pylori* (*H. pylori*) infection in Western Europe. Conversely, little is known regarding its prevalence in Central Europe, in which a substantial population resides in rural areas.

### Research motivation

The last Hungarian epidemiologic studies on *H. pylori* were carried out approximately two decades ago and showed high seroprevalence rates. Therefore we aimed to obtain new data and to test whether it decreases similarly to the Western European tendencies.

### Research objectives

The aims of the present study were to obtain data regarding the prevalence of *H. pylori* in Csongrád and Békés Counties in Hungary, evaluate the differences in its prevalence between urban and rural areas, and establish factors associated with positive seroprevalence.

### Research methods

One-thousand and one healthy blood donors were enrolled. Data collection was performed using an anonymous questionnaire including 26 questions associated with demographic parameters and medical status. All subjects were tested for *H. pylori* IgG antibody positivity using IgG enzyme-linked immunosorbent assay.

### Research results

The overall seropositivity of *H. pylori* was 32%. The prevalence of *H. pylori* was significantly higher in rural areas than in urban areas. Residence in rural areas for at least one year was associated with a significantly higher *H. pylori* prevalence than continuous urban residency. A significant positive association was observed between age, occupation, coffee consumption, pet or domesticated animal rearing and *H. pylori* positivity. Three age groups were formed for further analysis, in the youngest group, the presence of epigastric pain was an independent risk factor for *H. pylori* positivity.

### Research conclusions

The prevalence of *H. pylori* infection decreased in recent decades in Southeast Hungary, it remains high in middle-aged rural populations. Generally accepted risk factors for *H. pylori* positivity appeared to be valid for the studied population. Furthermore, a new original finding is that people who lived in rural conditions for at least one year also had an increased risk for *H. pylori* seropositivity.

### Research perspectives

The results of this study seems to consider the subsequent changes in seropositivity of *H. pylori* in Hungary. It would be interesting to test whether the significant positive association between age and *H. pylori* positivity continuous observed after 10 or 15 years or rather not, “new” infected will appear, or in the older age will stay low seropositivity. The other experience of this study is the link between epigastric pain and *H. pylori* seropositivity among young subjects, which supports the recommendation in countries with high *H. pylori* seropositivity, that patients with dyspeptic symptoms should be examined for *H. pylori* infection (Rome IV diagnostic protocol).

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