

WJG 20th Anniversary Special Issues (6): *Helicobacter pylori***Blood pressure and stature in *Helicobacter pylori* positive and negative persons**

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at the clinics of general practitioners. The overall prevalence of *H. pylori* infection was 30.4% (402/1321) in adults (≥ 18 year-old) and 5.2% (26/497) in children and adolescents (≤ 17 year-old). Once adjusted for age and gender, only a difference in body mass index remained statistically significant with *H. pylori* positive adults showing an increase of 0.6 kg/m² in body mass index. Once adjusted for age and gender, we found a difference in height between *H. pylori* positive and *H. pylori* negative children and adolescents. On further adjustment for place of residence, this difference became statistically significant, with *H. pylori* positive children and adolescents being on average 3.5 cm shorter. *H. pylori* positive adults were significantly older compared to *H. pylori* negative subjects. Once adjusted for age and gender, *H. pylori* infection had no impact on body weight, body mass index and vital signs either in adults or children and adolescents. Chronic *H. pylori* infection appeared to be associated with short stature in children. *H. pylori* infection did not influence blood pressure, body weight and body mass index either in adults or children and adolescents.

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Key words: Epidemiology; *Helicobacter pylori*; Czech Republic; 13C-urea breath test; Blood pressure; Heart rate; Weight; Stature; Body mass index

Abstract

To evaluate vital signs and body indices in *Helicobacter pylori* (*H. pylori*) positive and negative persons. A total of 22 centres entered the study. They were spread over the whole country, corresponding well to the geographical distribution of the Czech population. A total of 1818 subjects (aged 5-98 years) took part in the study, randomly selected out of 38147 subjects. *H. pylori* infection was investigated by means of a 13C-urea breath test. Data on height, weight, systolic and diastolic blood pressure and heart rate were collected

Core tip: Our group studied body indices and basic vital signs in *Helicobacter pylori* (*H. pylori*) positive and negative persons in 2001. The prevalence of *H. pylori* infection decreased significantly in the Czech Republic from 41.7% (2001) to 23.5% (2011). The aim of this multi-centre prospective study was to evaluate body indices and vital signs using comparable methods in the general population from identical geographical areas 10 years later. According to our current results, chronic *H. pylori* infection was associated with short stature

in children. *H. pylori* infection did not influence blood pressure, body weight and body mass index either in adults or children and adolescents.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) is the most common chronic bacterial infection in humans. *H. pylori* has been demonstrated worldwide and in individuals of all ages. Infection is acquired at an earlier age and is more frequent in developing countries compared with industrialised ones. *H. pylori* is a cause of chronic gastritis. About one third of all gastric cancers in developed and developing countries, respectively, are solely attributable to *H. pylori*. *H. pylori* infection is a major aetiological agent in peptic ulcer disease^[1].

It has been hypothesised that chronic *H. pylori* infection may be associated with and/or contribute towards several extra-gastric diseases, including ischemic heart disease^[2-12], arterial hypertension^[2,13-20], cerebral non-cardioembolic ischemic stroke^[21,22], peripheral arterial disease^[23,24], obesity^[13,25-27], metabolic syndrome^[28,29] and short stature^[30-36]. Our group studied body indices and basic vital signs in *H. pylori* positive and negative persons in a large prospective multi-centre study in 2001^[37,38]. In the meantime, prevalence of *H. pylori* infection decreased significantly in the Czech Republic from 41.7% to 23.5% within a 10-year period^[39,40]. The aim of our current multi-centre prospective study was to evaluate blood pressure and stature in *H. pylori* positive and negative persons in the Czech Republic using comparable methods in a representative sample of general unselected population from identical geographical areas 10 years after the initial study.

SEARCH

Ethics

The study was approved by the University Ethics Committee. All participants received detailed written information about the Project in advance and signed written consent (parents on behalf of their children). For all data obtained, all personal identification information was deleted in compliance with the laws for the protection of confidentiality of the Czech Republic.

Study population

A total of 22 centres entered the study. They included 15 centres of general practitioners for adults and 7 for

children and adolescents. These centres covered cities and towns with more than 20000 inhabitants (10 centres), smaller towns (≤ 20000 inhabitants) with surrounding villages (9) and rural areas (3 centres), and were spread over the whole country, corresponding well to the geographical distribution of the Czech population. A total of 1818 subjects (aged 5-98 years) took part in the study, randomly selected out of 38147 registered males and females in this age range.

Urea breath test

Urea breath tests were performed in the morning after overnight fasting by means of 13C-urea breath test^[41]. Citric acid solution (3 g dissolved in 150 mL of still water) was given initially as a test drink. Five minutes later two baseline exhaled breath samples were collected into 20-mL vacutainers using a straw. After this, all of the subjects ingested 75 mg 13C-urea (Helicobacter Test INFAI, INFAI GmbH, Köln, Germany) dissolved in 50 mL of still water with 1 g citric acid (at time 0). Breath samples were collected in duplicates using a straw in 20-mL vacutainers after 30 min. Tubes with breath samples were sent to a single analytical centre by post and measured within a one-week period. Breath samples in duplicates were analysed using isotope ratio mass spectrometry (AP 2003, Analytical Precision Products, Cambridge, United Kingdom). The cut-off point was 3.5.

Body indices and basic vital signs

Data on height and weight were collected at the clinics of general practitioners (measured in underwear by nurses). Body mass index was calculated as weight/height² (in kg/m²). Systolic and diastolic blood pressure measurements were performed by a trained nurse in a standard manner^[42] at the study clinics. Manual resting pulse measurement at the wrist (radial artery) was performed in sitting position by a trained nurse for 60 s. The blood pressure and heart rate were measured in the morning (from 8 to 12 a.m.).

Questionnaires

Data were collected by self-completed questionnaires distributed to adults and parents of children aged 5-15. The questionnaire included information on the place of residence in childhood, mother's and father's education, access to running warm water in childhood, crowding in childhood and number of siblings. Information on the study subjects' current place of residence, education, marital status, self-reported socio-economic group and smoking habits was also collected in the questionnaire and was used in the analysis of determinants of *H. pylori* positivity in subjects aged 15+ years of age. We combined the mother's and father's education and generated a variable indicating highest education achieved by any of the two parents (or the mother if single). This variable was used in analyses of blood pressure and stature in children and adolescents.

Table 1 Body indices, basic vital signs and socio-demographic characteristics in *Helicobacter pylori* positive and negative children and adolescents (≤ 17 years old)

Parameter	<i>Helicobacter pylori</i> negative <i>n</i> = 471 (mean \pm SD)	<i>Helicobacter pylori</i> positive <i>n</i> = 26 (mean \pm SD)	Statistical significance
Gender (% males)	47.1	46.1	NS
Age (yr)	11 \pm 3	12 \pm 3	NS
Weight (kg)	42.3 \pm 17.5	40.3 \pm 16.9	NS
Height (cm)	145.4 \pm 19.6	143.6 \pm 19.7	NS
BMI (kg/m ²)	19.1 \pm 3.9	18.6 \pm 3.7	NS
Systolic blood pressure (mmHg)	107.6 \pm 12.6	110.3 \pm 10.2	NS
Diastolic blood pressure (mmHg)	65.5 \pm 8.6	65.2 \pm 8.2	NS
Heart rate (beats per minute)	77.7 \pm 7.7	80.9 \pm 8.4	0.040
Residence ¹			NS
Larger town	32.0%	32.0%	
Smaller town	24.7%	32.0%	
Village	43.3%	36.0%	
Parental education			0.006
Secondary or higher	66.0%	57.7%	
Vocational	29.3%	23.1%	
Elementary	4.7%	19.2%	

¹Based on *n* = 491. NS: Not significant; BMI: Body mass index.

Statistical analysis

The data was analysed using STATA statistical software (StataCorp. 2011. Stata Statistical Software: Release 12, College Station, TX, United States)^[43]. Descriptive statistics, non-paired *t* test and Mann-Whitney test were used. Associations of *H. pylori* positivity with body indices and vital signs were analysed by univariable and multivariable linear regression. Crude and adjusted differences between groups of *H. pylori* positive and *H. pylori* negative study subjects are presented as beta coefficients with 95%CI.

RESULTS

The overall prevalence of *H. pylori* infection was 30.4% (402/1321) in adults (≥ 18 year-old) and 5.2% (26/497) in children and adolescents (≤ 17 year-old). There was no statistically significant difference in prevalence between males and females (Tables 1 and 2). *H. pylori* infection was strongly associated with higher age.

There were no significant differences in weight, height, body mass index or blood pressure among *H. pylori* positive and *H. pylori* negative children and adolescents, while heart rate was statistically significantly higher among those who were *H. pylori* positive (Table 1). There was a statistically significant difference in blood pressure, weight, height, and body mass index among *H. pylori* positive and *H. pylori* negative adults. *H. pylori* positive subjects were significantly older (Table 2).

Once adjusted for age and gender, we found a difference in height between *H. pylori* positive and *H. pylori*

Table 2 Body indices, basic vital signs and socio-demographic characteristics in *Helicobacter pylori* positive and negative adults (≥ 18 years old)

Parameter	<i>Helicobacter pylori</i> negative <i>n</i> = 919 (mean \pm SD)	<i>Helicobacter pylori</i> positive <i>n</i> = 402 (mean \pm SD)	Statistical significance
Gender (% males)	46.3	48.5	NS
Age (yr)	48 \pm 20	57 \pm 17	<i>P</i> < 0.001
Weight (kg)	76.3 \pm 16.2	79.1 \pm 16.4	<i>P</i> = 0.004
Height (cm)	171.6 \pm 9.9	170.2 \pm 9.9	<i>P</i> = 0.020
BMI (kg/m ²)	25.9 \pm 4.7	27.2 \pm 4.8	<i>P</i> < 0.001
Systolic blood pressure (mm Hg)	126.7 \pm 16.6	129.9 \pm 17.9	<i>P</i> = 0.001
Diastolic blood pressure (mm Hg)	77.0 \pm 9.2	78.5 \pm 9.8	<i>P</i> = 0.009
Heart rate (beats per minute)	71.1 \pm 7.8	71.0 \pm 8.0	NS
Residence ¹			<i>P</i> = 0.023
Larger town	59.0%	52.2%	
Smaller town	16.3%	22.1%	
Village	24.6%	25.6%	
Education ²			<i>P</i> < 0.001
University	28.9%	22.2%	
Secondary	39.5%	34.5%	
Vocational	20.1%	30.5%	
Elementary	4.2%	10.8%	
Studying	7.2%	2.0%	

¹Based on *n* = 1320; ²Based on *n* = 1313. NS: Not significant; BMI: Body mass index.

negative children and adolescents that was of borderline statistical significance. On further adjustment for place of residence, this difference became statistically significant, with *H. pylori* positive children and adolescents being on average 3.5 (95%CI: 0.2-6.7) cm shorter. This association was affected relatively little by further adjustment for parental education and remained of borderline statistical significance.

A higher average heart rate among *H. pylori* positive children and adolescents was consistently seen in all univariable and adjusted analyses with a difference of 3.4 (95%CI: 0.7-6.2) beats per minute in fully adjusted analysis (Table 3).

Although our crude analyses indicated differences in several body indices and vital signs between groups of *H. pylori* positive *vs* *H. pylori* negative study subjects aged 18+, these findings were mainly driven by substantial differences in age distribution among the *H. pylori* positive compared to *H. pylori* negative groups. Once adjusted for age and gender, only a difference in body mass index remained statistically significant with *H. pylori* positive adults showing an increase of 0.6 kg/m² in body mass index. This association weakened and became statistically non-significant on adjustment for place of residence and education (Table 4).

DISCUSSION

The prevalence of *H. pylori* in the Czech Republic in

Table 3 Association of *Helicobacter pylori* positivity with body size and blood pressure in 491 children and adolescents (≤ 17 years old) with no missing data on any variables used in the models; univariable and adjusted analysis

Parameter	β -coefficient (95%CI)			
	Crude	Adjusted for age and gender	+ place of residence	+ parental education
Weight (kg)	-1.1 (-8.2-5.9)	-3.4 (-7.4-0.6)	-3.4 (-7.4-0.5)	-3.4 (-7.4-0.7)
Height (cm)	-0.4 (-8.3-7.4)	-3.2 (-6.5-0.0)	-3.5 [-6.7-(-0.2)] ¹	-3.2 (-6.4-0.0)
Body mass index (kg/m ²)	-0.4 (-2.0-1.1)	-0.8 (-2.1-0.5)	-0.7 (-2.0-0.6)	-0.7 (-2.0-0.6)
Systolic blood pressure (mmHg)	3.5 (-1.5-8.5)	2.4 (-1.8-6.7)	2.3 (-1.9-6.6)	2.3 (-2.0-6.5)
Diastolic blood pressure (mmHg)	0.3 (-3.1-3.8)	-0.4 (-3.3-2.5)	-0.4 (-3.3-2.5)	-0.7 (-3.6-2.3)
Heart rate (beats per minute)	3.4 (0.2-6.5) ¹	3.5 (0.3-6.6) ¹	3.7 (0.9-6.5) ¹	3.4 (0.7-6.2) ¹

¹Statistical significance at 0.05 level.**Table 4 Association of *Helicobacter pylori* positivity with body size and blood pressure in 1312 adults (≥ 18 years old) with no missing data on any variables used in the models; univariable and adjusted analysis**

Parameter	β -coefficient (95%CI)			
	Crude	Adjusted for age and gender	+ place of residence	+ own education
Weight (kg)	2.8 (0.9-4.7) ¹	1.3 (-0.5-3.0)	1.1 (-0.6-2.8)	1.1 (-0.6-2.8)
Height (cm)	- 1.4 [-2.6-(0.2)] ¹	-0.5 (-1.4-0.3)	-0.5 (-1.3-0.4)	-0.2 (-1.1-0.6)
Body mass index (kg/m ²)	1.4 (0.8-2.0) ¹	0.6 (0.0-1.1) ¹	0.5 (0.0-1.1)	0.4 (-0.1-1.0)
Systolic blood pressure (mmHg)	3.3 (1.3-5.3) ¹	-0.7 (-2.5-1.1)	-1.0 (-2.8-0.8)	-1.1 (-2.9-0.6)
Diastolic blood pressure (mmHg)	1.5 (0.4-2.6) ¹	0.0 (-1.0-1.1)	-0.1 (-1.2-0.9)	-0.2 (-1.3-0.8)
Heart rate (beats per minute)	-0.1 (-1.0-0.8)	-0.2 (-1.1-0.8)	-0.2 (-1.1-0.7)	-0.2 (-1.1-0.8)

¹Statistical significance at 0.05 level.

2011 was significantly lower compared to the prevalence reported from identical geographical areas in 2001^[40]. In our previous project (run in 2001), we evaluated body indices and basic vital signs in *H. pylori* positive and negative persons in a large prospective study^[37]. The aim of current research was to assess same parameters in 2011 in a prospective setting, using the same methods in identical geographical areas of the Czech Republic.

In 2001, there was a negative effect of *H. pylori* infection on systolic and diastolic blood pressure in subjects below the age of 25 and a relatively strong positive effect on blood pressure in subjects over 65^[37]. We were not able to prove such an association in our current project.

Blood pressure, weight and body mass index were significantly higher in *H. pylori* positive adults compared to *H. pylori* negative ones in our current study. However, *H. pylori* positive adults were significantly older compared to *H. pylori* negative subjects. Once adjusted for age and gender, *H. pylori* infection did not influence body weight, body mass index and basic vital signs either in adults or children and adolescents.

Controversial data have been published in literature on the association of *H. pylori* infection and hypertension with both positive^[2,15,17,18] and negative results^[14,15]. In a large community-based cross sectional study (1634 *H. pylori* positive and 3267 *H. pylori* negative persons out of 10537 subjects enrolled), *H. pylori* infection had little effect on blood pressure in the general population, mean systolic blood pressure was higher in *H. pylori* infected individuals than in those who were not infected

and, although this was significant statistically, the authors concluded that it was unlikely to be clinically important and might be explained by unknown residual confounding factors^[15]. Migneco *et al*^[17] demonstrated a significant decrease in blood pressure values (in particular in the diastolic one) after successful *H. pylori* eradication. There are several methodological difficulties in carrying out studies to determine a possible relationship between *H. pylori* infection and raised blood pressure, there are several other factors that must be considered (weight gain, salt intake, aging, co-morbidity, antihypertensive therapy, and compliance of patients *etc.*)^[44,45].

Several epidemiological studies showed association between *H. pylori* infection and short growth in children^[46-49]. However, contradictory data are available on this topic, as other authors did not find any relationship^[31,32,50,51]. Results and conclusions of all published papers (including our findings) must be assessed with caution. It is necessary to distinguish intrinsic shortness and delayed or attenuated growth. Several factors can influence growth and stature, including chronic inflammation, nutrition and several gastrointestinal diseases^[52].

Family social conditions are possibly a common determinant of *H. pylori* infection and growth. However, quite a large difference in children's height remains after adjustment for parental education, indicating that there may be other mechanisms in place. Possibly, this also might be a causal effect of *H. pylori* infection on children's growth. The adults' socioeconomic conditions and life style may be a common cause of higher body mass index and *H. py-*

lori infection. Although our earlier paper^[39] indicated that most subjects become infected in childhood and childhood social conditions may thus be relevant for many different aspects of adult health, including *H. pylori* infection and higher body mass index (or overweight/obesity).

It is necessary to mention another interesting phenomenon: the decreased prevalence of *H. pylori* represents a prominent decline of CagA positive *H. pylori* strains^[53,54]. CagA positive *H. pylori* strains are more susceptible to eradication treatment than CagA negative strains. This might partly explain their more pronounced decline^[55]. It is necessary to admit that the reasons for decline of *H. pylori* infection have not been fully clarified yet. It is necessary to also consider that the fundamental environmental changes could cause gradual disappearance of *H. pylori* from the human microbiome^[56-58].

In conclusion, chronic *H. pylori* infection appeared to be associated with short stature in children. *H. pylori* infection did not influence blood pressure, body weight and body mass index either in adults or children and adolescents.

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