Helicobacter pylori Positivity in Asymptomatic and Symptomatic Bulgarian Adults Diagnosed by [13]C Urea Breath Test

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Abstract

Global prevalence of *Helicobacter pylori* infection is changing with socio-economic and household improvements, and the increasing use of eradication regimens. The aim of the present study was to assess the current *H. pylori* infection rates among various groups of untreated Bulgarian adults by gender, presence or absence of associated diseases, residence in the capital city versus residence elsewhere, and healthcare-related profession versus other professions. Totally, 373 adults untreated for *H. pylori* infection were evaluated by ^{13}C urea breath test (^{13}C UBT), among them 69 asymptomatic subjects, 33 ulcer patients, 221 non-ulcer patients, and 50 subjects prior to diagnosis. Overall, 57.9% of the adults were *H. pylori* positive, ranging from 47.8% in asymptomatic subjects to ≥66.0% in ulcer patients and symptomatic undiagnosed subjects. Gender of the patients, residence in the capital and healthcare-associated profession were not linked to significantly different positivity rates when compared to the other subgroups. In conclusion, ^{13}C UBT was used as the most accurate non-invasive test for *H. pylori* diagnostics since it detects not past but only present active infections and reflects the status not only of several biopsy specimens but of the whole gastric mucosa. The present results showed that *H. pylori* infection is still a frequent infection and an important healthcare problem in our country, affecting from one-half to two-thirds of all subgroups of Bulgarian untreated adults.

Keywords: *Helicobacter pylori,* adults, subgroups

Резюме

Глобалното разпространение на *Helicobacter pylori* инфекцията се променя със социално-икономическите и битови подобрения, и все по-широкото използване на режимите за ерадикация. Цел на настоящото проучване беше да се открие актуалната честота на *H. pylori* инфекцията сред различни групи от нелекувани възрастни у нас. Общо 373 възрастни, нелекувани за *H. pylori* инфекцията, бяха изследвани с [13]С уреен дихателен тест ([13]С UBT), от тях 69 безсимптомни, 33 пациенти с язва, 221 неязвено болни и 50 души още преди поставяне на диагноза. Общо 57.9% от изследваните възрастни бяха *H. pylori* положителни, вариращи от 47.8% от безсимптомните до ≥66.0% от пациентите с язва и недиагностицираните симптоматични изследвани. Полът на пациентите, местоживеенето в столицата и свързаната със здравеопазването професия не бяха асоциирани със статистически различни честоти на положителност в сравнение с другите подгрупи. В заключение, използвахме [13]С UBT като най-акуратния неинвазивен тест за диагностика на *H. pylori*, тъй като той открива не миналите, а само настоящите активни инфекции и отразява състоянието не в няколко биопсични проби, а на цялата стомашна лигавица. Настоящите резултати показаха, че *H. pylori* инфекцията с все още честа инфекция и важен проблем в здравеопазването в нашата страна и засяга от половината до две трети от всички подгрупи нелекувани възрастни у нас.

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Introduction

Helicobacter pylori causes one of the most common chronic infections in humans and it was estimated that more than half (about 60%) of the people worldwide were infected in 2015 (Sjomina *et al.,* 2018). The high *H. pylori* importance for the healthcare is due to the association of the infection with chronic gastritis, gastric and duodenal ulcers, gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma (Chmiela *et al.,* 2017). Moreover, *H. pylori* has been determined as class I (among the strongest carcinogens) human carcinogen for gastric cancer by the International Agency for Research of Cancer (Chmiela *et al.,* 2017). In most countries, *H. pylori* infection prevalence has been decreasing with socio-economic and living condition improvements, and the common use of regimens for eradication of the infection (Hooi *et al*., 2017).

The aim of the present study was to assess *H. pylori* infection rates among different groups of untreated Bulgarian adults according to ^{13}C urea breath test (^{13}C UBT), which is considered as the most reliable and the most accurate non-invasive test for *H. pylori* diagnostics (Józefczuk *et al.,* 2016). Importantly, unlike serology, ^{13}C UBT detects only the active present infection and, unlike most other diagnostic methods, reveals the state not of one or several biopsy samples but of the gastric mucosa as a whole (Gisbert and Pajares, 2004).

Material and Methods

Totally, 373 adults untreated for *H. pylori* infection were evaluated, including 69 asymptomatic subjects, 33 ulcer patients, 221 non-ulcer patients, and 50 subjects prior to diagnosis (Table 1).

The mean age of the subjects was 45.5 years (range, 18 to 88 years). Data about the place of living were available for 87.4% (326) subjects. Of all subjects evaluated, 11.8% (44 persons) had healthcare-associated professions.

^{13}C UBT evaluation was performed by HeliFANplus (Fischer ANalysen Instrumente GmbH, 04347 Leipzig, Germany) based on non-dispersive infrared spectroscopy (Fig. 1).

Fig. 1. HeliFANplus for ^{13}C urea breath test

^{13}C-UBT was carried out in patients after overnight fasting. After obtaining baseline breath samples, ^{13}C urea (75 mg) and citric acid (2 g) were administered in aqueous solutions. The second breath sample was collected 30 min after administering the test solutions.

Delta over baseline (DOB) cut-off value of 2.05 or higher was considered as a positive result according to a previously plotted ROC curve (Boyanova *et al.,* 2013a).

Results

Among all subjects evaluated by ^{13}C UBT, 216 (57.9%) were *H. pylori* positive. Positivity rate was 47.8% (33/69 subjects) in the group of asymptomatic patients, but significantly higher in the symptomatic but still undiagnosed subjects (66.0%, 33/50, p=0.049), (Table 1).

Table 1. *H. pylori* positivity among untreated Bulgarian adults

Group		No. of tested	No. of positive	% of positive	95% CI	P value
Gender	Women	215	131	60.9	54.3-67.2	0.168
	Men	158	85	53.8	46.0-61.4	
Status/ disease	Symptomatic, non-diagnosed	50	33	66.0	52.1-77.6	Non-diagnosed vs. Asymptomatic: 0.049
	Asymptomatic	69	33	47.8	36.5-59.4	Asymptomatic vs. Ulcer: 0.074
	Ulcer	33	22	66.7	49.5-80.3	
	Non-ulcer	221	128	57.9	51.3-64.2	Asymptomatic vs. Non-ulcer: 0.141
Place of living	Living in Sofia	285	160	56.1	50.3-61.8	0.240
	Living elsewhere	41	27	65.8	50.5-78.5	
Profession	Helthcare profession	44	24	54.6	40.1-68.3	0.630
	Other professions	329	192	58.4	53.0-63.6	
	All	**373**	**216**	**57.9**	**52.8-62.8**	

Totally, 66.7% (22/33) of ulcer patients and 57.9% (128/221) of and non-ulcer patients were positive.

No statistically significant differences were found between the subjects living in Sofia (56.1%, 160/285 subjects) and those living elsewhere (65.8%, 27/41, p=0.24). The positivity rates were similar in the subjects with healthcare professions (54.6, 24/44) and those with other professions (58.4%, 192/329, p=0.63).

Discussion

^{13}C UBT accuracy is very high, with sensitivity and specificity often of 90-100% (most often >95%), (Gisbert and Pajares, 2004). Using 75 mg of urea has been considered as optimal to obtain accurate UBT results, furthermore, citric acid test meal has been recommended to be added by leading specialists (Gisbert and Pajares, 2004). Moreover, DOB value for positive results was considered according to the ROC curve calculated beforehand (Boyanova *et al.,* 2013). This is a very important issue and in the study of Perets *et al.* (2019), optimizing ^{13}C UBT cutoff to 2.74 DOB provided about 1% more positivity to the test compared with the cutoff of 3.5 specified by the manufacturer.

In a meta-analysis (Hooi *et al.*, 2017), *H. pylori* infection has been most prevalent (>79%) in Africa and Latin America (>63%), while a two-fold lower (37.1%) prevalence has been observed in Northern America. Our prior results confirmed the still high prevalence of *H. pylori* infection in symptomatic Bulgarian children (Boyanova *et al.*, 2019). In 24.2% of asymptomatic children, the infection was also detected (Yordanov *et al.,* 2018).

In our previous work on asymptomatic Bulgarian adults, a high rate (72.4%) of *H. pylori* seroprevalence was observed (Yordanov *et al.,* 2016). In the present work, *H. pylori* positivity rate was lower (>47%), most probably because serology detects both present and past infections, whereas ^{13}C UBT detects only current active infections.

In the present study, the infection in asymptomatic subjects (47.8%) was more frequent than that in Germany (28.9%) and was similar to that in Denmark (42.9%) in 1982-1983, (Franck *et al.,* 2017; Levenstein *et al.,* 2017).

A striking result of the present study was the very high (66.0%) positivity rate in symptomatic but still undiagnosed subjects. This may be explained by the probable presence of severe or persistent pain and disturbing symptoms that make the subjects want to be tested for infection before being referred to specialist gastroenterologists.

As in our previous study (Boyanova, 2007), there was no significant difference in *H. pylori* positivity between men (53.8%) and women (60.9%, p=0.17) in the present study.

No significant differences were found according to the place of living in Sofia, the capital of the country, or according to the profession related to healthcare. The lack of statistical difference according to the place of living may be due to the relatively low (47 subjects, 12.6% of all adults evaluated) number of the subjects reporting a place of living outside the capital. However, in our previous study (Boyanova *et al.*, 2013b), the inhabitants of the capital were at a 1.4-fold higher risk of *H. pylori* resistance to antibiotics compared with those living in other settlements. In addition, Hadzhiyski (2019) observed a significantly higher (37.2%) *H. pylori* positivity rate in children living in villages compared to that (22.8%) in children living in towns. Thus, this topic merits further evaluation.

The differences in *H. pylori* prevalence among occupational groups is a topic of controversy. There are relatively few recent studies on occupational risk factors contributing to the infection (Leja *et al.*, 2019). In the study of Loster *et al.* (2009), gastric and oral *H. pylori* positivity rates in dentists were comparable to those in the general population; however, a difference was only related to the male sex and the length of professional exposure. In a systematic review, health professionals were *H. pylori* positive compared to those with other professions, the difference being the highest for the health professionals of gastroenterology units (Kheyre *et al.,* 2018).

In the present study, no data were available about the exact workplace of the health care workers (in hospitals or dental offices), however, the *H. pylori* positivity rates in them (54.6%) were very similar to those (58.4%, p=0.63) of the other adults evaluated. Therefore, the high similarity of the prevalence rates in both groups does not imply an increased risk of the infection in health professionals evaluated in the present work. However, as stated by Leja *et al.* (2019), the influence of the social origin and conditions, in addition to the specific profession is also very important and should also be taken into account.

Conclusion

In conclusion, ^{13}C urea breath test was used as the best non-invasive test for *H. pylori* diagnostics since it detects only the current active infection and reflects the status of the entire gastric mucosa. The present results revealed that *H. pylori* infec-

tion is still a frequent infection and an important healthcare problem in our country, affecting from one-half to two- thirds of all subgroups of Bulgarian untreated adults. The strikingly high (66.0%) positivity rate in the group of undiagnosed subjects can be explained by the intensity of the symptoms.

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