

Helicobacter Pylori Prevalence in Communities from Southern Regions of Romania with Limited Access to Health Services: A Cross-sectional Study

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ABSTRACT

Background & Aims: *Helicobacter pylori* (*H. pylori*) infection has an unknown prevalence in certain Romanian regions. We aimed to estimate it in communities from Southern regions of Romania with limited access to health services.

Methods: We designed a cross-sectional study to include adult voluntary participants in the “Health in the neighborhood” medical assistance program. This was offered in villages with deprived healthcare availability from Southern regions of Romania. An immunochromatographic assay for the qualitative detection of *H. pylori* stool antigen was used for testing.

Results: We included 708 adult voluntary participants in 10 villages, 6 from Muntenia and Oltenia Regions (Southern Romania), 2 from Dobrogea and 2 from Moldova (2.4% of all village inhabitants). *H. pylori* prevalence in Romanian Southern regions was 28.2%, (95%CI: 24-32.6%), and overall was 27.1%, (95%CI: 23.9-30.6%). There were no significant differences of *H. pylori* infection pertaining to regions distribution ($p=0.711$), gender ratio ($p=0.779$), age distribution ($p=0.471$) and hemoglobin value ($p=0.503$).

Conclusions: *H. pylori* prevalence in communities from Southern regions of Romania with limited access to health services was 28.2%, 95%CI: 24-32.6%.

Key words: *Helicobacter pylori* – prevalence – developing country – accessibility health services – iron deficiency.

Abbreviations: *H. pylori*: *Helicobacter pylori*; HDL: high density lipoprotein; PPI: proton pump inhibitor.

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a Gram-negative bacterium which colonizes gastric mucosa, often asymptomatic and sometimes with severe medium and long-term complications (chronic gastritis, peptic ulcer, gastric adenocarcinoma, MALT lymphoma) [1].

According to most recent Globocan Cancer Observatory 2020 data, the annual incidence of gastric cancer ranks 5th both worldwide (1,089,103 new cases in 2020) and in Romania (3,970 new cases in 2020), while mortality due to gastric cancer ranks 4th both worldwide (768,793 deaths due to gastric

cancer in 2020) and in Romania (3,246 deaths due to gastric cancer in Romania in 2020) [2].

Helicobacter pylori infection is grade I carcinogen for gastric cancer designated by the World Health Organization (WHO) [3]. Screening and eradication may be beneficial in prevention of its complications [4].

In Romania, in present, available data for *Helicobacter pylori* incidence comes from tertiary centers located mostly in Transylvania, Crisana, Banat and Moldova regions, and mostly in symptomatic patients [5-13] (Table I). Currently there are no epidemiological data in Muntenia Region and there are no epidemiological data in general population in Romania.

The aim of the study is to evaluate the prevalence of *Helicobacter pylori* infection in individuals from several villages of the Southern regions of Romania, considered vulnerable relative to healthcare availability.

METHODS

In the year 2023, MEDCORP Association developed the “Health in the neighborhood” program sponsored by

Table I. Published papers that have estimated *Helicobacter pylori* prevalence in Romania

Year	Paper	Study type, period	Study population	Diagnostic method	Positivity rate
2022	Negovan A, et al [5]	Retrospective, 2018 - 2021	Transylvania region (Mureş County) Patients with UGiE indication	UGiE + histology	35.9% (557 of 1552 patients)
2021	Loor A, et al [6]	Prospective, 2019	Crişana region (Cluj County) Medical University students	UBT	25.3% (38 of 150 students)
2021	Szoke A, et al [7]	Retrospective, 2016 - 2019	Transylvania (Mureş County) Patients with UGiE indication, with duodeno-gastric reflux at UGiE	UGiE + histology	34.8% (195 of 560 patients)
2020	Coroian Al, et al [8]	Retrospective, 2014 - 2018	Crişana Region (Sălaj County) Patients with dyspeptic syndrome	Serology IgG	40.8% (169 of 414 patients)
2020	Popovici et al [9]	Retrospective, 2018 - 2019	Moldova Region (Bacau County) Hospitalized patients	Fecal antigen	39.9% (819 of 2048 patients)
2017	Negovan A, et al [10]	Prospective, 2012 - 2015	Transylvania Region (Mureş County) Patients with UGiE indication, treated with LDA and PPI	UGiE + histology	30.8% (73 of 237 patients)
2017	Olar L, et al [11]	Retrospective, 2010 - 2014	Oltenia Region (Dolj County) Patients with UGiE indication	UGiE + histology	63.7% (971 of 1525 patients)
2016	Danciu M, et al [12]	Retrospective, 2014 - 2015	Moldova Region (Iasi County) Obese patients with UGiE indication before gastric sleeve surgery	UGiE + histology	51.4% (36 of 70 patients)
2003	Sporea I, et al [13]	Prospective, 2003	Banat Region (Timişoara County) Hospital employees	Serology IgG	71.9% (691 of 960 employees)

UGiE: upper gastrointestinal endoscopy; UBT: urea breath test; LDA: low dose aspirin; PPI: proton pump inhibitors; GERD: gastroesophageal reflux disease.

OMV PETROM Company. During this project, MEDCORP Association offered medical assistance in rural areas in the Southern Regions of Romania with limited access to health services. Participation was voluntary. The offered medical assistance included clinical evaluation (symptoms, medical history, physical examination), electrocardiogram, blood tests (full blood count, lipidic profile, urea, creatinine, transaminases, serum iron, serum calcium, sodium, potassium, hepatitis B virus surface antigen, hepatitis C virus antibody) and urinalysis. All participants with abnormal findings were offered further tailored medical evaluations and specific treatments.

We designed a prospective study to assess the prevalence of *H. pylori* infection in voluntary participants in the “Health in the neighborhood” program. All consenting adult individuals were tested with a single use immunochromatographic assay for the qualitative detection of *H. pylori* antigen in unpreserved stool specimens (Vitrotrack test, Vitrobiochem, Romania). This is a commercially available validated monoclonal test with a relative sensitivity of 99.9% (95%CI: 96.2–100%) and specificity of 98.1% (95%CI: 93.2–99.8%) (Supplementary file). Positive patients were offered eradication therapy according to current guidelines [14, 15]

Data recorded for categorical variables was expressed as absolute values and percentages. For normally distributed quantitative variables data was presented as mean and standard deviation, or else median and intervals. Univariate analysis was done using Fisher’s exact test for categorical variables and T test for quantitative variables if normally distributed, Mann-Whitney U otherwise. For multiple comparisons, Pearson Chi-Square and Kruskal-Wallis test were used. A general linear model was used for multivariate analysis. Sample size for incidence estimation in a population was calculated with a 95%

confidence level and a 5% margin of error. The Kolmogorov-Smirnov test was used to test for normal distribution. SPSS 29.0 software (IBM, USA) was used for statistical analysis.

The study protocol was approved by the Carol Davila University Ethical Committee decision number 11304/24.04.2023 and was registered in Clinical Trials (NCT05874960).

RESULTS

Between March and December 2023, we included 708 adult voluntary participants, in 10 villages, 6 from Muntenia and Oltenia Regions (Southern Romania), 2 from Dobrogea and 2 from Moldova (Fig. 1).

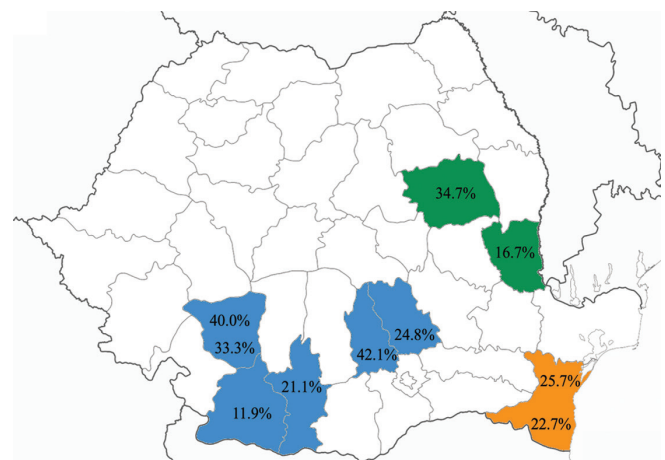


Fig. 1. Distribution of participants and *Helicobacter pylori* incidence in Romanian regions and counties for the included villages (some counties included two villages). Blue - Southern regions, orange - Dobrogea region, green - Moldova region.

The demographic data from each village and overall, in Southern, Moldova and Dobrogea regions and for all participants is presented in Table II.

There were no significant differences of *H. pylori* infection pertaining to regions distribution ($p=0.711$) and age distribution (positive 56.0 ± 13.4 years old vs. negative 55.2 ± 14.6 years old, $p=0.471$). However, amongst counties, significantly lower incidence of *Helicobacter pylori* was seen in Isalnita county from Southern region ($p=0.002$) and Schela county from Moldova region ($p=0.014$). Participants from these two counties also had significantly lower mean age in several pairwise comparisons (Isalnita vs. Tuzla $p<0.001$, Schela vs. Calnic $p=0.017$, Schela vs. Costinesti $p=0.006$, Schela vs. Tuzla $p<0.001$).

There were no significant differences of *H. pylori* infection concerning gender ratio (53 positives of 203 men vs. 139 positives of 505 women, $p=0.779$), and hemoglobin value (positive 14 g/dl (9-17.5) vs. negative 14 g/dl (9.4-17.5), $p=0.503$).

Helicobacter pylori positive patients and women had significantly lower iron levels (positive 92 $\mu\text{g/ml}$ (16.8–190.4) vs. negative 96.8 $\mu\text{g/ml}$ (15.5–253.6), $p=0.010$ and women 92.9 $\mu\text{g/ml}$ (15.5–223.6) vs. men 105.9 $\mu\text{g/ml}$ (23.3–253.6), $p<0.001$).

Most metabolic parameters had similar distribution in *H. pylori* positive and negative participants, glycemia ($p=0.205$), total cholesterol ($p=0.348$), low density lipoprotein (LDL) cholesterol ($p=0.713$) and triglycerides ($p=0.437$). Only high density lipoprotein (HDL) cholesterol was significantly lower in *H. pylori* positive patients - [positive 1.4 mmol/L (0.8–2.8) vs. negative 1.5 mmol/L (0.6–2.9), $p<0.001$; positive 54.3 mg/dl (29.1–110) vs. negative 59.1 mg/dl (23.7–114.3), $p < 0.001$].

Of the 192 positive *H. pylori* individuals, 6 of them (3.1%) had a personal history of gastroduodenal ulcer and 7 of them (3.6%) were known to have *H. pylori* and had had eradication therapy in the past, in a median period of 1.25 years (range 0.3 to 21 years). 51 of infected individuals (26.6%) had dyspeptic and or gastrointestinal reflux symptoms of which 22 (11.5%) had had proton pump inhibitor (PPI) therapy, currently or in the past. 21 of 192 (10.9%) had symptoms or diseases that could be associated with lower iron and/or hemoglobin levels: 6 individuals had digestive symptoms or diseases (2 individuals with rectal bleeding, 2 individuals had hemorrhoids, one had a large hiatal hernia and one had liver cirrhosis), 4 had hematological diseases, 6 had gynecological diseases and 5 had chronic kidney diseases.

20 of 192 *H. pylori* positive individuals (10.4%) were smokers.

DISCUSSION

Our sample of 708 individuals represent 2.3% of all adult inhabitants from the included counties, as determined by the 2021 Romanian census [16]. This is larger than a calculated hypothetical sample size to estimate *H. pylori* incidence in Romania (385 individuals of a 19,053,815 population) [17]. The mean percentage of participants included per county was $2.8\% \pm 1.3\%$, normally distributed ($p=0.372$).

Even though serology is mostly used for epidemiological studies, we used the *H. pylori* antigen stool test as these two methods have comparable sensitivities and specificities [14]. As serology does not indicate an active infection, for the benefit of the individual participants we considered the antigen stool test more appropriate, as eradication therapy was offered to positive individuals [14,15].

Table II. Demographic data for all participants

Region	County	Village	Participants, number, (% of adults*)	Age, years mean \pm SD	Male gender, number (%)	<i>H. pylori</i> positive, number (%)
Muntenia	Dambovița	Bucșani	57 of 4800 (1.2)	54.8 \pm 15.1	13 (22.8)	24 (42.1)
	Prahova	Scorțeni	117 of 4173 (2.8)	54.5 \pm 13.1	22 (18.8)	29 (24.8)
Oltenia	Dolj	Ișalnița	67 of 3284 (2)	52.0 \pm 13.6	19 (28.4)	8 (11.9)
	Olt	Poboru	71 of 1425 (5)	57.3 \pm 14.1	28 (39.4)	15 (21.1)
	Gorj	Câlnic	75 of 1802 (4.2)	57.3 \pm 13.2	24 (32.0)	30 (40.0)
		Hurezani	57 of 1244 (4.6)	47.9 \pm 13.8	14 (24.6)	19 (33.3)
Overall, Southern Regions			444 of 16728 (2.7)	54.4 \pm 14.3	120 (27)	125 (28.2) 95%CI: 24-32.6
Dobrogea	Constanța	Tuzla	73 of 5198 (1.4)	64.8 \pm 10.9	22 (30.1)	19 (26)
		Costinești	44 of 2461 (1.8)	59.7 \pm 13.1	15 (34.1)	10 (22.7)
Overall, Dobrogea			117 of 7659 (1.5)	62.9 \pm 11.9	37 (31.6)	29 (24.8) 95%CI: 17.3-33.6
Moldova	Galați	Schela	72 of 2734 (2.6)	47.9 \pm 12.1	28 (38.9)	12 (16.7)
	Bacau	Zemeș	75 of 3452 (2.2)	58.2 \pm 14.4	18 (24.0)	26 (34.7)
Overall, Moldova			147 of 6186 (2.4)	53.1 \pm 14.2	46 (31.3)	38 (25.9) 95%CI: 19-33.7
Overall, all participants			708 of 30573 (2.3)	55.4 \pm 14.1	203 (28.7)	192 (27.1) 95%CI: 23.9-30.6

* Proportion of all adults from the village as determined by the Romanian 2021 census [16]. SD: standard deviation. 95%CI: 95% confidence interval.

Helicobacter pylori prevalence in Romanian Southern regions was 28.2%, (95%CI: 24-32.6%), while for all included regions was comparable, at 27.1%, (95%CI: 23.9-30.6%). This is surprisingly much lower than the reported percentages of 50% and higher for western regions of Romania at the beginning of the years 2000 [11-13] (Table I). As we did not sample the same regions, we cannot infer a time tendency for *Helicobacter pylori* prevalence. Data suggest that *H. pylori* prevalence is decreasing in time. The worldwide prevalence in adults has been reduced from 52.6% (95%CI: 49.6-55.6%) before 1990 to 43.9% (95%CI: 42.3%-45.5%) during 2015 to 2022 [18].

Helicobacter pylori prevalence tends to increase with age, 29.8% in 30 to 34 years old, 48.8% in 40 to 44 years old, 66.2% in 50 to 54 years old and 69.2% in 60 to 64 years old in a study in the Welsh population from 1990 [19]. Similar results are also reported more recently [20]. Although the methodology used are different, the same tendencies were seen in Romania. In 2021 a prevalence of 25.3% in medical students aged 21.1±1.4 years was reported and in 2003 a prevalence of 71.9% in hospital employees aged 36.8±7.6 years [6, 13]. In our series, we could not find any differences in age distribution, as these were communities with low access to medical services, with possibly higher rates of *H. pylori* infection, irrespective of age distribution [21]. However, we could identify two counties (Isalnita from Southern region and Schela from Moldova region) with participants with a lower mean age and lower incidence of *H. pylori*, which may support this finding.

Prevalence in villages from Southern Regions varied between 11.9% to 42.1%. Similar variations among different nationwide communities are reported by other authors as well, partly explained by variable *H. pylori* prevalence in Caucasians and African Americans [20].

Men were about one quarter to one third of our included individuals. This is less than reported men to women sex ratio of 0.99 in the 15 to 64 years old group and 0.77 in the above 65 years old group, as reported by the 2021 census [16]. This may be that men are less likely to seek medical advice than women and therefore less likely to voluntarily participate in this project [22].

In our study, there were no significant differences in hemoglobin values between positive and negative *H. pylori* participants, only the serum iron levels were lower in positive ones. Although the differences were statistically significant, these were clinically non-significant. Literature data do report significantly lower hemoglobin and iron levels in *H. pylori* positive individuals, with arguable clinical significance [23, 24].

Of interest may be the finding that *H. pylori* positive patients have significantly lower HDL- cholesterol levels. It may explain the findings of a very recent meta-analysis of 24 studies on 5270 participants which proved that eradication of *Helicobacter pylori* significantly increases HDL cholesterol by 0.06 mmol/L (2.28 mg/dl) [25]. This is important as, up to 2.3 mmol/L (90 mg/dl), every increase with 0.03 mmol/L (1 mg/dl) of HDL cholesterol decreases the cardiovascular risk by 3 – 5% [26, 27].

26.6% of *H. pylori* positive participants had dyspeptic symptoms, which is in concordance of the reported 80% percentage in literature of asymptomatic infection [28]. 10.4% percent of our *H. pylori* individuals were smokers; this

is less than the reported 19.8% percentage for the Romanian population for the year 2020 [29]. Currently, there is no accepted association between tobacco consumption and *H. pylori* infection [30].

CONCLUSIONS

About a quarter of individuals from Southern part of Romania are estimated to be infected with *H. pylori*. As the included individuals were from areas with limited access to medical services, it is possible that the prevalence may actually be lower.

Conflicts of interest: None to declare.

Authors' contribution: R.F.P. designed the study, organized the epidemiological data collection, collected and analyzed data; C.A.P. and F.I.I. organized the epidemiological data collection. M.C. designed the study, analyzed data and wrote the paper. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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