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Динамика распространенности инфекции *Helicobacter pylori* с 2015 по 2023 год

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АННОТАЦИЯ

Обоснование. Глобальная распространенность инфекции *Helicobacter pylori* снизилась с 58,2 % (в 1980–1990 гг.) до 43,1 % (в 2011–2022 гг.). Для разработки клинических рекомендаций по профилактике заболеваний, связанных с *Helicobacter pylori*, важное значение имеет оценка изменения инфицированности *Helicobacter pylori* в мире и в Российской Федерации в частности.

Цель исследования — оценить динамику инфицированности *Helicobacter pylori* среди пациентов, направленных на диагностику хеликобактерной инфекции в г. Санкт-Петербурге и прошедших в период с 2015 по 2023 г. процедуру ^{13}C-уреазного дыхательного теста.

Материалы и методы. В описательное исследование включены все пациенты, направленные на ^{13}C-уреазный дыхательный тест (50 884 человек). При значении Delta Over Baseline менее 2,5 ‰ результат теста считали отрицательным, значение показателя более 2,5 ‰ свидетельствовало об инфицированности *Helicobacter pylori*. В базу данных для последующего статистического анализа вносили возраст, пол, факт предшествующей эрадикационной терапии и результат теста, включая степень инфицированности.

Результаты. *Helicobacter pylori* выявлен у 32,7 % (16 642; 95 % доверительный интервал 32,3–33,1 %) пациентов. Из 50 884 участников исследования 83,6 % (42 543; 95 % доверительный интервал 83,3–83,9 %) не получали эрадикационную терапию в прошлом (первичные, «наивные» пациенты), 16,4 % (8341; 95 % доверительный интервал 16,1–16,7 %) — получали (пролеченные, повторные пациенты). Средняя частота инфицированности среди первичных пациентов составила 36,1 % (15 358; 95 % доверительный интервал 35,6–36,6 %), среди повторных — 15,4 % (1284; 95 % ДИ 14,6–16,2 %). С 2015 по 2017 г. выявлено снижение инфицированности *Helicobacter pylori* у первичных и повторных пациентов во всех группах на 14,8 и 21,1 % соответственно, и с 2020 по 2023 г. — на 3,6 и 6,2 % соответственно. У большинства как первичных, так и повторных пациентов выявлена очень высокая (IV) степень инфицированности — у 73,0 и 66,5 % соответственно.

Заключение. Продемонстрированное в исследовании значимое снижение инфицированности *Helicobacter pylori* с 2015 по 2017 г. свидетельствует о том, что информирование врачей о важности диагностики и лечения *Helicobacter pylori*-инфекции является приоритетной задачей. Пандемия новой коронавирусной инфекции также повлияла на показатель инфицированности, однако до настоящего времени непонятны негативные последствия активного использования антибактериальных средств у пациентов с COVID-19, прежде всего, потенциальное изменение резистентности *Helicobacter pylori* к ключевым препаратам данной группы.

Ключевые слова: ^{13}C-уреазный дыхательный тест; хеликобактерная инфекция; эрадикация; распространенность; *Helicobacter pylori*.

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Dynamics of the prevalence of *Helicobacter pylori* infection from 2015 to 2023

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ABSTRACT

BACKGROUND: The global prevalence of *Helicobacter pylori* infection has decreased from 58.2% (1980–1990) to 43.1% (2011–2022). To develop clinical recommendations for prevention diseases associated with *Helicobacter pylori*, it is important to assess changes in *Helicobacter pylori* infection in the world and in the Russian Federation, in particular.

AIM: To assess the dynamics of *Helicobacter pylori* infection among patients in St. Petersburg, who undergone ^{13}C-urease breath test in the period from 2015 to 2023.

MATERIALS AND METHODS: All the patients have been included in the descriptive study to conduct ^{13}C-urease breath test. If the Delta Over Baseline was less than 2.5‰, the test was considered negative. The value of this indicator of more than 2.5‰ indicated infection with *Helicobacter pylori.* The database for subsequent statistical analysis included age, gender, the facts of prior eradicative therapy, test results, including degree of infection.

RESULTS: *Helicobacter pylori* was detected in 32.7% (16,642; 95% confidence interval 32.3–33.1%) of the patients. Of the 50,884 study participants, 83.6% (42,543; 95% confidence interval 83.3–83.9%) of the patients had not received eradication therapy in the past (primary "naive" patients), 16.4% (8,341; 95% confidence interval 16.1–16.7%) had undergone eradication therapy in the past therapy (treated "recurrent" patients). The average infection rate among primary patients was 36.1% (15,358; 95% confidence interval 35.6–36.6%), among recurrent patients — 15.4% (1,284; 95% confidence interval 14.6–16.2%). From 2015 to 2017, a decrease in *Helicobacter pylori* infection was detected in "naive" and "recurrent" patients in all the groups by 14.8 and 21.1%, respectively, and from 2020 to 2023 — by 3.6 and 6.2%, respectively. The majority of both primary and recurrent patients showed a very high (IV) degree of infection — 73.0 and 66.5%, respectively.

CONCLUSIONS: The study demonstrated significant reduction of *Helicobacter pylori* infection from 2015 to 2017 indicating that information from doctors about the importance of diagnosing and treating *Helicobacter pylori* infection is a priority task. The new coronavirus infection also had an impact on the incidence of the infection; however, it is still unclear what the negative consequences of the active use of antibacterial agents in patients with COVID-19 are, first of all, potential impact on *Helicobacter pylori* resistance to key antibacterial drugs.

Keywords: ^{13}C-urease breath test; *Helicobacter pylori* infection; eradication; prevalence; *Helicobacter pylori*.

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BACKGROUND

Helicobacter infection is the most prevalent chronic bacterial infection [1]. About 90% of gastric cancer cases are associated with *Helicobacter pylori* [2]. The guidelines on preventing, diagnosing, and treating gastric cancer indicate that eradicating *H. pylori* is a very effective approach to preventing gastric cancer [3].

The epidemiology of *H. pylori* infection has been determined through noninvasive diagnostic techniques, including identifying *H. pylori* antigens in fecal specimens and class G immunoglobulins to *H. pylori* antigens in the blood (serologic method), along with the ^{13}C-urease breath test (^{13}C-UBT). The ^{13}C-UBT is recommended for the primary diagnosis and to monitor eradication efficiency because of its equivalent sensitivity and specificity compared with other invasive and noninvasive methods. The Delta over Baseline value, which measures the increase in ^{13}C content in exhaled air after administering ^{13}C-labeled urea, is positively correlated with Helicobacter urease activity and the number of microbes and reflects the degree of *H. pylori* contamination of the gastric mucosa [4].

In 2014, approximately 7 million ^{13}C-UBTs were taken in the USA [5]. In contrast, the national 2014 publication reported a maximum of 15–20 thousand such tests per annum in the Russian Federation [6]. According to data from a laboratory that has provided the ^{13}C-UBT service since May 2017 with extensive representation in our country, 42,843 individuals were examined using this method in 2019–2020. These findings suggest a favorable trend toward the use of a noninvasive reference diagnosis of *H. pylori* infection in Russia [7]. However, this quantity of tests is inadequate for prompt identification and treatment of *H. pylori* infection to prevent cancer. Russia should conduct at least 1–1.5 million ^{13}C-UBTs annually. Notably, despite regulatory measures, the ^{13}C-UBT is not covered by compulsory health insurance [8].

Assessing the changes in *H. pylori* infection worldwide and in the Russian Federation in particular is important to develop clinical recommendations to prevent *H. pylori*-related diseases. Half of the world's population is thought to be infected with *H. pylori*; however, annually updated data indicate a decrease in the prevalence of this infection, suggesting the effectiveness of treatment and prevention strategies. The prevalence of *H. pylori* infection decreased globally from 58.2% during 1980–1990 to 43.1% during 2011–2022 [9].

Significant variations in the prevalence of infection are observed between different countries and within countries, as well as between different subgroups within populations in those countries (such as people of different ages, social statuses, or educational backgrounds). An examination of 410,879 patients from 73 countries across six continents revealed that Nigeria, Serbia, South Africa, Nicaragua, and Colombia have the highest incidence rates of *H. pylori* infection (89.7%, 88.3%, 86.8%, 83.3%, and 83.1%, respectively), while Yemen, Indonesia, Belgium, Ghana, and Sweden have the lowest (8.9%, 10.0%, 11.0%, 14.2%, and 15%, respectively) [10].

Children are a unique group regarding the diagnosis of Helicobacter infection. Unlike adults, children infected with *H. pylori* usually show no symptoms, particularly no abdominal symptoms [11]. The "test and treat" strategy, which is popular in some countries, is not recommended for the pediatric population [12]. Studying the prevalence of *H. pylori* infection in children is valuable for predicting future associated diseases. The prevalence of *H. pylori* infection varies by country and diagnostic test type. Countries with higher income levels have lower infection rates (21.7%) than low- and middle-income countries (43.2%). Serologic diagnostic methods produce lower infection rates (28.6%), whereas the ^{13}C-UBT produces higher rates (35.9%) [13]. Most studies indicate a rate of asymptomatic *H. pylori* infection >30% in children, and the overall prevalence among children with digestive symptoms is 40% [14]. Developed countries, such as Japan, Germany, the Netherlands, and the USA, have relatively low reported serologic detection rates of *H. pylori* in children (7.7%, 11.8%, 9.8%, and 5.7%, respectively). High rates of infection among children have been recorded in Chile, Venezuela, Iran, and Nigeria, with percentages of 27.2%, 65.9%, 25.8%, and 40.4%, respectively [15].

The prevalence of *H. pylori* infection in Russia, as per the outcome of the ^{13}C-UBT (n = 19,875) between 2017 and 2019, was 38.8%–42.5% [16]. The Southern and Northern Caucasus Federal Districts recorded the highest levels. *H. pylori* infection among patients aged 41–50 years [17]. Based on the findings from a 2016 study in St. Petersburg among patients with gastrointestinal symptoms (n = 4,181), *H. pylori* infection was prevalent in 50% of cases. In addition, 55% of patients revealed a substantial level of contamination [18].

Data on the effect of the COVID-19 pandemic on the prevalence of Helicobacter infection are limited, including in the Russian Federation.

A register was established at the North-Western State Medical University named after I.I. Mechnikov, St. Petersburg to evaluate the infection trends among patients referred for Helicobacter diagnosis. This registry, reflecting clinical indicators, encompasses data from 50,884 patients who underwent the ^{13}C-UBT procedure between 2015 and 2023 at the time of data analysis for this study.

MATERIALS AND METHODS

The North-Western State Medical University named after I.I. Mechnikov conducted a descriptive study on the prevalence of Helicobacter infection from 2015 to 2023.

This study is a continuation of the research conducted in 2015 [18].

All patients referred for UBT enriched with carbon-13 were included. The ^{13}C-UBT procedure was performed according to a standardized technique using an IRIS infrared spectrometer (Kibion/Wanger, Erlangen, Germany). The principle and the examination procedure for the ^{13}C-UBT have been explained previously [18]. The test was performed using the 4-point technique, which helped to lower the likelihood of false negatives.

The study excluded patients who were administered antimicrobials, bismuth preparations for 1 month, or antisecretory drugs for 2 weeks before testing. The test results were evaluated according to the manufacturer's instructions. A negative test result (minimal enzymatic hydrolysis of urea) was recorded if the Delta over Baseline value was <2.5. An index value >2.5 indicated the presence of *H. pylori* infection. This citation verified our research, which compared the accuracy of the ^{13}C-UBT with the *H. pylori* morphological method for diagnosis, confirming its sensitivity and specificity.

Age, gender, previous eradication treatment, and the test results, including the severity of infection were recorded in the database for subsequent statistical analysis.

The participants were classified into four age categories for the statistical analysis: children (2–17 years), young adults (18–44 years), middle-aged adults (45–59 years), and older adults (>60 years). In addition, cases of infection diagnosed in older individuals (>75 years old) and long-lived individuals (>90 years old) were assessed alongside the elderly population. A comparative analysis was conducted on the frequency of infection during 2015–2017, 2018–2020, and 2021–2023. The key point of division occurred in 2020, which marked the onset of the COVID-19 pandemic in the Russian Federation. The incorporation of azithromycin into the treatment protocols for patients with the new coronavirus infection, in addition to the excessive administration of amoxicillin, clarithromycin, and azithromycin, may have had a significant effect on the occurrence of *H. pylori* infection.

Data analysis was performed using Microsoft Excel 2016 (Microsoft Inc., Redmond, WA, USA), GraphPad Prism 10.1.0, (GraphPad Software Inc., La Jolla, CA, USA), and Statistica 10 (Statsoft Inc., Tulsa, OK, USA). The Kolmogorov–Smirnov test was used to assess the normality of the distribution with the Lilliefors correction for quantitative indicators. The median and interquartile range [Me (Q25%; Q75%)] was used to explain quantitative indices that were abnormally distributed. Differences were detected using Pearson's χ^2 test. Confidence intervals (CIs) were determined using Fisher's angular transformation. A p-value < 0.05 was considered significant.

RESULTS

The study included 50,884 patients, and *H. pylori* was found in 32.7% [16,642; 95% CI 32.3%–33.1%].

Of the 50,884 participants in the study, 83.6% (42,543; 95% CI 83.3%–83.9%) were primary or "naïve" patients who had not undergone eradication therapy, whereas 16.4% (8,341; 95% CI 16.1%–16.7%) were recurrent patients who had received treatment. Primary patients had a younger mean age than the treated patients, with an age of 42.9 (95% CI 31.0–55.0) years compared with 45.8 (34.0–58.0) years (p < 0.05). No differences were observed in the gender composition between the primary and recurrent patients.

Group of patients who have not received eradication therapy in the past (primary patients)

The prevalence of *H. pylori* infection among primary care patients was 36.1% (15,358; 95% CI 35.6%–36.6%).

No significant differences were observed between the infected and noninfected primary patient groups of males or females. However, infected patients tended to have a higher median age of 44.5 years (33.0; 56.0) compared to 41.9 years (30.0; 55.0) for noninfected patients (p < 0.05). Details of the primary patients, including the distribution by time triad, are presented in Table 1.

The majority of primary patients, 73.0% (11,215; 95% CI 72.3%–73.7%), had a very high (IV) grade of infection; a high (III) grade of infection was detected in 11.7% (1,802; 95% CI 11.2%–12.3%), moderate (II) in 10.5% (1,605; 95% CI 10.0%–10.9%), and mild (I) in 4.8% (736; 95% CI 4.5%–5.1%). Table 2 shows a higher number of patients with grade IV infection across all age groups (p < 0.0001). Notably, the *H. pylori* detection frequency was highest among patients aged 18–44 years, reaching 51.5% (7,918; 95% CI 50.8%–52.3%; p < 0.0001). A significantly higher prevalence of infection was observed among middle-aged patients (aged 45–59 years) than among children, young, or elderly patients. The rates of infection were 76.1% (95% CI 74.8–77.3%) in middle-aged patients vs. 55.0% (95% CI 48.8%–61.1%) in children, 71.7% (95% CI 70.7%–72.7%) in young adults, and 73.5% (95% CI 71.9%–75.2%) in the elderly (p < 0.0001). A higher infection rate was found more frequently in females than males, with 77.3% (6,808; 95% CI 76.4%–78.2%) vs. 67.2% (4,407; 95% CI 66.1%–68.4%) of cases (p < 0.0001).

A significant decrease of 18.7% in *H. pylori* infection was observed among primary patients during the follow-up period, ranging from 51.4% (874; 95% CI 49.0%–53.8%) in 2015 to 32.7% (1,450; 95% CI 31.3%–34.1%) in 2023 (p < 0.0001). The lowest index value was recorded in 2022 at 32.2% (1,904; 95% CI 31.0%–33.4%) (Fig 1).

Table 1. Characteristics of the primary patients included in the study

Таблица 1. Характеристики первичных пациентов, включенных в исследование

Indicator	Positive ^{13}C-urease breath test result	Negative ^{13}C-urease breath test results	Total	Statistical significance
Total number of patients, *n* (%)	15,358 (36.1)	27,185 (63.9)	42,543 (100)	–
Those examined in 2015–2017, *n* (%)	3,537 (41.4)	5,016 (58.6)	8,553 (20.1)	
Those examined in 2018–2020, *n* (%)	6,431 (36.2)	11,354 (63.8)	17,785 (48.1)	$p < 0.0001$
Those examined in 2021–2023, *n* (%)	5,390 (33.3)	10,815 (66.7)	16,205 (52.8)	
Women, *n* (%)	8,804 (57.3)	15,901 (58.5)	24,705 (58.1)	$p < 0.05$
Men, *n* (%)	6,554 (42.7)	11,284 (41.5)	17,838 (41.9)	
Mean age, median and interquartile range, years	44.5 (33.0; 56.0)	41.9 (30.0; 55.0)	42.9 (31.0; 55.0)	$p < 0.05$
Age range, years	4–97	2–93	2–97	

Table 2. Characteristics of the primary patients who had taken the ^{13}C-urease breath test (+) according to sex, age, and degree of infection

Таблица 2. Характеристики первичных пациентов с ^{13}C-уреазным дыхательным тестом (+) в зависимости от пола, возраста, степени инфицированности

Indicator	Patients aged 2–17 years, *n* (%)	Patients aged 18–44 years, *n* (%)	Patients aged 45–59 years, *n* (%)	Patients over 60 years of age, *n* (%)	Total number of patients, *n* (%)	Statistical significance
Total	247 (1.6)	7,918 (51.6)	4,401 (28.6)	2,792 (18.2)	15,358 (100)	–
Women	134 (54.3)	4,076 (51.5)	2,675 (60.8)	1,919 (68.7)	8,804 (57.3)	$p < 0.0001$
Men	113 (45.7)	3,842 (48.5)	1,726 (39.2)	873 (31.3)	6,554 (42.7)	
IG I (2.5–3.4)	32 (13.0)	357 (4.5)	183 (4.2)	164 (5.9)	736 (4.8)	
IG II (3.5–6.4)	47 (19.0)	861 (10.9)	407 (9.2)	290 (10.4)	1,605 (10.5)	$p < 0.0001$
IG III (6.5–9.4)	32 (13.0)	1,023 (12.9)	463 (10.5)	284 (10.2)	1,802 (11.7)	
IG IV (over 9.5)	136 (55.0)	5,677 (71.7)	3,348 (76.1)	2,054 (73.5)	11,215 (73.0)	

Note. IG, infection grade (with reference values).

The infection rate among primary patients decreased 41.4% (3,537; 95% CI 40.3%–42.4%) between 2015 and 2017, 36.2% (6,431; 95% CI 35.5%–36.9%) from 2018 to 2020, and 33.3% (5,390; 95% CI 32.5%–34.0%) between 2021 and 2023 ($p < 0.0001$). The prevailing age group among the primary patients with confirmed *H. pylori* infection was 18–44 years. However, prevalence increased significantly during 2021–2023, comprising 54.4% (2,931; 95% CI

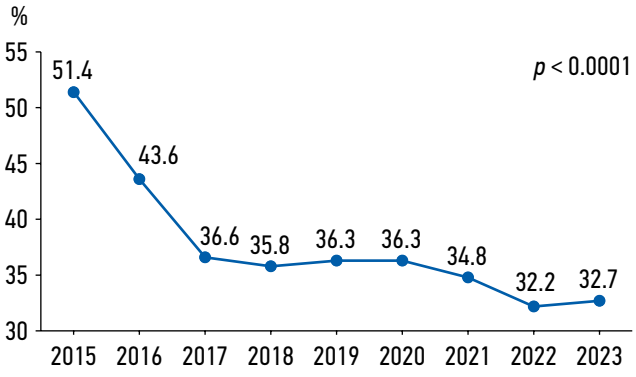

Fig. 1. Change in degree of *Helicobacter pylori* infection in the primary patients from 2015 to 2023

Рис. 1. Изменение показателя инфицированности *Helicobacter pylori* у первичных пациентов с 2015 по 2023 г.

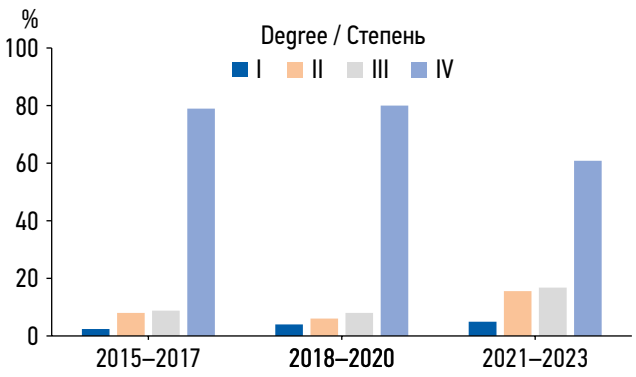

Fig. 2. Distribution of the primary patients according to time triads and degree of infection

Рис. 2. Распределение первичных пациентов по временным триадам и степени инфицированности

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Table 3. Characteristics of the primary patients who received the ^{13}C-urease breath test (+) according to the year of the test, sex, age, and degree of infection

Таблица 3. Характеристика первичных пациентов с ^{13}C-уреазным дыхательным тестом (+) в зависимости от года выполнения теста, пола, возраста и степени инфицированности

Indicator	2015–2017	2018–2020	2021–2023	Total	Statistical significance
Total, *n* (%)	3,537 (23.1)	6,431 (41.8)	5,390 (35.1)	15,358 (100)	–
Women, *n* (%)	2,210 (62.5)	3,596 (55.9)	2,998 (55.6)	8,804 (57.3)	$p < 0.0001$
Men, *n* (%)	1,327 (37.5)	2,835 (44.1)	2,392 (44.4)	6,554 (42.7)	
Mean age, median and interquartile range, years	44.72 (34; 56)	44.68 (33; 56)	44.09 (33; 55)	44.5 (33.0; 56.0)	–
2–17 years old, *n* (%)	57 (1.6)	121 (1.9)	69 (1.3)	247 (1.6)	$p < 0.0001$
18–44 years old, *n* (%)	1,729 (48.9)	3,258 (50.7)	2,931 (54.4)	7,918 (51.5)	
45–59 years old, *n* (%)	1,147 (32.4)	1,864 (28.9)	1,390 (25.8)	4,401 (28.7)	
Over 60 years old, *n* (%)	604 (17.1)	1,188 (18.5)	1,000 (18.5)	2,792 (18.2)	
IG I (2.5–3.4), *n* (%)	116 (3.3)	304 (4.7)	316 (5.8)	736 (4.8)	$p < 0.0001$
IG II (3.5–6.4), *n* (%)	313 (8.9)	438 (6.8)	854 (15.9)	1,605 (10.5)	
IG III (6.5–9.4), *n* (%)	334 (9.4)	542 (8.4)	926 (17.2)	1,802 (11.7)	
IG IV (over 9.5), *n* (%)	2,774 (78.4)	5,147 (80.1)	3,294 (61.1)	11,215 (73.0)	

Note. IG, infection grade (with reference values).

53.0%–55.7%) ($p < 0.0001$) (Table 3). The analysis revealed a significant prevalence of very high (IV) grade of infection ($p < 0.0001$) during all follow-up periods (Fig. 2).

Group of patients with a history of eradication therapy (recurrent patients)

In patients with a previous history of eradication therapy, a positive ^{13}C-UBT was detected in 15.4% (1,284; 95% CI 14.6%–16.2%). Therefore, eradication efficacy was 84.5%, which is not acceptable for therapy.

The median age was not significantly different between the infected and noninfected groups: 45.8 (35.0–57.0) and 45.8 (34.0–58.0) years respectively ($p = 0.85$). Furthermore, gender was not a distinguishing factor between the two groups.

Among the primary patients, most of the recurrent patients exhibited a very high (IV) infection grade of 66.5% (854; 95% CI 63.9%–69.0%), followed by a high (III) grade of infection in 10.3% (132; 95% CI 8.7%–12.1%), a moderate (II) grade in 13.9% (179; 95% CI 12.2%–15.9%), and a mild (I) grade in 9.3% (119; 95% CI 7.8%–11.0%). Table 4 shows that patients with grade IV infection were predominant in all age groups ($p < 0.0001$), despite undergoing antibiotic therapy. Additionally, patients between the ages of 18–44 years had the highest frequency of *H. pylori* infection at 47.7% (613; 95% CI 45.0%–50.5%) ($p < 0.0001$). The prevalence of high infection rates was greater in middle-aged patients (aged

Table 4. Characteristics of the recurrent patients who received the ^{13}C-urease breath test (+) according to sex, age, and degree of infection

Таблица 4. Характеристика повторных пациентов с ^{13}C-уреазным дыхательным тестом (+) в зависимости от пола, возраста и степени инфицированности

Indicator	Patients aged 2–17 years, *n* (%)	Patients aged 18–44 years, *n* (%)	Patients aged 45–59 years, *n* (%)	Patients aged over 60 years, *n* (%)	Total number of patients, *n* (%)	Statistical significance
Total	17 (1.3)	613 (47.7)	403 (31.4)	251 (19.6)	1284 (100)	$p < 0.0001$
Women	12 (70.6)	311 (50.7)	236 (58.6)	169 (67.3)	728 (56.7)	
Men	5 (29.4)	302 (49.3)	167 (41.4)	82 (32.7)	556 (43.3)	
IG I (2.5–3.4)	1 (5.9)	51 (8.3)	33 (8.2)	34 (13.5)	119 (9.3)	$p = 0.0497$
IG II (3.5–6.4)	2 (11.8)	96 (15.7)	43 (10.7)	38 (15.1)	179 (13.9)	
IG III (6.5–9.4)	3 (17.6)	71 (11.6)	37 (9.2)	21 (8.4)	132 (10.3)	
IG IV (over 9.5)	11 (64.7)	395 (64.4)	290 (72.0)	158 (62.9)	854 (66.5)	

Note. IG, infection grade (with reference values).

Table 5. Characteristics of the recurrent patients who received the ^{13}C-urease breath test (+) according to year of test performance, sex, age, and degree of infection

Таблица 5. Характеристика повторных пациентов с ^{13}C-уреазным дыхательным тестом (+) в зависимости от года выполнения теста, пола, возраста и степени инфицированности

Indicator	2015–2017	2018–2020	2021–2023	Total	Statistical significance
Total	410 (31.9)	487 (37.9)	387 (30.2)	1,284 (100)	
Women, *n* (%)	244 (59.5)	278 (57.1)	206 (53.2)	728 (56.7)	$p = 0.1971$
Men, *n* (%)	166 (40.5)	209 (42.9)	181 (46.8)	556 (43.3)	
2–17 years old, *n* (%)	3 (0.7)	10 (2.1)	4 (1.0)	17 (1.3)	
18–44 years old, *n* (%)	188 (45.9)	241 (49.5)	184 (47.5)	613 (47.7)	$p = 0.0721$
45–59 years old, *n* (%)	146 (35.6)	148 (30.4)	109 (28.2)	403 (31.4)	
Over 60 years old, *n* (%)	73 (17.8)	88 (18.1)	90 (23.3)	251 (19.5)	
IG I (2.5–3.4), *n* (%))	40 (9.8)	35 (7.2)	44 (11.4)	119 (9.3)	
IG II (3.5–6.4), *n* (%)	49 (12.0)	61 (12.5)	69 (17.8)	179 (13.9)	$p < 0.0001$
IG III (6.5–9.4), *n* (%)	35 (8.5)	34 (7.0)	63 (16.3)	132 (10.3)	
IG IV (over 9.5), *n* (%)	286 (69.8)	357 (73.3)	211 (54.5)	854 (66.5)	

Note. IG, infection grade (with reference values).

45–59 years) than in pediatric, young, or elderly patients, with rates of 72.0% (290; 95% CI 67.4%–76.1%), 64.7% (11; 95% CI 41.3%–82.7%), 64.4% (395; 95% CI 60.6%–68.1%), and 62.9% (158; 95% CI 56.8%–68.7%), respectively ($p < 0.05$). Women with a significantly higher level of infection were more frequent than men, with prevalence rate of 71.3% (519; 95% CI 67.9%–74.5%) compared with 60.3% (335; 95% CI 56.1%–64.2%) in males ($p < 0.0006$).

Helicobacter infection was detected in 17.8% (410; 95% CI 16.3%–19.5%) of recurrent patients in 2015–2017, 16.0% (487; 95% CI 14.8%–17.4%) in 2018–2020, and 12.9% (387; 95% CI 11.7%–14.1%) in 2021–2023. The rate of *H. pylori* infection during the follow-up in recurrent patients decreased threefold from 2015 to 2023, dropping from 39.1% to 13.2% ($p < 0.001$). Table 5 presents the data on recurrent patients based on age, gender, grade of infection, and time of study. The change in the rate of *H. pylori* infection in recurrent patients from 2015 to 2023 is depicted in Fig. 3.

Figure 4 illustrates the variation in the *H. pylori* infection rates among the primary and recurrent patients between 2015 and 2023. Notably, the infection rates for primary and recurrent patients decreased significantly by 14.8% and 21.1%, respectively from 2015 to 2017. The rates remained relatively stable from 2017 to 2020. However, there were additional decreases of 3.6% and 6.2% for the primary and recurrent patients, respectively from 2020 to 2023.

DISCUSSION

Helicobacter infection is the primary cause of chronic gastritis, precancerous changes in the mucosa (atrophy, metaplasia, and dysplasia), and gastric adenocarcinoma [2].

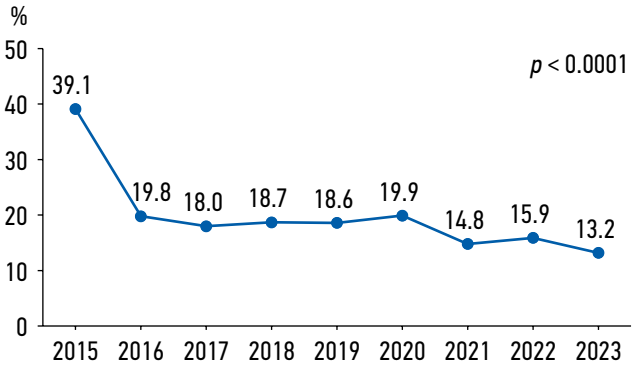

Fig. 3. Change in degree of *Helicobacter pylori* infection in the recurrent patients from 2015 to 2023

Рис. 3. Изменение показателя инфицированности *Helicobacter pylori* у повторных пациентов с 2015 по 2023 г.

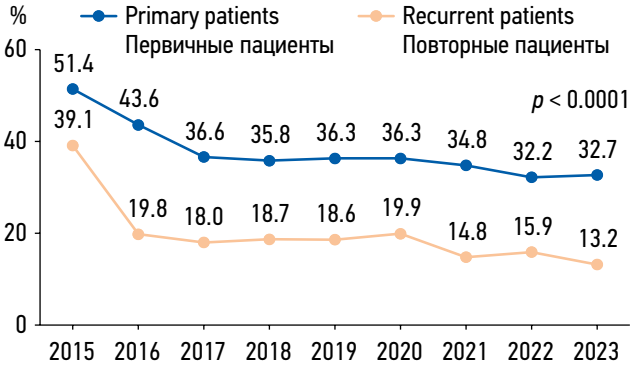

Fig. 4. Change in degree of *Helicobacter pylori* infection in the primary and recurrent patients from 2015 to 2023

Рис. 4. Изменение показателя инфицированности *Helicobacter pylori* у первичных и повторных пациентов с 2015 по 2023 г.

The infection rate of *H. pylori* among the population changes [9]. The decrease in infection in recent decades has been associated with the use of eradication therapy. Y. Zhou et al. reported that the rate of spontaneous eradication is 2.9% in children aged 7–12 years [19]. Spontaneous eradication can be induced by antibacterial drugs for indications unrelated to eradication [20].

Given the widespread use of antibacterial drugs against the backdrop of the COVID-19 pandemic in 2020–2021, current research on the dynamics of *H. pylori* infection among gastroenterology patients from 2015 to 2023 is significant.

Of the 50,884 patients who underwent the ^{13}C-UBT between 2015 and 2023, 83.6% were primary (never having received eradication therapy) and 16.4% were recurrent (indicating at least one course of eradication therapy in the past). The mean incidence of infection among the primary patients was 36.1% (15,358; 95% CI 35.6%–36.6%), whereas the rate was 15.4% (1,284; 95% CI 14.6%–16.2%) among recurrent patients. The prevalence of *H. pylori* infection was 38.8% among 19,875 patients in a national study conducted between 2017 and 2019 [21]. According to the study design, the detection frequency of *H. pylori* in patients who had previously undergone eradication therapy may have been associated with eradication failure instead of reinfection.

Our study revealed that the primary and recurrent patients within the 18–44-year age group had the highest frequency of infection at 51.6% and 47.7%, respectively. However, the frequency was the lowest in children, with only 1.6% of primary patients and 1.3% of recurrent patients infected. This finding suggests that social contact after reaching 18 years of age may have contributed to the majority of infections in the study participants. The infection rates were significantly lower in the primary and recurrent patient groups (18.2% and 19.5%, respectively) aged >60 years. This decrease in infection frequency with age could be associated with spontaneous eradication due to the use of antibacterial drugs and/or the progression of atrophic mucosal changes in patients with chronic gastritis [22].

The ^{13}C-UBT enabled the detection of Helicobacter infection and a determination of its severity based on the Delta over Baseline value. The data show that most of the primary and recurrent patients exhibited a very high (IV) grade of infection, with rates of 73.0% and 66.5%, respectively. Bacterial contamination of the gastric mucosa suggests a severe course of Helicobacter gastritis and an increased risk of complications [23].

The infection rate among primary patients decreased during the time triads, with decreases of 41.4% (2015–2017), 36.2% (2018–2020), and 33.3% (2021–2023). The analysis revealed an 18.7% decrease in the incidence of *H. pylori* infection among primary patients during the follow-up period, from 51.4% in 2015 to 32.7% in 2023 ($p < 0.0001$). The largest decreases occurred from 2015 to 2016 (7.8%) and from 2016 to 2017 (7%). The percentage of infected patients decreased by 3.6% between 2020 and 2023.

The infection rates in the recurrent patients decreased during the time triads, amounting to 17.8% for 2015–2017, 16.0% for 2018–2020, and 12.9% for 2021–2023. Notably, the indicator decreased nearly threefold from 39.1% to 13.2% during 2015–2023 (Fig. 4) when analyzing the infection rate in recurrent patients. The most significant decrease occurred from 2015 to 2016 (by 19.3%) and from 2020 to 2021 (by 5.1%). The proportion of infected patients decreased by 6.7% from 2020 to 2023.

The infection rates of all groups decreased between 2015 and 2023. The infection rates were 14.8% and 21.1% between 2015 and 2017, respectively, and 3.6% and 6.2% between 2020 and 2023, respectively.

The significant decrease in the incidence of infection in St. Petersburg from 2015 to 2017 was associated with the dissemination of the initial stage of the study findings in 2015 and the proactive execution of eradication work with general practitioners and gastroenterologists. The potential correlation between the repeated decrease in infection rates after 2020 and the spontaneous elimination of *H. pylori*, coupled with the extensive use of antibacterial agents during the new coronavirus pandemic, specifically amoxicillin, clarithromycin, azithromycin, and levofloxacin, warrants further investigation.

CONCLUSIONS

The findings demonstrated a significant decrease in *H. pylori* infection between 2015 and 2017, emphasizing the importance of physician education in diagnosing and treating this infection. The COVID-19 pandemic influenced the infection rate, but the adverse effects of antibacterial medications, particularly on *H. pylori* resistance to some key drug groups, remain uncertain.

ADDITIONAL INFORMATION

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Author contributions. Thereby, all the authors confirm that their authorship complies with the international ICMJE criteria (all the authors have made a significant contribution to the development of the concept, research, and preparation of the article as well as read and approved the final version before its publication).

Personal contribution of the authors: *N.V. Bakulina* — experimental design, collecting and preparation of the samples, GC–MS, data analysis, writing the main part of the text, literature review,

making final edits, funding acquisition; *S.V. Tikhonov, A.V. Zharkov* — gas chromatography – mass spectrometry, data analysis, writing the main part of the text; *I.V. Savilova* — data analysis, writing the main part of the text; *V.A. Ponomarenko* — collecting and preparation of the samples, writing the main part of the text, literature review.

Ethics approval. Non-interventional study.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Источник финансирования. Исследование проведено без финансового обеспечения и спонсорской поддержки.

Конфликт интересов. Авторы заявляют об отсутствии потенциального конфликта интересов, требующего раскрытия в данной статье.

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