



THE MANAGEMENT OF HELICOBACTER PYLORI INFECTION IN THE POST-COVID-19 ERA: A BRIEF COMMUNICATION

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The COVID-19 pandemic has undoubtedly reshaped many aspects of healthcare, but one of its most concerning impacts has been on antibiotic use and the growing crisis of antibiotic resistance, particularly in relation to Helicobacter pylori (H. pylori) infections. In Croatia, as in many other parts of the world, the pandemic led to significant shifts in antibiotic prescription practices. This was driven by early, and often unproven, claims of the effectiveness of certain antibiotics in treating COVID-19, along with shortages of commonly used medications like penicillin. These factors resulted in a marked increase in the use of macrolides, such as azithromycin, which has been linked to worsening antibiotic resistance in H. pylori. In Croatia, antibiotic use in 2022 surpassed 2019 levels, driven by increased consumption of macrolides and other antibiotics. However, as resistance to these drugs rises, the effectiveness of these regimens diminishes. To address these challenges, healthcare providers must adopt more personalized approaches to treating H. pylori infections. One potential solution is the use of tailored antibiotic therapy, based on local resistance patterns or individual susceptibility testing.

Keywords: HELICOBACTER PYLORI, COVID-19, PANDEMIC, ANTIBIOTIC RESISTANCE, ERADICATION THERAPY, CHALLENGES

The COVID-19 pandemic has undoubtedly reshaped many aspects of healthcare. One of its most concerning impacts has been on antibiotic use and the growing crisis of antibiotic resistance, particularly concerning Helicobacter pylori (H. pylori) infections. In Croatia, as in many other parts of the world, the pandemic led to significant shifts in antibiotic prescription practices. This was driven by early, and often unproven, claims of the effectiveness of certain antibiotics in treating COVID-19, along with shortages of commonly used medi-

cations like penicillin. These factors resulted in a marked increase in the use of macrolides, such as azithromycin, which has been linked to worsening antibiotic resistance in H. pylori (1-3).

H. pylori is already a challenging pathogen to treat due to its high rates of antibiotic resistance, and the pandemic has only exacerbated this issue. In Croatia, antibiotic consumption surged, particularly in 2022, surpassing pre-pandemic levels. The increased use of azithromycin and other antibiotics during the pandemic was concerning, as it directly contributed to higher resistance rates in H. pylori. Specifically, resistance to clarithromycin and levofloxacin—two key antibiotics in H. pylori eradication regimens—has risen due to mutations in the bacterium's 23S rRNA, gyrA, and gyrB genes. These mutations alter the target sites of the antibiotics, reducing their effectiveness and complicating treatment efforts (4).

This rise in resistance poses a significant threat to public health, both in Croatia and worldwide. The increased anti-

biotic use during the pandemic, though understandable in the context of a viral outbreak, has had far-reaching implications. Overuse and misuse of antibiotics, particularly without confirmed bacterial infections, are major drivers of resistance. The pandemic emphasized the need for stronger antimicrobial stewardship, highlighting the importance of judicious antibiotic use and reserving them for cases where they are truly necessary. The challenges presented by the pandemic's impact on antibiotic resistance are particularly evident in the case of H. pylori. Standard treatment regimens for H. pylori infections often rely on a combination of antibiotics, including clarithromycin, levofloxacin, and metronidazole (5).

However, as resistance to these drugs rises, the effectiveness of these regimens diminishes. This creates a situation where treatment failures become more common, leading to prolonged infections, higher healthcare costs, and increased risk of complications such as gastric cancer.

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To address these challenges, healthcare providers must adopt more personalized approaches to treating *H. pylori* infections. One potential solution is tailored antibiotic therapy, based on local resistance patterns or individual susceptibility testing. This approach, already being explored in Croatia, has shown promise in improving eradication rates and reducing the risk of resistance (6). Additionally, next-generation sequencing and other advanced diagnostic tools can help identify resistant strains more quickly, enabling more targeted and effective treatments.

However, the need for action extends beyond individual treatment strategies. The pandemic has underscored the importance of robust antimicrobial stewardship programs at both national and global levels. These programs must prioritize promoting the responsible use of antibiotics, educating healthcare providers and the public about the dangers of overuse, and developing new antibiotics and treatment strategies to outpace evolving resistance patterns. In Croatia, where macrolide-resistant *H. pylori* strains are already widespread, these efforts are particularly critical.

Before the onset of the COVID-19 pandemic, our research group focused on the challenges of *H. pylori* eradication in Croatia. We identified a significant deficiency in the knowledge of general practitioners (PCPs) and medical students regarding the management of *H. pylori* infection and poor adherence to the Maastricht/Florence Consensus Report. Bismuth-based quadruple therapy (BQT) or concomitant therapy (if BQT is not available) should be the first-line treatment for *H. pylori* infection. Unfortunately, it was the choice of only 4.8% of PCPs and 13% of students. Only 2.8% of PCPs and 7.1% of students would correctly recommend the first and second line of treatment for *H. pylori* infection (7). According to our previous research tetracycline hydrochloride, oral 500 mg metronidazole, tinidazole, and bismuth subsalicylate are not registered in Croatia (8).

A search of the Croatian Agency for Medicinal Products and Medical Devices (HALMED) database reveals that tetracycline hydrochloride is not yet registered in Croatia, despite being a first-line therapy for *H. pylori* eradication.

According to the results from our last research, we can conclude that the COVID-19 pandemic has led to significant fluctuations in community antibiotic consumption within the European Union/European Economic Area. In Croatia, antibiotic use in 2022 surpassed 2019 levels, driven by increased consumption of macrolides and other antibiotics (10).

In conclusion, the COVID-19 pandemic has brought to light the delicate balance between managing immediate healthcare needs and protecting the long-term efficacy of antibiotics. While the surge in antibiotic use during the pandemic was, in many cases, a necessary response to an unprecedented crisis, it has also accelerated the rise of antibiotic resistance, especially in pathogens like *H. pylori*. Moving forward, healthcare systems must prioritize judicious antibiotic use, develop new treatment strategies, and strengthen antimicrobial stewardship programs to combat this growing threat. Failure to do so risks leaving us ill-equipped to manage bacterial infections in the future, with potentially dire consequences for public health. The pandemic has taught us many lessons, and one of the most important is the need for a more cautious and strategic approach to antibiotic use in everyday medical practice and during global health emergencies.

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Sažetak

LJEČENJE HELICOBACTER PYLORI INFEKCIJE U POST-COVID-19 RAZDOBLJU: KRATKO PRIOPĆENJE

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COVID-19 pandemija nedvojbeno je promijenila mnoge aspekte zdravstvene skrbi, ali jedan od njezinih učinaka koji stvaraju najveću zabrinutost bila je uporaba antibiotika i rastuća kriza rezistencije na antibiotike, osobito u vezi s infekcijom Helicobacter pylori (*H. pylori*). U Hrvatskoj, kao i u mnogim drugim dijelovima svijeta, pandemija je dovela do značajnih promjena u praksi propisivanja antibiotika. To je bilo potaknuto ranim i često nedokazanim tvrdnjama o učinkovitosti određenih antibiotika u liječenju COVID-19 infekcije, zajedno s nedostatkom inače često korištenih lijekova poput penicilina. Ovi čimbenici rezultirali su značajnim povećanjem upotrebe makrolida, poput azitromicina, koji je povezan s porastom antibiotske rezistencije *H. pylori*. U Hrvatskoj je upotreba antibiotika 2022. godine premašila razinu iz 2019. godine, potaknuta povećanom potrošnjom makrolida i drugih antibiotika. Međutim, kako otpornost na ove lijekove raste, učinkovitost ovih eradikacijskih protokola za *H. pylori* se smanjuje. Kako bi odgovorili na te izazove, potrebni su personalizirani pristupi liječenju infekcija *H. pylori*. Jedno od mogućih rješenja je korištenje personalizirane prilagođene antibiotske terapije, temeljene na podacima i uzorcima lokalne rezistencije ili mikrobiološkom testiranju individualne osjetljivosti *H. pylori* kod bolesnika.

Ključne riječi: HELICOBACTER PYLORI, COVID-19, PANDEMJA, REZISTENCIJA NA ANTIBIOTIKE, ERADIKACIJSKA TERAPIJA, IZAZOVI

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