

KAKO JE COVID-19 PROMJENIO MAPU ANTIMIKROBNE REZISTENCIJE U CRNOJ GORI

HOW COVID-19 CHANGED THE ANTIMICROBIAL RESISTANCE MAP IN MONTENEGRO

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SAŽETAK

Nedvosmisleno je dokazano da je glavni pokretač razvoja i širenja rezistencije bakterija na antibiotike: generacionalna i prekomerna upotreba antibiotika (1). Iako su podaci pokazali da je kod manje od 10% hospitalizovanih i ambulantnih pacijenata s COVID-19 širom sveta dijagnostikovana sekundarna bakterijska infekcija koja zahteva terapiju antibioticima, procenjuje se da je 75% pacijenata dobilo antibiotik na recept (2-7).

U ovom istraživanju ispitivali smo uticaj pandemije COVID-19 u Crnoj Gori na rezistenciju najčešćih Gram „-“ invazivnih izolata važnih patogena, kao i patogenih Gram „+“ bakterija na ključne antibiotike, uzimajući u obzir već prisutnu prekomernu upotrebu antibiotika u zemlji (8).

Analizirani su podaci Instituta za javno zdravlje Crne Gore o rezistenciji Gram „-“ invazivnih izolata važnih patogena (*Klebsiella pneumoniae*, *Escherichia coli*) i Gram „+“ bakterija (*Staphylococcus aureus*, *Streptococcus pyogenes*) na ključne antibiotike u periodu od 2019. do 2023. godine, te upoređeni sa podacima Crnogorskog Instituta za lekove i medicinska sredstva o potrošnji antibiotika u predpandemijskim (2019.) i pandemijskim godinama (2020, 2021 i 2022).

Rezultati su pokazali da je rezistencija *Escherichia coli* na cefalosporine III generacije porasla sa 38% u 2019. na 67% u 2022. godini. Stopa rezistencije *Klebsiella pneumoniae* na fluorohinolone je narasla sa 48% (2019) na 75% (2021), dok se rezistencija na karbapeneme povećala sa 17% (2019) na 47% (2022). Takođe, zabeležen je porast rezistencije *Staphylococcus aureus*-a na makrolide sa 11% u 2019. na 18% u 2022. godini. Kod *Streptococcus pyogenes*, rast rezistencije na makrolide u 2023. godini bio je na granici statističke značajnosti u poređenju sa 4% u 2019. i 2022. godini. Analiza potrošnje antibiotika ukazuje da se trend porasta rezistencije kod ispitivanih bakterija može dovesti u vezu s promenama u upotrebi određenih antibiotika tokom pandemije. Naime, podaci ukazuju da je tokom pandemije COVID-19 porasla ukupna upotreba ceftriaksona (sa 1,03 u 2019. na 2,57 DDD/1000/dan u 2021) i ciprofloxacina (sa 1,74 u 2019. na 2,92 DDD/1000/dan u 2021). U bolničkoj potrošnji zabeležen je porast potrošnje karbapenema sa 0,05 DDD/1000/dan u 2019. na 0,21 DDD/1000/dan u 2021, a ukupna potrošnja azitromicina je porasla sa 2,59 DDD/1000/dan (2019) na 6,19 DDD/1000/dan (2022).

Na osnovu prikazanih podataka može se zaključiti da je pandemija COVID-19 izmenila mapu rezistencije važnih patogena na ključne antibiotike u Crnoj Gori, dodatno podstičući praksu prekomerne i iracionalne upotrebe antibiotika. Ovakav trend rezistencije ukazuje na hitnu potrebu za razvijanjem sveobuhvatnog nacionalnog programa racionalne upotrebe antibiotika, kako bi se sprečili dalji negativni ishodi i suočavanje sa novim izazovima.

ABSTRACT

It has been unequivocally proven that the main driver of the development and spread of bacterial resistance to antibiotics is their irrational and excessive use (1). Although data show that fewer than 10% of hospitalized and outpatient COVID-19 patients worldwide were diagnosed with a secondary bacterial infection requiring antibiotic therapy, it is estimated that 75% of patients received a prescription for antibiotics (2-7).

In this study, we examined the impact of the COVID-19 pandemic on the resistance of the most common Gram-negative invasive isolates of important pathogens, as well as pathogenic Gram-positive bacteria to key antibiotics in Montenegro, taking into account the already existing overuse of antibiotics in the country (8).

Data from the Institute of Public Health of Montenegro on the resistance of Gram-negative invasive isolates of important pathogens (*Klebsiellapneumoniae*, *Escherichia coli*) and Gram-positive bacteria (*Staphylococcus aureus*, *Streptococcus pyogenes*) to key antibiotics from 2019 to 2023 were analyzed and compared with data from the Montenegrin Institute for Medicines and Medical Devices on antibiotic consumption in the pre-pandemic year (2019) and the pandemic years (2020, 2021, and 2022).

The results showed that resistance of *Escherichia coli* to third-generation cephalosporins increased from 38% in 2019 to 67% in 2022. The resistance rate of *Klebsiellapneumoniae* to fluoroquinolones rose from 48% (2019) to 75% (2021), while resistance to carbapenems increased from 17% (2019) to 47% (2022). There was also a recorded increase in resistance of *Staphylococcus aureus* to macrolides from 11% in 2019 to 18% in 2022. For *Streptococcus pyogenes*, the increase in resistance to macrolides to 8% in 2023 was at the borderline of statistical significance compared to 4% in both 2019 and 2022. Analysis of antibiotic consumption suggests that this trend of increasing resistance among the studied bacteria may be associated with changes in the use of certain antibiotics during the pandemic. Specifically, data indicate that the overall use of ceftriaxone increased from 1.03 DDD/1000/day in 2019 to 2.57 in 2021, and ciprofloxacin from 1.74 in 2019 to 2.92 DDD/1000/day in 2021. Hospital use of carbapenems rose from 0.05 DDD/1000/day in 2019 to 0.21 in 2021, and overall consumption of azithromycin increased from 2.59 DDD/1000/day (2019) to 6.19 DDD/1000/day (2022).

Based on the presented data, it can be concluded that the COVID-19 pandemic altered the resistance map of important pathogens to key antibiotics in Montenegro, further encouraging the practice of inappropriate and overuse of antibiotics. This resistance trend indicates an urgent need to develop a comprehensive national antibiotic stewardship program, to prevent further negative outcomes and to address emerging challenges.