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Review Article

Impact of COVID-19 on antimicrobial resistance: revealing the hidden threats

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ABSTRACT

The COVID-19 pandemic, which was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has impacted every area of life, including efforts concerning antibiotic resistance (AMR). Antibiotic usage in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients exceeded the incidence of bacterial coinfections and secondary infections during the COVID-19 pandemic, suggesting irrational and excessive prescribing. Even in settings with established antimicrobial stewardship (AMS) programs, weaknesses were seen regarding the optimal use and administration of antibiotics during the epidemic. This irrational use and prescribing threaten the future of antimicrobial use and imply the possibility of another pandemic caused by multidrug-resistant pathogens. In this review, we summarized the important aspects of COVID-19's impact, specifically on antimicrobials and other aspects. Antimicrobial stewardship programs are to be reinforced if not already implemented in all hospital settings to guide antimicrobial selection. This could contribute to combating this emerging concern of antimicrobial resistance.

Keywords: COVID-19, Antimicrobial resistance, Stewardship, Antibiotics, Secondary bacterial infection

INTRODUCTION

The COVID-19 pandemic, which was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has impacted every area of life, including efforts concerning antibiotic resistance (AMR).[1-4] The pandemic has shown that a greater burden on healthcare systems may result in increased, often inappropriate antibiotic usage and de-prioritization of antimicrobial resistance surveillance and antimicrobial stewardship (AMS).[5]

Over the last two decades, antimicrobial resistance (AMR) has grown to such proportions that it has been identified as one of the most serious threats to global health and economic growth.[6,7] In settings with a high rate of antibiotic prescriptions, such as medical wards and intensive-care units, infections caused by difficult-to-treat bacteria are becoming increasingly correlated with increased mortality and hospital expenditures.[8-10] The European centre for disease prevention and control (ECDC) reported more than 670,000 infections and 33,000 deaths caused by resistant bacteria in 2019, while fungi and resistant bacteria were responsible for at least 3 million new infections and 35,900 deaths in the United States alone each year.[11,12]

Globally, the response to SARS-CoV-2 was variable, owing to variances in the severity of the pandemic, local and national policy, resource availability, social factors, and public awareness. However, the majority of countries attempted to prepare their healthcare systems for a high predicted number of severe cases by implementing all available resources, but still, some different practices were employed, ranging from strict, enforced curfews to physical distancing guidelines. Some of the most important epicenters were in areas where AMR is a concern.[13,14]

ANTIBIOTICS AND ANTIMICROBIAL RESISTANCE DURING THE COVID-19 ERA

There has been widespread usage of broad-spectrum antibiotics in patients with COVID-19.[4] Although complete data is lacking, early evidence suggests that outpatient antibiotic usage may have decreased in certain contexts. This might be a result of limited access to healthcare as a consequence of lockdowns and physical distancing or decreased community spread of other ailments in some settings, or it could be a simultaneous process of both reasons. However, antibiotic treatment of the majority of hospitalized COVID-19 patients in the early stages of the pandemic increased antibiotic consumption compared to the pre-pandemic era.[3,15,16]

Irrational antibiotic use leads to the development and spread of antimicrobial resistance (AMR), a major global health concern. One of the fundamental strategies for tackling this issue is to optimize antibiotic usage by ensuring that the appropriate antibiotic is administered at the correct therapeutic dose, for the optimal period, and in a way that results in the best outcome and minimizes adverse effects and AMR.[17] In fact, these are the core elements of antimicrobial stewardship programs. Conversely, since the outbreak of the COVID-19 pandemic, there has been increasing concern about the possibility of an increase in AMR as a result of increased antibiotic use for COVID-19 patients.[18]

The initial stage of the pandemic was aggravated by the interplay of inappropriate and excessive antibiotic prescribing and a lack of access to appropriate therapy. Coinfections are infections caused by pathogens that are present concomitantly with COVID-19 at the time of admission to a hospital or upon COVID-19 diagnosis, whereas secondary infections occur after the occurrence of COVID-19 disease and are generally associated with healthcare and exacerbated by invasive procedures and the use of immunosuppressive drugs.[19,20] Coinfections are the primary reason for empirical treatment during hospitalization, while secondary infections are the main reason for antimicrobial therapy after hospitalization and are probably more preventable with appropriate infection prevention and control techniques.[21]

According to meta-analyses, 7-8% of hospitalized COVID-19 patients were diagnosed with a bacterial or fungal infection.[2,22,23] These were more prevalent in intensive care unit (ICU) patients (8-14%) than in other wards (4-6%). Only 3.5% of patients had coinfections (95% CI 0.4 to 6.7%), while 14.3% developed secondary infections (95% CI 9.6 to 18.9%).[23,24]

The reason behind using antimicrobials in COVID-19 patients was the presumption of having a direct effect on SARA-CoV-2. This may cause a notable emergence of resistance in co-colonizing or co-infecting pathogens.[25] For example, despite the evidence of chloroquine's ineffectiveness, an antimalarial drug, it has been widely used to treat COVID-19. This is of potential concern in regions with a high non-*Plasmodium falciparum* rate of malaria, where chloroquine remains the treatment of choice for malaria and its use for COVID-19 may accelerate the development of chloroquine resistance.[26,27]

Because COVID-19 patients may develop non-specific symptoms (e.g., fever and/or persistent cough), they could be misdiagnosed with other diseases such as malaria or tuberculosis (TB), or vice versa.[28,29] Depending on the incidence of COVID-19, these interconnected symptoms may result in inaccurate prescribing and/or misdiagnosis. This could potentially have an impact on future drug resistance levels of pathogens in other diseases. The significance of such bystander selection has been noticed following the widespread use of azithromycin in the WHO-recommended mass drug administration program for trachoma. This is of particular concern for COVID-19 since azithromycin has been proposed as a drug with promising activity against COVID-19.[30]

The majority of COVID-19 patients (80%) have uncomplicated infections and are treated on an outpatient basis. While the data on the treatment of COVID-19 patients in the community is limited, there is enough evidence of inappropriate antibiotic usage in self-limiting viral upper respiratory tract infections in non-hospitalized settings. Thus, inappropriate antibiotic use is comparable, if not more, in community settings, specifically when antibiotics can be accessed online, without a prescription, and from informal drug suppliers.[31,32]

The variation between the proportion of patients with bacterial coinfections or nosocomial infections and those receiving antibacterial agents could be explained by several hypotheses, including the response to medical uncertainty regarding the optimal management of COVID-19 patients during the early weeks of the pandemic. The probability of medical personnel getting SARS-CoV-2, the burden on health resources, and supply chain issues all resulted in a reduction in sample collection for microbiological evaluations, influencing options for informed therapy in place of empirical antibiotics.[33] Reduced antibiotic stewardship activities are most likely a result of the COVID-19 spread, diverting healthcare resources and expertise.[2,34]

To determine whether antibiotic use is appropriate during the first stage of the COVID-19 pandemic, it is crucial to consider specific criteria for different patient populations, including ventilated critically ill patients, hospitalized but non-ventilated patients, outpatients, and the COVID-19-naive population. Although bacterial coinfections are uncommon among critically ill COVID-19 patients, they often emerge in the latter stages of hospitalization and are caused by the respiratory tract microbiota or the nosocomial environment.[35] Diagnosis of ventilator-associated pneumonia (VAP) is challenging, both clinically and epidemiologically. Antibiotic therapy should be initiated after the collection of sufficient samples in patients with hemodynamic instability or severe hypoxemia, as well as in patients with a high pretest risk of VAP based on clinical criteria.[36] However, if these criteria are not met, therapy can be delayed.

CHALLENGES OF THE CHOICE OF ANTIBIOTIC FOR COVID-19 PATIENTS

If the risk of needing invasive mechanical ventilation justifies the use of antibiotics to treat nosocomial bacterial coinfections, the scarcity of ventilators in low- and middle-income countries (LMIC) reduces this risk, which should result in significant reductions in unnecessary antimicrobial prescribing.[2,37] Because short-term peripheral venous catheters are linked to more bloodstream infections in low- and middle-income countries than in high-income countries, there is a risk that more COVID-19 patients will be hospitalized and need antibiotics to treat infections caused by catheters in the hospital.[38] Implementing infection prevention and control strategies may help manage these risks.[39] It would be insightful to research bacterial co-infections in COVID-19 patients in LMIC, as previous studies have revealed significant differences between HIC and LMIC regarding populations at risk, clinical manifestations, pathogen distribution frequency, and antibiotic susceptibility for the same bacterial pathogens. The threat posed by COVID-19 may provide an opportunity for LMICs to implement antimicrobial stewardship programs following WHO guidelines: education and training of an antimicrobial stewardship team, development of clinical guidelines, and surveillance of resistance and antimicrobial use.[40]

THE NEED FOR REINFORCEMENT OF ANTIMICROBIAL STEWARDSHIP PROGRAMS AMS DURING COVID-19 PANDEMIC

It is critical to maintain the sustainability of AMS programs. Due to the multidisciplinary approach used by many institutions in managing COVID-19 patients, stewardship programs should be reinforced through training activities directed at non-infectious disease specialists, including prospective prescription audits, and data feedback.

Diagnostic stewardship of community-acquired pneumonia (CAP) by general practitioners is essential to minimize unnecessary antibiotic use, not only in patients not infected with SARS-CoV-2 but also in those with moderate COVID-19 who are managed at home. Evaluating the influence of interventions should be carried out correctly.[41] Antibiotic consumption, appropriateness of use, rates of antibiotic-related adverse events, overall mortality, length of hospital stay, rates of antibiotic resistance, and the necessity for readmission after discharge may all be considered endpoints of AMS.

CONCLUSION

The COVID-19 pandemic revealed the economic and social impacts of an uncontrolled infectious epidemic, which are comparable to those anticipated for AMR in multiple reports. Among the numerous consequences of the COVID-19 pandemic, the significant potential influence on AMR through changes in antibiotic usage and health-seeking behavior, as well as infection prevention and control methods, is worth noting. Determining these AMR-related impacts is crucial for promoting best practices and directing research. Being proactive amid predictable AMR enables us to avoid being reactive in the future, as we have been with COVID-19. However, if AMR is not addressed, comparable consequences are expected to take place over a longer period.

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REFERENCES

1. Xiaobo Y, Yuan Y, Jiqian X, Huaqing S, Jia'an X, Hong L, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Med. 2020;8(5):475-81.
2. Rawson TM, Moore LSP, Zhu N. Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis. 2020;71(9):2459-68.
3. Abelenda-Alonso G, Padullés A. Antibiotic prescription during the COVID-19 pandemic: A biphasic pattern. Infection control and hospital epidemiol. 2020;41(11):1371-2.
4. Bojana B, Doušak M. Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey. J Antimicrobial Chemotherapy. 2020;75(11):3386-90.
5. Lynch C, Mahida N, Gray J. Antimicrobial stewardship: a COVID casualty? J Hospital Infection. 2020;106(3):401-3.
6. World Health Organization 10 Global Health Issues to Track in 2021. Available at: https://www.who.int/news-room/spotlight/10-global-health-issues-to-track-in-2021. Accessed on 26 April 2022.
7. The World Bank Drug-Resistant Infections: A Threat to Our Economic Future. Available at: https://www.worldbank.org/en/topic/health/public

ation/drug-resistant-infections-a-threat-to-our-economic-future. Accessed on 26 April 2022.
8. Anton PY, Hooper DC. Hospital-acquired infections due to gram-negative bacteria. N Eng J Med. 2010;362(19):1804-13.
9. Matthew NJ. Costs of healthcare- and community-associated infections with antimicrobial-resistant versus antimicrobial-susceptible organisms. Clin Infect Dis. 2012;55(6):807-15.
10. Richard NE. National Estimates of Healthcare Costs Associated with Multidrug-Resistant Bacterial Infections Among Hospitalized Patients in the United States. Clin Infect Dis. 2021;72(1):S17-26.
11. European Centre for Disease Prevention and Control Antimicrobial resistance in the EU/EEA (EARS-Net)-Annual Epidemiological Report for 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2019. Accessed on 26 April 2022.
12. Steven SL, Oliver KB. Antibiotic resistance threats in the United States: stepping back from the brink. Am Family Physician. 2014;89(12):938-41.
13. Clancy CJ, Nguyen MH. Coronavirus Disease 2019, Superinfections, and Antimicrobial Development: What Can We Expect? Clin Infect Dis. 2020;71(10):2736-43.
14. European Centre for Disease Prevention and Control. "Surveillance of antimicrobial resistance in Europe–annual report of the European antimicrobial resistance surveillance network (EARS-Net) 2017." ECDC: Surveillance Report. 2018.
15. Velasco-Arnaiz E, López-Ramos MG, Simó-Nebot S. Kids Corona Project. Pediatric 205 antimicrobial stewardship in the COVID-19 outbreak. Infect Control Hosp Epidemiol. 2020;206:1-3.
16. Deanna JB. Antibiotic Consumption and Stewardship at a Hospital outside of an Early Coronavirus Disease 2019 Epicenter. Antimicrobial Agents Chemotherapy. 2020;64(11):e01011-20.
17. Matthew D. Using antibiotics responsibly: right drug, right time, right dose, right duration. J Antimicrobial Chemotherapy. 2011;66(11):2441-3.
18. Timothy RM. Antimicrobial use, drug-resistant infections and COVID-19. Nature reviews Microbiol. 2020;18(8):409-10.
19. Bengoechea JA, Bamford CG. SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19? EMBO Mol Med. 2020;12(7):e12560.
20. Lansbury L, Lim B, Baskaran V. Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect. 2020:S0163-4453(20)30323-6.
21. Rodríguez-Baño J, Rossolini GM, Schultsz C. Key considerations on the potential impacts of the COVID-19 pandemic on antimicrobial resistance research and surveillance. Trans R Soc Trop Med Hyg. 2021;115(10):1122-9.
22. Langford BJ, So M, Raybardhan S. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect. 2020;26(12):1622-9.
23. Garcia-Vidal C, Sanjuan G, Moreno-García E. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study. Clin Microbiol Infect. 2021;27(1):83-8.
24. Vaughn VM, Gandhi TN, Petty LA. Empiric Antibacterial Therapy and Community-onset Bacterial Coinfection in Patients Hospitalized with Coronavirus Disease 2019 (COVID-19): A Multi-hospital Cohort Study. Clin Infect Dis. 2021;72(10):e533-41.
25. Tedijanto C, Olesen SW, Grad YH, Lipsitch M. Estimating the proportion of bystander selection for antibiotic resistance among potentially pathogenic bacterial flora. Proc Natl Acad Sci USA. 2018;115(51):E11988-95.
26. Zakariya K. Efficacy of chloroquine or hydroxychloroquine in COVID-19 patients: a systematic review and meta-analysis. J Antimicrobial Chemotherapy. 2021;76(1):30-42.
27. WHO. Solidarity' Clinical Trial for COVID-19 Treatments. Solidarity Clinical Trial for COVID-19 Treatments, www.who.int. 2021. Available online: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments. Accessed on 26 April, 2022.
28. Chanda-Kapata P, Kapata N, Zumla A. COVID-19 and malaria: A symptom screening challenge for malaria endemic countries. Int J Infect Dis. 2020;94:151-3.
29. Hiv L. When pandemics collide. The Lancet HIV. 2022;7(5):e301.
30. O'Brien KS, Emerson P, Hooper PJ. Antimicrobial resistance following mass azithromycin distribution for trachoma: a systematic review. Lancet Infect Dis. 2019;19(1):e14-25.
31. Dekker AR, Verheij TJ, van der Velden AW. Inappropriate antibiotic prescription for respiratory tract indications: most prominent in adult patients. Fam Pract. 2015;32(4):401-7.
32. Gulliford MC, Dregan A, Moore MV. Continued high rates of antibiotic prescribing to adults with respiratory tract infection: survey of 568 UK general practices. BMJ Open. 2014;4(10):e006245.
33. Hughes S, Troise O, Donaldson H, Mughal N, Moore LSP. Bacterial and fungal coinfection among hospitalized patients with COVID-19: a retrospective cohort study in a UK secondary-care setting. Clin Microbiol Infect. 2020;26(10):1395-9.
34. Huttner BD, Catho G, Pano-Pardo JR, Pulcini C, Schouten J. COVID-19: don't neglect antimicrobial stewardship principles! Clin Microbiol Infect. 2020;26(7):808-10.
35. François B, Laterre PF, Luyt CE, Chastre J. The challenge of ventilator-associated pneumonia diagnosis in COVID-19 patients. Crit Care. 2020;24(1):289.

36. Fu Y, Yang Q, Xu M. Secondary Bacterial Infections in Critical Ill Patients with Coronavirus Disease 2019. Open Forum Infect Dis. 2020;7(6):ofaa220.
37. Losonczy LI, Barnes SL, Liu S. Critical care capacity in Haiti: A nationwide cross-sectional survey. PLoS One. 2019;14(6):e0218141.
38. Rosenthal VD, Belkebir S, Zand F. Six-year multicenter study on short-term peripheral venous catheters-related bloodstream infection rates in 246 intensive units of 83 hospitals in 52 cities of 14 countries of Middle East: Bahrain, Egypt, Iran, Jordan, Kingdom of Saudi Arabia, Kuwait, Lebanon, Morocco, Pakistan, Palestine, Sudan, Tunisia, Turkey, and United Arab Emirates-International Nosocomial Infection Control Consortium (INICC) findings. J Infect Public Health. 2020;13(8):1134-41.
39. Phan HT, Vo TH, Tran HTT. Enhanced infection control interventions reduced catheter-related bloodstream infections in the neonatal department of Hung Vuong Hospital, Vietnam, 2011–2012: a pre- and post-intervention study. Antimicrob Resist Infect Control. 2020;9(9).
40. Aston SJ. Pneumonia in the developing world: Characteristic features and approach to management. Respirol. 2017;22:1276-87.
41. Schweitzer VA, Van Werkhoven CH, Rodríguez Baño J. Optimizing design of research to evaluate antibiotic stewardship interventions: consensus recommendations of a multinational working group. Clin Microbiol Infect. 2020;26(1):41-50.

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