COVID-19 and Antimicrobial Resistance: Parallel and Interacting Health Emergencies

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Summary:

1. The COVID-19 pandemic and antimicrobial resistance are parallel and interacting health emergencies with opportunity for mutual learning
2. Researchers should now start collecting data to measure the impact of current COVID-19 policies and programs on antimicrobial resistance

Abstract

The COVID-19 pandemic and antimicrobial resistance are parallel and interacting health emergencies with opportunity for mutual learning. As their measures and consequences are comparable, the COVID-19 pandemic helps to illustrate the potential long-term impact of AMR, which is less acute but not less crucial. They may also impact each other as there is a push to resort to existing antimicrobials in critically ill COVID-19 patients in the absence of specific treatments, while attempts to manage the spread of COVID-19 may also lead to a slow down AMR. Understanding how COVID-19 affects AMR trends and what we can expect if these remain the same or worsen, will help us plan next steps to tackle AMR. Researchers should now start collecting data to measure the impact of current COVID-19 policies and programs on AMR.

Introduction

The COVID-19 pandemic has been spreading swiftly, absorbing enormous resources from public health and healthcare systems to limit its damage. This emergency has vast health consequences, not only in terms of the direct health impact on COVID-19 patients, but also indirectly on the global economy and societies across the globe.[1,2] Most countries are activating all possible countermeasures towards containing and treating COVID-19.[3] Inevitably, other health care issues need to adjust and may temporarily receive less attention.[4,5] Antimicrobial resistance (AMR) is an emergency that should not fall off the radar.[6] Certain actions to alleviate COVID-19 suffering might represent a rapid and far-reaching risk to AMR, a phenomenon projected to afflict our society well over the COVID-19 crisis.

Two health emergencies

AMR exists because micro-organisms who are resistant to antimicrobial agents survive and replicate. The overuse and inappropriate use of antibiotics in humans and animals, and their contamination of the environment, are substantial contributors to AMR. In the United States alone, each year at least 2.8 million people become infected with bacteria that are resistant to antibiotics and at least 35,000 people (1.3%) die as a result.[7] It was estimated in 2014 that globally, if there was no change in the increasing trend and resistance grows apace, AMR could result in as many as 10 million deaths in 2050 and have a cumulative loss in economic output of at least 60 trillion USD by 2050.[8] Whether or not these estimates are accurate, the significant negative trends in damage to the economy and population health are certain.[9]

AMR has recognized as a pervasive public health threat national and international organizations for decades, with gradually increasing perceived urgency, modest dedicated funding, and international treaties and initiatives.[10] Now, the COVID-19 pandemic has further complicated the era of AMR. As of April 30 (2020) there have been over 6 million cases and over 300,000 deaths.[2] Having recently become a WHO Collaborating Center for Infectious Diseases, Research Methods and Recommendations with a focus on AMR, we believe the COVID-19 pandemic helps to illustrate the potential impact of AMR *(Table 1)*.[11] Alongside, it is sensible to discuss the potential effects of the COVID-19 pandemic on AMR and the opportunities that may arise.

Parallels

COVID-19 is a new infectious disease caused by SARS-CoV-2 requiring swift knowledge creation and innovation, and its outbreak has been declared a global pandemic by the World Health Organization (WHO) on March 11, 2020. AMR is also pandemic in nature, but in contrast a gradual but implacable process affecting multiple microorganisms for which we have some established knowledge. Despite these differences, the required behaviour changes that have been implemented to deal with the COVID-19 pandemic would also benefit AMR that faces a similar path. Infection protection and control measures such as handwashing, physical distancing, quarantining, and travel restrictions can be seen as an effective adaptation to reduce the health risks of AMR.[12] In addition, the healthcare system will be seriously tested, for example when there are insufficient prophylactic antimicrobials for invasive procedures, and social inequalities will be amplified, for example when certain sociodemographic

groups are at increased risk of infection.[12] The occurrence of infections due to resistant pathogens can be significantly mitigated by evidence-based antimicrobial stewardship across all sectors (agriculture, veterinary and human medicine). Although this buys us time, AMR will not be restrained if we do not also develop new vaccines, drugs and rapid tests that are scalable, as is the mandate for COVID-19. The deaths from COVID-19 may overtake the deaths from AMR for 2020, but the estimated annual number of deaths from AMR of 10 million by 2050 may well be higher than the toll from the entire COVID-19 pandemic (currently just crossed the 200,000 mark worldwide). A potentially high use of antimicrobials in COVID-19 patients may also shift gains in short-term COVID-19 mortality to an increase in long-term AMR mortality. Those deaths and impact on our social and health systems will likely have lasting negative effects on the economy as COVID-19 will, but over a much longer period of time. Similarly, the current strategies to combat COVID-19 using urgent action, international collaboration, and development of new treatments, vaccines and rapid tests are required for AMR. These approaches were already underway, but at a much slower pace and smaller scale, considering, for example, the lack of investment in developing new antimicrobials and vaccines.[13] In other words, the measures and consequences of both COVID-19 and AMR are comparable, although the urgency of action is largely in favor of COVID -19. The response to the high-speed pandemic of COVID-19 shows that initiatives tackling AMR could be done faster. And vice versa, the response to COVID-19 needs to be informed by lessons learned from studying the slow-motion problem of AMR.

Interactions

The two emergencies are also intertwined. There is a push to resort to existing antimicrobials in critically ill COVID-19 patients, in the absence of specific treatments when supportive care alone is not enough. As with other viral infections, severely ill patients are at increased risk of secondary infections that can be fatal and require additional treatment.[14] These issues are further complicated by the fact that the most prevalent symptoms of SARS-CoV-2, cough and fever, are independent factors associated with overuse of antibiotics in hospitals and communities.[15] One has to keep in mind that the role of macrolides, quinolones and other antimicrobials such as chloroquine and its derivative has not yet been proven, and can be harmful.[16] The bottom line is that to identify the most effective medicine to improve outcomes for COVID-19 patients, multiple antimicrobials are being tested in formal research settings (randomized trials) as well as in ad hoc studies, and this may further exacerbate rates of AMR. As of June 3 in ClinicalTrials.gov, 211 COVID-19 records contained 'hydroxychloroquine' and 93 contained 'azithromycin', a common antibiotic for the treatment of bacterial infections. Until the findings of these studies are released, use of antimicrobials might be inspired by the principle of parsimony recommended by WHO.[17]

Attempts to manage the spread of COVID-19 may also lead to a lower use of antimicrobials and slow down AMR, particularly if the pandemic is going to last over a long period.[18] Behavioural interventions, including physical barriers, to prevent the spread of SARS-CoV-2 will likely decrease the spread of other infections, and thus the use of antimicrobials. Furthermore, there are signals that patients with other health issues, acute or less urgent, are reluctant to seek care, which may also be true for patients with other types of infections.[19,20] Finally, shortages in certain antimicrobials due to

stress on the global supply chain could lead to a further reduction in their use.[21] In short, COVID-19 and AMR have multiple potential interactions, but at present it is uncertain how they will unfold.

<u>What to do?</u>

The COVID-19 pandemic currently requires our full commitment to limit its harm. We expect that it will serve as an illustration to recognize the potential effects of AMR, which is less acute but not less crucial, and that there are lessons to be learnt by carefully examining the parallels and interactions between COVID-19 and AMR. Understanding how COVID-19 affects AMR trends and what we can expect if these remain the same or worsen, will help us plan next steps to tackle AMR. Researchers should now start collecting data to measure the impact of current COVID-19 policies and programs on AMR.

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Table 1. Comparison of COVID-19 and AMR

	COVID-19	AMR
Characteristics		
Number affected worldwide	6.28 million[*] (annually: unknown)	64.5 million annually[$]
Knowledge of problem	Developing	Established
Spread	Fast	Gradual
Mechanism	New transfer from non-human host	Natural selection in humans, animals, and environment
Behaviour change required		
Handwashing	Continuously needed	Continuously needed
Physical distancing	Urgent, possibly recurrent	Probably recurrent
Travel restrictions	Urgent, possibly recurrent	Probably recurrent
Quarantine	Confirmed and suspected cases	Confirmed and suspected cases
Impacts		
Mortality worldwide	379,000[*] (annually: unknown)	812,000 annually[#]
Economic impact	Unknown	400 billion USD[†]
Health inequity	Increased	Increased
Management Needs		
Vaccine	In development	Not available for resistant microbes
Augmented testing	Real-time picture of spread	Surveillance of problem
Rapid diagnostics	In development	Some useful tests (procalcitonin, CRP)
New drugs	In development	Few in development
Stewardship	In time	Continuously & internationally

* December 2019 to June 3, 2020 – World Health Organization.[2] $ Extrapolated based on the US having 2.8 million annually, and 4.31% of global population.[7] # Extrapolated based on the US having 35,000 annually, and 4.31% of the global population.[7] † 0.5% of 80 trillion GWP.[7]

WHO = World Health Organization; CDC = Centers for Disease Control and Prevention; HAI = hospital-acquired infections; QoL = quality of life; USD = US Dollar; GWP = Gross world product; CRP = C-reactive protein