Pontificia Universidad JAVERIANA Bogotá

Univ. Sci. 28(2): 183–199, 2023
doi: 10.11144/Javeriana.SC282.taoc

REVIEW

The aftermath of corona virus disease on antimicrobial resistance across low- and middle-income countries

Pia Dey[1], Debaprasad Parai[2], Sk Tofajjen Hossain[1], Samir Kumar Mukherjee*[1]

Edited by
Angela Johana Espejo Mojica
editorus@javeriana.edu.co

1. Department of Microbiology, University of Kalyani, Kalyani, India

2. ICMR-Regional Medical Research Centre, Bhubaneswar, India

*dr.samirmukherjee@gmail.com

Received: 11-12-2022
Accepted: 19-05-2023
Published online: 15-06-2023

Citation: Dey P, Parai D, Hossain S, Kumar S, Mukherjee SK. The aftermath of corona virus disease on antimicrobial resistance across low- and middle-income countries, *Universitas Scientiarum*, 28(2): 183–199, 2023.
doi: 10.11144/Javeriana.SC282.taoc

Funding: n.a.

Electronic supplementary material: n.a.

OPEN ACCESS

Abstract

Antimicrobial resistance (AMR) poses a critical challenge to modern medicine. The number of resistance cases worldwide has been increasing exponentially, and it is estimated that by 2050, the AMR mortality rate will be ten times higher than it is today. The emergence of the coronavirus disease 2019 (COVID-19) pandemic compromised the research on AMR by deprioritizing proper monitoring of preventive measures and control programs, innovation and global health programs, and use antimicrobial stewardship (AS). With the current scenario of sporadic COVID-19 cases around the world, it is impossible to accurately evaluate the impact that the pandemic had on AMR and AS due to insufficient reports. However, it's possible to speculate what the scenario will look like by surveying the escalation in unmethodical antimicrobial, the increase in secondary bacterial and fungal infections, and the extension in hospital stay and adverse medical exigency during the second wave when compared to the first wave. COVID-19 exposed the harsh reality that even countries with the best medical facilities struggled to meet national healthcare needs during a pandemic. In such circumstances, the clinical and scientific communities need to understand that available global medical amenities would be insufficient to face an upcoming AMR pandemic. Therefore, international surveillance systems need to highlight the deficiencies in AMR containment and mitigation and develop strategies to address future challenges.

Keywords: antimicrobial resistance; corona virus disease; antimicrobial stewardship; antimicrobial usages; public health

1. Introduction

The pandemic caused by COVID-19, a virus that causes severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has impacted almost every aspect of the society. It has placed the available healthcare facilities in a questionable state, severely disrupted the global economy, intensified the existing threats to healthcare such as antimicrobial resistance (AMR), and resulted in the loss of innumerable human lives [1]. As of April 2022, there have been more than 50 million confirmed COVID-19 cases, and over 6.2 million people have died worldwide. The only silver lining in the dashboard of global COVID-19 management is that more than 11 billion vaccine doses have been administered. This includes double doses, as well as booster doses [2]. With a world population of 7.9 billion and subsequent peaks of the disease on the horizon, overcoming the pandemic emergency through double-dose vaccination is an ongoing challenge, especially in low- and middle-income countries (LMICs). While high-income countries (HICs) have started administering booster vaccine doses, LMICs are still struggling to provide the initial two doses of the COVID-19 vaccine, and in some cases, even the first dose poses a challenge. The crisis persists due to concurrent COVID-19 waves, continuous cycles of lockdown and unlocking of social activities in various countries, an indifferent frame of mind towards the use of face masks, and the inevitable rise of several mutant variants of SARS-CoV-2 [3]. Withstanding the current scenario, we have seen a simultaneous increase in the use of broad-spectrum antibiotics and prophylactic drugs along with the deprioritization of AMR surveillance and antimicrobial stewardship (AS) during the pandemic [4, 5]. AMR was considered to be a moderate ongoing pandemic that mostly went unnoticed before the onset of COVID-19 [6]. AMR somehow got subsided due to extreme medical exigency and the huge loss of human lives posed by the COVID-19 pandemic. An indiscriminate use of antibiotics and steroids, if not regulated, can lead to a future pandemic in the form of AMR as antibiotics are a critical component of all health systems. The possible impact of the subsequent COVID-19 waves on global AMR and AS cannot be exactly validated due to a lack of data. But recent reports on the irrational use of antiviral, antibacterial, antiparasitic, and anti-inflammatory drugs for the prevention of secondary infections in COVID-19 patients during a prolonged period of the pandemic in both HICs and LMICs have raised concerns among global public health surveillance systems about the possible exacerbation of AMR and future complications in a post-COVID-19 world [7]. This review examines the different aspects and unavoidable negative impacts of the coronavirus disease on antimicrobial resistance in low- and middle-income countries.

2. Antimicrobial resistance

AMR has been established as a significant challenge to global public health in the current century. A wide array of infections caused by bacteria, viruses, fungi, and parasites that no longer respond to the application of prescribed commercialized drugs come under the umbrella of AMR [8]. The current crisis encircling AMR can be better understood by considering the widespread antibiotic resistance in bacteria, which causes significant problems in communities across multiple continents [8]. Indiscriminate use of antibiotics across sectors such as medical care, animal health, and agriculture including animal feed production has increased the incidence of antibiotic resistance across the globe. For a long time, the true extent number of resistance cases along with its impact went unnoticed, even in developed countries, due to large gaps in the existing surveillance systems. AMR cases are reported all over the world, but LMICs continue to face challenges in terms of either being under the radar of surveillance systems or struggling to implement the necessary preventive measures to control them. The situation is exacerbated in these countries due to inappropriate antibiotic use, the dissemination of misinformation, and the negative impact of political influences. [9]. Detailed studies have concluded that antibiotic usage among humans, animals, and the environment are interconnected and therefore, resistant microorganisms easily spread across environments [10]. Two global surveillance agencies, the World Health Organization (WHO) and the Centres for Disease Control and Prevention (CDC) work in coordination supervising the current AMR status, chalking out strategies for prevention and control of AMR, and alerting about upcoming global threats. The number of AMR deaths reported by the CDC in 2019, was lower than that reported in 2013, but the number of people affected by AMR-associated infections in the United States remains high [11]. Each year, the United States reports more than 2.8 million cases of acquired antibiotic-resistance with a mortality rate of almost 35,000 people as a result of such infections [11].

Antibiotic resistance demands a 'One Health Approach,' which implies that human health is connected to animal and environmental health [11]. Excessive use of antibiotics in agriculture, including livestock feeds, environmental perturbation arising due to human and animal waste, as well as clinical and pharmaceutical waste amplifies antibiotic resistance. The One Health Approach will not only impact humans but also livestock, aquaculture, wildlife, and the environment because wildlife is considered to serve as a reservoir of resistance and the other factors mentioned are directly connected to human existence [12].

3. The global antibiotic resistance scenario before and during COVID

3.1. The global antibiotic resistance scenario before COVID

AMR has been an ongoing, if partially invisible menace that caused distress in humans of different races, ages, and kinds. Although the exact number of cases associated with antibiotic resistance cannot be calculated, the CDC estimates the burden of AMR associated with the healthcare system through several electronic health databases [11]. Several international initiatives were taken to combat this crisis. In 2001, the WHO provided the 'Global Strategy for Containment of Antimicrobial Resistance,' which presented several interventions that could slow down the advent and consequent spread of AMR [13]. In 2012, the WHO published 'The Evolving Threat of Antimicrobial Resistance – Options for Action,' which provided a discrete list of strategies to strengthen health systems, including proper surveillance of antimicrobial usage in hospitals, prevention and control of community infection, development of novel antimicrobials, targeted vaccines, and political commitment [14]. Following the release of the 2013 CDC report on 'Antibiotic Resistance Threats in the United States', the U.S. government released a roadmap of actions for a five-year goal-driven assessment to detect, prevent, and respond to drug-resistant threats. It was named 'National Action Plan for Combating Antibiotic Resistant Bacteria'(CARB), and its main objectives included, i) Detection and tracking of resistance cases along with resistance threats and antibiotic use, ii) Prevention of infection using a national alert system and containment when needed by providing resources and expertise in response to outbreak, iii) Appropriate use of antibiotics by implementing antibiotic stewardship practices and programs that encourages the same, iv) Better understanding of the environment along with proper sanitation to reduce the need for antibiotics, and v) Identification of novel therapeutics along with administration of vaccines and proper diagnostics as a source of promising treatment facilities.

Several annual programs such as 'World Antibiotic Awareness Week' and the 'Hand Hygiene Day' are observed to raise awareness about AMR and AS [15], and to emphasize the importance of maintaining personal hygiene in the form of frequent hand washing, respectively. In LMICs such as India, the WHO proposed the formation of a national committee for the formulation of numerous AMR-related policies. It also aims to guide standards, training, regulations, and awareness of antibiotic usage, as well as popularizing the concept of AMR. An ideal surveillance system should include indicators to assess and evaluate the impact of AMR while focussing on prevention and control strategies [16]. A registration system should be established to ensure that antimicrobials are only dispensed with a valid prescription. Additionally, the registration scheme should require manufacturers to strictly report accurate data on antimicrobial distribution, imposing legal obligations on them. The schemes can further be popularized by declaring incentives for the rational use of antimicrobials to suppress the further spread of AMR [16]. Furthermore, national standard treatment guidelines should be established, enhancing coverage of immunization along with a proper essential drug list (EDL) [13].

Following these propositions, a national policy was introduced in 2011, for detailed surveillance of AMR, which mainly focussed on the emergence, spread, and influencing factors related to AMR. The aim was to organize various antimicrobial programs to promote the rational use of antimicrobials and encourage the development of new antimicrobial leads. The national policy was expected to act as an authoritative platform for AMR surveillance, enhancing infection prevention and the dissemination of accurate information by educating, training, and motivating all stakeholders on the rational use of antimicrobials [17]. Before the emergence of the COVID-19 pandemic, India was under the supervision of the National Action Plan (NAP) on AMR (2017–2021), which was based on the Global Action Plan (GAP) submitted at the 70th World Health Assembly (WHA) in Geneva in May 2017 [18]. However, despite rigorous planning and implementing policies and guidelines, the WHO estimates that less than 50 % of all countries are able to implement fundamental policies for the appropriate use of medications [19].

3.2. Indiscriminate use of antibiotics during COVID-19

Antibiotic resistance was already a great concern in the 21st century, and the advent of COVID-19 made the scenario even more critical. The inappropriate use of antibiotics as a part of prophylaxis and therapeutic management of COVID-19 further escalated global AMR cases [20]. Malpractices like self-medication and selling over-the-counter antibiotics substantially increased during the pandemic, which inevitably contributed to the emergence of AMR strains and related complications [21]. At the beginning of the pandemic, medical professionals were unable to distinguish COVID-19 from other respiratory co-infections, such as hospital-acquired or ventilator-associated pneumonia and thus prescribed broad-spectrum antibiotics irrationally [22]. Recent global studies have shown an overall occurrence of bacterial co-infection in 6.9 % of hospitalized COVID-19 patients, of which 3.5 % had a bacterial co-infection and 14.3 % had a secondary bacterial infection [23]. *Haemophilus influenza, Mycoplasma* species, and *Pseudomonas aeruginosa* were identified as the most common bacterial co-pathogens [23, 24]. A large percentage (between 27 % and 84 %) of hospitalized patients had already received empiric antibacterial therapy before their admission [23, 25]. A comparative case series carried out by Xu et al. (2020) reported that almost 45 % of hospitalized COVID-19 patients were inaccurately treated with antibiotics despite a relatively low rate of ICU admission [26]. The rate of antibiotic usage increased (91.4 %) in ICU-admitted COVID-19 patients even with a low number of confirmed bacterial co-infections [27]. Moreover, as many as 72 % of COVID-19 patients from a series of reports mainly carried out in China in 2020 received empiric, broad-spectrum antibiotic therapy, making the patients more susceptible to multidrug-resistant (MDR) strains [4]. A review by Chedid et al. (2021) reported fluoroquinolones as the most widely used (56.8 %) antibiotics in COVID-19 patients, followed by azithromycin (29.1 %) and ceftriaxone (39.5 %) [28]. The usage of empiric and broad-spectrum antibiotics could lead to an underestimation of co-infections [29]. In a retrospective cohort study by Garcia-Vidal et al. (2021), it was reported that all the patients admitted for COVID-19 treatment in the Hospital Clinic of Barcelona (Spain) were initially administered antibiotics regardless of severity and medical diagnosis [24]. The reliance on telemedicine during COVID-19 further exacerbated the problem of irrational antibiotic use. Previous research on telemedicine already reported considerably higher rates of prescribed antibiotics in this modality than during in-person visits in clinics, with patient satisfaction being the main reason for these prescriptions rather than an actual need for antibiotics [30,31].

The situation was very similar in different parts of the world during the inception period of the COVID-19 pandemic. But, a lack of stewardship about the rational distribution and use of broad-spectrum antimicrobials ultimately led to the emergence of AMR strains and nosocomial superinfections [32]. Keeping this in mind, the COVID-19 Treatment Guidelines Panel of the National Institutes of Health recommends the prophylactic use of empiric antibiotics only for COVID-19 patients whose health condition is moderate and severe and who are suspected to have bacterial pneumonia, co-infection, or sepsis. For patients who do not show clear evidence of bacterial infection, the guidelines recommend reduced or no antibiotic therapy with a daily re-evaluation of the patient condition [33].

3.3. Misinformation about antibiotics as a cure for COVID-19

AMR was already a lurking global threat by the time a new worldwide medical emergency materialized in the form of the COVID-19 pandemic. Medical emergencies are hard to tackle, especially when they are enveloped in misinformation and misbeliefs. Many epidemics had previously witnessed the effect of misinformation but the situation worsened in the face of the pandemic [34]. A survey reported that about a fifth of online popular articles published in several languages across the world wrote about the cure and treatment of COVID-19 without proper data-based evidence [35]. Early release of preprints was thought to encourage easy circulation of important research findings but it ended up causing confusion due to the simultaneous release of inappropriately conducted studies, which lacked substantial findings. This phenomenon was further fuelled by inaccurate media reporting [36]. Initially, the momentum and intensity of the pandemic were underestimated by prime public health stakeholders. This ultimately led to the inconsistent spread of messages and widespread public confusion [37]. In many countries, the politicization of the critical situations that prevailed during the pandemic became a leading source of misinformation [38]. Not only in LMICs but also in HICs, misinformation heightened the inappropriate use of commercial antibiotics such as macrolides, which did not have any reported efficacy for the treatment of COVID-19 [39]. The overuse of antibiotics might have contributed to an increase in the existing burden of resistance across the globe, especially in LMICs [9]. A study conducted in the United States unveiled that about 71 % of COVID-19 patients received antibiotic therapy while only 4 % of them needed it due to bacterial co-infection [40]. It was a common theme worldwide that the general population and medical professionals (in some countries) lacked basic knowledge of the SARS-CoV-2 epidemiology and its proper treatment guidelines, with a balance between transmission and economic stability [41]. This hypercritical situation demanded open and honest communications from clinicians but a lack of meticulous observation, overburdened number of patients, and inadequate trained medical personnel further deteriorated the situation.

3.4. Possible implications of the COVID-19 pandemic on antimicrobial resistance

The extent of the implications imposed by the COVID-19 pandemic on AMR is still unknown [20]. However, it's reasonable to expect that COVID-19 will have a huge impact on the global healthcare systems. It might force countries with well-equipped healthcare systems to rethink their preparedness and prioritization of sudden medical emergencies [42] and it might create a predicament in LMICs, which have limited resources to cope with the emergence of another pandemic. Moreover, the dissemination rates of AMR are supposed to be 4-7 times higher in LMICs than in the rest of the world [43]. The ongoing campaigns and implementation of policies against AMR have been hampered by the COVID-19 pandemic, which has forced the LMICs, with their inadequate healthcare systems, to take the tough decision of cutting back on apparent non-urgent medical needs. Henceforth, AS efforts might be compromised because of unrestrained workloads and priority shifts towards COVID-19-related emergencies [44]. Inappropriate use of antibiotics both as prescribed for COVID-19 patients and as prophylactic measures accelerate the threat of AMR [45]. The same applies to excessive use of hand sanitizers and other disinfectants due to fear of SARS-CoV-2. Preventive measures are protecting us from COVID-19 but they are simultaneously exposing us to an increase in AMR, which could potentially be more detrimental.

The emergence of more AMR strains will enforce longer treatment time for patients, longer hospitalizations, and increased risk associated with routine surgical procedures and hospital-borne nosocomial outbreaks. This will in turn put an extra burden on the overall healthcare system and its providers, leading to a dilemma regarding the prioritization of treatment types and the selection of recipients [46]. Decreased laboratory surveillance for culture and antimicrobial susceptibility testing would also be hampered because of limited resources due to the prioritization of COVID-19 diagnosis [47]. The excessive stress on the physical and mental health of healthcare workers should not be ignored. Broadening the lens, the global economy will be highly affected by COVID-19 and associated AMR cases. Industries and institutions that rely on human interactions are expected to be highly perturbed as the surging number of AMR-related cases can lead to an increase in leaves and recovery time, hindering workforces at their workspaces [48]. Another concerning area is the possible disturbance in national/international labour markets that would have further socio-economic impacts [49]. COVID-19 has forced us to rethink the current guidelines implemented by international organizations, as they may no longer be the most suitable and should be reevaluated in the post-COVID world. The probable impact of the COVID-19 pandemic on the elevated emergence of AMR is summarized in Table 1.

Table 1. Probable impact of COVID-19 pandemic on antimicrobial resistance in post COVID-19 world.

	Observable changes during COVID-19	Hypothesized changes post COVID-19
Impact of COVID-19 on AMR	Reckless use of antimicrobials along with reduced AMR surveillance and AS	AMR cases might shoot up due to unrestrained use of broad spectrum antimicrobials
	Prevalence of secondary bacterial and fungal infections	Longer period of hospitalization, increased risk of nosocomial outbreaks
	Excessive use of biocides	Detrimental effect on global economy
	Prophylactic use and self-medication of broad spectrum antibiotics	Persistence of restrictions on social interactions, public gatherings and travel
	Huge COVID-19 patient burden along with depriortization of patients with diseases other than COVID-19	Rise in medical leaves pertaining to increase in AMR cases, hindering workforces at their respective workspaces
	Excessive physical and mental stress on healthcare workers	Disturbance in national/ international labour markets impacting socio-economic solidarity
	Decreased laboratory surveillance for antimicrobial susceptibility due to focus on COVID-19 diagnosis as a priority	Delayed detection of antimicrobial resistant organisms along with sub-optimal diagnosis and treatment

3.5. Prophylactic drugs, self-medication, and host immune system

Initially, the main obstacle to managing the spread of the coronavirus disease was the lag between the optimization of its treatment and its rapid rate of transmission. Moreover, immunocompromised patients affected by COVID-19 required intensive care devices along with the administration of antibiotics. The situation worsened during the second wave of the pandemic when patients who were hospitalized at ICUs experienced concurrent comorbidities with a higher risk of bacterial infections [50]. Therefore, there was a great reliance on the prophylactic use of antibiotics to prevent bacterial respiratory diseases, as well as an approach for the management of COVID-19 [4]. This prophylactic administration was consciously done to cope with a demanding situation: 50 % of COVID-19 mortalities were associated with either bacterial or fungal secondary infections. This indicated that secondary co-infections were one of the main factors increasing fatalities during the second wave when compared to the first wave [29, 51,52]. But one thing went unnoticed; the increase in the percentage of secondary infections during the second wave of the pandemic was due to the indiscriminate use of antibiotics during the first wave. Meta-data analyses of COVID-19 co-infection showed that antibiotics were prescribed to approximately 72 % of COVID-19 patients, but only 8 % of them had a bacterial or fungal co-infection, and thus needed the treatment [4]. Additionally, selective therapeutics, such as chloroquine, were prescribed for COVID-19, despite a lack of evidence for their efficacy [53, 54, 55]. This irresponsible antibiotic usage raised concerns in certain settings, such as the zones of high prevalence of non-*Plasmodium falciparum* malaria, where chloroquine remains the drug of choice for malaria treatment, [56] since its use for COVID-19 might indirectly promote chloroquine resistance. The overuse of antimicrobials and steroids for COVID-19 is evident, and this unfortunately might continue during the successive waves of the pandemic.

Self-medication is another critical problem that is more common in LMICs, where over-the-counter antibiotics are easily available to the public [27]. The situation worsens because fewer efforts are being made towards COVID-19 testing, there is a financial crisis, and people are unable to access healthcare facilities. As a result, undiagnosed individuals with symptoms are more likely to resort to self-medication. [57, 58]. The pandemic further escalates these practices, which will inevitably increase AMR cases. Although vaccines are available, there is no specialized drug for the treatment of COVID-19 patients, hence a combination of available commercial drugs (antiparasitic/antiviral) is administered along with broad-spectrum antibiotics such as macrolides. Unfortunately, a majority of the approved antibiotics have off-target sites in the host's mitochondrial system. Since mitochondria are evolutionary linked to prokaryotic cells, antibiotic therapy either causes a malfunction of mitochondrial physiology, disrupts their function, interferes in ATP production, or induces cell death pathways. This in turn is speculated to weaken the host's immune response against COVID-19 infection [59]. However, it should be kept in mind that the magnitude of antibiotic sensitivity varies with the immunity of patients. Patients with already-diagnosed mitochondrial disorders are much more susceptible to certain antibiotics than the general population [60].

4. Conclusion

The consequences of AMR in the post-COVID-19 world are currently speculative, but preliminary findings and scientific evidence from the ongoing pandemic and past experiences strongly indicate a potentially alarming situation. Despite the availability of vaccines, the risk of infection and the emergence of severe medical situations cannot be completely disregarded due to the emergence of waves caused by new variants in multiple countries. [61]. On the one hand, the implementation of regulations such as the use of face masks, increased hand hygiene, physical distancing, stay-at-home orders, mandatory lockdowns, mandatory vaccination, travel bans, and transportation restrictions during the pandemic might have lowered the spread of infections, but on the other hand, reckless usage of antimicrobials might have planted the seeds of an upcoming threat. Governments worldwide are under tremendous pressure of maintaining a delicate balance between addressing the medical emergency and ensuring the economic stability of their countries. The world needs to understand that managing an AMR crisis requires increased vigilance and cooperation of people from every stratum of society, starting with healthcare professionals, industry, academia, politicians, and social workers, as well as maintaining healthy habits at the household level in order to minimize the need for antibiotics.

The challenge arises from the fact that the pandemic has been prolonged, and we cannot predict the duration of successive waves due to the continuous emergence of mutant strains and the unequal distribution of vaccines worldwide. This has resulted in a two-track pandemic that disproportionately affects LMICs. To bridge the existing knowledge gap regarding the occurrence and impact of co-infections in COVID-19 patients it is crucial to conduct ongoing epidemiological, microbiological, and clinical studies on AMR and nosocomial infections in both HICs and LMICs. These studies would help to improve COVID-19 treatment guidelines and future strategies and precautions to be taken, especially as international travel restrictions are lifted. Furthermore, it is crucial to promote antibiotic awareness among the general public, provide explicit AS training for frontline healthcare professionals, and implement legislation related to AMR. These measures are particularly important for addressing AMR-related challenges, especially in LMICs [27]. The interim guidelines by the WHO recommended the inclusion of AS principles during the clinical management of COVID-19 [62]. The guidelines also recommend stopping antibiotic therapy or prophylaxis for mild or moderate COVID-19 patients if no signs or symptoms of bacterial infection are reported [63]. Nevertheless, LMICs face challenges in adhering to these guidelines. Therefore, it is crucial to enhance global efforts by promoting effective leadership, increasing public involvement, and fostering international cooperation. These measures are necessary to effectively mitigate the adverse effects of the coronavirus disease on AMR in the future.

5. Acknowledgements

The authors acknowledge the various support received from DST-PURSE programme, University of Kalyani.

6. Funding

The paper was not funded.

7. Declaration of interest

It is being declared that the contents of the paper along with the opinions expressed within are those of the authors, and it was the decision of the authors to submit the manuscript for publication.

References

[1] Scott J. The economic, geopolitical and health impacts of COVID-19, *World Economic Forum*, 2020.

https://www.weforum.org/agenda/2020/03/the-economic-geopolitical-and-health-consequences-of-covid-19/

[2] WHO. WHO Coronavirus (COVID-19) Dashboard, *World Health Organiztion*, 1–5, 2021.

https://covid19.who.int/

[3] Callaway E. Could new COVID variants undermine vaccines? Labs scramble to find out, *Nature*, 589: 177–178, 2021.

https://media.nature.com/original/magazine-assets/d41586-021-0-00310/d41586-021-00031-0.pdf

[4] Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M,et al. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support covid-19 antimicrobial prescribing, *Clinical Infectious Diseases*, 71(9): 2459–2468, 2020.

doi: https://doi.org/10.1093/cid/ciaa530Lynch C

[5] Mahida N, Gray J. Antimicrobial stewardship: a COVID casualty?, *Journal of Hospital Infection*, 106(3): 401–403, 2020.

doi: https://dx.doi.org/10.1016%2Fj.jhin.2020.10.002

[6] Monnet DL, Harbarth S. Will coronavirus disease (COVID-19) have an impact on antimicrobial resistance?, *Eurosurveillance*, 25(45): 2001886, 2020.

doi: https://doi.org/10.2807/1560-7917.ES.2020.25.45.2001886

[7] Afshinnekoo E, Bhattacharya C, Burguete-García A, Castro-Nallar E, Deng Y, Desnues C, et al. COVID-19 drug practices risk antimicrobial resistance evolution, *The Lancet Microbe*, 2: 135–136, 2021.

doi: https://doi.org/10.1016/S2666-5247(21)00039-2

[8] Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance : a global multifaceted phenomenon, *Pathogens and Global Health*, 109: 309–318, 2016.

doi: https://dx.doi.org/ 10.1179%2F2047773215Y.0000000030

[9] Arshad M, Mahmood SF, Khan M, Hasan R. Covid -19, misinformation, and antimicrobial resistance, *BMJ*, 371: m4501, 2020.

doi: https://doi.org/10.1136/bmj.m4501

[10] WHO. Antimicrobial resistance,*World Health Organization*, 2020.

https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

[11] US Department of Health and Human Services, CDC. Antibiotic resistance threats in the United States, *Centers of Disease Control and Prevention*, 1–113, 2019.

https://www.cdc.gov/drugresistance/biggest_threats.html

[12] Pelfrene E, Botgros R, Cavaleri M. Antimicrobial multidrug resistance in the era of COVID-19: a forgotten plight?, *Antimicrobial Resistance & Infection Control*, 10: 21, 2021.

doi: https://doi.org/10.1186/s13756-021-00893-z

[13] WHO. Global strategy for containment of antimicrobial resistance. *World HealthOrganization*, 105, 2001.

https://www.who.int/drugresistance/WHO_Global_Strategy_English.pdf

[14] WHO. The evolving threat of antimicrobial resistance: options for action,*World Health Organization*, 1–119, 2014.

https://apps.who.int/iris/handle/10665/44812

[15] WHO. World antimicrobial awareness week,*World Health Organization*, 2015.

https://www.who.int/news-room/events/detail/2020/11/18/default-calendar/world-antimicrobial-awareness-week-2020

[16] Regional Committee for Europe. European strategic action plan on antibiotic resistance, 6: 12–15, 2011. https://www.euro.who.int/_data/assets/pdf_file/0008/147734/wd14E_AntibioticResistance_ 111380.pdf

[17] NCDC. National policy for containment of antimicrobial resistance, India, 2011.

http://www.indiaenvironmentportal.org.in/files/ab_policy.pdf

[18] National action plan on antimicrobial resistance (NAP-AMR), India, 2017.

https://ncdc.gov.in/WriteReadData/l892s/File645.pdf

[19] Dijk KH and Van L. The world medicines situation: rational use of medicines, *World Medicine Situation*, 2: 24–30, 2011.

[20] Ansari S, Hays JP, Kemp A, et al. The potential impact of the COVID-19 pandemic on global antimicrobial and biocide resistance: an AMR insights global perspective, *JAC-Antimicrobial Resistance*, 3(2). 2021.

doi: https://doi.org/10.1093/jacamr/dlab038

[21] Zhu X, Ge Y, Wu T, et al. Co-infection with respiratory pathogens among COVID-2019 cases, *Virus Research*, 285: 198005, 2020. doi: https://doi.org/10.1016/j.virusres.2020.198005

[22] Rodríguez-Baño J, Rossolini GM, Schultsz C, et al. Key considerations on the potential impacts of the COVID-19 pandemic on antimicrobial resistance research and surveillance, *Transactions of the Royal Society of Tropical Medicine & Hygiene*. 2021.

doi: https://doi.org/10.1093/trstmh/trab048

[23] Langford BJ, So M, Raybardhan S, Leung V, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis, *Clinical Microbiology and Infection*, 26(12): 1622–1629, 2020.

doi: https://doi.org/https://doi.org/10.1016/j.cmi.2020.07.016

[24] Garcia-Vidal C, Sanjuan G, Moreno-García E, et al. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study, *Clinical Microbiology and Infection*, 27(1): 83–88, 2021.

doi: https://doi.org/10.1016/j.cmi.2020.07.041

[25] Vaughn VM, Gandhi TN, Petty LA, et al. Empiric antibacterial therapy and community-onset bacterial coinfection in patients hospitalized with Coronavirus Disease 2019 (COVID-19): A multi-hospital cohort study, *Clinical Infectious Diseases*, 72(10): 533–541, 2021.

doi: https://doi.org/10.1093/cid/ciaa1239

[26] Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series, *BMJ*, 368: 606, 2020. doi: https://doi.org/10.1136/bmj.m606

[27] Subramanya SH, Czyż DM, Acharya KP, et al. The potential impact of the COVID-19 pandemic on antimicrobial resistance and antibiotic stewardship, *Virus Disease*, 23(2): 1–8, 2021.

doi: https://doi.org/10.1007/s13337-021-00695-2

[28] Chedid M, Waked R, Haddad E, et al. Antibiotics in treatment of COVID-19 complications: a review of frequency, indications, and efficacy, *Journal of Infection and Public Health*, 14(5): 570–576, 2021.

doi: https://doi.org/10.1016/j.jiph.2021.02.001

[29] Chang CY, Chan KG. Underestimation of co-infections in COVID-19 due to non-discriminatory use of antibiotics, *Journal of Infection*, 81(3): 29–30, 2020.

doi: https://doi.org/10.1016/j.jinf.2020.06.077

[30] Martinez KA, Rood M, Jhangiani N, et al. Association between antibiotic prescribing for respiratory tract infections and patient satisfaction in direct-to-consumer telemedicine, *JAMA-Internal Medicine*, 178(11): 1558–1560, 2018.

doi: https://doi.org/10.1001/jamainternmed.2018.4318

[31] Ray KN, Shi Z, Gidengil CA, et al. Antibiotic prescribing during pediatric direct-to-consumer telemedicine visits, *Pediatrics*, 143(5): e20182491, 2019.

doi: https://doi.org/10.1542/peds.2018-2491

[32] Clancy C, Nguyen M. COVID-19, superinfections and antimicrobial development: What can we expect?, *Clinical Infectious Diseases*, 71(10): 2736–2743, 2020.

doi: https://dx.doi.org/10.1093%2 Fcid%2Fciaa524

[33] NIH, COVID-19 treatment guidelines. Clinical spectrum of SARS-CoV-2 infection, 2021.

[34] Sell TK, Hosangadi D, Trotochaud M. Misinformation and the US Ebola communication crisis: analyzing the veracity and content of social media messages related to a fear-inducing infectious disease outbreak, *BMC Public Health*, 20(1):550, 2020.

doi: https://doi.org/10.1186/s12889-020-08697-3

[35] Islam MS, Sarkar T, Khan SH, et al. COVID-19-Related infodemic and its impact on public health: a global social media analysis, *American Journal of Tropical Medicine and Hygeine*, 103: 1621–1629, 2020.

doi: https://doi.org/10.4269/ajtmh.20-0812

[36] Glasziou PP, Sanders S, Hoffmann T. Waste in covid-19 research, *BMJ*, 369: 1847, 2020.

doi: https://doi.org/10.1136/bmj.m1847

[37] Wang Y, Hao H, Platt LS. Examining risk and crisis communications of government agencies and stakeholders during early-stages of COVID-19 on Twitter, *Computers in Human Behaviours*, 114: 106568, 2021.

doi: https://doi.org/10.1016/j.chb.2020.106568

[38] Gonsalves G, Yamey G. Political interference in public health science during Covid-19, *BMJ*, 371:19–20, 2020.

doi:https://doi.org/10.1136/bmj.m3878

[39] Azad A. Antimicrobial crisis, *DAWN.COM.*, 2020.

https://www.dawn.com/news/1578514

[40] Nori P, Cowman K, Chen V, et al. Bacterial and fungal coinfections in COVID-19 patients hospitalized during the New York City pandemic surge, *Infection Control & Hospital Epidemiology*, 42(1): 84–88, 2021.

doi: https://doi.org/10.1017/ice.2020.368

[41] Shehadeh M, Suaifan G, Darwish RM, et al. Knowledge, attitudes and behavior regarding antibiotics use and misuse among adults in the community of Jordan. A pilot study, *Saudi Pharmaceutical Journal*, 20(2): 125–133, 2012.

doi: https://doi.org/10.1016/j.jsps.2011.11.005

[42] Wang Z, Wang J, He J. Active and effective measures for the care of patients with cancer during the COVID-19 spread in China, *JAMA Oncology*, 6(5): 631–632, 2020.

doi: 10.1001/jamaoncol.2020.1198OECD

[43] Stemming the superbug tide: just a few dollars more, *OECD Health Policy Studies, OECD Publication Paris*, 2018.

https://doi.org/10.1787/9789264307599-en

[44] Mazdeyasna H, Nori P, Patel P, et al. Antimicrobial stewardship at the core of COVID-19 response efforts: implications for sustaining and building programs, *Current Infectious Disease Reports*, 22(9): 23, 2020.

doi: https://doi.org/10.1007/s11908-020-00734-x

[45] Usman M, Farooq M, Hanna K. Environmental side effects of the injudicious use of antimicrobials in the era of COVID-19, *Science of the Total Environment*, 745: 141053, 2020.

doi: https://doi.org/10.1016/j.scitotenv.2020.141053

[46] Wilson LA, Rogers Van Katwyk S, Fafard P, et al. Lessons learned from COVID-19 for the post-antibiotic future, *Global Health*, 16: 94, 2020.

doi: https://doi.org/10.1186/s12992-020-00623-x

[47] CantoÂ NR, GijoÂn D, Ruiz-Garbajosa P. Antimicrobial resistance in ICUs: an update in the light of the COVID-19 pandemic, *Current Opinion in Critical Care*, 26(5): 433–441, 2020.

doi: https://doi.org/10.1097/MCC.0000000000000755OECD

[48] Waiting Times for Health Services: Next in Line, *OECD Health Policy Studies,OECD Publication Paris*, 2020.

https://doi.org/10.1787/242e3c8c-en

[49] CCA. When antibiotics aail: the expert panel on the potential socio-economic impacts of antimicrobial resistance in Canada, *Council of Canadian Academies*, 2019.

https://cca-reports.ca/reports/the-potential-socio-economic-impacts-of-antimicrobial-resistance-in-canada/

[50] Liberati A, D'Amico R, Pifferi S, et al. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care, *Cochrane Database System Reviews*, 4: CD000022, 2009.

doi: https://doi.org/10.1002/14651858.CD000022.pub3

[51] MacIntyre CR, Chughtai AA, Barnes M, Ridda I, et al. The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09, *BMC Infectious Diseases*, 18(1): 637, 2018.

doi: https://doi.org/10.1186/s12879-018-3548-0

[52] Morris DE, Cleary DW, Clarke SC. Secondary bacterial infections associated with influenza pandemics, *Frontiers in Microbiology*, 8: 1041, 2017.

doi: https://dx.doi.org/10.3389%2Ffmicb.2017.01041

[53] Kashour Z, Riaz M, Garbati MA, et al. Efficacy of chloroquine or hydroxychloroquine in COVID-19 patients: A systematic review and meta-analysis, *Journal of Antimicrobial Chemotherapy*, 76(1): 30–42, 2021.

doi: https://doi.org/10.1093/jac/dkaa403UKRI

[54] The recovery trial, 2022.

https://www.ukri.org/our-work/tackling-the-impact-of-covid-19/vaccines-and-treatments/recovery-trial-identifies-covid-19-treatments/

[55] WHO. "Solidarity" clinical trial for COVID-19 treatments, *World Health Organization*, 2021.

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

[56] Maugueret TMJ, Walker SL. Rapid detection of *Obesumbacterium proteus* from yeast and wort using polymerase chain reaction, *Letters in Applied Microbiology*, 35(4): 281–284, 2002.

doi: https://doi.org/10.1046/j.1472-765x.2002.01179.x

[57] Molento MB. COVID-19 and the rush for self-medication and self-dosing with ivermectin: a word of caution, *One Health*, 10:100148, 2020.

doi: https://dx.doi.org/10.1016%2Fj.onehlt.2020.100148

[58] Torres NF, Chibi B, Middleton LE, et al. Evidence of factors influencing self-medication with antibiotics in low and middle-income countries: a systematic scoping review, *Public Health*, 168: 92–101, 2019.

doi: https://doi.org/10.1016/j.puhe.2018.11.018

[59] Rezasoltani S, Yadegar A, Hatami B, et al. Antimicrobial resistance as a hidden menace lurking behind the COVID-19 outbreak: the global impacts of too much hygiene on AMR, *Frontiers in Microbiology*, 11: 590683, 2020.

doi: https://doi.org/10.3389/fmicb.2020.590683

[60] Stoker ML, Newport E, Hulit JC, et al. Impact of pharmacological agents on mitochondrial function: a growing opportunity?, *Biochemical Society Transactions*, 47(6): 1757–1772, 2019.

doi: https://doi.org/10.1042/BST20190280The

[61] Economic Times. Third wave of COVID-19 definitely underway in Britain, says vaccine expert, 2021.

https://economictimes.indiatimes.com/news/international/world-news/third-wave-of-covid-19-definitely-underway-in-britain-says-vaccine-expert/articleshow/83666378.cms

[62] WHO. Clinical Management of COVID-19, *World Health Organization*, 2020.

https://apps.who.int/iris/handle/10665/332196

[63] Getahun H, Smith I, Trivedi K, et al. Tackling antimicrobial resistance in the COVID-19 pandemic, *Bulletin of the World Health Organization*, 98(7): 442–442A, 2020.

doi: https://doi.org/10.2471/BLT.20.268573

Las secuelas de la enfermedad del coronavirus en la resistencia a los antimicrobianos en países de bajos y medianos ingresos

Resumen: La resistencia a los antimicrobianos (RAM) plantea un desafío crítico para la medicina moderna. El número de casos de resistencia en todo el mundo ha ido aumentando de manera exponencial y se estima que para el año 2050, la tasa de mortalidad por RAM será diez veces mayor que la actual. La aparición de la pandemia de la enfermedad del coronavirus 2019 (COVID-19) comprometió la investigación sobre la RAM al darle menor prioridad al monitoreo adecuado de medidas preventivas y programas de control, la innovación y los programas de salud global, y el manejo de los antimicrobianos (MA). Con el escenario actual de casos esporádicos de COVID- 19 en todo el mundo, es imposible evaluar de manera precisa el impacto que la pandemia tuvo en la RAM y la MA ya que no hay suficientes reportes. Sin embargo, es posible especular cómo será el escenario al observar el aumento en el uso no metódico de antimicrobianos, el incremento en las infecciones bacterianas y fúngicas secundarias, y la prolongación de la estadía hospitalaria y las emergencias médicas adversas durante la segunda ola en comparación con la primera. La COVID-19 reveló una dura realidad: incluso los países con las mejores instalaciones médicas tuvieron problemas para satisfacer las necesidades nacionales de atención médica durante una pandemia. En dichas circunstancias, las comunidades clínicas y científicas deben comprender que los recursos médicos globales disponibles serían insuficientes para enfrentar una próxima pandemia de RAM. Por lo tanto, los sistemas de vigilancia internacionales deben destacar las deficiencias actuales en la contención y mitigación de la RAM y desarrollar estrategias para enfrentar los desafíos futuros.

Palabras Clave: resistencia a los antimicrobianos; enfermedad del coronavirus; manejo de los antimicrobianos; uso de los antimicrobianos; salud pública.

As consequências da doença do coronavírus na resistência aos antimicrobianos em países de baixa e média renda

Resumo: A resistência aos antimicrobianos (RAM) representa um desafio crítico para a medicina moderna. O número de casos de resistência em todo o mundo tem aumentado exponencialmente e estima- se que em 2050, a taxa de mortalidade devido à RAM será dez vezes maior do que a atual. A chegada da pandemia da doença do coronavírus 2019 (COVID-19) comprometeu a pesquisa sobre a RAM ao dar menor prioridade ao monitoramento adequado de medidas preventivas e programas de controle, inovação e programas de saúde global, e á gestão dos antimicrobianos (GA). Com o cenário atual de casos esporádicos de COVID-19 em todo o mundo, é impossível avaliar de forma precisa o impacto que a pandemia teve na RAM e no MA, devido à falta de relatórios suficientes. No entanto, é possível especular como será o cenário ao observar o aumento no uso não metodológico de antimicrobianos, o aumento nas infecções bacterianas e fúngicas secundárias e a prolongação da internação hospitalar e emergências médicas adversas durante a segunda onda em comparação com a primeira. A COVID-19 revelou uma dura realidade: mesmo os países com as melhores instalações médicas tiveram dificuldades para atender às necessidades nacionais de atendimento médico durante uma pandemia. Nessas circunstâncias, as comunidades clínicas e científicas devem compreender que os recursos médicos globais disponíveis seriam insuficientes para enfrentar uma próxima pandemia de RAM. Portanto, os sistemas de vigilância internacionais devem destacar as atuais deficiências na contenção e mitigação da RAM e desenvolver estratégias para enfrentar os desafios futuros.

Palavras-chave: resistência aos antimicrobianos; doença do coronavírus; gestão dos antimicrobianos; uso dos antimicrobianos; saúde pública.

Pia Dey is a Microbiologist who obtained her doctoral degree from the University of Kalyani, India. Her field research is focused on antimicrobial and antibiofilm research.

ORCID: 0000-0002-2085-4252

Debaprasad Parai is a Microbiologist working as a Scientist at ICMR-Regional Medical Research Centre, Bhubaneswar, India. He obtained his doctoral degree from the University of Kalyani, India. His area of interest is on infectious disease management, antimicrobial resistance, and bacterial biofilm.

ORCID: 0000-0003-0266-5623

Sk Tofajjen Hossain is an Assistant Professor in Microbiology, University of Kalyani, India. He obtained Ph.D. from University of Kalyani, India, and then did post-doctoral work at University of Miami Miller School of Medicine, USA. He has focused his area of research on RNA metabolism, antimicrobials, and bacterial biofilm.

ORCID: 0000-0002-1448-1015

Samir Kumar Mukherjee is a Professor in Microbiology, University of Kalyani, India. He has contributed to various research fields in Microbiology. His major fields of research are metal- microbe interaction, antimicrobials, and bacterial biofilm.

ORCID: 0000-0001-8841-6817