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The Role of Bioethics in Antimicrobial Resistance Response: The COVID-19 Perspective

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Abstract

Background: AMR, a global health risk continues to pose a public health challenge during the COVID-19 due to an increase in the use, misuse, and overuse of antimicrobials during the pandemic. This study, therefore, aims to explore the drivers of antimicrobial resistance during the COVID-19 pandemic and the role of bioethics in guiding actions against AMR.

Methods: Google Scholar and PubMed were used to retrieve articles published between 2019 and 2022, using search terms such as: COVID-19 and antimicrobial resistance, co-infections in COVID-19 patients, including bioethics in COVID-19 response.

Results: Widespread empiric antibiotic therapy in the near absence of microbial co-infections was the most cited reason for the propagation of AMR in COVID-19 patients. AMR is at risk of being exacerbated by the COVID-19 pandemic due to unethical practices. The resurfacing and indiscriminate use of antimicrobials for which resistance has been recorded is alarming. Although papers concentrating on applying ethical measures to the control of antimicrobial resistance during the pandemic were lacking, we have attempted to contextualize the role of bioethics in AMR response as it relates to the COVID-19 pandemic. Countries and regulatory bodies need to develop and establish the appropriate implementation of actions to ensure the judicious use of antimicrobials during the pandemic as well as check the questionable prescription practices of healthcare professionals through well restructured antimicrobial stewardship programs in healthcare settings.

Conclusion: The COVID-19 pandemic has brought about an upsurge in the use of antimicrobials and consequently, the exacerbation of the problem of AMR. Bio-ethic will definitely play a massive role in mitigating the spread of AMR in the face of the persistent the COVID-19 pandemic.

Keywords: Antimicrobial resistance; COVID-19; Pandemic; Bio-ethics

Introduction

The discovery of antibiotics by Alexander Fleming revolutionized medicine to what we have come to know it as. However, nearly a century down the line, the medical world is once again faced with the menace of Antimicrobial Reistance (AMR) and an impending era where these wonder drugs are rendered ineffective in combatting common infectious disease. AMR is an intricate threat to public health that requires equally intricate solutions but decisions made by individuals and institutions accountable for its control may either make or mar healthcare provisions for both present and future patients [1]. The continuous decline in the availability of effective antimicrobials while AMR thrives has raised several ethical concerns; the Coronavirus Disease-2019 (COVID-19) pandemic, caused by the Severe Acute Respiratory Virus Coronavirus (SARS-CoV-2), further complicates efforts of healthcare professionals, researchers, public health institutions, and international community such as the Centers for Disease Control and Prevention (CDC), the World Helath Organization (WHO), the Food and Agricultural Organzation of the United Nations (FAO). Estimating the exact impact and mortality rates of AMR is tedious especially for Low to Middle Income Countries (LMIC), due to negligence, gross underreporting, and lack of surveillance and in Nigeria in particular, availability of studies that estimate the full burden, health and economic impact of AMR on Nigerians is wanting. However, reports from the WHO and the World Bank put the global mortality rate from AMR resistant diseases at 700,000 deaths annually, including 230,000 people who die from multi-drug resistant tuberculosis, a projected million people could die from AMR related deaths by 2050 if left unaddressed [2]. While much research have been conducted on AMR and its impact on treatment of infectious diseases, the ethical issues of AMR have not been prioritized especially its ethical implications on drug resistance and the problem it exacerbates, associated with infectious disease control. In this paper, we discuss the pre-existing global response to antimicrobial resistance before COVID-19, the drivers of AMR during COVID-19, and the role of bioethics in concerted efforts to combat it while the world faces a pandemic [3].

Literature Review

Antimicrobial resistance and global response

AMR is a threat to global health and development and one of the top 10 public health threats facing humanity. AMR is the survival mechanism put up by microorganisms that enables them to withstand treatment with antibiotics. Resistance developed by microorganisms makes treatment and control of infectious diseases more difficult, transmission easier and quality healthcare more expensive to obtain especially in developing countries where access to quality healthcare is already limited. The use and misuse of antibiotics are the most common causes of AMR and this applies to both human and veterinary health [4]. The fight against AMR is ongoing globally but disparities in responses and data coverage of various countries exist and have made progress in combating AMR and tracking antimicrobial consumption tedious and disproportionate, the greater of which can be found in developing countries [5]. Some of the frameworks put in place by the WHO and other international organizations to foster actions against AMR include:

- The one health plan, a tripartite collaboration between the Food and Agriculture Organization (FAO), WHO, and World Organization for Animal Health (OIE) employs a multi-sectoral approach that integrates epidemiological, environmental, and socio-economic factors.
- The WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) which since its establishment in 2015 has provided an annual report on AMR, use, and recently, antibiotic consumption surveillance systems of its 109 participatory countries. It aims to engender and strengthen national AMR surveillance systems to provide standard AMR surveillance data.
- The WHO global action plan is committed to developing and implementing national action plans in WHO member countries.
- Global Antibiotic Research and Development Partnership (GARDP) which by 2025 aims to have developed five new treatments against antibiotic-resistant bacteria.

In this section, we shall be discussing the drivers of AMR in both developed and developing countries as well as respective actions taken to ameliorate the issue while adhering to WHO guidelines.

Europe and America

The most developed continents in the world are not spared from the revolving threats of AMR. Antimicrobial resistance in most parts of Europe and America stems from the inappropriate use of antimicrobials in agriculture, veterinary and human healthcare [6]. A report from the Organization for Economic Cooperation and Development (OECD) showed that the United States of America, Italy, and France have the highest death rates from antimicrobial resistance. The annual epidemiological report of the European Union/European Economic Area (EU/EEA) for 2019 showed that the EU countries are most burdened with antibiotic resistance from bacterial species such as *Escherichia coli*, *Staphylococcus aureus, Klebsiella pneumonia, Enterococcus faecalis, Enterococcus faecium, Pseudomonas aeruginosa*. An updated report however observed a decline in antimicrobial resistance in most bacterial species under surveillance except carbapenem-resistant *E. coli*, *K. pneumoniae*, and vancomycin-resistant *E. faecium*. The EU's response to antimicrobial resistance can be seen in the various national action plans devised by the EU countries with central foci on the judicious use of antimicrobials, prevention, and control of infectious diseases, and research and development. The EU One health action plan against AMR was established in 2017 with the objectives of boosting research, development, and innovation and improving practice in the EU region [7].

In response to the 2013 CDC report on antimicrobial resistance threats in the United States, the US took several One health actions and partnerships with the EU, Canada, and Norway; countries with which they formed the transatlantic taskforce on antimicrobial resistance [8-12]. They also founded the Global Antimicrobial Resistance Research and Development (GARRD) hub and created and implemented national action plans. Other regional networks put across Europe and America include the European Antimicrobial Resistance Network (EARS-Net) coordinated by the European Centre for Disease Control (ECDC) and the Latin American Network for AMR surveillance (ReLAVRA) established in 1996 by the WHO/region for Pan American Health Organization (PAHO) Regional Office.

Asia and Africa

Low to Medium Income Countries (LMIC) in Asia and Africa alike are faced with high burdens on infectious diseases which leave the population vulnerable to the continuous development and spread of antimicrobial resistant organisms. The emergence, persistence, and spread of AMR in these regions are exacerbated by a plethora of factors, some of which include limited access to healthcare facilitated by poverty and ignorance, ease of accessing Over The Counter (OTC) drugs, inappropriate sanitary practices amongst the general public and healthcare providers, extensive use of antibiotics in food and animal production, overprescribing by healthcare professionals encouraged by a low diagnostic capacity to properly diagnose infectious diseases. The data gap between High Income Countries (HIC) and LMICs makes the estimation of antimicrobial resistance tedious. Notwithstanding, a review of the global burden of antibiotic resistance by the Lancet showed that the highest death rates both attributed and associated with antibiotic resistance were in Sub-Saharan Africa and South Asia, with an all-age death rate of 75 per 100,000s. Despite various programs of action recommended by the WHO, many LMICs in Asia and Africa have made comparatively slower advances in the formulation and implementation of policies. However, some countries have developed national action plans to tackle the issue of AMR. A report on the preparedness of Sub-Saharan Africa on AMR, based on the WHO Joint External Evaluation (JEE), showed that East Africa had the highest percentage of countries with well implemented AMR national action plans. As of 2019 before the pandemic, the WHO African region reported that 33 member countries had developed national action plans for AMR based on the "one health" approach, with 18 already approved at their respective national levels. The list of African countries and their respective National Action Plans can be found in the WHO library of AMR national action plans. As of 2022, these numbers have progressed to 39 member states having finalized national action plans [13].

The reasons for AMR in China are not far removed from those of Africa. South and Southeast Asia are laden with infectious diseases and antimicrobial resistance as well. A systematic review on the statistics of the resistance of critical and high priority pathogens in South and Southeast Asian countries reported that the organisms which show the most resistance in their regions are carbapenem resistant *Acinetobacter* spp, third or fourth generation cephalosporin-resistant *E. coli*, Methicillin Resistant *Staphylococcus Aureus* (MRSA), ciprofloxacin resistant *Salmonella typhi* and cefotaxime resistant *E. coli*, although the rate of resistance varied amongst the countries due to lack of surveillance and detailed reports on the incidence of resistance. Countries of South and Southeast Asia also developed national action plans, with a majority of objectives that aligned with the global action plan [14-16].

Policy implementation remains a critical point between planning and action. In Nigeria, some of the hindrances that have been identified include the lack of technical know-how, lack of funding directed towards AMR policy implementation, insufficient data on AMR and insufficient communication amongst stakeholder. These reasons also hold for some other LMICs Notwithstanding, successes have been recorded for WHO Africa region member countries enrolled in the GLASS program, Nigeria included, with various collaborations amongst stakeholders to improve implementation and AMR surveillance [17-20].

Antimicrobial resistance in the COVID-19 era

The outbreak of the COVID-19 not only brought about a crackdown on global healthcare services but also revealed certain inadequacies in healthcare services. Understandably, COVID-19 has become the health issue of utmost priority of the past two years but the menace of AMR lingers with concerns of it being exacerbated by the pandemic. Some of the factors that may play a role in propagating AMR in the COVID-19 era are empirical antibiotic therapy encouraged by the lack of antimicrobial stewardship, overuse, and misuse of hygiene products, indiscriminate consumption of antimicrobials at the community level.

COVID-19 and microbial co-infections

As observed with most viral respiratory disease outbreaks and pandemics in the past, the emergence of COVID-19 raised concerns over bacterial co-infections. Secondary bacterial infections were identified as the cause of the majority of deaths in the 1918 to 1919 influenza pandemic; AMR contributed a minimum of 1% to 8% to the mortality recorded in the 2009 influenza pandemic. Reports also exist of a rise in MRSA in the hospital environment during the SARS pandemic. The use of antimicrobials to treat COVID-19 can be found in studies at the beginning of the pandemic supporting the use of repurposed hydroxychloroquine and chloroquine for the treatment of COVID-19, often administered in combination with antibiotics like azithromycin. However, these reports were subsequently disregarded as further research proved the hydroxychloroquine and azithromycin combination therapy in effective against COVID-19 treatment and in preventing secondary bacterial infection. Notwithstanding, there have been reports of fatal outcomes of COVID-19 infections attributed to super infection and co-infections by other pathogens of non-viral origins. Song, et al. screened for 28 microorganisms in 89 COVID-19 patients with varying severity of illness and detected bacterial co-infections (64.3%); no viral co-infections were detected. They did, however, raise concerns over patients in intensive care being infected with the rapidly prone to resistance *Acinetobacter baumanni*. Similarly, other research raised concerns over Intensive Care Unit (ICU) acquired infections. Soriano, et al. observed an incidence rate of 51.2% of ICU acquired infection in critically ill patients, accompanied by a high mortality rate (57.1%) in patients with bacterial co-infections although its prevalence was relatively low in comparison. Their studies corroborated a meta-analysis previously carried out by Lansbury, et al. involving a larger number of cohorts (3834), which also saw a higher rate of ICU acquired infections in ICU admitted patients (14%) than in overall hospitalized COVID-19 patients (7%).

Although substantial literature on the global estimate of incidence and prevalence of viral co-infections and super infections in COVID-19 patients is limited, some studies have reported incidence but prevalence has varied. The most commonly reported virus found in viral co-infected patients is the Influenza A virus. This should be of particular concern in areas where there is a high prevalence of the flu and more importantly, a high risk population of immunosuppressed and immunocompromised patients. Now, while the consequences of influenza a viral co-infection with COVID-19 have not been fully understood, previous studies have linked influenza virus with a patient predisposition to super infection by bacterial pathogens *S. aureus* and *S. pneumonia* leading to complications such as the development of acute respiratory distress syndrome or lung endothelial leakage. Such disruption of the endothelial barrier is one of the drivers of severe COVID-19 associated with multiple organ failure. The shared clinical symptoms and the manifestation of influenza and other microbial co-infections and COVID-19 may make a co-infection highly fatal if not properly diagnosed and timely managed. The co-infection might further complicate efforts in countries with limited diagnostic capacity.

Empiric antimicrobial therapy and its contribution to AMR

Empiric antibiotic treatment is defined according to the World Health Organization as "the initial antibiotic treatment targeted at the most probable causative microorganisms". Despite supporting evidence that disproves the use of antibiotics to manage a viral disease such as COVID-19, it is still highly relied upon as a means of treatment and symptom management of COVID-19 especially in LMICs. The outcomes of empiric antimicrobial therapy vary in different infectious diseases but sometimes the detriments outweigh the benefits. The use of broad spectrum antibiotics during this COVID-19 era has been well documented. A meta-analysis carried out by Rawson, et al. of studies representing 3338 patients, 6.9% of COVID-19 patients were found to have bacterial infections which were more common in critically ill patients. Disproportionately, 71.9% of those patients received antibiotics based on empiric antibiotic prescriptions. Coenan, et al. noted the "overtreatment" of COVID-19 patients in their study who underwent a median duration of antibiotic therapy even though 83% of COVID-19 patients observed had no co-infection. 81% of these patients received antibiotic treatment. Vaughn, et al. observed an inordinate difference in their study of 1705 randomly sampled cohort of patients, where for only 3.5% confirmed community onset bacterial co-infections, 56.6% of hospitalized COVID-19 patients received early empiric antimicrobial therapy. Furthermore, other studies have also observed that the empiric use of antimicrobials does not necessarily target the infections pathogens they're meant for, therefore contributing to the onset of multidrug resistance in bacteria. The emergence of extensive Drug Resistant (XDR) *Salmonella typhi* in Pakistan has been attributed to empiric antibiotic therapy by pharmacists and non-adherence to dosage by patients. The authors also raised concern for a possible emergence of azithromycin-resistant XDR *S. typhi* as azithromycin is a crucial means of treatment of both XDR *S. typhi* and for COVID-19 prophylaxis. The PAHO reported a rise in drug-resistant infections due to over-prescribing of drugs such as azithromycin, ivermectin, and chloroquine across countries in the Americas despite efforts put into reinforcing antimicrobial stewardship programs.

Self-medication, poor regulation infrastructure and, antimicrobial resistance

Poor regulation and enforcement lead to the overuse and misuse of antimicrobials in developing countries where often substandard or falsified antimicrobials are made easily available to the public by unqualified drug store owners and patented pharmacies. In Nigeria, the term "chemist" is used to refer to individuals who run drug stores, most often unlicensed and without proper oversight from authorized government agencies. Antimicrobials are sold on the streets, marketplaces, and road transport vehicles with misleading information about the purpose of the drugs. It is very common to find vendors recommending antibiotics for non-bacterial diseases. In grassroots communities where access to healthcare is arduous, residents self-medicate and more often than not, do not appropriately consume these drugs leading to medication with sub-optimal doses that aid in the buildup of resistance in organisms.

Before the pandemic, self-medication was commonplace in the global community but the bulk of occurrence and the brunt have been seen in low to medium income countries with fragile healthcare systems and less than standard practices amongst healthcare workers and the general public. Studies conducted across different countries in Africa have all identified reasons for self-medication, the most common of which are, the distance to healthcare facilities some ill equipped to deliver timely services-, ease and convenience of acquiring drugs used for self-medication, and the cost of healthcare it saves, and the perceived potential to manage common illnesses by oneself through self-medication.

The onset of the pandemic and restrictions that followed after did nothing to reduce the use of self-medication. The uncertainty and fear of contracting the virus fuelled by the lack of a drug to treat COVID-19, the fear of stigmatization, and quarantine have been cited as some of the reasons people self-medicate. Misinformation also caused anxiety and led more people to self-medicate. Because of the commonalities in clinical manifestation of COVID-19 and other diseases such as malaria, especially in Africa where it is endemic, it was easy for the general public to mistake COVID-19 symptoms as malaria leading to a surge in the purchase of and self-medication with anti-malarial and antibiotics and consequent hike in prices of these drugs. A population-based study carried out in Nigeria by Wegbom, et al. reported a 41% prevalence of self-medication for the prevention and treatment of COVID-19. 24.9% of the most commonly used drugs were antimalarials. Onchonga, et al. observed an increase in the prevalence of self-medication among health workers in Kenya which went from 36.2% before the pandemic to 60.4% during the pandemic while 84.1% of participants reported the pandemic prompted the need to self-medicate. A cross-sectional study to assess the prevalence of self-medication against COVID-19 yielded heterogeneous results where prevalence ranged from <4% to 88.3% in studies conducted in a general population and 33.9% to 51.3% in specific populations which included hospitalized COVID-19 infected adults, students, and workers.

Uninformed and irresponsible self-medication has been identified as a challenge to the fight against antimicrobial resistance. The drugs most used for self-medication during the pandemic include multivitamins, antibiotics such as azithromycin, analgesics; chloroquine, hydroxychloroquine, and ivermectin traditional medicines were also used in some cases. The questionable composition, potency, and efficacy of locally sourced herbal mixtures could instigate the onset of virulence.

Mutation

SARS-COV-2 belongs to the class IV group of RNA viruses known for their high rate of mutation. However, the notably low genomic diversity of SARS-CoV-2 gives it a comparatively low rate of mutation than other RNA viruses such as Hepatitis C virus, HIV, Influenza virus, and other coronaviruses. Mutations in coronaviruses could occur as a result of errors during viral replication, recombination or may be induced by host RNA editing actions. Recurrent mutations affecting changes in viral proteins have been found in the SAR-COV-2 genome. Van Dorp, et al. detected recurrent mutations in the regions encoding for spike protein and non-structural proteins. Alterations in spike proteins could lead to the onset of resistance in SARS-COV-290. Research has suggested that the longer the pandemic goes on, the higher the chances of it amassing mutations that contributes to immunological resistance and are advantageous to its viral fitness.

A missense mutation in the amino acid sequence in the SARS-CoV-2 spike protein, D614G, has been identified in dominant variants of SARS-CoV-2 and has been found to have higher transmissibility and increases the infectivity of the virus. To track mutation and subsequent variants of COVID-19, the WHO coined the terms "variants of interest" and "variants of concern". Variants of interest were defined as "variants with mutations known to cause significant changes and are circulating widely" while variants of concern were defined as variants of interest with more transmissibility, evades host immune attack, changes clinical presentation, and decrease the effectiveness of public health measures, diagnostics, treatments, and vaccines. As of January 2022, four variants of concern have been identified including the Beta variant first identified in South Africa, gamma variant first identified in Brazil, delta variant first identified in India, and most recently, the omicron variant first detected in South Africa and Botswana. All three variants before omicron have the D614G spike mutation amongst others and its presence is still not known in the omicron variant. The emergence of these variants has raised concerns over the effects they may have on the existing vaccines available against COVID-19 as vaccines are well-known tools in controlling antimicrobial resistance.

The role of bioethics in antimicrobial response

Bioethics addresses ethical, social, and legal issues that occur in biomedicine and biomedical research such as research ethics, medical ethics, dental ethics, public health ethics and environmental ethics (citation). In the context of Antimicrobial Resistance (AMR), bioethics deal with the ethical changes arising from the use, misuse and abuse of antimicrobials to the poor regulations and policy implementation of such antimicrobials (citation). Recently, a number of global ethical issues have been raised about the use of AMR in human health which posed questions on whether we could and should consider benefits in the distant future for unidentified patients as being more important than benefits in the near future for an identified patient.

Discussion

This must be discussed within a broader ethical debate by considering diverse ethical theories, principles and values. Bioethics can help healthcare experts and public policy makers to recognize the ethical dilemmas surrounding antibiotic use as well as strategies to reduce the extent of AMR.

The risk of the world emerging into a phase of multidrug resistance to essential antimicrobials post-COVID-19 should not be handled with kids' gloves. However, every measure taken to ensure this does not happen must stay within the confines of bioethical considerations so they don't become detrimental in the long run. Antimicrobial resistance has since been established as an ethical issue that affects both HICs and LMICs; the control of which requires equally ethical approaches. The aftermath effect of the pandemic on healthcare systems around the world has exposed the health systems to unethical practices. Some of the major areas of concern for bioethical intervention in the control of antimicrobial resistance include

Vaccines: Vaccines are effective in curbing antimicrobial resistance as the buildup of immunity protects the population against pathogenic infections that would otherwise require the use of antimicrobials. Considering the successes of many vaccines beforehand, one would expect people to welcome the swift development of vaccines against the virus responsible for the high rate of morbidity and mortality the world has witnessed. However, vaccine hesitancy has become a bottleneck situation in the fight against COVID-19. While the race to develop a vaccine by big pharmaceutical companies may seem like concerted efforts to "heal the world", most researchers fear the ulterior motives behind them, as they stand to gain billions in revenue generated from the sales of vaccines, especially to heavily burdened countries and the political affiliations they might have. The drivers of vaccine hesitancy in both HICs and LMICs have most been associated with poor education, especially on the benefits of the vaccine and the herd immunity it could engender, the female gender, religious beliefs, financial status, and an outright lack of confidence in the vaccine. In a country like Nigeria, for example, there is a particular lack of trust in the vaccines from Pfizer pharmaceutical company due to fatalities that occurred during the 1996 Trovan antibiotic drug trials which brought about Taths of children enrolled in the trials. This and other reasons have raised ethical concerns on where the line should be drawn between profiteering and saving lives. With many countries deciding on compulsory vaccination s especially for front line healthcare workers ethical considerations have to be made so as not to further discourage an already skeptical population or infringe on their rights. The World Health Organization provided some considerations that should predicate mandatory vaccinations.

- The absolute necessity of such mandate should be weighed while less forceful/intrusive policies are sought.
- Sufficient evidence of vaccine safety, efficacy, and effectiveness should be made available to the public. The absence of such does not ethically justify mandatory vaccination as going ahead with such a policy would expose the general public to the risk of harm.

- They also spoke on the need for an equitable supply of vaccines, especially for people with limited access for whom vaccination would be made compulsory before such a mandate could be considered.
- The effect on public trust and consequently, vaccine hesitancy should also be put into consideration while building on the fundamental frameworks of ethics and ethical analysis to make transparent, non-discriminatory decisions that would justify the mandate.

More efforts need to be put in place to properly inform public consciousness on the benefits of vaccination as patients have the ethical right to be informed of risks and benefits involved with taking the vaccine. Misinformation about COVID-19 vaccine is a contributing factor to the low acceptance rates of the vaccine, especially in LMICs. Civic dialogue, building trust in vaccines, public service messages on traditional media amongst other action cues were found to improve vaccine acceptance in a study carried out by Jin, et al. Similarly, Schwarzinger, et al. also observed a reduced reluctance to accept the vaccine when the benefits of herd immunity were properly communicated to the cohort in their study.

Antimicrobial stewardship

To control and soften the impact of easy antimicrobial usage during this pandemic, certain restrictive measures must be put in place; the mantle falling on health regulatory bodies to make policies as well as oversee the implementation and on physicians and other healthcare professionals to regulate their prescribing practices. As antimicrobial resistance is a multifaceted issue, it requires a multifaceted solution. The findings of Schuts, et al. who noted the infectiveness of a single, short-term stewardship strategy in combatting AMR, support this. In response to the quandary of inappropriate antibiotic prescribing amongst physicians due to patient influence, Meeker, et al. proposed a solution that involved employing a simple yet effective means of communication between patients and clinicians. In a randomized trial, clinicians provided patients with commitment letters that reinforced their commitment to avoid inappropriate antibiotic therapy for acute respiratory infections. Their stewardship intervention brought about a noteworthy reduction in inappropriate antibiotic prescribing practices and was low cost. Yen, et al. agreed with their interventions and deemed it ethical as it preserves patient autonomy and the bioethical frameworks of beneficence and maleficence but called for the need of any antimicrobial stewardship program to recognize and properly enunciate the ethics in such a program given the importance of antimicrobial stewardship in providing quality healthcare and driving research and innovation.

A pre-COVID-19 meta-analysis by Baur, et al. showed the significance of antibiotic stewardship programs in curbing AMR. The indiscriminate use of antimicrobials during the pandemic especially of those which have existing records of multidrug resistance is a wake-up call to the need development of effective antimicrobial stewardship programs across countries and strengthening already established ones. Martin, et al. summarized the challenges to antimicrobial stewardship in the hospital setting brought on by the COVID-19 pandemic. Existing antimicrobial stewardship activities have been proposed to be refocused on COVID-19 response efforts. Mazdyasna, et al. recommended tools such as prospective audit with intervention and feedback, formulary restriction and, preauthorization to check the usage and shortages of key antimicrobials and other drugs used in the management of the COVID-19 streamlining/de-escalating therapy and, antibiotic time outs to give room for errors in diagnosis. Assi, et al. also proposed collaborations between infection prevention programs and antimicrobial stewardship programs since they both have common objectives of reducing healthcare associated infections and the subsequent emergence of multi-drug resistant microorganisms, both issues of high concern during this pandemic.

Conclusion

The concept of AMR pre-COVID, during COVID, and projected outcomes of the heavy usage of antimicrobials in the previous year's calls for the need to develop strategies to address it. These strategies should not only seek to curb AMR but must also make sure that ethical boundaries are not crossed and human rights to life and healthcare are preserved. Aside from timely ethical interventions, a structural reform that includes the creation of local regulatory bodies that will provide oversight on ethics should be carried out in weakened healthcare systems with well-implemented stewardship programs. Diagnostic methods to properly differentiate COVID-19 infection and co-infections should be developed and made easily accessible to developing countries at subsidized cost to encourage seeking proper healthcare support rather than resolving to self-medication practices. Governments also must clamp down on illegal sales of antimicrobials to ill-informed consumers and make room for rational ethical considerations when implementing action plans on the control of AMR.

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