

Antimicrobial Resistance: A Global Public Health Concern that Needs Perspective Combating Strategies and New Talented Antibiotics

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Since the last century, antibiotics have been our reliable weapons against infectious diseases. In addition to their medicinal applications in human and veterinary medicine, antibiotics are also used in agriculture. However, the uncontrolled usage of antibiotics has led to the emergence of drug-resistant microbial strains and the rise of their incidence, representing a huge global concern in this century. All microbial populations, such as fungi, bacteria, parasites, and viruses, have the potential of developing antimicrobial resistance (AMR), which, in the medical realm, leads to a decrease in the standard pharmaceutical treatment efficacies—the starting point for a range of negative consequences such as an increase in global healthcare costs, a rise in the number of infectious diseases, and an increase in morbidity and mortality rates among patients [1–3]. Given the gravity of these impacts, the AMR is recognized as one of the top 10 threats in the healthcare domains worldwide [4,5].

In a systematic analysis, Murray *et al.* [6] estimated that the AMR caused by bacterial strains was responsible for 4.95 million deaths in 2019, of which 1.27 million fatalities had direct association with bacterial AMR [7]. Furthermore, Murray *et al.* [6] also found that in 2019, AMR was the third leading cause of death according to the Global Burden of Diseases (GBD) Level 3 death etiologies, following ischemic heart disease and stroke. This highlights the significance of bacterial AMR as a major public health concern, supported by various metrics. The analysis further revealed that the top six most fatal bacterial causative agents with high potential of causing bacterial AMR in 2019 were *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. Each of these bacterial species was responsible for >250,000 deaths in association with AMR in 2019 [6–8]. Thus, the emergence and rise of superbugs or multi-drug resistant (MDR) bacteria such as Gram-positive and Gram-negative bacteria and fungi represents a global problem with close association with bacterial and fungal hospital-acquired and community-acquired infections [1,9].

The ESCAPE group (which is composed of six highly virulent and antibiotic resistant superbugs) encompasses Enterobacterales, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *Enterobacter*. This implies that extended-spectrum β -lactamase (ESBL)-producing Enterobacterales, carbapenem-resistant *A. baumannii* (CRAB), MDR *A. baumannii*, carbapenem-resistant *K. pneumoniae* (CRKP), carbapenem-resistant Enterobacterales (CRE), vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant *S. aureus* (MRSA), and MDR *P. aeruginosa* are recognized the leading global superbugs [10,11]. The overuse or misuse of antibiotics, the lack of sanitation and safe water, low incomes, the use of low-quality medications, poor private hygiene, self-medication, and misdiagnosis are all important factors that may lead to the emergence of AMR attributed to the microbial pathogens dwelling in or having close association with humans [2,5]. On the other hand, microbial abilities and factors are involved in the emergence of AMR. In this regard, the microbial genomic plasticity, genetic exchanges (*e.g.*, horizontal genetic transfer [HGT], genetic elements such as transposons, retrotransposons, insertion sequences, integrons, and plasmids) and mutations, microbial enzyme modifications, microbial degradative enzymes, alterations in microbial pathways, activation of microbial efflux pumps are critical microbial factors underlying the emergence and rise of AMR. Furthermore, a wide range of environmental and intrinsic factors may lead to the emergence of AMR. For instance, microbial events, like biofilm formation, effectively create a suitable condition for the development of AMR features among microbial pathogens populations. The microbial strains with AMR features may manifest as diverse MDR strains, extensively drug-resistant (XDR) strains, and/or pan-drug resistant (PDR) strains [9,10,12]. To address the inevitable rise of these strains, some other treatment strategies rather than antibiotic therapeutics have recently been considered. The use of vaccines (prophylactic and preventive), immunotherapy, phage therapy, new line of drugs and antibiotics, probiotics, agonists, and antagonists are some of the significant strategies rolled out to replace traditional antibiotic therapy [1,2,5].

In this editorial, we would also like to discuss about a new antibiotic called “Lolamicin”, which acts selectively and kills only pathogenic Gram-negative bacteria by targeting their lipoprotein transport system (Lol system)—a system that is innately absent in the Gram-positive bacteria due to the lack of outer membrane. It has been proven that it does not target the useful gut microbiome of the host (mice). Hence, the antimicrobial mechanism of Lolamicin is a doubly selective strategy [13,14]. Moreover, the experimental results showed that the Lol system sequences in some pathogenic Gram-negative bacteria differ from those in beneficial Gram-negative bacteria residing among the gut microbiota [13,15]. The discovery of Lolamicin has the potential to pave way for the development of a reliable and effective treatment regimen for infected individuals.

Challenges of Combating Antimicrobial Resistance on Global Scale

Firstly, a significant restriction in obtaining comprehensive data on AMR across different regions poses a substantial hindrance to drawing definitive conclusions about the global state of AMR and its trends. Secondly, the variability in reporting standards among countries is a source of inconsistencies in the data collected. This inconsistency may affect the reliability of the findings and the comparisons made across regions. Thirdly, focusing solely on certain resistant strains, such as ESBL-producing Enterobacteriales and MRSA, limits the understanding of the full spectrum of AMR challenges and their broader implications on a global scale. Fourthly, having a limited understanding of the effectiveness of potential and existing interventions could affect medical recommendations by physicians. Next, without conducting longitudinal studies, it is difficult to assess the long-term effectiveness of interventions and the evolving nature of AMR. This necessitates more longitudinal studies in future to track the progression of AMR over time. Finally, it is important to note that the research findings obtained at the current state may not be fully generalizable to all populations or settings due to the differences in healthcare practices, antibiotic usage, and public health policies across countries. This limitation could impact the applicability of new interventions as recommended therapeutic strategies. In summary, the challenges mentioned above highlight the complexities involved in addressing AMR and the need for ongoing research and improved data collection methods to better understand and combat AMR, a rising global public health threat.

Author Contributions

AA and PB conceived this study. AA and PB were involved in the drafting and critical revision of the manuscript. Both authors have read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest. Abdelazeem Mohamed Algammal is serving as one of the Editorial Board members of this journal. We declare that Abdelazeem Mohamed Algammal had no involvement in the peer review of this article and has no access to information regarding its peer review. Payam Behzadi has no conflict of interest.

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