Antimicrobial-resistant *Acinetobacter*: Where do we go next?

Respected Editor,

The "Antibiotic Era," initiated with Fleming's 1928 penicillin discovery, is potentially nearing cessation due to bacterial resilience. The initial seemingly unbeatable success of antibiotics, the fruit of human ingenuity, has been countered by bacterial resistance mechanisms. Antimicrobial resistance (AMR), a "silent pandemic" continuing around the world, poses a serious threat to human health and development. Each year, AMR causes 7,00,000 deaths worldwide, and if no action is taken, it is estimated to kill 10 million people per year by 2050. Updated statistics from surveillance data illustrate the emergence of many genera of bacteria that are resistant to almost all classes of antibiotics. The genus *Acinetobacter*, a notorious nosocomial pathogen, also epitomizes this trend and displays resistance to almost all existing antibiotic classes. The escalating detection of extensively drug-resistant/multidrug-resistant *Acinetobacter* in hospital settings, particularly in intensive care units (ICUs), is a disconcerting reality warranting immediate attention.[1]

Acinetobacter baumannii (clinically most important species of the genus *Acinetobacter*) is a gram-negative coccobacillus ubiquitously found in hospital environments. It is an important opportunistic pathogen associated with severe nosocomial infections and causes approximately 10,00,000 cases per year worldwide. It belongs to the category of "ESKAPE" pathogens, which have the potential to exhibit high antibiotic resistance.[2] *A. baumannii* is implicated in a range of infections including pneumonia, bacteremia, meningitis, endocarditis, and surgical site infections, predominantly affecting immunocompromised patients or those undergoing invasive procedures. Over the last decade, due to a significant increase in mortality rate and its extensive resistance to a variety of antibiotic classes, the World Health Organization (WHO) classified it as a "critical-priority pathogens" for efficient drug development.[3] Therefore, "an old friend but new enemy": antibiotic-resistant *Acinetobacter* raised the question in our mind, "Where do we go next?"

Carbapenems are the cornerstone of treatment for *Acinetobacter* infections, with other antibiotics such as polymyxins, sulbactam, tigecycline, and aminoglycosides. However, the global emergence of carbapenem-resistant *A. baumannii* (CRAB) worsens the scenario. Colistin and tigecycline still remain effective against it, although resistance to colistin has been increasingly reported.[4] A new and promising treatment option for CRAB is sulbactam–durlobactam but recent evidence raises a number of questions related to its safety and efficacy, that need to be addressed in future research.[2] Microbiome restoration such as faecal microbiota transplantation (FMT) has been tested successfully for the treatment of a few bacterial infections such as *Clostridium difficile* and carbapenem-resistant *Klebsiella pneumonia*, although FMT for the management of *Acinetobacter* infections has not been studied in depth. The use of probiotics and synbiotics is gaining importance as a treatment option for *Acinetobacter* infections. Antimicrobial peptides (AMPs) may be another alternative to antibiotics. The interest in using bacteriophage therapy has reemerged for the treatment of *Acinetobacter* infections and recently developed gene-editing tools CRISPR-Cas9 also can be used to combat resistant strains of *Acinetobacter* species.[5] In response to the increasing concern related to this resistant bug, the most realistic and practical alternative strategy is to develop a vaccine. Several multivalent vaccines have been tested successfully in animal models but their effectiveness in humans still remains uncertain.[3] However, we are hopeful for the vaccine of *Acinetobacter* because of today's advancement in vaccine development. Very recently, on October 2023, the WHO approved a second malarial vaccine R21/Matrix-M for children, and pioneers of the mRNA COVID vaccine were awarded "The Nobel Prize in Medicine 2023."[6,7]

We would like to conclude by stating that the growing prevalence of antimicrobial-resistant *Acinetobacter* species in clinical settings is a "ticking time bomb" requiring new interventions to tackle catastrophic consequences in public health.

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Conflicts of interest

There are no conflicts of interest.

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