Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Rising antimicrobial resistance: an evolving epidemic in a pandemic

Published Online
July 1, 2021
https://doi.org/10.1016/
S2666-5247(21)00173-7

While the second wave of the COVID-19 pandemic is sweeping through India, causing unprecedented human tragedy, the prescription of a plethora of unnecessary antibiotics—without regard for the potential for increased antimicrobial resistance—is widespread and unchecked. In *The Lancet Microbe*, Clark Russell and colleagues[1] highlight the overuse of antimicrobials during the first wave of COVID-19 in the UK, despite the rare incidence of bacterial coinfections. This problem occurs to a greater magnitude in low-income and middle-income countries (LMICs). Antimicrobial resistance is a serious public health threat to progress achieved against infectious diseases, cancer therapy, organ transplant, and intensive care. Globally, drug-resistant infections caused due to antimicrobial resistance contribute to about 700 000 deaths annually, and without effective intervention are projected to cause 10 million deaths and a global economic loss of US$100 trillion by 2050.[2] Furthermore, the direct and indirect consequences of antimicrobial resistance are predicted to disproportionately affect LMICs in Asia and Africa.

India has one of the highest age-standardised infectious disease mortalities in south Asia, and the rates of antibiotic resistance are alarming. More than half of the *Klebsiella* spp isolates from hospital-acquired infections are resistant to carbapenems, with case fatality rates of around 50%.[3] A significant proportion of these are also resistant to polymyxins, with a case fatality rate of almost 70%.[4] Carbapenem-resistant *Acinetobacter baumannii* is the leading cause of ventilator-associated pneumonia in Indian intensive care units.[3]

Simultaneously, India leads the world in human antibiotic use, a prime driver of antimicrobial resistance, at 10·7 units per person.[5] Widespread resistance increases the use of broad-spectrum empiric antibiotic therapy, narrowing treatment options and worsening patient outcomes. Over-the-counter use of antibiotics, lack of awareness, inadequate use of diagnostics, overcrowding, cross-infections, financial compensation of doctors by pharmaceuticals, and poor health infrastructure also amplify India's antimicrobial resistance problem.

In response, the Indian Council of Medical Research established the Antimicrobial Resistance Surveillance Research Network to evaluate the burden of resistance among seven critical pathogens and initiate stewardship activities.[6] Since 2017, India has contributed to the Global Antimicrobial Resistance Surveillance System. Although surveillance is being addressed, the clinical management of drug-resistant infections remains undefined, resulting in the continued cycle of inappropriate prescribing and worsening resistance.

To address clinical research in drug-resistant infections in a collaborative fashion, initiatives such as the Antibacterial Resistance Leadership Group have been created.[7] Although these consortia have significantly progressed drug-resistant infection research through uniformity in data collection and reporting, Indian populations are often unrepresented. Furthermore, most Indian studies on drug-resistant infections are small scale, retrospective, single institutional, have significant biases, and tend to report limited surveillance data on molecular patterns of resistance.[8] Hence, the collaboration of governments, academia, and private sector stakeholders to address the paucity of clinical research in drug-resistant infections in India is vital.

More than 70% of the population use private healthcare services, and many urban private sector hospitals provide cancer therapy and transplants. The private sector is currently invisible in academically funded research; however, any attempt to answer questions in drug-resistant infections in India should involve it.

Drug-resistant infections complicate other health conditions and are not standalone problems;[9] hence, they are often not captured in standardised registries as the cause of mortality or morbidity. Because patients with drug-resistant infections are distributed across various specialities and departments, clinicians and scientists from across specialities should participate.

When bringing together institutions and hospitals from various sectors for large-scale studies, ethical clearances and regulatory approvals must be standardised. Evidence-based approaches in diagnosis and treatment of drug-resistant infections need to be emphasised within clinical settings. To increase clinical

use of data generated across centres, data need to be homogenised, shared, FAIR (findable, accessible, interoperable, and reusable), and focus on core clinical outcomes.[10] Collaborator autonomy, open data sharing, and logistics support are needed to accelerate and enable buy-in for clinical research.

Incorporating these principles to decrease the burden of antimicrobial resistance and improve outcomes of drug-resistant infections, we formed a cross-disciplinary coalition, which synergises with existing national and international initiatives, and has expertise in clinical management, laboratory capabilities, and research capacity. We envision the initiative, the Clinical Research Network for Drug-Resistant Infections (CENDRIC), where scientists and clinicians come together to use existing research capabilities, design and execute high-quality research in the diagnosis, treatment, risk-stratification, and prevention of relevant drug-resistant infections. The short-term, specific aim of this initiative is the identification of optimal management of serious carbapenem-resistant Gram-negative bacterial infections. CENDRIC will facilitate and empower the research agenda. We believe this will become a collaborative international platform for high-quality clinical research, harmonising with existing initiatives to decrease the burden of antimicrobial resistance and improve patient outcomes.

We declare no competing interests. The CENDRIC Investigators and Collaborators are listed in the appendix.

See Online for appendix

*Abi Manesh, *George M Varghese, on behalf of the CENDRIC Investigators and Collaborators*
georgemvarghese@hotmail.com

Department of Infectious Diseases, Christian Medical College, Vellore, Tamil Nadu 632004, India (AM, GMV)

1 Russell CD, Fairfield CJ, Drake TM, et al. Co-infections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre, prospective cohort study. *Lancet Microbe* 2021; published online June 2. https://doi.org/10.1016/S2666-5247(21)00090-2.

2 O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf (accessed June 23, 2021).

3 Hsu L-Y, Apisarnthanarak A, Khan E, Suwantarat N, Ghafur A, Tambyah PA. Carbapenem-resistant *Acinetobacter baumannii* and Enterobacteriaceae in south and southeast Asia. *J Clin Microbiol Rev* 2017; **30:** 1–22.

4 Kaur A, Gandra S, Gupta P, Mehta Y, Laxminarayan R, Sengupta S. Clinical outcome of dual colistin- and carbapenem-resistant *Klebsiella pneumoniae* bloodstream infections: a single-centre retrospective study of 75 cases in India. *Am J Infect Control* 2017; **45:** 1289–91.

5 Van Boeckel TP, Gandra S, Ashok A, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. *Lancet Infect Dis* 2014; **14:** 742–50.

6 Walia K, Madhumathi J, Veeraraghavan B, et al. Establishing antimicrobial resistance surveillance & research network in India: journey so far. *Indian J Med Res* 2019; **149:** 164–79.

7 Marimuthu K, Ng O-T, Bagdasarian N, Tambyah PA. The global challenge of carbapenemases and the critical need for more data. *Int J Infect Dis* 2019; **84:** 141–42.

8 Department of Biotechnology, Ministry of Science and Technology, Government of India. Scoping report on antimicrobial resistance in India. November 2017. 2017. http://dbtindia.gov.in/sites/default/files/ScopingreportonAntimicrobialresistanceinIndia.pdf (accessed June 23, 2021).

9 Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance—the need for global solutions. *Lancet Infect Dis* 2013; **13:** 1057–98.

10 Wilkinson MD, Dumontier M, Aalbersberg IJ, et al. The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data* 2016; **3:** 160018.