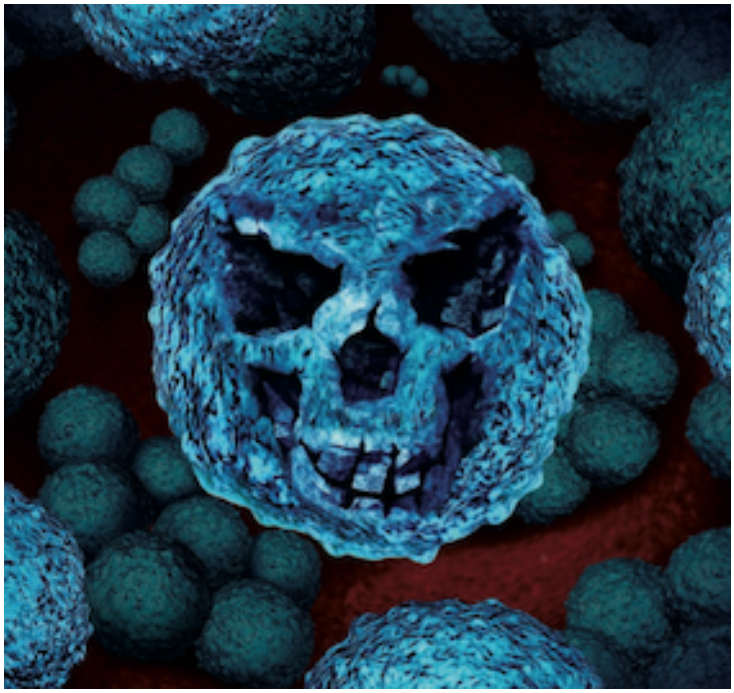
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Is AMR Modern-day Frankenstein's Monster?

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Antimicrobial Resistance (AMR) continues to pose a significant public health problem in terms of mortality and economic loss. The rising AMR is a matter of huge concern that needs to be tactfully handled and health authorities of several countries, including India, have formulated action plans for its containment. Significant efforts by the government, an active involvement of startups and diagnostic players is a good start. The question remains, whether this will be enough. Let's find out.



According to an Indian Council of Medical Research (ICMR) study, a big chunk of patients in India may no longer benefit from carbapenem, a powerful antibiotic administered mainly in ICU settings to treat pneumonia and septicemia, as they have developed antimicrobial resistance to it. This is alarming as Antimicrobial resistance (AMR) is on the rise in India and continues to pose a significant public health problem in terms of mortality and economic loss. The World Health Organisation (WHO) has declared that AMR is one of the top 10 global public health threats facing humanity.

Timely and accurate diagnosis through rapid tests can reduce the time to pathogen identification and facilitate faster, optimised antimicrobial treatment. Diagnostic players can play a major role when it comes to counter AMR. While there are diagnostic tests available to rapid detection of AMR in a hospital setting, there is a clear unmet need for a point of care (POC) diagnostic test to guide antibiotic prescriptions, in both urban and rural settings.

Current lab based tests such as Next-Generation Sequencing (NGS), Polymerase Chain Reaction (PCR), microbiology cultures and immunoassays that are used to determine the causative infectious agent are either time consuming, costly, or difficult to access. These may not be sufficient to quickly differentiate between bacterial and viral infections. In addition, strong AMR surveillance along with rapid diagnostics will help in finding the correct treatment fast.

While attending the 26th Maharashtra Chapter conference of the Indian Association of Medical Microbiologists in Pune, **Prof. Justin O'Grady, Professor of Medical Microbiology at the University of East Anglia in Norwich**, spoke about the rise in antimicrobial resistance (AMR) which could cause 10 million deaths per year by 2050 unless authorities take steps to prevent this.

"Microbial culture is the gold standard for the diagnosis of bacterial/fungal pathogens and AMR and takes 48 hours or longer. Hence, antibiotic prescriptions are empiric and patients often receive inappropriate treatment. Rapid tools are urgently required to guide appropriate antimicrobial therapy, thereby improving patient outcomes and slowing the development of AMR," feels Prof. O'Grady.

Drastic measures should be in place to prevent AMRs and proper diagnosis can make a difference in how treatment can be done. A report by Grand View Research states that the growth of the AMR diagnostics market is attributed to the increased risk of developing drug-resistant bacterial infections, the introduction of novel technologies, and increasing government initiatives to diagnose and reduce AMR infections. To address the global health challenge of AMR, government bodies such as the United States Food and Drug Administration (FDA) support the development of next-generation sequencing-based diagnostic tests to identify the right pathogen to help healthcare providers to treat infections more accurately. The Asia Pacific

is expected to grow at the fastest rate for AMR diagnostics.

Government in combat mode

India, one of the many developing countries of the world, is intending to be future ready through the National Patient Safety Implementation Programme and National Action Plan – AMR (2018-2025) to combat multi drug resistant organisms (MDRO). The Government of India has increased its focus on combating AMR through various national and state level programmes.

As a step in this direction ICMR has developed a real time online AMR data entry system for its network and will have AMR data analysis capacity. It is a user-friendly web-based informatics solution/suite for collection, storage and analysis of surveillance data. ICMR initiated Antimicrobial Resistance Surveillance and Research Network (AMRSN) a few years back that includes six Nodal Centers (NCs) for each pathogenic group and are located in four tertiary care medical institutions. There are 16 Regional Centers (RCs) in the network. 16 regional labs from tertiary care hospitals provide data across the country as RCs which are providing data on fixed number of isolates for each pathogenic group.

The NCs and RCs follow standard operating procedures (SOPs) of Bacteriology and Mycology formulated by ICMR to collect resistance data. The NCs focus on the identified resistant organisms and also exchange organisms amongst each other according to their expertise for in-depth molecular studies of the group of pathogens for which they are responsible.

“In developing countries, the major source of antibiotic contamination in surface water is improper disposal of effluents from industries, hospitals and domestic wastewater treatment plants. Industrial emissions of antibiotics can contribute to AMR. Awareness of AMR and monitoring of antibiotics from manufacturing needs to improve to address the issue of discharged antibiotics as significant contributors to AMR. Industry and government competence, policy and access to technical solutions can play a pivotal role in controlling the contribution of antibiotic manufacturing to AMR,” says **Dr Suman Kapur, Senior Professor, BITS Pilani, Hyderabad Campus**.

Dr Suman Kapur and her team have developed a platform called RightBiotic for rapid bacterial culture and antibiotic sensitivity test results in just four hours as opposed to two to four days and is suitable for both biological and environmental samples.

In addition to BITS Pilani, Hyderabad Campus, the Centre for Cellular and Molecular Platforms (C-CAMP), an initiative supported by the Department of Biotechnology, Government of India, has a key focus area on AMR. Bangalore-based C-CAMP has funded, incubated and mentored many innovative startups in this domain. C-CAMP is also part of the CARB-X Global Accelerator Network. CARB-X is one of the largest not-for-profit partnerships, dedicated to accelerating the early development of antibacterial products. C-CAMP, in association with CARB-X, conducts an AMR Quest annually, to identify and support promising innovations that can combat AMR. The three month AMR Accelerator Programme that follows the AMR Quest, supports innovators, startups and SMEs to validate and fast-track their solutions to the market.

C-CAMP’s AMR portfolio in diagnostics includes Achira Labs that has developed Bug Check, a rapid molecular diagnostics platform for identification of microbial species and antimicrobial resistance genes in urinary tract infections (UTI); Module Innovations, which is developing Antimicrobial Susceptibility Testing (AST) assays for UTI that has a rapid turnaround time of less than two hours, and WeInnovate Biosolutions’ RAPID, is a device for fast and affordable solution for AST of various pathogens.

The C-CAMP expects to see many exciting innovations reaching the market to create wider impact at scale. This can be further boosted by a collective effort among stakeholders, including product developers, policy makers, regulatory bodies, and health organisations. Concerted efforts can bring in the required policies for quality systems, supply-chain, incentivising the healthcare system, etc., for the deployment of these new-age diagnostics.

The AST determines the most effective antibiotic treatment for bacterial infection. Antimicrobial stewardship is advocated for the rational use of antibiotics to preserve their efficacy in the long term. Rapid diagnostic tests can play a pivotal role in

efficient and timely treatment. Many startups have been working in this area and have developed devices / tests related to AMR.

Gizmos from startups

Papyrus Diagnostics has developed Papyrus UTI AST, a paper-based device that can determine AMR in urinary tract infections. The device is designed to be used at the doctor's clinic and has the capability to test the response of the infection-causing organism to at least six antibiotics. The device is designed to give a colorimetric signal to report whether the organism is sensitive or resistant to each antibiotic. This device will enable the clinician to prescribe antibiotics that are already proven to work on the infection-causing organism, and prevent empirical prescription of antibiotics.

“Given the historic indiscriminate use of antibiotics in India, the burden of AMR in India is very high. Therefore, funding agencies as well as diagnostic companies are currently very keen on developing solutions for the diagnosis of antimicrobial resistance. CARB-X, an international AMR innovations accelerator, is now working closely with Bengaluru-based C-CAMP to scout for innovations in AMR diagnostics. The AMR diagnostics market in India is expected to grow rapidly in the coming years,” says **Dr Bhushan J Toley, Co-Founder, Papyrus Diagnostics**.

Other players in this field include Bengaluru-based Spotsense headed by Amrita Sukrity, is fast developing a test for diagnosing sepsis in newborns followed by Pune-based startup Module Innovations, that is building innovative solutions for infectious diseases and AMR. It is revolutionising the UTI management and treatment clinical pathway with solutions that work at all levels of healthcare settings. Bengaluru-based Achira has developed and commercialised innovative technologies for POC medical testing.

It may be noted that the Foundation for Neglected Disease Research (FNDR) is working on developing a POC test that can differentiate between viral and bacterial infections based on a combination of host and pathogen biomarkers that are found in the patients’ blood. The biomarkers are validated in the preclinical setting and have completed an initial proof of concept clinical study in patients with fever of unknown origin. FNDR is also working on a device that eliminates antibiotics from wastewater, thereby helping reduce AMR in the environment (can share more information if needed). Both of these projects have been funded by Biotechnology Industry Research Assistance Council (BIRAC).

Shridhar Narayanan, CEO, FNDR, says, “An affordable rapid POC that can determine whether the infection is bacterial or viral, and the drug resistance profile of the infection, will be essential. The goal is that the right drugs be administered in a timely manner. The currently available technologies will continue to evolve to become quicker and accurate, and will be guided by technologies like artificial intelligence/machine learning.”

Market potential

Looking at the growth of the POC market in India, a leading pharma player such as Cipla is showing keen interest in this area and started making investments in. Cipla has acquired 21.05 per cent stake (on a fully diluted basis) for Rs 25 crore in Achira Labs. The pharma major said that this investment will facilitate a Cipla entity’s strategic participation in the POC diagnostics and AMR space through the design, development, and manufacturing of microfluidics-based technologies.
Achin Gupta, CEO, One India Business, Cipla said, “This investment will further our commitment of bringing innovative, affordable and quality diagnostic solutions for all. We are guided by our purpose of caring for life and will continue to make strategic investments to ensure access to POC test kit solutions.”

Besides making investments in startups focussing on POC, creating awareness and providing education to the healthcare professionals has become an integral part of the healthcare system. In this regard Pfizer India and Americares India Foundation announced the launch of OPEN-AMR, an Online Platform for Education among Nurses on Antimicrobial Resistance. Americares India Foundation, a health-focused relief and development organisation, has joined as the execution partner.

Speaking about the market potential Manish **Dattatraya Karekar, Chief Operating Officer - Lab Operations, Krsnaa Diagnostics** says, “With rising incidences of AMR, treatment based on evidence-based medicine, greater acceptance of health insurance, availability of sensitive value for money diagnostics, shall all result in increase in adoption and starting of antimicrobial (resistance) tests in tier III and smaller cities.”

Sharing his views on AMR tests, **Dr Vishal Wadhwa, Head Scientific Affairs, Metropolis Healthcare**, says “Health will come at a cost and when a doctor prescribes a diagnostic test patients should undertake it. Information coming out of laboratory tests is needed to supplement and complement the clinical inputs for treatment. Labs entrusted with testing samples for infectious agents and reporting AMR should follow international standards of testing.”

Diagnostic tests can help doctors wield antimicrobial treatments more effectively. It can play a key role in community and primary care settings to lower unnecessary antibiotic prescribing, particularly in respiratory tract infections, and protect the healthcare system in the decades to come. Policy and frontline challenges need to be looked into and then only AMR can be eradicated by using proper diagnostic measures. Public private partnership in this regard is going to make a positive impact in combating AMR in the long run.

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