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ANTIMICROBIAL RESISTANCE AS A GLOBAL CONCERN

[1]Swetha S Babu, [2]Dr. Noha Laj, [3]Abhinsha Z, [4]Dr. Raishy R Hussain

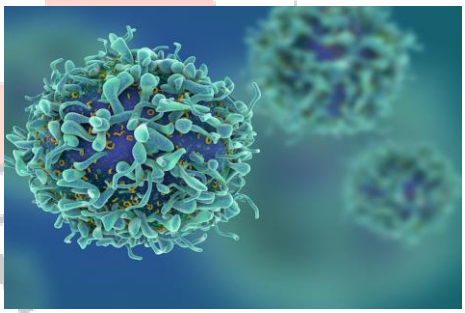
[1]B.Sc Student, [2,4]Associate Professor, [3]M.Sc Student,
[1]Department of Biochemistry and Industrial Microbiology,
[1]A J College of Science and Technology, Trivandrum, Kerala, INDIA

Abstract: Antimicrobial resistance (AMR) has emerged as one of the 21st century's key public health issues, challenging the successful prevention and treatment of an ever-increasing number of infections caused by bacteria, parasites, viruses and fungi that are no longer susceptible to the common medicines used to treat them. Concerning antibiotic resistance in bacteria, the issue of AMR is extremely urgent. Bacteria causing common or serious infections have established resistance to each new antibiotic coming on the market over many decades, to varying degrees. The need for action to avert a developing global health care crisis is imperative in the face of this reality.

Index Terms **- AMR, global concern, TB, malaria, *Staphylococcus aureus***

I. INTRODUCTION

Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. AMR is an increasingly serious threat to global public health that requires action across all government sectors and society. Without effective antibiotics, the success of major surgery and cancer chemotherapy would be compromised. The cost of health care for patients with resistant infections is higher than care for patients with non-resistant infections due to longer duration of illness, additional tests and use of more expensive drugs. In 2016, 490 000 people developed multi-drug resistant TB globally, and drug resistance is starting to complicate the fight against HIV and malaria, as well. Antimicrobial tolerance occurs when microorganisms (such as bacteria, fungi, viruses, and parasites) alter when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics). Microorganisms that establish antimicrobial resistance are often referred to as "superbugs". As a consequence, the medications become ineffective and diseases in the body remain, raising the risk of spreading to others.



Courtesy:
https://scandiononcology.com/news/eu-publication-on-scanresist-project/

II. WHAT ACCELERATES THE EMERGENCE AND SPREAD OF ANTIMICROBIAL RESISTANCE?

Antimicrobial tolerance, typically by genetic variations, develops gradually over time. However, this process is being accelerated by the misuse and overuse of antimicrobials. In many areas, in people and animals, antibiotics are overused and misused, and sometimes provided without clinical supervision. Examples of misuse include when people with viral infections such as colds and flu are taken and when they are given as growth promoters in animals or used in healthy animals to prevent diseases.

In humans, livestock, food, and the atmosphere (in water, soil and air), antimicrobial resistant microbes are present. They can spread from person to person, including from food of animal origin and from person to person, between people and animals. The spread of antimicrobial resistance is facilitated by ineffective infection control, insufficient sanitary conditions and improper food handling.

Patients with drug resistant bacteria infections are at higher risk of worse clinical conditions and death and use more health care services than patients with the same bacteria infected with non-resistant strains.

III. RESISTANCE IN *KLEBSIELLA PNEUMONIAE*

Common intestinal bacteria that can cause life threatening infections to a last resort treatment (carbapenem antibiotics) has spread to all regions of the world. *K. pneumoniae* is a major cause of hospital acquired infections such as pneumonia, bloodstream infections, and infections in newborns and intensive care unit patients. In some countries, because of resistance, carbapenem antibiotics do not work in more than half of people treated for *K. pneumoniae* infections.

IV. RESISTANCE IN *E. COLI*

To one of the most widely used medicines for the treatment of urinary tract infections (fluoroquinolone antibiotics) is very widespread. There are countries in many parts of the world where this treatment is now ineffective in more than half of patients.

Treatment failure to the last resort of medicine for gonorrhoea (third generation cephalosporin antibiotics) has been confirmed in at least 10 countries (Australia, Austria, Canada, France, Japan, Norway, Slovenia, South Africa, Sweden and the United Kingdom of Great Britain and Northern Ireland).

The treatment recommendations for gonorrhoea have recently been revised by WHO to counter emerging resistance. Due to widespread high resistance levels, the current WHO recommendations do not prescribe quinolones (a class of antibiotic) for the treatment of gonorrhoea. In addition, treatment recommendations for chlamydia and syphilis infections have also been revised.

V. RESISTANCE TO FIRST-LINE DRUGS

To treat infections caused by *Staphylococcus aureus* a common cause of severe infections in health facilities and the community is widespread. People with MRSA (methicillin-resistant *Staphylococcus aureus*) are estimated to be 64% more likely to die than people with a non-resistant form of the infection.

Colistin is the last line medication for life threatening, carbapenem resistant Enterobacteaceae induced infections. In multiple countries and regions, resistance to colistin has recently been observed, rendering infections caused by such bacteria untreatable.

Courtesy: https://www.biomerieuxconnection.com/2018/07/12/explain-antimicrobial-resistance-friends-family-infographics/

VI. RESISTANCE IN TUBERCULOSIS (TB)

WHO estimates that, in 2014, there were about 480 000 new cases of multidrug-resistant tuberculosis (MDR-TB), a form of tuberculosis that is resistant to the 2 most powerful anti-TB drugs. Only about a quarter of these (123 000 cases) were detected and reported. MDR-TB requires treatment courses that are much longer and less effective than those for non-resistant TB. Globally, only half of MDR-TB patients were successfully treated in 2014. Among new TB cases in 2014, an estimated 3.3% were multidrug-resistant. The proportion is higher among people previously treated for TB, at 20%. In 105 countries, extensively drug-resistant tuberculosis (XDR-TB), a form of tuberculosis resistant to at least four of the core anti-TB drugs, has been reported. 9.7 per cent of people with MDR-TB are estimated to have XDR-TB.

VII. RESISTANCE IN MALARIA

As of July 2016, in five countries of the Greater Mekong sub region (Cambodia, the Democratic People's Republic of Lao, Myanmar, Thailand and Viet Nam), resistance to first-line treatment of P. falciparum malaria (artemisinin-based combination therapies, also known as ACTs) was verified. Patients with artemisinin-resistant infections recover completely after treatment in most areas, provided they are treated with an ACT containing an appropriate partner medication. However, P. falciparum has been immune to nearly all available antimalarial medicines along the Cambodia-Thailand border, making treatment more difficult and requiring close monitoring. There is a real risk that multidrug resistance will soon emerge in other parts of the sub region as well. The spread of resistant strains to other parts of the world could pose a major public health challenge and jeopardize important recent gains in malaria control.

VIII. RESISTANCE IN HIV

In 2010, an estimated 7 percent of people in developing countries who started antiretroviral therapy (ART) had drug-resistant HIV. The same figure was 10-20 percent in developing countries. Some nations have recently recorded levels among those beginning HIV treatment at or above 15 percent, and up to 40 percent among people re-starting treatment. This requires urgent attention.

As second and third-line regimes are three times and 18 times more costly, respectively, than first-line medications, rising levels of resistance have significant economic consequences.

Since September 2015, the WHO has recommended that antiretroviral treatment be initiated for anyone living with HIV. In all regions of the world, greater use of ART is expected to further increase ART resistance. In order to optimize the long-term efficacy of first-line ART regimens and to ensure that people are getting the most efficient regimen, it is important that resistance tracking continues and that its further growth and spread is minimized. In consultation with countries, partners and stakeholders, WHO is currently developing a new "Global Action Plan for HIV Drug Resistance (2017-2021)".

IX. RESISTANCE IN INFLUENZA

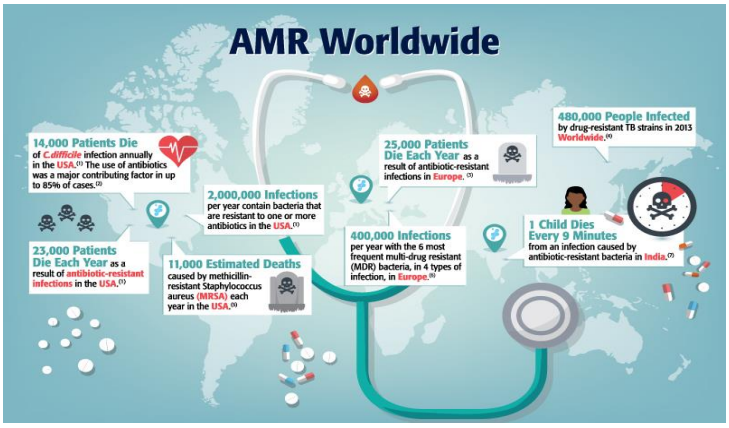
For the treatment of epidemics and pandemic influenza, antiviral drugs are essential. To date, one class of antiviral drugs, M2 inhibitors (amantadine and rimantadine), has been immune to nearly all influenza A viruses circulating in humans. The level of resistance to oseltamivir, a neuraminidase inhibitor, remains low (1-2%), however. Through the WHO Global Influenza Surveillance and Response Framework, antiviral susceptibility is continuously monitored.

X. NEED FOR COORDINATED ACTION

Antimicrobial resistance is a complex issue that affects all of society and is motivated by multiple factors that are interconnected. There is minimal influence of discrete, independent interventions. Coordinated action is required to minimize the emergence and spread of antimicrobial resistance.

All countries need national action plans on AMR.

Greater innovation and investment are required in research development of new antimicrobial medicines, vaccines, and diagnostic tools.



Courtesy: https://www.biomerieuxconnection.com/2018/07/12/explain-antimicrobial-resistance-friends-family-infographics/

and

XI. STAPHYLOCOCCUS AUREUS

S. aureus is a Gram-positive bacterium that forms part of the normal anterior nar flora, but is one of the most common causes in almost all geographic areas of nosocomial and community-acquired Blood Stream infections, skin and soft tissue infections (SSTIs) and pneumonia. Strains belonging to antistaphylococcal penicillin resistant aureus is called MRSA. In the 1960s, the first strains of MRSA developed and spread in subsequent years, in conjunction with an increase in the number of elderly and immunocompromised patients. MRSA may cause serious infections such as bloodstream infections, sepsis, pneumonia, and surgical site infections in the healthcare environment.

Hospital acquired MRSA (HA-MRSA) infections are associated with insertion of medical devices such as central vein catheters, with haemodialysis, or with surgical procedures such as joint replacement. MRSA has recently become a common cause of community based infections (CA-MRSA) that affect children and young people with no underlying diseases. Community acquisition In particular, MRSA can infect individuals in activities that cause skin damage and near contacts or crowding (athletes, military personnel, prisoners, etc.). While most CA-MRSA infections involve the skin, some symptoms (necrotic pneumonia, fasciitis) can be very serious. Methicillin proof *S. Aureus* infections need less effective, more costly, and close monitoring of second-line antibacterials, such as vancomycin, to prevent adverse side effects. New treatment options for MRSA are also costly and not free of side effects, such as linezolid and daptomycin.

XII. NON-TYPHOIDAL SALMONELLA (NTS)

Salmonellosis is one of the most common and widely spread foodborne diseases of the genus Salmonella and is caused by bacteria. NTS is an infection caused by all *Salmonella enterica* serotypes, with the exception of the Typhi and *Paratyphi serovars*, which are more invasive and are associated with enteric fever.

About 1500 NTS serotypes are present, the most prevalent being *S. Typhimurium*, *Enteritidis* and *S. Heidelberg*, where domestic and wild animals (including birds and amphibians) can be found worldwide. The incidence of NTS infection has risen dramatically in recent years; a report on the global burden of NTS reported that there are 94 million cases of NTS gastroenteritis per year, resulting in 155,000 deaths worldwide.36 The South-East Asian region accounts for the majority of the disease burden.

As for all zoonotic pathogens, also for NTS, the widespread use of antimicrobial agents in food animal production for growth promotion, prophylaxis or treatment purposes has contributed to the spread of antibiotic resistance. There is regular multidrug resistance in NTS to various widely used antimicrobial agents (ampicillin, chloramphenicol, sulphonamides and tetracycline). Compared to infections caused by susceptible strains, multidrug resistance has been associated with a higher risk of invasive infection, a higher prevalence and length of hospitalization and an increased risk of death. In addition, from 2000, several studies have shown a decreased susceptibility to fluoroquinolones, drugs of choice for treatment of invasive gastrointestinal infections, in many parts of the world.

XIII. KLEBSIELLA PNEUMONIAE

K. pneumoniae causes infections (bloodstream infections, infections of the urinary and respiratory tract) that are especially prevalent in vulnerable people in hospitals, such as preterm babies, elderly people and patients with compromised immune systems. In intensive care units and hospitals for neonatal care, *K. Pneumoniae*, which contributes to nosocomial outbreaks, can spread easily among patients.

In recent years, the number of multidrug-resistant *K. pneumoniae* has risen rapidly. Resistance mediated by extended spectrum beta-lactamases (ESBLs) includes all penicillins, cephalosporins (including third-generation cephalosporins) and aztreonam. Recent studies showed a prevalence of ESBL-producing *K. pneumoniae* of 38.9% in Europe, 8.8% in the USA and 21.5% in the Asia-Pacific region. WHO reported that third-generation cephalosporins resistance in *K. pneumoniae* was higher than 30% worldwide and higher than 60% in some countries. This high proportion of cephalosporin resistance means that treatment for severe *K. pneumoniae* infections have to rely on carbapenems.

XIV. CONCLUSION

Antimicrobial resistance is now recognized by the scientific community, the society at large and most policy-makers as an important problem to confront. The WHO Global Surveillance Study on AMR, which offers a global image of the magnitude of AMR for the first time, also shows the lack of adequate surveillance in many parts of the globe and wide gaps in knowledge on microbes of significant public health significance that prevent an accurate analysis of the real situation and trends over time.
Strengthening and harmonizing AMR surveillance is crucial through the implementation of accepted epidemiological and microbiological approaches, the adoption of common concepts to boost the capacity to exchange and compare information on resistance, and better coordination of surveillance networks.

With this aim, the WHO regional office for Europe (EURO) supports a new project (CAESAR-Central Asian and Eastern European Surveillance of Antimicrobial Resistance) to develop a network of national surveillance systems in the countries of the region that are not part of the EU and do not participate to EARS-Net, facilitating comparison of data throughout the entire European region. Different but coordinated strategies against AMR should be implemented, considering the type of pathogen (human or zoonotic), the setting in which it spreads (hospital or the community) and possible other specific factors contributing to the emergence of resistance.

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