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ANTIMICROBIAL RESISTANCE: SILENT PANDEMIC OF MODERN ERA

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ABSTRACT

Antimicrobial resistance (AMR) is a growing global public health threat. AMR occurs when microorganisms such as bacteria, viruses, fungi and parasites become resistant to the antimicrobials deigned to kill them become less effective. Antimicrobial resistance develop naturally or with multiple use of the drug. With rampant use of antibiotics for minor infection like viral infections antimicrobial resistance is gaining importance and if left uncontrolled will be responsible for miilions of death in the coming years. Multidrug resistant organisms such as Methicillin resistant staphylococcus aureus, extended spectrum beta lactamases and carbapenem resistant organisms pose significant therapeutic challenges. To decrease AMR Antibiotic stewardship programs and infection control programmes are held in the hospitals and the clinicians are advised to rationally prescribe the antibiotics

Keywords*: Natural resistance, Acquired resistance, Antibiotic stewardship programme*

INTRODUCTION

Antimicrobial resistance (AMR) is one of the major health concerns in this century.[1] Antimicrobial resistance (AMR) is when microorganisms — such as bacteria, viruses, fungi, and parasites — evolve so that the medicines designed to kill them (antibiotics, antivirals, antifungals, antiparasitics) become less effective or stop working. AMR happens when microbes adapt in response to exposure to antimicrobial drugs. Over time, they survive treatment and continue to multiply, leading to infections that are harder to treat. The WHO calls AMR one of the top 10 global public health threats. Projections estimate millions of potential deaths per year by 2050 if resistance trends continue.[2]

Antibiotic resistance is a natural phenomenon that occurs when microorganisms are exposed to antibiotic drugs. Under the selective pressure of antibiotics, susceptible bacteria are killed or inhibited, while bacteria that are naturally (or intrinsically) resistant or that have acquired antibiotic-resistant traits have a greater chance to survive and multiply. Not only the overuse of antibiotics but also the inappropriate use (inappropriate choices, inadequate dosing, poor adherence to treatment guidelines) contribute to the increase of antibiotic resistance.[3]

It is a silent pandemic of the modern era and if proper precautions are not taken to control the resistance, by 2050 AMR could potentially supersede all other causes of mortality worldwide.[2] Globally, estimates indicate that by 2019 there were 1.2 million deaths and these would escalate to approximately 10 million deaths annually by 2050 if measures are not implemented to decrease AMR.[4]

The history of AMR traces back to the discovery of penicillin in 1928 by Alexander Fleming[5] and there was mass production and utilization of antibiotics in the 1940 s. However, resistant organisms emerged almost immediately thereafter. The first cases of penicillin-resistant Staphylococcus aureus were reported in 1942[6], along with tetracycline resistance by 1953[7]. The widespread agricultural use of antibiotics in the 1950–60s also accelerated resistance. The MRSA was reported in 1961, followed by resistance to multiple antibiotic classes[8,9]. The 1980s saw a global epidemic of MDR tuberculosis[10]. In the 1990s, gram-negative pathogens such as Escherichia coli and Klebsiella pneumonia developed ESBL resistance.[11]

AMR is dangerous because common infections become difficult or impossible to treat. Medical procedures like surgeries, chemotherapy, and organ transplants become riskier and leads to longer illness durations, higher medical costs, and increased mortality.

MECHANISM OF RESISTANCE

Microbes develop resistance to the antimicrobials either innate or by multiple intake of the drug through various mechanisms:[12-17]

- Genetic mutations — natural changes in their DNA.
- Gene transfer — bacteria can pass resistance genes to one another by conjugation, transformation and transduction.
- Efflux mechanism – Energy dependent pumps expel antibiotics from the cell. Common with Tetracyclines, FQs and macrolides
- Enzymatic Inactivation of drugs- Bacteria produce enzymes that destroy or modify antibiotics. Beta lactamases that hydrolyse penicillins and cephalosporins. ESBL, Carbapenemases
- Enzymatic modifications
- Alteration of Target Site ie drug's binding site. Eg. Altered Penicillin binding proteins is resp. for beta lactam resistance in MRSA. Modified ribosomal subunits is responsible for macrolide and tetracycline resistance
- Limiting entry by decreasing antibiotic entry into the bacterial cell by loss or alteration of porin channels in Gram negative bacteria
- Alteration of metabolic pathways: Bacteria use alternative metabolic pathway. Resistance to sulphonamide via altered folate synthesis. Eg Trimethoprim and sulphamethoxazole.
- Biofilm formation: Bacteria in biofilms are protected from antibiotics by reduced penetration eg Catheter associated infection commonly by S epidermidis. Seen in device associated infection

Examples of microorganisms prone to resistance:

- MRSA (Methicillin-resistant Staphylococcus aureus)
- Drug-resistant mycobacterium tuberculosis
- Ciprofloxacin-resistant E. coli
- Carbapenem resistant Enterobacteriaceae ie Klebsiella, E.Coli
- Carbapenem resistant Acinetobacter Baumanii
- Carbapenem resistant Pseudomonas Aeroginosa
- Vancomycin resistant enterococci
- MDR Neisseria Gonorrhoea
- Fluconazole resistant Candida and Fungi
- HIV and Influenza resistant to antivirals

Major causes leading to AMR

1. Innapropriate use of antibiotic: Overuse or misuse of antibiotics (e.g., taking them for viral illnesses), wrong drug selection and incorrect dose or duration.
2. Poor patient compliance: Incomplete antibiotic courses, skipping doses and selfmedication without prescription.
3. Over the counter availability – easy access to antibiotics without medical supervision
4. Use of antibiotics in livestock and agriculture – Growth promotion in poultry and livestock and transmission of resistant organisms in humans via food chain. The excessive and improper utilization of antibiotics in agricultural practices, and veterinary medicine, has increased the emergence of drug-resistant strains of microorganisms. The excessive dependence on antibiotics has resulted in the emergence of antibiotic-resistant bacteria, commonly known as superbugs, which pose significant challenges in treatment efficacy and can lead to severe infections.[18]
5. Poor infection control in hospitals also is one of the leading cause of AMR. Inadequate hand hygiene, improper sterilization of instruments and overcrowding in healthcare settings are the causes of AMRs.
6. Lack of clean water and sanitation in some regions.
7. Biofilm formation: Reduces antibiotic pentration. Seen in device associated infection
8. Lack of rapid diagnostics leads to empirical broad spectrum therapy and delay in culture guided treatment
9. Use of substandard and counterfeit drugs leading to low antibiotic concentration and survival of resistant bacteria.

Anti microbial resistance can be prevented by

- Using antibiotics only when prescribed by a certified healthcare provider.
- Avoiding self-medication.
- Good hygiene and vaccination.
- Responsible use of antimicrobials in agriculture.

Various ways to decrease antimicrobial resistance:

- HOSPITAL LEVEL STRATEGIES:
  1. Antimicrobial Stewardship Programme: A good antimicrobial stewardship programmes includes formulary restrictions (only specific antibiotics allowed), preauthorization for higher antibiotics ie carbapenems and colistin. Prospective audit and feedback by physicians. Daily review of antibiotic prescriptions. Dose optimization based on pharmacokinetic and pharmacodynamic based dosing and renal dose adjustments. prescribing only when necessary and appropriate dosage. Policies to switch from intravenous to oral therapy equipment. Advantage of antimicrobial stewardship programme is it preserves antibiotic effectiveness and reduces resistance. [19]

  2. Infection Prevention and Control: Strict hand hygiene, use of personal protective equipment. Isolating or cohorting of MDR patients, Environmental Disinfection and proper sterilization of instruments. Surveillance is done by Hospital antibiogram every 6-12 months for monitoring rates of MRSA, VRE, ESBL, CRE etc.[20]

- CLINICIAN LEVEL MEASURES
  1. Rational Antibiotic Prescribing: Do not give antibiotics for viral infections, Always take culture/sensitivity before starting antibiotics, choose narrow spectrum antibiotic whenever possible, use correct dose, route, duration. Apply de-escalation once culture results are available.
  2. Avoid empirical overuse: Follow local treatment guidelines. Don't treat asymptomatic bacteruria
- PATIENT/COMMUNITY LEVEL MEASURES
  1. Public Awareness Programmes: Do not demand antibiotic for cold, flu and sorethroat. Do not self medicate and do not buy antibiotic OTC.
  2. Adherence: Complete the full antibiotic course. Do not share left over antibiotic and do not stock antibiotic at home.
  3. Vaccination: Influenza, Pneumococcal, Typhoid and Hib reduce infections and antibiotic use.
  4. HYGEINE: Clean water, Proper sanitation, handwashing and avoid misuse of antibiotics in animals.
- POLICY and GOVERNMENT MEASURES
  1. Strong regulation against OTC sale of antibiotics
  2. Ban on misuse in poultry/fish farming
  3. Mandatory ASP in hospitals
  4. Public reporting of AMR trends
  5. National AMR action plans.
- IN AGRICULTURE AND VETERINARY USE:
  Stop using antibiotic as growth promoters in animals and use only veterinary approved antibiotics.
  OTHER MEASURES TO REDUCE AMR
  1. Development of New Antibiotics: Research and development of novel antibiotics targeting new bacterial mechanisms. Addresses resistance to existing drugs. High cost, lengthy development process, potential for cross-resistance.
  2. Combination Therapies: Using multiple antibiotics with different mechanisms of action to treat infections. Synergy can enhance effectiveness, reduce resistance. Complex dosing regimens, increased risk of side effects, potential for antagonism.
  3. Phage Therapy: Using bacteriophages (viruses that infect bacteria) to target specific bacterial strains. Highly targeted approach, can be rapidly adapted. Limited knowledge of phage-bacteria interactions, regulatory challenges, variable effectiveness.
  4. Probiotics and Prebiotics: Promoting the growth of beneficial bacteria to remove the harmful strains. Supports healthy microbiota, reduces space for pathogens. Limited knowledge of optimal strains, challenges in colonization and persistence.
  5. Immunotherapy Enhancing the body's immune response to fight infections. Diverse targets, potential for long-lasting protection. Specific to certain infections, risk of autoimmunity, complex development.
  6. Repurposing Existing Drugs: Identifying nonantibiotic drugs with antimicrobial properties. Faster development, potentially lower costs. Limited candidates, potential for off target effects, dose optimization required.
  7. Alternatives to Antibiotics: Developing nonantibiotic treatments, like antimicrobial peptides, bacteriocins, or metal nanoparticles. Reduced risk of resistance, diverse mechanisms. Limited clinical data, potential for toxicity, delivery challenges.
  8. Education and Public Awareness: Promoting proper hygiene, antibiotic use, and understanding of resistance. Reduces unnecessary antibiotic demand and misuse. Behaviour change is gradual, hard to measure impact, requires ongoing efforts.
  9. Surveillance Systems: Monitoring and tracking resistance patterns to inform treatment guidelines. Provides real time data, guides treatment decisions. Resource intensive, challenges in data sharing and harmonization.

10. Environmental Regulations: Reducing antibiotic use in agriculture and industry to limit resistance spread. Mitigates selection pressure for resistance. Regulatory enforcement, global coordination, economic implications. Stop
11. One Health Approach: Coordinating efforts across human, animal, and environmental health to tackle resistance. Addresses complex sources of resistance spread. Requires interdisciplinary collaboration, challenges in communication and policy alignment.

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