WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Antibiotic Resistance: Current Trends and Strategies

***Mr.Sudhanshu Shingare*[*1] , *Dr.L..D.Hingane*[*2]**

[*1] Student of Aditya pharmacy college, beed

[*2] Principal of Aditya pharmacy college, beed

University – Dr. Babasaheb Ambedkar Marathwada University

ABSTRACT :

Antibiotic resistance is a pressing global issue, with the misuse and overuse of antimicrobials in humans, animals, and plants driving the development of drug-resistant pathogens. This resistance affects countries at all income levels and threatens modern medicine, making infections harder to treat and increasing the risks of other medical procedures. The world faces an antibiotics pipeline and access crisis, with an inadequate research and development pipeline and urgent needs for equitable access to new and existing vaccines, diagnostics, and medicines. Priorities to address AMR in human health include preventing infections, ensuring universal access to quality diagnosis and appropriate treatment, and strategic information and innovation. Antibiotic resistance can arise from mutations in the pre-existing genome of a bacterium and from the uptake of foreign resistance factors. The environment plays a significant role in the evolution of resistance and as a route for the transfer of bacteria and genes between humans, animals, and the environment. Studies of resistance in the environment could provide a reflection of the regional clinical resistance, complementing traditional surveillance. Strategies to reduce risks should focus on challenges in low- and middle-income countries and emissions from antibiotic manufacturing.

KEYWORDS:- Antibiotic resistance , Antibiotic stewardship , Future challenges and solutions

INTRODUCTION :

Antibiotic resistance is a growing public health crisis that threatens the effectiveness of antibiotics, which have been instrumental in treating and preventing infections in humans, animals, and plants. The misuse and overuse of antibiotics, as well as a lack of new drug development, have contributed to the rapid emergence of resistant bacteria, making bacterial infections difficult or impossible to treat. This issue is further exacerbated by poverty and inequality, particularly in low- and middle-income countries, where the consequences of antibiotic resistance are more severe.

The World Health Organization has identified antibiotic resistance as one of the top global public health threats, with bacterial resistance directly responsible for 1.27 million global deaths in 2019 and contributing to nearly 5 million deaths in the same year.The economic costs of antibiotic resistance are also significant, with estimates suggesting that it could result in US$ 1 trillion additional healthcare costs by 2050, and US$ 1 trillion to US$ 3.4 trillion gross domestic product (GDP) losses per year by 2030.

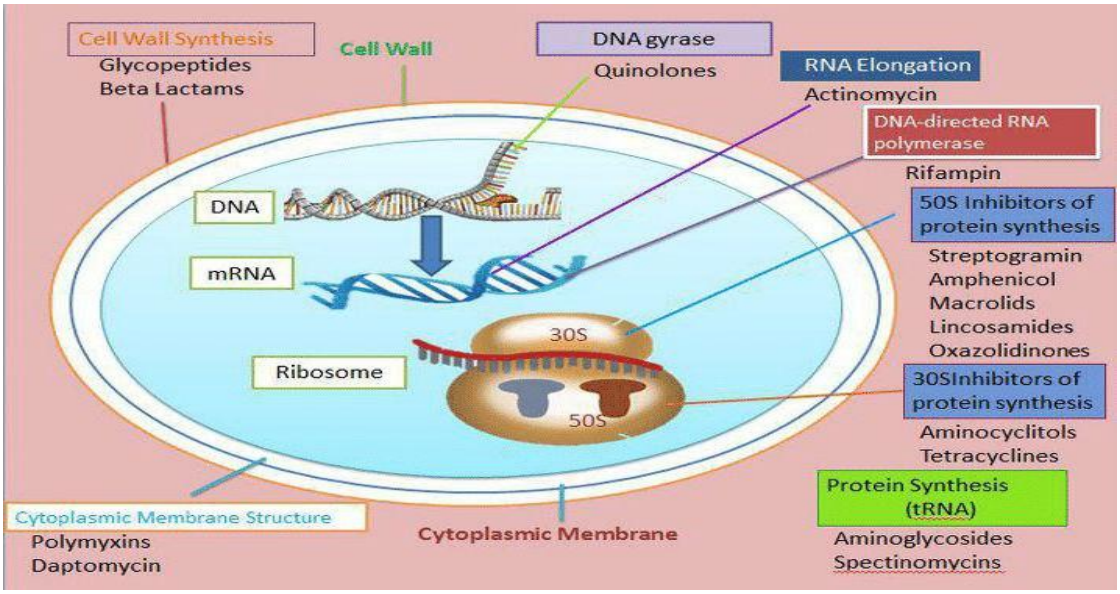
To address this crisis, it is crucial to understand the mechanisms and drivers of antimicrobial resistance, as well as to develop and implement strategies to manage the crisis and discover new agents for the treatment of bacterial infections. This article will explore the current trends and strategies in combating antibiotic resistance, including surveillance and monitoring, prevention and control measures, research and development of new antibiotics, and the promotion of responsible use of antibiotics in human and animal health.

Mechanism of action of antibiotics :

Antibiotics are chemical substances that are used to treat bacterial infections. They work by targeting specific mechanisms in bacteria that are essential for their growth and survival. The mechanism of action of antibiotics can be broadly classified into the following categories:

1. **Antibiotics inhibiting cell wall synthesis**:-Antibiotics that inhibit cell wall synthesis are a class of antibiotics that target the peptidoglycan layer in bacterial cell walls. Peptidoglycan is a polymer made up of sugars and amino acids that provides structural support to bacterial cells and protects them from osmotic lysis. Inhibiting the synthesis of peptidoglycan weakens the cell wall, making the bacteria more susceptible to lysis and death.
2. **Antibiotics that affect cell membrane**:-Antibiotics that affect cell membrane function disrupt or injure the bacterial plasma membrane, leading to rapid depolarization and a loss of membrane potential. This inhibits protein, DNA, and RNA synthesis, ultimately resulting in bacterial cell death.
3. **Antibiotics that inhibit protein synthesis**:-Antibiotics that inhibit protein synthesis target the ribosomes in bacterial cells, disrupting various stages of mRNA translation into proteins. These antibiotics interfere with the initiation, elongation, or termination stages of protein synthesis by binding to specific sites on the ribosomal subunits.

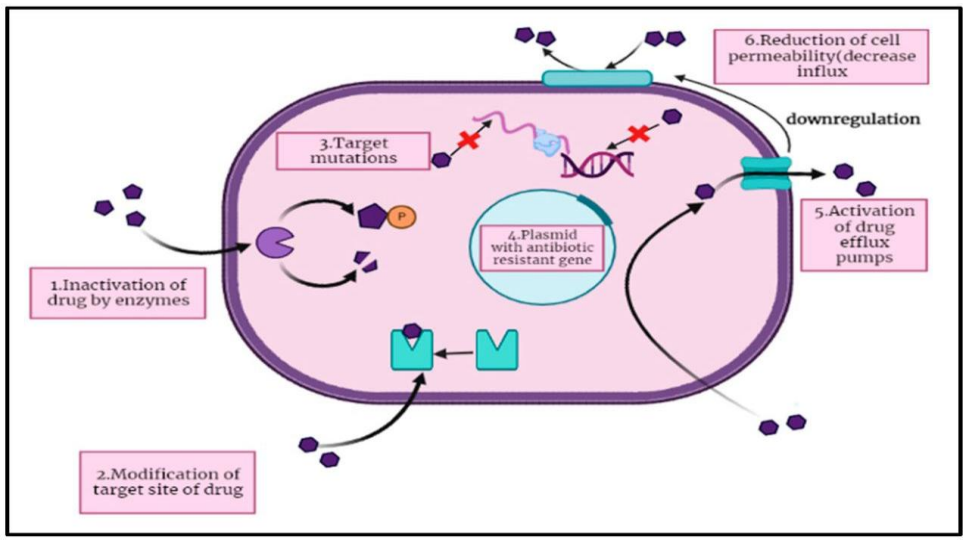
4. **Antibiotics that inhibit DNA gyrase**:-These antibiotics inhibit the activity of DNA gyrase, an enzyme that is essential for bacterial DNA replication. For example, fluoroquinolones inhibit DNA gyrase, leading to bacterial DNA damage and cell death.
5. **Antimetabolites**:-Antimetabolites, when used as antibiotics, interfere with the synthesis of essential metabolites in bacteria, disrupting their normal metabolic pathways and inhibiting their growth.



Mechanisms of antibiotic resistance :

Natural and acquired resistances to antibiotics are the two main Forms of antibiotic resistance. Normal resistance may be innate (it is often expressed in the organisms), or mediated (the genes arenormally present in the bacteria but are only activated to resistance levels following antibiotic treatment). On the other side,acquired resistance may be the result of the bacteria acquiring genetic material by translation, conjugation, or transposition or mutations in its own chromosomal DNA.AMR mechanisms May be divided into Three categories :-

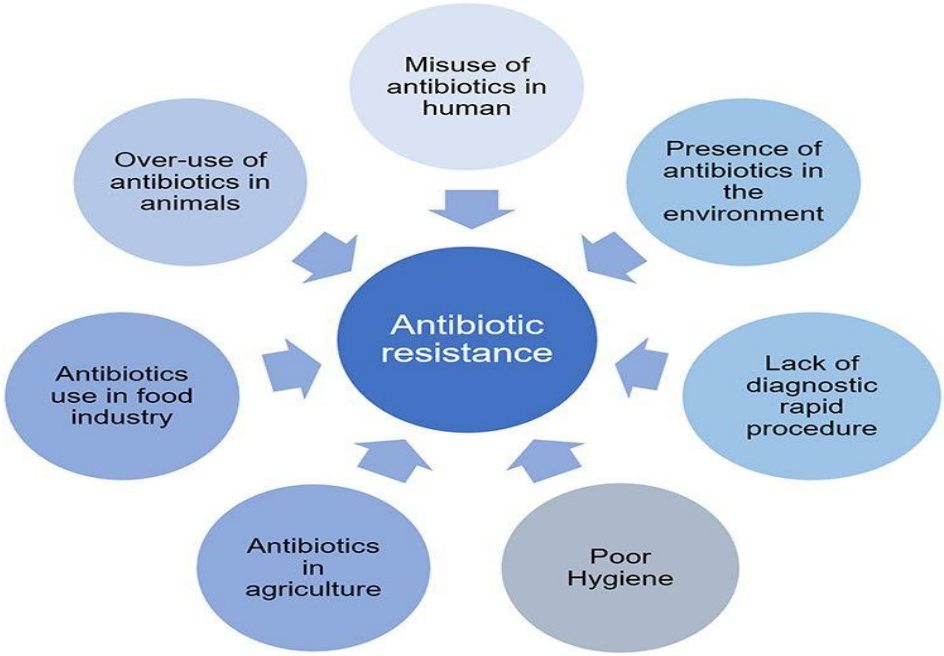
1. **Drug target modification:**-The modification of the antibiotic's target is a common mechanism by which bacteria become resistant to antibiotics .Changes in the arrangement and/or amount of PBPs are one of the mechanisms of resistance towards lactam drugs. The amount of drug that can attach to the target is affected by changes in the number of PBPs . A structural alteration e.g. the development of the mecA gene in S. aureus will reduce or completely prevent drug binding . Another example is the erythromycinRibosomemethylase (erm) gene family, whichmethylates 16S rRNA and changes the drug-binding site, blocking macrolides, strepTogramins, and lincosamines from binding . Resistance to drugs that inhibit nucleic acid synthesis e.g.fluoroquinolones,is mediated By changes in DNA gyrase or topoisomerase IV. These mutations alter the composition of gyrase and topoisomerase, reducing or Excluding the drug's ability to attach to these components .
2. **Drug inactivation:**-Bacteria inactivate antibiotics in one of the two ways: by Destroying the drug or by the chemical alteration of the drug .
3. **Drug efflux :-** Many antibiotics are actively transported out of the cell by bacterial efflux pumps, which are important contributors to Gram-negative bacteria's intrinsic resistance. Efflux pumps come in a variety of forms of most bacteria. The ATP-binding cassette (ABC) family, small multidrug resistance (SMR) family, multidrug and toxic compound extrusion (MATE) family, resistance-nodulation-cell division (RND) family, and large facilitator superfamily (MFS) Are the five primary families of efflux pump, which are categorized considering its structure and energy supply . Except For the RND family which are multi part pumps that efflux substrate across the cell envelope, all other efflux pump families are singular pumps that transfer substrates across the cytoplasmic membrane . Tetracycline resistance is a textbook



example of Efflux-mediated resistance, in which Tet efflux pumps (of the MFS family) use proton exchange as a source of energy to extrude tetracyclines. Several MDR efflux pumps, such as MexAB-OprM in P.aeruginosa and AcrAB-TolC in Enterobacterales (of the RND family) can extrude tetracyclines as part of their contribution to MDR .Resistance to macrolides is another clinically relevant phenotype induced by the effluxmechanism. Themef genes, which extrude the macrolide class of antibiotics, encode the most well-characterized effluxpumps (e.g., erythromycin). MacB, an ABC family member,Acts as a tripartite pump (MacAB-TolC) for extruding macrolide drugs.

Reasons behind antibiotic resistance :

1. **Genetic mutation:**-Changes in few base pairs may occur during bacterial replication (point mutations), resulting in the replacement of one or a few
   Amino acids in a critical target (enzyme, cell wall, or cell structure),as well as control genes or chromosomal structural, resulting in New resistant strains. The newly developed defense may render antibiotics ineffective, which were meant to be able to handle the Organism for years.
2. **Inaccurate diagnosis** :-While diagnosing an infection, healthcare professionals sometimes rely on unreliable or inaccurate knowledge, prescribing an Antibiotic "just in case" or a wide-spectrum antibiotic when a particular narrow spectrum antibiotic might be more appropriate. These circumstances exacerbate selective pressure and hasten antimicrobial resistance .
3. **Inappropriate prescription of antibiotics:**-When doctors are unclear if an infection is exacerbated by bacteria or a virus, they may prescribe antibiotics. Antibiotics, on the other hand, do not act against viral infections, and resistance may develop .
4. **Inadequate and overuse of antibiotics**:-If an individual does not finish a course of antibiotics, some bacteria may thrive and develop resistance to that antibiotic. Again,In the year 1945, the discoverer of antibiotics, Alexander Fleming,had issued a public warning against the overuse of antibiotics, as He had realized the dangers associated with the inappropriate use of these drugs. Taking antibiotics too often for the wrong reasons Can develop modifications within the bacteria that antibiotics do not work against them .
5. **Poor hospital environment:**-Thousands of patients, staff, and visitors arrive at hospitals every day, each with their own set of microbiome and colonizing bacteria on their clothing and on/inside their bodies. Bacteria can spread if hospitals do not have adequate procedures and protocols in place to help maintain spaces clean. As a result, the emergence and spread of AMR is aided.



CONSEQUENCES OF ANTIBIOTIC RESISTANCE :

Antibiotic resistance is a pressing global health issue, contributing significantly to both mortality rates and economic burdens worldwide. Despite some progress in reducing deaths attributed to antimicrobial resistance (AMR), alarming trends reveal a concerning increase in severe infections caused by multidrug-resistant (MDR) bacteria. Since 2013, the US Centers for Disease Control and Prevention (CDC) have reported an 18% decrease in AMR-related deaths. However, this decline is overshadowed by surges in MDR bacterial infections, including a staggering 315% increase in erythromycin-resistant group A Streptococcus, a 124% rise in drug-resistant Neisseria gonorrhoeae, and a 50% uptick in extended-spectrum β-lactamase-producing Enterobacteriaceae. Similarly, the prevalence of vancomycin-resistant Staphylococcus aureus (VRSA) has shown a worrisome 3.5% increase between 2006 and 2020, with Africa recording the highest rates at 16%.

Multidrug-resistant tuberculosis (MDR-TB) presents another formidable challenge, infecting an estimated 3.4% of new tuberculosis (TB) cases and a staggering 18% of previously treated cases in 2018, as reported by the World Health Organization (WHO). The emergence of resistance to "last resort" TB drugs further compounds the threat posed by MDR-TB.

Low- and middle-income countries bear the brunt of antibiotic resistance, exacerbated by widespread antibiotic misuse, agricultural antibiotic use, poor drug quality, insufficient surveillance, and substandard healthcare practices. Factors such as malnutrition, chronic and recurring infections, and limited access to effective and costly drugs further exacerbate the situation in these regions.

The consequences of antibiotic resistance are profound, leading to limited treatment options, prolonged illnesses, treatment failures, increased healthcare costs, and compromised effectiveness of critical interventions such as surgery, chemotherapy, and organ transplantation.

Addressing antibiotic resistance requires a multifaceted approach, including promoting responsible antibiotic use, enhancing surveillance systems, fostering innovation in antimicrobial development, and improving healthcare infrastructure, particularly in resource-limited settings. Only through concerted global efforts can we hope to mitigate the devastating impact of antibiotic resistance and ensure the continued efficacy of these essential medications.

STRATEGIES FOR TACKLING ANTIBIOTIC RESISTANCE :

1. **Targeting antimicrobial-resistant enzymes:** This involves using enzyme inhibitors or medicinal plants and phytochemicals to inhibit the activity of enzymes responsible for antibiotic resistance.
2. **Combination therapy:** Combining antibiotics with each other or with other agents such as β-lactamase inhibitors or biocides can improve the effectiveness of antibiotic therapy and reduce the risk of resistance development.
3. **Physiochemical methods**: Physiochemical methods such as plasma washing and the use of gallium-laced drugs can disrupt bacterial biofilms and starve bacteria of essential nutrients, making them more susceptible to antibiotics.
4. **New antibiotic developments:** The development of new antibiotics with unique mechanisms of action can help to combat antibiotic resistance.
5. **Education**: Education for patients, healthcare professionals, and the public about antibiotic resistance, prudent antibiotic prescribing, and personal hygiene can help to reduce the risk of antibiotic resistance development.
6. **Controlled use of antibiotics in food animals:** The controlled use of antibiotics in food animals can help to reduce the risk of antibiotic resistance development in animals and humans.
7. **Surveillance and research**: Enhanced surveillance and research can help to improve knowledge and understanding of antibiotic resistance and inform the development of new strategies to combat it.

CONCLUSION :

Antibiotic resistance is a significant global health issue, with bacterial pathogens becoming increasingly resistant to available drugs, leading to reduced drug efficacy and increased mortality rates. The causes of antibiotic resistance are complex, involving environmental factors that favor bacterial mutation, overuse and misuse of antibiotics in healthcare and agriculture, and the lack of new antibiotic development.

In conclusion, antibiotic resistance remains a pressing global health concern, posing significant challenges to healthcare systems worldwide. Current trends indicate a worrisome escalation in resistance rates across various pathogens, jeopardizing our ability to effectively treat common infections. However, concerted efforts are underway to combat this crisis through multifaceted strategies, including antimicrobial stewardship, surveillance, research into novel therapies, and public education. Addressing antibiotic resistance demands a collaborative approach involving healthcare providers, policymakers, researchers, and the public. Only through sustained commitment and innovation can we hope to mitigate the impact of antibiotic resistance and safeguard the efficacy of these life-saving drugs for generations to come.

REFERENCE :

1. Antibiotic Drug Resistance, edited by Ying Zhang. Wiley, 2019.
2. Antibiotics: Current Strategies and Future Directions, edited by David M. Shlaes and David P. Nicolau. Springer, 2016.
3. Antibiotic Resistance: Understanding and Responding, edited by Mark A. Schelley and Stuart B. Levy. ASM Press, 2013.
4. Antibiotic Resistance: A Comprehensive Review, edited by Ying Zhang. Springer, 2010
5. Gajdács M, Albericio F. Antibiotic resistance: from the bench to patients.Antibiotics 2019.
6. Watkins RR, Bonomo RA. Overview: global and local impact of antibiotic resistance. Infect Dis Clin North Am 2016.
7. Antimicrobial Resistance Collaborators (ARC). Global burden of Bacterial antimicrobial resistance in 2019: a systematic analysis.
8. Letek M. Alexander Fleming, the discoverer of the antibiotic effect Of penicillin.
9. Isaacs D, Andresen D. Combating antibiotic resistance: the war on error. Arch Dis Child 2013
10. European Centre for Disease Prevention and Control. Antimicrobial Resistance Surveillance in Europe 2014.