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Review On: Antibiotic Resistance Challenges and Strategies

Neha M. Jadhav *, Nida N. Mulla, Sanjay K. Bais

Fabtech College of Pharmacy, Sangola, Solapur, Maharashtra, India

*Corresponding Author: nj9148480@gmail.com

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Abstract

Resistant to antibiotic is a severe threat to global health because it allows for treating serious infections more challenging and increases medical expenses. An overuse and abuse within antibiotics causes this complex problem by causing resistant bacterial strains to evolve. Important obstacles include the need for efficient public health policies, the absence of new antibiotic research, and insufficient surveillance systems. In order to address this epidemic, strategies include developing vaccines, funding in research for new treatments, improving antibiotic stewardship, and encouraging international cooperation. Coordination between many sectors is necessary to address antibiotic resistance in order to control antibiotic use effectively and maintain current treatments.

Keywords - Antibiotic resistance, infection control, antimicrobial stewardship, surveillance, novel therapeutics.

INTRODUCTION

Definition of Antibiotic resistance

Bacterial resistance is the ability of microorganism to expand and survive when exposed to antibiotics that normally destroy them.

Classification of Resistance to Antibiotics

Intrinsic resistance

Some bacterial species naturally contain this kind because of innate structural or functional traits. For example, Mycoplasma species are resistant to beta-lactam medicines because they do not have cell walls. [1]

Acquired Resistance

Through genetic alterations, frequently through horizontal gene transfer, this resistance arises. It may be brought on by modification and a introduction of genes that resist through of bacteriophages, transposable elements (TEs) or plasmids. It is possible to further classify acquired resistance into:

Chromosomal Resistance: The bacterial chromosome can experience genetic alteration.

Gene Transfer: Transformation, transduction, conjugation, or other processes can result in the collection of resistance genes from other bacteria. [2]

Cross-Resistance

This describes the situation in which an antibiotic's resistance to one antibiotic spreads to another, typically as a result of comparable methods of action.

Multidrug Resistance (MDR)

Bacteria that is resistant to several antibiotics, frequently by different methods, which makes illnesses challenging to cure. [3]

Bacterial infections can be controlled and also treated using antibiotics. Inhibition to antibiotics is the result of pathogen becoming resistant for antibiotics due to continuous use.[4]Resilience of microbes is the ability of microorganisms to resist the effects of medication therapeutically acceptable doses.[5]When an antibiotic becomes less effective in treating infectious illnesses for which it was designed, it becomes a big global problem.

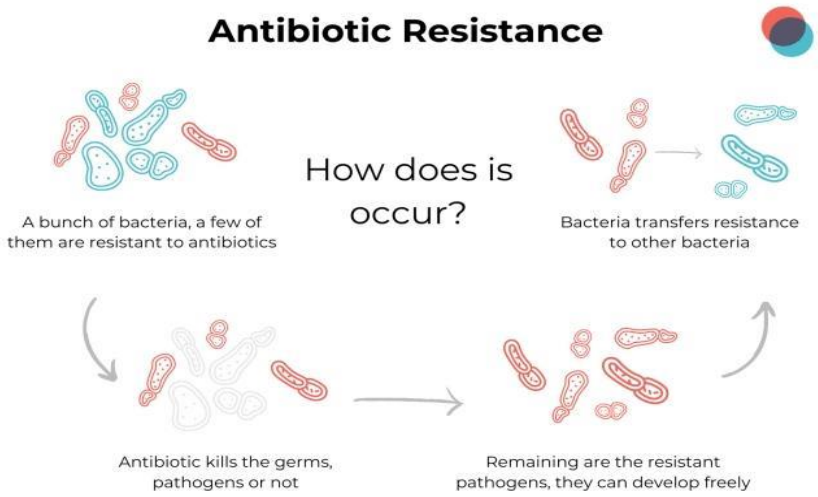

Figure 1*: *Antibiotic resistance

The WHO has issued a warning, explaining that the globe is "running out of antibiotics" has prompted issues that antibiotic resistance may reach previously unheard-of levels worldwide. Because of drug-resistant bacteria, which have become a significant barrier to dealing with of clinical communicative disease, nosocomial infections have progressively become more prevalent. [6]

Epidemiology of AR

It is a significant factor of dying & a costly impose on people worldwide. American agency for illness prohibits and inhibit report, since 2013, there has been a rise in the prevalence of numerous dangerous immune to many drugs caused by bacteria, such as a set sensitive to azithromycin. There has been a 315% increase in streptococcus infections, Neisseria gonorrhoea infections. [7]

A most common cause to prevent infections linked to hospitalization globally in fact, MRSA illness result in longer hospital stays, higher rates of mortality, and extremely significant social and financial consequences. [8] Seven European nations reported a noteworthy decline in MRSA transmission in 2010 as a result of strong control measures. In Italy, % reached 38%, which is among the highest in Europe and has been steadily rising in recent years. Use of anti-MRSA is necessary in cases where a potential staphylococcal infection etiology is suspected due to this epidemiological condition. [9] Gram-negative pathogen strains have spread rapidly. The usage of carbapenems has significantly

increased as a result of this phenomenon, which is aiding in the dissemination to resistant organisms of Enterobacteriaceae and Acinetobacter.

Certain kinds of Gram-negative bacteria, like A. baumanii, may be resistant to every antibiotic that is currently on the market. [10] multi-drug-resistant tuberculosis (MDR-TB) is projected to have infected 3.3% of new (TB) patients and eighteen percent of those who have already received treatment, according to a WHO report. Illness to newer "last resort" tubercular drugs, which are used in the treatment of resistant to medication of TB, poses big risk. [11]

Advantages of antibiotic resistance

Though there are some possible benefits to antibiotic resistance, especially in ecological and evolutionary contexts, it is generally thought ofas a grave risk to the human welfare. A few points are as follows:

Evolution and Natural Selection

Natural selection can be influenced by antibiotic resistance, which can result in the survival of more robust and resilient microorganisms. Ecosystem-related consequences may arise from this contribution to the evolution of microbial diversity.

Applications in Biotechnology

By analysing resistant strains, biotechnology can learn more about resistance mechanisms and design novel antibiotics or therapeutic approaches. [12]

Microbial Interactions:

Under certain conditions, resistant bacteria may out complete susceptible strains that show outcome in more stable microbial regions with greater durability to antibiotic stresses.

Informed Healthcare Practices

The issue with resistance to antibiotics forces healthcare systems to implement improved prescribing guidelines, which in turn promotes the prudent use of antibiotics and the development of novel treatment approaches.

These benefits highlight how complicated antibiotic resistance is as phenomena as well as need for a deeper comprehension that goes beyond its detrimental effects. [13]

Disadvantages of antibiotic resistance

Antibiotic resistance has serious drawbacks that affect treatment effectiveness, public health, and healthcare expenditures. The following are some salient points:

Increased Morbidity and Mortality

Bacteria that are resistant to infection can cause infections that result in greater rates of complications and mortality. Patients may need more intensive therapy if their ailments are chronic.

Longer Hospital Stays

Resistant illnesses frequently require longer hospital stays, which raises the risk of infections linked to medical care and puts additional strain on healthcare systems. [14]

Limited Treatment Options

As antibiotic resistance increases, there are fewer effective antibiotics available, which make treating common infections more challenging and necessitate the use of less effective or more dangerous substitutes.

Increased Healthcare Costs

The financial cost of antibiotic resistance is significant. Longer hospital stays, extra testing, and more involved therapies come with a price tag that has a big effect on patients care and healthcare systems. [15]

Effect on Medical Procedures

The use of efficient antibiotics helps prevent infections during several medical procedures, including chemotherapy and surgery. Resistance may put these procedures in danger and increase the chance of postoperative infections.

Spread of Resistance

Resistant bacteria have the ability to spread throughout societies and medical environments, increasing the difficulty of illnesses to treat & potentially causing outbreaks. [16]

The rise in multidrug resistance and the resistance to antibiotics

A Fleming identified a risk of improper application of penicillin with emergence in 1945. [17] Antimicrobial agents were not discovered until after many microbes developed innate resistance mechanisms. [18] The microbial population is under selective pressure when antibiotics are utilized, and the demand rises as more medications are prescribed. In recent decades, the quantity of microorganisms tolerant to many drugs has grown. Alarmingly, leading to major issues Here must be a pressing requirement for discover ways for prevent infection for a growth for an illness brought on the germs has caused illnesses & fatalities. [19] MDR organisms should be especially avoided. [20] One or more of the antibiotics used for cure MDR have that reduce to them. When medication that not utilized appropriately, an organism may acquire multi-drug resistance. [21]

Strategies of Bacterial Resistance with Antibiotics

Ability of bacterial strains to obstruct one or more of the crucial steps necessary for the antibiotics Successful action is a prerequisite for survival in the presence of an antibiotic.

One of the four Fundamental survival strategies used by bacterial species is:

Lowering the antibiotics penetration capacity into the bacterial cell, therefore preventing it from reaching its integrating target.

Through the efflux pump, antibacterial drugs are ejected from the cell.

Alteration or degradation of antibiotics to render them inactive.

Within the bacteria, alteration or modification of the antibacterial target. [22]

Antibiotic Resistance consequence

Globally, antibiotic resistance is a significant contributor to both mortality and economic hardship. Microbes that are resistant to antibiotics can have a number of effects. The following consequences may arise from infectious microbial organisms developing resistance to certain antibiotics. [23]

Ineffectiveness in responding to therapy results in a protracted illness &a higher chance of dying. A likelihood as more community members being impacted increases with lengthier hospital stays and disease. Third- or second-systemic antibacterial agents is invariably most costly & sometimes most perilous must be used to 1st-line antibiotics are never working. The lack of numerous second- and third-line treatments for illnesses resistant to drugs in low-income nations raises the possibility of first-line antibiotic resistance. These countries' supply of medications in order to address infections caused by mold is running lowas well as the set of necessary drugs is missing vital antibiotics that are needed to address illnesses caused by bacteria that are tolerant.

Origin of Antibiotic Resistance

A capacity of disease to endure being exposed to and treatment with antibiotics that have the potential to either kill it or drastically slow its growth is known as antibiotic resistance. [24] the manifestation

of susceptibility to drugs is influenced by several elements, such as the bacterial strain's level of resistance expression & capacity for live via means of systems of resistance. [25] Microbiological viruses might show intrinsic opposition of effective response an transgenic thing.[26]

Since it is connected to elevated rates of illness and mortality, the issue has surfaced. As a world-wide medical problem. The infections caused by gram +ve & gram -ve bacteria were challenging to cure because of resistance to many drugs, which prevented the use of conventional antibiotics. It has negatively impacted antibiotic effectiveness in medical settings during both the pre-antibiotic and antibiotic eras. [27] Because pharmacological agents have the power to inactivate their cell walls, Sensitivity to antibiotics is as old for antibacterial used therapeutically. It has developed into widespread and resistant. Scientific data indicates that antibiotics can be chemically modified to prevent or restrict the cleavage by β-lactamases or penicillinases. [28]

Mechanism of antibiotic resistance

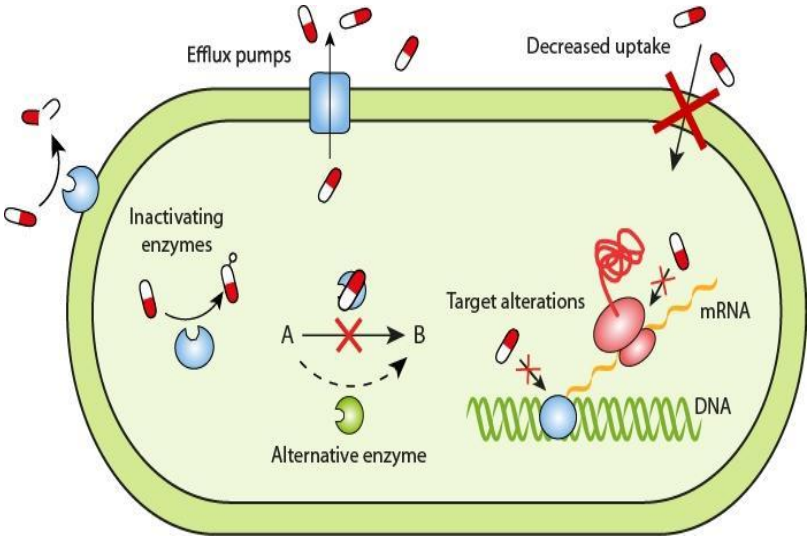

Figure 2*: *Antibiotic resistance mechanism

When bacteria develop defences against medicines that originally killed them or stopped their growth, it's known as resistance to antibiotics. The following are a few longest pathways:

Enzymatic Degradation

Antibiotics are rendered inactive by enzymes produced by bacteria. For instance, beta-lactamases degrade cephalosporins and penicillins.

Modified Target Sites

By altering the antibiotic's target, bacteria lessen drug binding. For example, ribosomal RNA alterations can impart macrolide resistance.

Efflux Pumps

Efflux pumps are the active mechanisms by which bacteria actively remove antibiotics from their cells. Multi-drug resistant bacteria, such as Pseudomonas aeruginosa, frequently use this method. [29]

Reduced Permeability

Modifications to the bacterial cell wall may result in a decreased antibiotic absorption. To restrict the entry of antibiotics, certain Gram-negative bacteria alter their porins.

Biofilm formation

Because of their altered microenvironment and decreased penetration, bacteria within biofilms can be substantially more resistant to antibiotics.

Horizontal Gene Transfer

Plasmids, transposons, and bacteriophages can all facilitate A transmission of genes that resist horizontally within bacteria. [30]

The result of billions of years of evolution, antibiotic resistance is a natural ecological occurrence. Pathogens with resistance to antibiotics found among individuals who spend time in hospitals and germs that cause harmful health effects, however, have received a lot of attention. [31]

In Gram-negative bacteria, the most common resistance mechanism that synthesis of β-lactams; The ability to withstand infection in gram +ve bacteria usually occurs to changing the target site. [32] The efflux pump system is one of the different processes of antibiotic resistance, as it facilitates the removal of toxins and drugs from cells. Bacteria developing antibiotic resistance are largely dependent on this process. Tet efflux pumps, in particular, are responsible for tetracycline export from cells via proton exchange, which is how Gram-negative bacteria develop tetracycline resistance. [33]

Bacteria's growing the primary cause of tolerance to various medicines is multiple export pathways. The identification of molecules it One crucial problem is to inhibit the flow processes. In the creation of efficient medicines versus microorganisms immune to drugs. [34]

Antibiotics known as β-lactams are the most commonly prescribed drugs for treating various bacterial infections, as they prevent the bacterial cell wall from being synthesized. Opposition to Medications beta-lactamase, however, to emerged a global wellness concern. Antibiotic resistance to β-lactams is primarily and seriously threatened by the production of β-lactamases. Recent work in epidemiology has shown that Salmonella enetrica Serovar Infantis is resistant to cefotaxime due to β-lactamase action. Extensive research conducted over the past three decades has concentrated on finding novel compounds that prevent that combat β-lactam resistance in pathogenic bacteria. [35]

Studies on tolerance mechanisms are continuous, and it has been established that the primary cause of antibiotic tolerance is persistent bacteria because of their ability to persist. These cells are inactive and resistant to drugs that are disinfecting, that require overwatch in action in order that cause cell death. [36]A processes behind the development of persistent cells are not entirely understood since they not only influence the emergence of resistance but also have significant implications for the clinical symptoms of infection. In actuality, persistent cells are resistant to antibiotics and grow back more quickly when the drug's concentration drops, which makes relapses easier to cause. [37]

Causes of resistance to antibiotics

Inhibition to antibiotics is a major wellness problem, which is brought about by a number of factors:

Overuse of Antibiotics

Resistance is exacerbated by the over prescription of antibiotics for viral illnesses when they are not effective. Studies have demonstrated that one of major problem as a resistance as incorrect medication. [38]

Lack of New Antibiotics

We are running out of effective therapies quicker than we can discover new ones due to the sluggish rate of antibiotic research. [39]

Inadequate Treatment Courses

Patients who fail to finish the entire term of antibiotics given to them may be playing a role in emergence of resistant to medication in surviving bacteria. [40]

Agricultural Use

Animals are routinely given medicines to encourage development and avoid illness, which increases risk of resistant bacteria getting into the food chain. [41]

Poor Infection Control in Healthcare Settings

According to, hospitals with inadequate hygiene and infection control procedures encourage the spread of resistant pathogen

Global Travel and Trade

As people and goods move more often across international orders, resistance to local outbreaks can spread beyond national boundaries. [42]

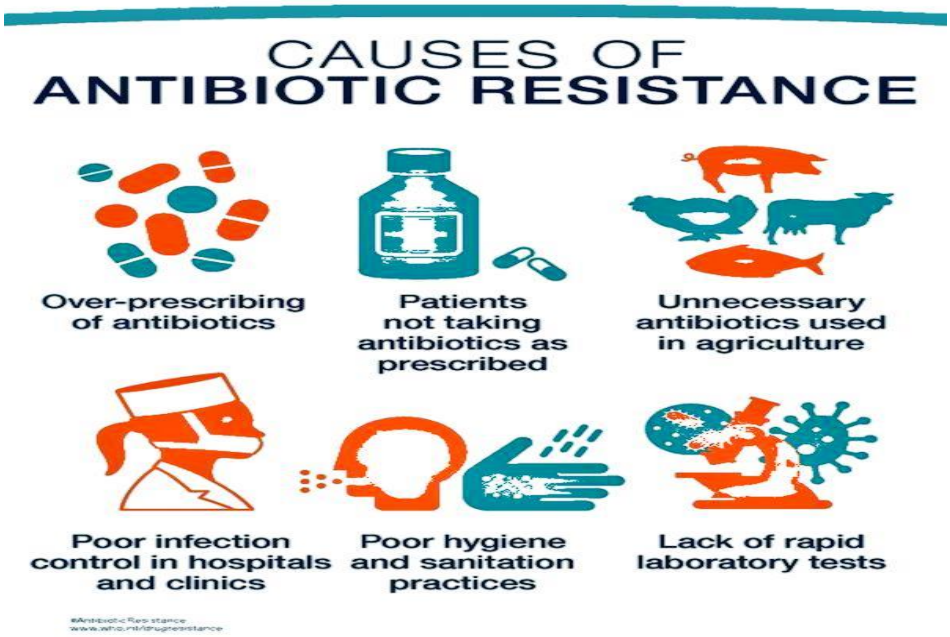

Figure 3*: *Causes of antibiotic resistance

Prevention of antibiotic resistance

Prevention Strategies

Using antibiotics responsibly means avoiding abuse and only prescribing when necessary.

Enhancing Public Awareness & Education

Motivating people to stop from requesting medications for viral infections and to promote the value of finishing antibiotic treatments. [43]

Hand hygiene, sanitization, and sterilization in healthcare environments are examples of infection control procedures. [44]

Research and pharmaceutical development

Ongoing efforts to produce new antibiotics.

International collaboration and surveillance, as well as global policies

Tracking and controlling antibiotic use. [45]

Vaccines, probiotics, and other methods of treatment as alternatives to antibiotics. [46]

The following are some practical guidelines for preventing antibiotic resistance.

Use Antibiotics Carefully

Only take antibiotics as directed by a medical expert. Remaining antibiotics should not be used.

Finish the Prescribed Course

Even if you begin to feel better, you should always take antibiotics as directed for the whole prescribed time.

Vaccination

Maintain current immunization records to prevent against diseases that can require antibiotic therapy.

Safe Food Practices

To avoid contracting foodborne illnesses, handle and cook food properly. Hand washing, fully cooking meat, and preventing cross-contamination are all part of this.

Don't Share Antibiotics

Since various infections require different treatments, never share your antibiotics with anybody else.

Educate Others and Yourself

Recognize the value of antibiotics and the dangers of overusing them. Inform your friends and family about this information. [47]

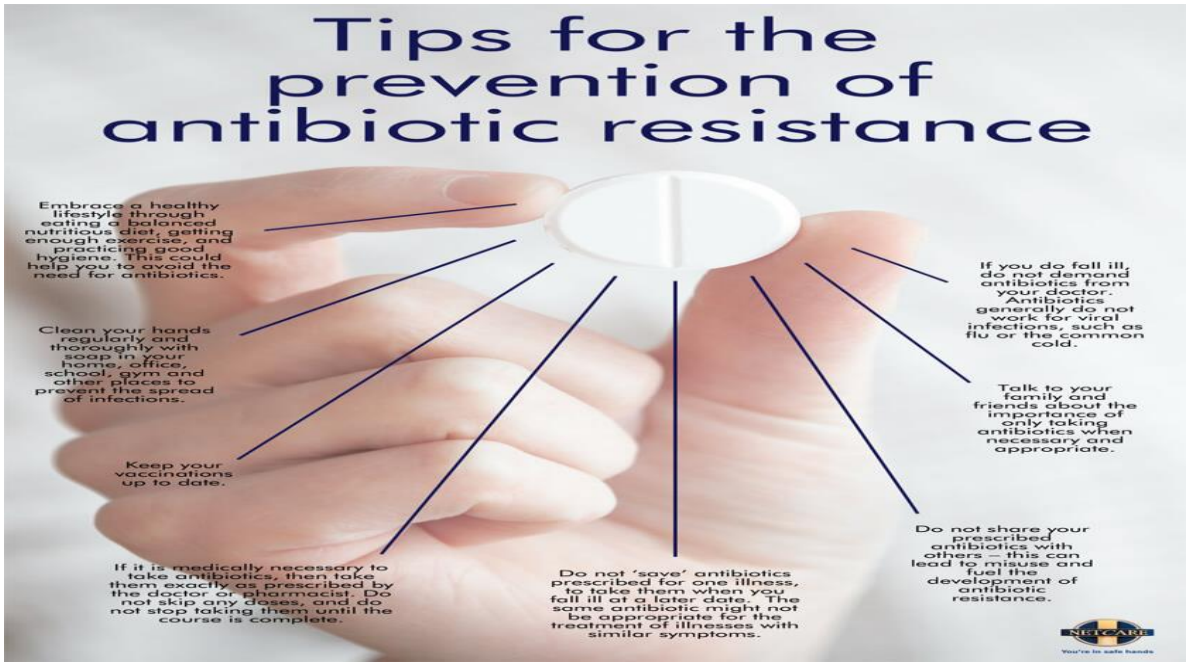

***Figure 4*:** *Tips for the prevention of antibiotic resistance*

The causes and consequences of drug resistance

Natural Element**.**

Factors connected to Drugs.

Factors connected to the Patient.

Factors connected to Physicians.

Environmental elements

High population and cramped conditions.

Quick spread – more travel.

Unsanitary conditions.

Strengthens community-acquired resistance.

Inadequate program for infection control.

A rise in both domestic and foreign travel.

The common practice of using medicines as medicated cleaning agents & an agricultural and animal husbandry.

Factors Associated with Drug Use

Fake medications.

The drug's quality.

A major development antibiotic use.

An availability of medicine over-a-counter

Antimicrobial combinations with irrational fixed doses.

Lower-than-ideal blood concentration due to fake and inferior medication.

Factors Related to Patients

Insufficient adherence to dosing routines.

Impoverishment.

Inadequate understanding of hygiene.

Insufficient studies.

Treating oneself.

Inaccurate faith.[48]

Irrational use of antibiotics in hospitals

The welfare of people in general & patient safety that seriously impacted by excessive use of antibiotics in hospitals. These are some salient points:

Increased Antimicrobial Resistance

Overprescribing antibiotics can result in the emergence of bacterial strains that are resistant to treatment, making antibiotics may cause the formation of drug-resistant organisms, which makes infections tougher to treat. [49]

Adverse Drug responses

Patient recovery may be impacted by side effects from unnecessary antibiotic treatment, such as allergic responses and gastrointestinal issues. [50]

Longer Hospital Stays

Effects or treatment failures may result in patients receiving the wrong antibiotics having to stay in the hospital for longer. [51]

Higher Healthcare costs

Longer treatments, more testing, and the management of problems are some of the ways that irrational usage raises healthcare expenses. [52]

Effect on the microorganism

Antibiotics can cause secondary infections like Clostridium difficile by upsetting the normal bacteria. [53]

Absence of Stewardship Programs

Appropriate antibiotic usage is guided by the presence of competent antimicrobial stewardship programs, which are lacking in many hospitals. [54]

Antibiotics drugs and its resistance mechanism

The following list includes instances of resistance mechanisms, common antibiotic classes, and their modes of action

Penicillins

Examples: Amoxicillin and Penicillin G.

Mechanism: Attach that drug binds to prevent a production for infected tissue walls.

Resistance: The generation of beta-lactamase enzymes, which convert the beta-lactam ring.

Cephalosporins

Examples: Cephalexin and Ceftriaxone.

Mechanism: Inhibits the formation of cell walls, much like penicillins do.
Resistance: PBP changes and beta-lactamase synthesis.

Macrolides
Examples: Azithromycin and erythromycin.
Mechanism: Attach for 50S synaptic compound for inhibition process of proteins.
Resistance: Efflux pumps; adenine methylation in rRNA (change of the ribosomal target). [55]
Tetracycline
Examples: Doxycycline and Tetracycline.
Mechanism: Bind to the 30S synaptic compound to inhibit process of proteins.
Resistance: Synaptic protection proteins; efflux pumps.
Aminoglycosides
Examples: Tobramycin, gentamicin
Mechanism: By attaching to the 30S ribosomal subunit and causing mRNA to be misread, it inhibits the synthesis of proteins.
Resistance: The drug's enzymatic alteration (phosphorylation, adenylation etc). [56]
Fluoroquinolones
Examples: Ciprofloxacin and Levofloxacin
Mechanism: Prevent DNA replication by inhibiting topoisomerase IV and DNA gyrase.
Resistance: Efflux pumps and target enzyme mutations.
Glycopeptides
Examples: Teicoplanin and Vancomycin
Mechanism: By attaching to D-CycloserineTerminal precursors for PGN, inhibit the production of cell walls.
Resistance: Target site modification. [57]
Lincosamides
Example: Clindamycin
Mechanism: By attaching a 50S synaptic component, prohibit the production of proteins.
Resistance: rRNA target site methylation, efflux pumps.
Oxazolidinones
Example: Linezolid.
Mechanism: Block the development for starting point by attaching to 50Ssynaptic component and prohibiting protein synthesis.
Resistance: Changes in ribosomal proteins or 23S rRNA.
Rifamycins
Examples: Rifampicin
Mechanism: Prevent RNA production by inhibiting bacterial RNA polymerase.
Resistance: RNA polymerase gene (rpoB) mutations. [58]
Polymyxins
Examples: Colistin and Polymyxin B.
Mechanism: Interact with phospholipids to break down the bacterial cell membrane.
Resistance: Lipids A modifications, such as added of L-Arap4N, are a kind of resistance.
Sulphonamides

Examples: Sulfamethoxazole
Mechanism: By competitively inhibiting dihydropteroate syntheses, folic acid production is inhibited.
Resistance: Target enzyme mutations; excessive para-aminobenzoic acid (PABA) synthesis.

Trimethoprim

Example: Trimethoprim
Mechanism: Prevents the formation of folic acid by inhibiting dihydrofolate reductase.
Resistance: Dihydrofolate reductive mutations; reduced drug buildup through efflux.

Chloramphenicol

Example: Chloramphenicol
Mechanism: Attached to theto nucleotide component 50S, it inhibits the production of proteins.
Resistance: C11H12CI2N2O5 acetyltransferase-induced acetylation. [59]

Streptogramins

Examples: Quinupristin/Dalfopristin (Synercid)
Mechanism: By attaching to the production of the 50S synaptic component, blocking of proteins.
Resistance: Efflux pumps and enzymatic modification.

Bacitracin

Mechanism: By preventing bactoprenol from being dephosphorylated, it prevents the formation of cell walls.
Resistance: Target molecule modification; efflux mechanisms. [60]

Challenges of antibiotics resistance

Increasing Infections and Mortality

Extended hospital stays, greater medical expenses, and a higher death rate are all consequences of resistant bacteria. Even easily curable conditions can develop into potentially fatal ones.

Limited Treatment alternatives

It becomes harder to treat common infections as resistance grows since there are fewer effective antibiotic alternatives available. This makes using older medications more common, which may have more negative effects or be less effective.

The impact on Medical Procedures

A number of medical procedures, such as chemotherapy and surgery, depend on the use of antibiotics. In certain situations, resistance may raise the risk of infections and consequences. [61]

Economic Burden

The cost implications of antibiotic resistance include increased medical expenses, decreased productivity, and the requirement for more costly medications or therapies. By 2050, it is predicted that resistance will cost the world economy trillions of dollars.

Global Spread

There is no border to antibiotic resistance. The international movement of people, products, and animals speeds up the spread of resistant germs and makes containment more difficult. [62]

Limited Research and Development

The lack of novel antibiotic development is partly attributable to financial incentives for pharmaceutical corporations, which results in a static pipeline of therapeutic interventions.

Public Education and Awareness

To prevent resistance, there is a need for heightened public understanding according to proper the application of medicines & a significance in following prescribed dosage schedules. [63]

Complications in the Management of Chronic Diseases

Individuals who have long-term conditions like diabetes or cancer are more susceptible to infections. Their treatment is complicated by antibiotic resistance, which has a negative impact on health outcomes.

Impact on Veterinary and Agricultural Practices

The usage of drug in farm & animals raises a risk in control. Animal to person pathogen transmission can make food safety and public health more difficult. [64]

To Avoid Infections in Medical Environments

Were vulnerable populations is treated, such as a hospitals and long-term care institutions, antibiotic-resistant illnesses can spread quickly. Oftentimes, effective infection control strategies fall short.

Disparities in Treatment Access

It is possible that low- and middle-income nations may not have access to adequate diagnostic resources and antibiotics, which exacerbates the effects of antibiotic resistance and raises morbidity and mortality rates. [65]

Environmental Contamination

Hospital and farm waste can release pharmaceuticals and resistant bacteria into the surrounding area, which can further disperse resistance across the community.

Diagnostic Difficulties

In order to diagnose illnesses and direct therapy, quick and precise diagnostics are essential. However, because there aren't many readily available diagnostic tools, antibiotics are sometimes recommended based only on intuition, which results in improper use. [66]

Misunderstanding and Misuse by the Public

A lot of people continue to misuse antibiotics by not finishing courses or by using them for viral diseases, which increases resistance.

Threat to Global Health Security

It is acknowledged as a serious danger in security for global health system, necessitating international action and collaboration to control its spread. [67]

Therapeutic strategies of antibiotic resistance

The following are some therapeutic approaches to combat antibiotic resistance:

Phage Therapy

Targeting and eliminating microorganisms resistant to antibiotics by using bacteriophages. Without damaging human cells, phases can selectively infect and lyse bacteria.

Combination Therapy

To increase effectiveness to prohibit barriers from growing, many antibiotics are used, or antibiotics are combined with adjuvants.

Novel Antimicrobials

To combat resistant bacteria, new classes of antibiotics are being developed or old medications with distinct modes of action are being repurposed.

Antibiotic Stewardship

Putting in place initiatives to maximize the application of drugs in medical situations for making sure that a right prescription is written to reduce the emergence of resistance.

Vaccination

Creating vaccinations to stop bacterial illnesses, which will lessen the prescription of antibiotics. [68]

CONCLUSION

A major risk to world health is antibiotic resistance, which raises morbidity, death, and healthcare costs. An expanded strategy and immediate action are required to combat the rise of resistant diseases. Developing new medicines and alternatives, improving infection control measures, encouraging acceptable antibiotic use, and putting in place reliable surveillance systems to track resistance trends are among strategies.For effective actions and to raise awareness, cooperation between the public, legislators, and healthcare professionals is necessary. By targeting the fundamental causes of resistance and using a complete strategy, we can reduce the effects of it & safety current and upcoming antimicrobial treatments continue to be effective.

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