IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Systematic Review on Antibiotic Resistance which is Knocking the Upcoming Challenges

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Abstract

Antibiotics are often called "wonder drugs" because they have been used for decades to fight infections caused by microbes. These drugs are not only used for treating illnesses but are also widely used in agriculture and animal farming to prevent disease. However, a serious problem has emerged: microbes are becoming resistant to common antibiotics, and many people aren't aware that this resistance is developing.

The purpose of this review is to look into where antibiotic resistance comes from, how it has developed, and the current challenges in fighting it. Our findings show that antibiotic resistance is growing rapidly. Many infections, like pneumonia, tuberculosis, and gonorrhoea, are becoming harder to treat, and in some cases, antibiotics no longer work at all. This is because the more antibiotics are used, the more likely it is that resistance will develop. The overuse and misuse of antibiotics, especially outside of medical settings (such as in farming), is a major factor in making microbes resistant.

Currently, there are very few treatment options for hard-to-treat bacterial infections caused by multidrug-resistant bacteria, leading to higher rates of illness and death. This review emphasizes the need to use antibiotics more carefully in both humans and animals to slow down antibiotic resistance. It also highlights that the public's understanding of antibiotic resistance is still very limited. For this reason, educating both patients and the general public is crucial in the fight against antibiotic resistance.

INTRODUCTION

Antibiotic resistance is something that happens naturally over time. To stay alive, some bacteria can find ways to protect themselves from antibiotics. This happens when their genes change. These bacteria that can resist antibiotics don't die — instead, they keep growing and spreading [1].

Every time you take antibiotics, there is a chance that some bacteria will become resistant. That's why it's important to take antibiotics only when you really need them [2]. Antibiotics are ineffective against viral infections such as the common cold or the flu. And not all bacterial infections need antibiotics either — for example, some sinus infections and ear infections can get better without them [3]. Antibiotics work by either killing harmful microorganisms (cytotoxic) or stopping their growth (cytostatic), which helps the body's natural defences, like the immune system, to remove them [4]. They usually act by blocking the bacteria's ability to make their cell wall, proteins, DNA, or RNA. Some antibiotics also damage the bacterial cell

membrane or perform other specific actions [4] . In some cases, antibiotics enter the bacterial cell by attaching to it and using energy to reach the ribosomes, where they stop protein production [5].

Antibiotics have been a true blessing for humanity in the fight against infections, saving millions of lives. Many different types of antibiotics have been used over the years for medical treatment. During the mid-20th century, they were seen as "wonder drugs," and there was great hope that infectious diseases would soon be fully controlled [6]. The modern antibiotic era is closely linked to scientists Alexander Fleming and Paul Ehrlich. Antibiotics were thought to be "magic bullets" that would kill only the disease-causing microbes without harming the human body. Fleming was also the first to warn that penicillin might become less effective if not used properly—such as using too little or stopping treatment too soon [7] .

The period from the 1950s to the 1970s is known as the golden age for discovering new classes of antibiotics. Since then, millions of tons of antibiotics have been made. Due to high demand in healthcare, farming, and other sectors, antibiotics became cheaper and were often used for purposes not originally intended. However, overuse and misuse of antibiotics have played a big role in the rise of drug-resistant bacteria [8].

In the past, new antibiotics were discovered regularly, keeping pace with the development of resistance. But today, the focus has shifted to improving existing antibiotics to fight the growing number of drug-resistant germs [8].

Antibiotic resistance can develop very quickly, which makes it a serious issue. Although more people now understand that antibiotic resistance is dangerous, very few take real steps to prevent it—like avoiding the unnecessary use of antibiotics [9] . In many developing countries, antibiotics can be bought easily without a doctor’s prescription, which is a major cause of resistance [10].

To reduce antibiotic resistance, it is important to educate patients and the general public. This review is one step toward raising awareness by explaining how antibiotic resistance has developed, what the future might look like, and what rules exist to control the spread of resistance [9].

1.Origin of Antibiotic Resistance

Antibiotic resistance happens when a drug can no longer stop bacteria from growing effectively. In this case, bacteria are called "resistant" because they continue to grow and multiply even when treated with antibiotics at normal doses [11]. Normally, antibiotics can kill or stop the growth of bacteria, but when bacteria become resistant, a higher dose of the same drug is needed to have any effect [12].

The issue of antibiotic resistance began to appear soon after new antibiotics were introduced. Resistance can happen naturally through a process called natural selection, where all bacteria have some ability to survive, even if only slightly, against antibiotics [13].

For example, one study found that antibiotics like sulfamethoxazole, trimethoprim (TMP-SMZ), ampicillin, and tetracycline—which were once effective—are no longer useful for treating non-cholera diarrhoea in Thailand [14] . However, another study in Bangladesh showed that these same drugs still work well for the same condition. Interestingly, signs of antibiotic resistance were seen even before antibiotics started being used widely to treat infections [2] .

The improper or unnecessary use of antibiotics plays a major role in causing resistance. Since sulfonamides were introduced in 1937, bacteria have developed ways to resist them. In fact, resistance to sulfonamides was reported as early as the 1930s, and the same type of resistance still exists today—over 80 years later [15].

Aminoglycoside antibiotics were followed by the development of resistant strains of Staphylococcus aureus just six years after they were first made [16] . Methicillin, a special type of penicillin introduced in 1961 to fight penicillin-resistant Staphylococcus aureus, also faced resistance shortly after it started being used [17] .

Fluoroquinolones were first used in the 1980s to treat infections caused by Gram-negative bacteria. Later, they were also used for Gram-positive infections. Over time, resistance to fluoroquinolones developed, especially in methicillin-resistant bacteria [17].

2.Mechanisms of AMR and microbes involved

Antimicrobial resistance (AMR) occurs when harmful microorganisms, like bacteria and viruses, evolve and become resistant to drugs that were once effective in treating them. This resistance can happen for several reasons, including natural selection, misuse and overuse of antibiotics, poor sanitation, and substandard or fake drugs [18].

Overusing or misusing antibiotics—such as not completing the full course, prescribing them for viral infections, self-medicating, or using leftover antibiotics—can lead to AMR. When bacteria survive a partial antibiotic treatment, they may develop resistance [19]. Poor hygiene and lack of clean water contribute to the spread of infections, which increases the use of antibiotics and the risk of resistance. Additionally, low-quality drugs may not provide the proper dose, leading to incomplete treatment and resistance Microbes have evolved clever ways to survive the effects of antibiotics [20]. They may alter their structure, use different metabolic pathways, or develop mechanisms like producing enzymes that break down the antibiotics. Other methods include changing the drug's target sites, blocking the antibiotic from entering, or actively pumping it out before it can work [21]. Bacteria can also form biofilms—groups of bacteria stuck to surfaces, which are harder to treat because the antibiotics can't penetrate them easily [22].

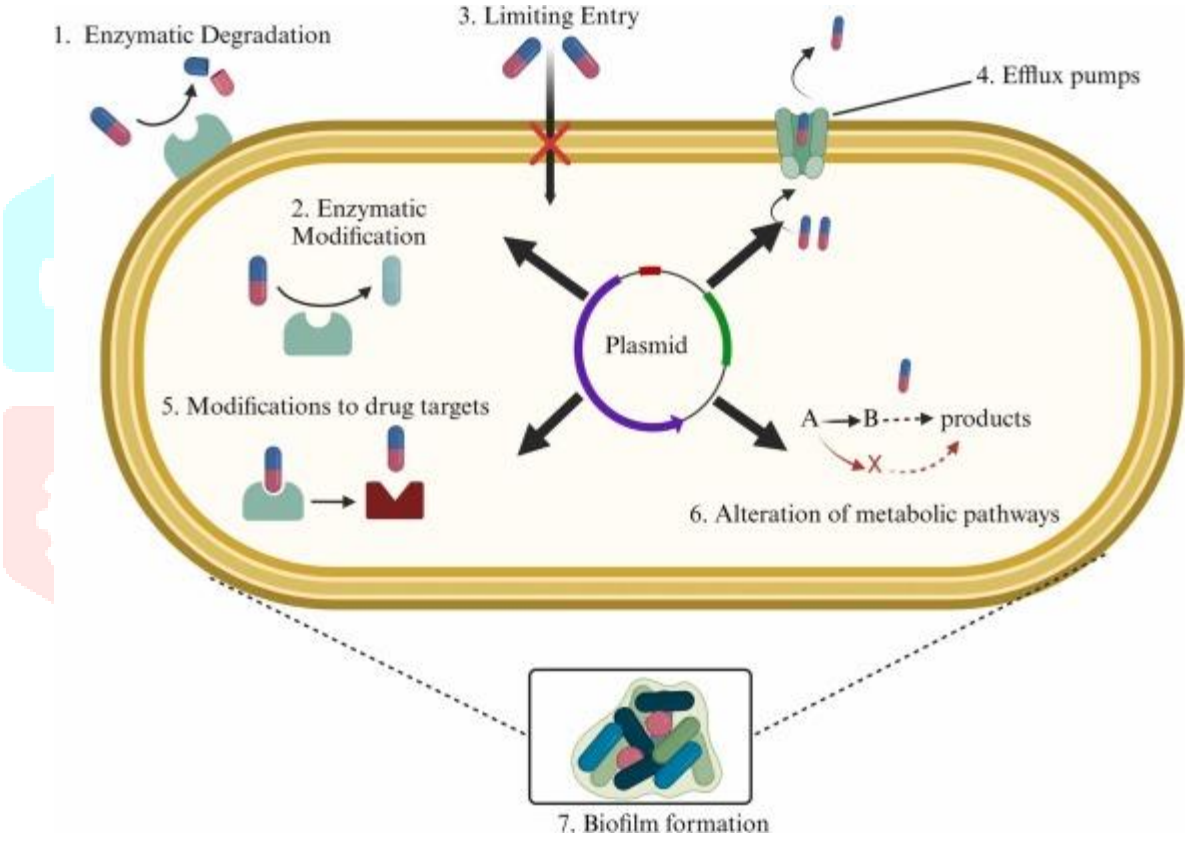

Fig 01: Mechanism of AMR and microbes involved [23]

Furthermore, bacteria can exchange resistance genes with other bacteria through a process called horizontal gene transfer. This allows bacteria to quickly spread resistance within their population [24]. Some bacteria, like Staphylococcus aureus and Escherichia coli, have acquired resistance through gene mutations or by taking up resistance genes from other bacteria. These genetic changes can make them resistant to many types of antibiotics, leading to multidrug-resistant (MDR) strains [25].

Examples of bacteria and fungi with AMR include methicillin-resistant Staphylococcus aureus (MRSA), carbapenem-resistant Enterobacteriaceae (like Klebsiella pneumoniae), and fluconazole-resistant Candida fungi, which cause infections in high-risk patients. Even viruses like HIV and influenza can develop resistance to antiviral treatments [25].

3.The impact of ABR on human and animal populations

Antibiotic resistance (ABR) has become a complex problem affecting both human and animal health. The overuse and misuse of antibiotics in healthcare, farming, and veterinary medicine have sped up the development of drug-resistant microorganisms [26]. This has led to the rise of so-called "superbugs"—bacteria that are resistant to multiple drugs, making them harder to treat and causing serious infections. Additionally, the slow development of new antibiotics is making the problem worse, as resistance is growing faster than new treatments are being discovered [27].

ABR is now one of the biggest health threats of the 21st century. Infections that were once easily treatable are becoming harder to manage, creating major challenges for doctors. As first-line antibiotics lose their effectiveness, doctors are turning to more expensive and toxic second- and third-line drugs, which also require longer treatments. This not only puts a strain on individuals' health and healthcare systems but also costs more money. People may have to stay in the hospital longer, which affects their recovery and productivity at work. ABR infections also require more visits to outpatient clinics, more tests, and extra precautions. It's estimated that ABR causes over a million deaths each year. Without effective antibiotics, basic medical procedures like surgery, organ transplants, chemotherapy, and neonatal care could become much more risky. Some bacteria, known as "ESKAPE" pathogens (like Enterococcus faecium, Staphylococcus aureus, and Klebsiella pneumoniae), are particularly dangerous because they're resistant to many antibiotics and are major threats in hospitals [27].

ABR also affects food production and human health by allowing resistant pathogens to pass from animals to humans. The overuse of antibiotics in livestock, both to treat disease and promote growth, has created large reservoirs of resistance. This can spread dangerous bacteria like Salmonella and Campylobacter through the food chain or by people handling animals. Even wildlife is getting exposed to ABR through environmental contamination. Resistant bacteria can spread through fertilizers made from manure, contaminate water supplies, and end up on food. These bacteria can even pass on resistance genes to other microbes in the environment or human body. The spread of ABR in animals is also causing outbreaks of infections in livestock, leading to culling (destroying infected animals) and major financial losses. It's estimated that ABR could cost \$3–4 billion in losses in the livestock industry over the next few decades [28].

This growing problem is not only an agricultural and economic concern but also a threat to national security and international trade. To fully tackle ABR, a "One Health" approach is needed—this means combining efforts in human, animal, and environmental health to monitor and address the issue from all angles [28].

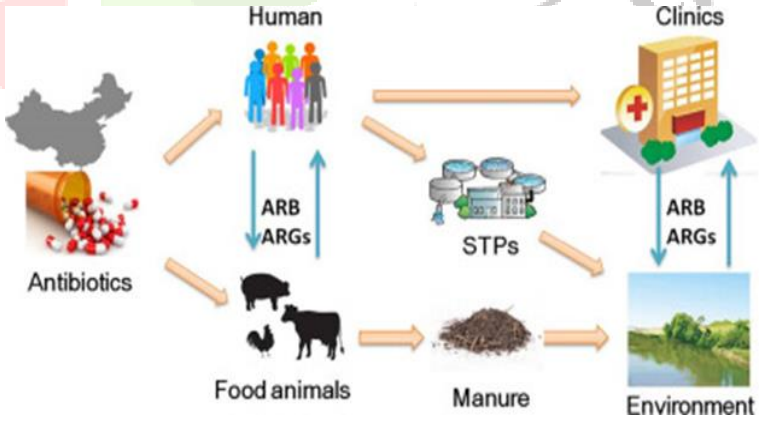

Fig 02: The impact of ABR on human and animal populations [29]

4. Antibiotic Use in Agriculture and Resistance Spread

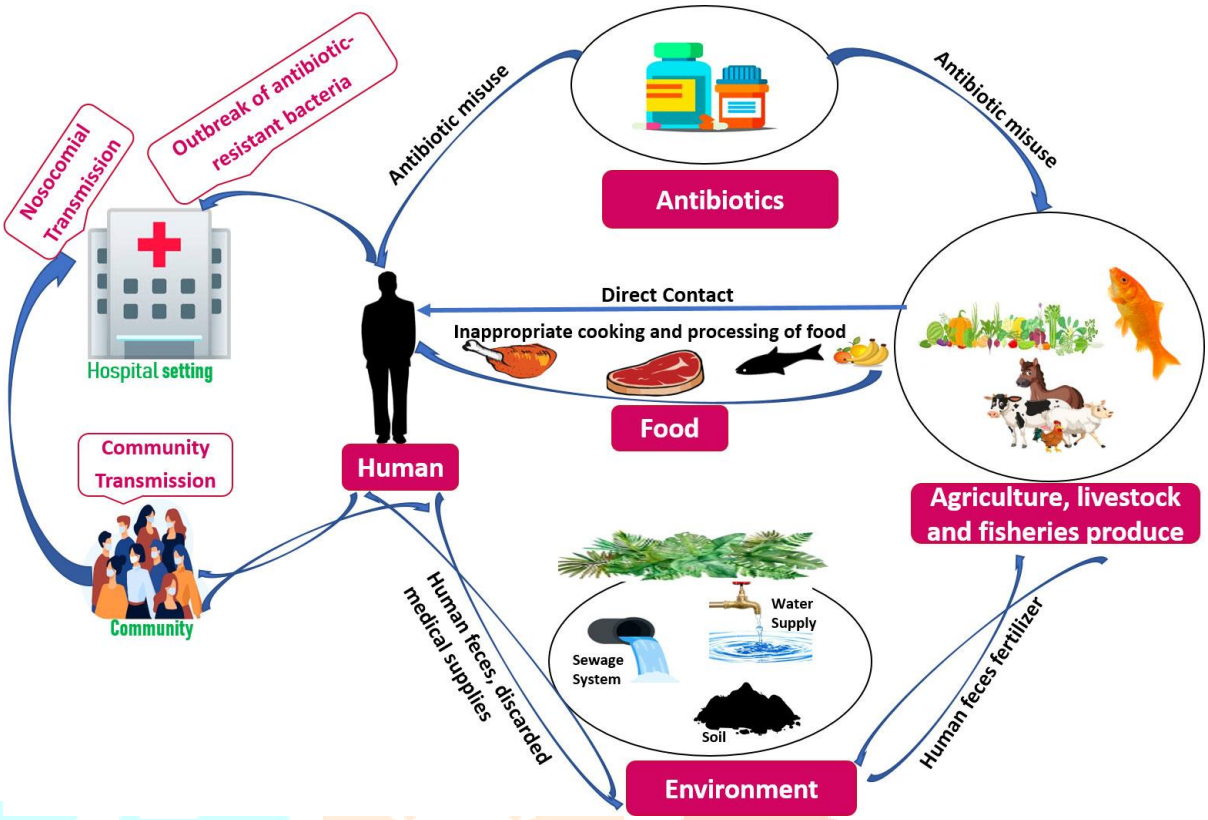

Fig 03: Antibiotic use in Agriculture and Resistance Spread [30]

Many antibiotics used in farming are the same or similar to those used in human medicine. Overusing them in agriculture can lead to drug resistance. One major way resistant bacteria spread from animals to humans is through the food chain [31] . In some developed countries, animals are given antibiotics through food, water, or injections, which can help bacteria become resistant to those antibiotic. For example, using antibiotics in cattle feed to promote growth has been linked to increased resistance [32] .

Recent studies show that poultry and pork may be sources of quinolone-resistant Escherichia coli (E. coli). In rural villages in Barcelona, one-fourth of children were found to carry these bacteria in their faeces, even though they had never taken quinolone antibiotics [33] .

5.How Antibiotic Resistance Develops

Antibiotics work by killing bacteria. In response, bacteria have natural ways to become resistant. This usually happens through changes (mutations) in their genes. When antibiotics are used, they create pressure that encourages bacteria with resistance genes to survive and multiply [2] .

Bacteria can also share resistance genes with other bacteria by passing small DNA pieces called plasmids [2]. This means resistance can spread even without natural selection. In hospitals, broad-spectrum antibiotics are often used to treat infections, but this can increase resistance [34].

While antibiotics kill most bacteria in an infection, some may survive due to genetic mutations. These surviving bacteria can multiply and lead to resistance [23] . There is a strong link between how much antibiotics are used and how many resistant infections occur [9] .

Resistance can also develop when people don’t finish their full course of antibiotics. The remaining bacteria survive and become stronger [9]. Over time, bacteria can gather multiple resistance traits and become resistant to many types of antibiotics [2].

For example, Staphylococcus bacteria became resistant to aminoglycosides due to mutations, poor drug transport into the bacteria, and enzyme changes. One antibiotic can also cause resistance to other drugs in the same family. For instance, if bacteria become resistant to tetracycline, they may also resist oxytetracycline, doxycycline, and others [35] .

Some microbes have long had resistance genes to protect themselves from natural antibiotics—even before humans started using antibiotics for treatment [36] .

6.Common Mode of Drug Resistance (Table 1)

Antibiotic class	Example(s)	Mode(s) of resistance
P-Lactams	Penicillin, Cephalosporins, Penems, Monobactams	Hydrolysis, efflux, altered target
Aminoglycosides	Gentamicin, Streptomycin, Spectinomycin	Phosphorylation, acetylation, nucleotidylation, efflux, altered target
Glycopeptides	Vancomycin, Teicoplanin	Reprogramming peptidoglycan biosynthesis
Tetracyclines	Minocycline, Tigecycline	Monooxygenation, efflux, altered target
Macrolides	Erythromycin, azithromycin	Hydrolysis, glycosylation, phosphorylation, efflux, altered target
Lincosamide	Clindamycin	Nucleotidylation, efflux, altered target
Streptogramins	Synergid	Carbon-Oxygen lyase, acetylation, efflux, altered target
Oxazolidinones	Linezolid	Efflux, altered target
Phenicol	Chloramphenicol	Acetylation, efflux, altered target
Quinolones	Ciprofloxacin	Acetylation, efflux, altered target
Pyrimidines	Trimethoprim	Efflux, altered target
Sulfonamides	Sulfamethoxazole	Efflux, altered target
Rifamycin	Rifampicin	ADP-ribosylation, efflux, altered target
Lipopeptides	Daptomycin	Altered target
Cationic peptides	Colistin	Altered target, efflux

(Table 1) Mode of Drug Resistance [37]

7.Causes of Antibiotic Resistance

a. Overuse of antibiotics

- Taking antibiotics when they aren't needed (e.g., for viral infections like colds or flu).
- High antibiotic use in healthcare and community settings increases selective pressure for resistant bacteria [9].

b. Misuse of antibiotics

- Not finishing prescribed courses.
- Taking incorrect doses.
- Using leftover or non-prescribed antibiotics [38].

c. Overuse in livestock and agriculture

- Routine use of antibiotics in animals to promote growth or prevent disease.
- Resistant bacteria can spread to humans through food, water, or the environment [39].

d. Poor infection prevention and control

- Inadequate sanitation, hygiene, and infection-control practices in hospitals and communities.
- Allows resistant bacteria to spread more easily [40].

e. Lack of new antibiotics

- Very few new antibiotics have been introduced over the past several decades.
- Existing drugs are used repeatedly, increasing resistance [41].

f. Global travel and trade

- Resistant bacteria can spread quickly across countries through travel, food supply chains, and migration [42].

g. Environmental contamination

- Antibiotic waste from pharmaceutical factories, farms, and hospitals can enter water or soil.
- Creates "hotspots" where resistant bacteria develop [43].

8.Consequences of Antibiotic Resistance

Bacteria that resist antibiotics are often called "superbugs." These aren't just a concern for scientists—they're a global health crisis. Superbugs cause life-threatening infections and many deaths. In times of crisis—such as war, famine, or natural disasters—the situation becomes worse [44].

The World Health Organization (WHO) warns that if we don't act now, we may enter a "post-antibiotic era" where even minor infections or injuries could become deadly. In the U.S., over 63,000 people die every year from infections they got in hospitals. In Europe, around 25,000 people die each year from infections caused by multi-drug resistant bacteria [45].

One major cause is the spread of Staphylococcus aureus in hospitals, especially the methicillin-resistant strain (MRSA), which is spreading quickly across the globe. Treating these infections leads to higher healthcare costs and lost productivity [46] .

Some pharmaceutical companies still sell antibiotics that don't work or lack proper approval. Research shows that more use of antibiotics leads to more resistant bacteria. People who have taken antibiotics before are more likely to be infected with resistant bacteria. Restarting the same antibiotic after a break makes resistance even worse [47] .

9.Regulations and the Global Response

Currently, there is no unified global guideline on how to use antibiotics every day. Different countries have different rules. Some, like the UK, have taken steps to manage antibiotic use. Others have not made much progress [48].

The WHO recommends that in developing countries, antibiotics should only be used for serious illnesses like bloody diarrhoea or cholera [49].

Since the industrial revolution, humans have polluted land, water, and air with harmful substances. Household products with high levels of antibacterial chemicals also increase the risk of resistance, yet regulations for these are lacking [2] .

There is overwhelming evidence that antibiotic resistance is a serious global issue. Countries where antibiotics are cheap and easy to get—especially without a prescription—see the highest levels of misuse. In places without universal healthcare, controlling antibiotic use is difficult [50] .

A study in the UK found that 11.3% of people didn't finish their last course of antibiotics. Most said it was because they either felt better or forgot [51] .

This crisis affects everyone—not just doctors and scientists. Farmers, factory workers, policymakers, and the public all need to act. We need awareness, strong laws, responsible use, and behaviour changes across industries. Technology can also help—for example, reminding patients to take their medicine on time. [48]

10.Artificial intelligence in combating ABR

Artificial intelligence (AI) is being used in many areas of healthcare today, showing its broad potential in modern medicine. Studies have shown that AI is effective in fighting antibiotic resistance (ABR) by quickly detecting patterns in bacterial behaviour and improving treatment strategies. These advancements offer great potential for creating more effective and personalized treatments for ABR, which is a growing global health threat. AI and machine learning technologies are expected to improve antimicrobial stewardship (responsible use of antibiotics) and precision medicine, which can help address the ABR crisis [52].

As more bacteria become resistant to standard antibiotics, AI tools that improve diagnostics, optimize antibiotic prescriptions, and help replenish antibiotic pipelines will be extremely useful. AI can enhance traditional antibiotic stewardship programs, which usually rely on specialized staff and strict drug policies. For example, AI systems using advanced neural networks can help identify infections faster based on a patient's symptoms, allowing doctors to start targeted treatments sooner. AI prescription assistants can also combine patient data, local microbiology reports, and treatment guidelines to recommend the best antibiotics to use [53].

By using AI, doctors can reduce the unnecessary use of broad-spectrum antibiotics (which are used for a wide range of infections) when they're not needed, helping to prevent further resistance. AI can also help monitor patients continuously to ensure antibiotics are stopped when they're no longer needed, reducing the risk of overuse. In addition, AI-powered tools can track local outbreaks of resistant bacteria, helping health authorities update their treatment policies. AI systems can also analyse large datasets (such as omics data and published research) to find new drug targets or ideas for developing new antibiotics [54].

Despite these benefits, there are still limitations that need to be addressed. One challenge is the quality of the data AI systems are trained on. Most healthcare AI systems use narrow, specialized neural networks based on limited clinical data, which can lead to biases or incorrect predictions. Inaccurate predictions can cause doctors to over-prescribe antibiotics or use them inappropriately, which could worsen the problem. Most antibiotic prescription data comes from developed countries, so AI models may not work as well in other regions. Additionally, many AI systems still lack transparency, meaning doctors don't fully understand how the AI makes its recommendations, which can reduce trust in the technology [55].

Another issue is that while AI has shown success in predicting drug targets and understanding how drugs work, these predictions often haven't been validated through experiments yet. Plus, many AI tools for ABR are still mostly in research stages and haven't yet been fully integrated into clinical practice. Despite these challenges, with careful development and proper application, AI holds great promise in helping combat the growing AMR crisis [56].

11.Current Situation and Future Solutions

The most dangerous superbug today is Staphylococcus aureus. Its resistance is rising fast. It is deeply linked to human history, yet its behaviour is still not fully understood. This makes it a serious health threat. Antibiotic misuse in animals is also a major problem. Antibiotics are often given to livestock to help them grow faster or prevent disease. Strict rules are needed in farming to prevent further harm [57].

Treating bacterial infections is becoming harder each day. Resistance causes treatment failures, as seen in diseases like tuberculosis. We need new antibiotics that bacteria can't resist. Researchers are also exploring alternative treatments [57].

One such method is passive immunization, where antibodies are given to people to help prevent infections. Another option is phage therapy, which uses viruses that attack bacteria. New antibiotics and treatments are being tested in clinical trials. Modern research focuses not just on single targets, but also on the entire biological systems that bacteria use to survive. Promising results are seen in using a mix of antibiotics and phases together, which might become a powerful future treatment [58].

Conclusion

Antibiotic resistance is now at its highest level worldwide. Even though some countries have taken steps to control it, the use of antibiotics in people, animals, and farming continues to rise. This has created a major problem for healthcare systems, including longer hospital stays, the need for special isolation rooms, strict infection control, and treatments that often fail. To manage this growing issue, public health leaders should create a strong surveillance system that works at both national and international levels. This system should include regular monitoring, analysis, and mandatory reporting of antibiotic resistance cases.so the antibiotic should only take in required condition.

Antibiotic resistance is a rapidly growing global threat driven by overuse, misuse, and agricultural practices. It endangers human and animal health, increases healthcare costs, and limits treatment options. Combating this crisis requires coordinated efforts: responsible antibiotic use, public education, strict regulations, surveillance, and the development of new therapies. Emerging tools like AI, phage therapy, and novel antibiotics offer hope, but urgent global action is essential to prevent a post-antibiotic era.

Both national and global rules must be consistent and strictly followed to prevent the overuse and misuse of antibiotics. This review involved mechanism of antibiotic resistance, also the origin of antibiotic resistance, use of AI in antibiotic resistance, and how the impact of antibiotic resistance on human body.

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