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Antibiotic Resistance: Understanding the Threat and Exploring New Antimicrobial Strategies A Review
Short Running Title: Innovating Antimicrobial Strategies

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ABSTRACT
One of the most crucial public health concerns of the twenty-first century is antimicrobial resistance (AMR), which represents a danger to the prevention and treatment of a number of diseases brought on by bacteria, viruses, parasites, and fungi. Treatment for common illnesses is becoming more and more challenging due to the overuse and misuse of antibiotics, which has expedited the evolution of resistant microorganisms. This review examines the multifaceted issue of AMR, with a focus on its global impact, the mechanisms behind drug resistance in various pathogens, and the critical need for novel antimicrobials. It highlights the alarming rates of resistance in bacterial infections, fungal diseases, tuberculosis, malaria, and neglected tropical diseases (NTDs). Additionally, it addresses the inappropriate prescribing practices and the over-the-counter availability of antibiotics that exacerbate the problem. The review also explores current and potential strategies to combat AMR, including the rational use of existing antibiotics, regulatory measures, and the advancement of new drugs and technologies. By presenting a comprehensive overview of the current state of AMR and the urgent demand for innovative solutions, this article aims to underscore the necessity of coordinated global action to avert a looming healthcare catastrophe.

Keyword: antimicrobial, antifungal, antioxidant, antituberculosis

I. INTRODUCTION

One of the main issues that humanity is currently experiencing is antibiotic resistance. The demand for novel antimicrobials has surged significantly. (**1**)A growing number of diseases caused by bacteria, viruses, parasites, and fungi that are resistant to the conventional antibiotics used to treat them are being prevented and treated at risk due to antimicrobial resistance (AMR), which has emerged as a significant public health concern of the twenty-first century. The problem of antibiotic resistance in bacteria makes AMR an especially pressing concern. For many years, every new antibiotic that enters the market has led to some degree of resistance among bacteria that cause common or serious diseases. Considering this, action is needed to stop the escalating global healthcare crisis. (**2**) Higher rates of illness and mortality are linked to the global issue of antibiotic-resistant microorganisms. Certain infections are now resistant to the effects of conventional antimicrobials due to the presence of multidrug-resistant bacteria, which can be Gram-positive or Gram-negative. (**3**)Antimicrobial resistance (AMR) develops more quickly when antibiotics are overused and abused. The accessibility of antibiotics without a prescription and the absence of expert supervision are two factors that contribute. (**4**)India has one of the world's topmost levels of infectious illness burden. A latest study revealed that antimicrobial resistance has increased because of the inappropriate and illogical use of antimicrobial medicines to treat infectious diseases. Furthermore, research has demonstrated that the health system in India is severely underfunded by the government, which creates an environment that is conducive to the emergence of drug resistance. (**5**) By the year 2050, antimicrobial resistance, or AMR, has grown to be a major public health risk that may cause 10 million deaths annually. India has one of the highest rates of drug-resistant infections in the world. By 2050, it's estimated that AMR would kill two million people in India. (**6**) The number of individuals dying from AMR alone is higher than the total deaths from cancer and traffic accidents. Action plans have been developed by health authorities in several nations, including India, to contain it. It is critical to acknowledge the role that each of the following four domains plays in the fight against AMR: the environment, food, animals,

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and humans. One of the greatest rates of antibiotic resistance in both humans and food animals is seen in India. (**7**)

Examination of agents that cause antimicrobial resistance

1. Drug resistance in bacteria

In the early 1900s, many thought the war against microorganisms had been won when antibiotics were discovered. Nevertheless, it was soon discovered that the microorganisms can develop resistance to any drugs being given. It seems that most pathogenic bacteria have the capability to develop resistance to certain antimicrobial agents. The worldwide rise of antibiotic resistance is posing a danger to the efficiency of conventional antibiotics against common bacterial illnesses. Draws attention to the concerning rates of resistance among common bacterial infections.Antimicrobial medications such as aminoglycosides, macrolides, tetracycline, fluoroquinolones, and others are severely resistant to Methicillin-resistant S. aureus (MRSA). (**9**)

2. Drug-resistance in fungi

Fungi are some of the most significant eukaryotic microorganisms on the planet; they are linked to massive agricultural losses as well as the extinction of numerous other life forms. Common fungus species that weaken the immune system have the potential to become invasive diseases. They do this by moving methodically and developing invasive fungal infections (IFIs), which can damage several organs and organ systems. The most clinically significant pathogens causing invasive fungal infections are species of fungi found in the genera Candida, Aspergillus, Cryptococcus, and Pneumocystis. There are only a few types of antifungals, which fall into three main categories: azoles (fluconazole, itraconazole,voriconazole,etc.), echinocandins (caspofungin and micafungin), and polyenes such as (amphotericin B). (**10**)

3. Drug resistance in tuberculosis

Around the world, tuberculosis (TB) remains a serious infectious illness and public health issue. An estimated 8.6 million tuberculosis (TB) incidence cases were reported in 2012, and the disease was responsible for 1.3 million fatalities, according to the most recent World Health Organization (WHO) study. 320,000 HIV-related deaths were recorded, while more than 500,000 paediatric cases were recorded. However, the rise in drug resistance is even more concerning. Approximately 450,000 instances of multidrug-resistant (MDR) tuberculosis were reported in 2012; 170,000 deaths were attributed to the illness. Multidrug-resistant tuberculosis, or MDR-TB, is caused by strains of Mycobacterium tuberculosis that are resistant to isoniazid and rifampicin, two of the most important drugs used to treat the disease. (**11**)

4. Drug resistance in malaria

A hematoprotozoan parasitic disease called malaria is spread by several anopheline mosquito species. Although people are often infected by four species of Plasmodium, the majority of cases of morbidity and mortality are caused by Plasmodium falciparum. Chloroquine resistance in P. falciparum has increased significantly in most malaria affected countries. In cases of falciparum malaria, the death rate related to this presentation is approximately 0.1% if there are easily accessible, effective treatments. A very minor proportion of P. falciparum infections result in significant parasite burdens due to unchecked parasite development. These parasite burdens impair crucial organ function, causing acidosis, more severe anaemia, and impaired consciousness. (**12**)

5. Drug resistance in neglected tropical diseases (NTDs)

A threat to global public health, antimicrobial resistance (AMR) has the potential to claim millions of lives. Antimicrobial usage has skyrocketed due of preventive chemotherapy eradication and control initiatives targeting neglected tropical diseases (NTDs). Neglected tropical diseases (NTDs) have afflicted more than 2 billion of the world's poorest people within the last 20 years. Infections caused by viruses, parasites, and bacteria account for the majority of NTDs in America, Asia, and Africa. The two primary strategies for treating NTDs are preventive chemotherapy and transmission control (PCT), which consists of innovative and intensified disease management (IDM) and mass drug administration (MDA). (**13**)

Issuesabout the excessive use of antibacterial agents

1. Resistance against microbes

Antibiotic-treated bacteria are the source of the naturally occurring antibiotic resistance. The drugs put vulnerable bacteria under selection pressure by either killing or inhibiting them; on the other hand, bacteria that have grown or are

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inherently resistant to the medications are more likely to endure and spread.misuse of antibiotics, as well as inappropriate use (inadequate dosage, inappropriate decisions, and noncompliance with treatment protocols) can exacerbate antibiotic resistance. (**14**)Antimicrobial resistance (AMR) rates are steadily rising globally, which is concerning and a serious threat to public health. One of the most significant strategies for combating AMR is the creation of novel antimicrobial agents. But when it comes to creating new strategies to tackle antimicrobial resistance (AMR), it seems that the scientific community is lagging due to the ability of multi-drug resistant bacteria to evolve. The "pioneering strategy" of developing entirely new medications is a reasonable approach, but it takes a lot of time and effort. Rather, the advancement of drug development could be accelerated by concentrating on enhancing the efficacy of presently accessible antibiotics via combination medicines, bacteriophage therapy, antimicrobial adjuvant therapy, or nanotechnology.(**15**)

2. Adverse effect

One of our most often-used medications is an antibiotic. They are helpful in the treatment of serious and sometimes lethal infections. On the other hand, using them may have negative consequences and increase bacterial resistance. Adverse effects may vary in severity, be common or uncommon, and be depending on the dosage or duration of the medication or wholly unique. Unfortunately, neither the patient nor the doctor are often aware of the direct risks associated with antibiotics. This is partially because many common side symptoms (such as nausea and vomiting) are covered up by the infection or illness itself, and patients may choose not to disclose them. (**16**) Additionally, secondary Candida species overgrowth is likely to be brought on by broad-spectrum antibiotics, particularly in diabetes. Amoxicillin or ampicillin, clindamycin,third-generation cephalosporins (including cefotaxime and ceftazidime), and fluoroquinolones are the main culprits behind Clostridium difficile infections. (**17**)

3. Resistance against host

The more concerning development in the current treatment landscape is the introduction of multidrug-resistant strains of Gram-positive (Staphylococcus, Enterococcus, Streptococcus species) and Gram-negative (Pseudomonas, Klebsiella, Enterobacter, Acinetobacter, Salmonella species) bacteria. Resistance to many drugs in tuberculosis is a further grave public health concern. Certain agents can be used to treat resistance by changing the dosage schedules (e.g., by using high-dose therapy) or by blocking the resistance mechanism (e.g., by using beta-lactamase inhibitors). Other compounds can only be used to treat resistance by blocking other mechanisms of resistance. The selling of antibiotics without a prescription must be outlawed immediately, hospital staff must be extensively trained in the responsible use of antibiotics, and better controls must be put in place to prevent nosocomial infections. (**18**)

4. Inappropriate Prescribing

The spread of resistant germs is also facilitated by medications that are wrongly given. Studies have shown that treatment indications, agent selection, and antibiotic drug duration are incorrect in 30 to 50% of instances. A study carried out in the United States found that only 7.6% of the 17,435 patients hospitalized for community-acquired pneumonia (CAP) had a pathogen identified. Antibiotics that are given incorrectly expose patients to potential side effects and have dubious therapeutic value. (**19**)

Techniques for Countering Antimicrobial Resistance

1. Over the counter (OTC) antibiotics

The major focus of measures to maintain the effectiveness of antibiotics is on hospitals, drug suppliers, and preventing the use of antibiotics without a prescription. The systematic study undertaken by Morgan et al. revealed that non-prescription antibiotic use varied widely, from as low as 3% in studies conducted in northern Europe to 100% in studies conducted in Africa. This implies that regulatory monitoring of the use of over-the-counter antibiotics is desperately needed. (**20**)

2. Rational use of antibiotics

The misuse of medications is an international issue. According to estimates, less than half of all patients take their medications as directed by a doctor or pharmacist, and less than half of all medications are prescribed, distributed, or marketed improperly. Patients who use medications excessively run the risk of experiencing negative side effects, wasting money on out-of-pocket expenses, and poor patient outcomes. This requires Both the general public

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and specialists need to be informed about the proper use of antibiotics. (**21**)

3. Invention of novel medications and technologies

Growing worries about antibiotic resistance make it imperative to focus on developing new medications and vaccines to address AMR. Finding novel classes of antibiotics and developing diagnostic tools requires cooperation between national, international, governmental, and academic networks. Encouraging pharmaceutical companies to create innovative antimicrobials for diseases of public health concern can expedite the development of new drugs. (**22**)

II. CONCLUSION

Antimicrobial resistance represents a critical threat to global health, necessitating immediate and concerted efforts to mitigate its impact. The review underscores the complexity and scale of AMR, driven by factors such as the abuse and overuse of antibiotics, inadequate healthcare infrastructure, and the availability of non-prescription antibiotics. The increasing resistance among bacterial, fungal, and parasitic pathogens, particularly in high-burden countries like India, highlights the urgent requirement for novel antimicrobial agents and effective stewardship programs. Strategies to combat AMR must include stringent regulatory frameworks, enhanced surveillance, public and professional education, and significant investment in research and development of new antibiotics and alternative therapies. Collaborative efforts at the national and international levels are essential to curtail the spread of resistance and ensure the continued efficacy of antimicrobial treatments for future generations.

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