RESEARCHERID THOMSON REUTERS

International Journal of Research in Engineering and Applied Sciences(IJREAS)
Available online at http://euroasiapub.org/journals.php
Vol. 14 Issue 3, March -2024,
ISSN(O): 2249-3905, ISSN(P) : 2349-6525 | Impact Factor: 8.202| Thomson Reuters ID: L-5236-2015

STUDY ON COMBATING ANTIMICROBIAL RESISTANCE

Ms Anu sharma

Research scholar ,Department of pharmacy

Dr Ajit kiran kaur

Principal ,Department of pharmacy

Monad,university

ABSTRACT

In addition to the fact that conventional antibiotics are not always successful, antimicrobial resistance (AMR) also poses a threat to our ability to manage infectious diseases. This is one of the most significant obstacles that traditional medicines face. Among the several kinds of antibiotics that are used in the treatment of clinical bacterial diseases, beta-lactam antibiotics are among the most essential. A growth of antibiotic-resistant bacteria, viruses, fungi, and parasites has developed as a result of the rising overuse and misuse of these antibiotics, which has rendered treatments that were previously successful ineffective. This is a cause for concern. As the pandemic continues to deteriorate, it is imperative that novel and comprehensive techniques be developed to combat antimicrobial resistance (AMR). This research examines the issue from every viewpoint, from the reasons and effects of its formation to the catastrophic repercussions it presents to public health. Antimicrobial resistance is a complicated topic, and this study looks at all of the sides of the problem simultaneously. To put the cherry on top of everything, we are going to study a number of novel techniques that have the potential to be the driving force behind overcoming this massive challenge. Our objective is to shed light on the complexities of antimicrobial resistance (AMR) and to study novel options in order to safeguard the effectiveness of antimicrobials and to have an impact on the management *practices of infectious diseases in the future. Antimicrobial resistance is a process that occurs when bacteria and other germs develop to resist antimicrobial treatments.*

Keywords: *Elements of AMR, Antimicrobial, Treatments,*

INTRODUCTION

Antimicrobial resistance (AMR), it is essential to have a comprehensive understanding of the mechanisms that are at play. Microbes use a wide variety of resistance tactics, some of which include the production of biofilms, horizontal gene transfer, and mutations in genes. The problem is made even more problematic by the phenomenon of collateral sensitivity, which is a situation in which resistance to one antimicrobial treatment results in a rise in susceptibility to another. It is possible that researchers may discover vulnerabilities in these systems that can be used in the development of novel medicines by dissecting them at the molecular level.

This process is known as antimicrobial resistance, and it reduces the efficiency of these drugs in treating diseases. In terms of the treatment of bacterial infections, antibiotics have been a game-changer and have been responsible for saving the lives of countless people over the course of history.

There has been an increase in the rate at which resistance strains have arisen as a consequence of the excessive and inappropriate use of antibiotics in human health, agricultural, and veterinary operations. In the event that this issue continues to deteriorate, we can soon find ourselves in a world where antibiotics are no longer available, where routine ailments pose significant hazards to our health. It is vital to do research on the epidemiology, socioeconomic impacts, and historical history of antimicrobial resistance (AMR) in order to put into perspective, the magnitude of the issue and the need of developing new treatments.

Contributing Elements to the Resistance to Antimicrobials

The problem of antimicrobial resistance is caused by a complex interaction between a number of factors, including those that are biological, environmental, and social in nature.

Overprescribing antibiotics in clinical settings, excessive usage of subtherapeutic doses in agricultural settings, and inadequate sanitation and hygiene practices are some of the many factors that contribute to the development of bacteria that are resistant to antibiotics. The ease with which microorganisms that are resistant to antibiotics may cross international borders is another consequence of worldwide business and travel. It is necessary to first have an understanding of the factors that lead to antimicrobial resistance (AMR) before we can design comprehensive tactics to address AMR and its underlying causes.

Consequences for Public Health

In addition to having a significant influence on healthcare systems and economies, the repercussions of antibiotic resistance that is not under control reach well beyond the health impacts that are experienced by people. The absence of efficient antimicrobial medicines leads to a rise in the rates of death and morbidity, as well as an increase in the risk of normal medical procedures, such as organ transplants, chemotherapy, and surgical procedures. There is a significant effect on the economy as a result of the rising costs associated with prolonged treatments, hospitalizations, and the development of new antimicrobial medications. In order to generate political, social, and financial support for the development and implementation of new initiatives, it is necessary to have knowledge of the far-reaching repercussions of antimicrobial resistance (AMR).

Across the world, particularly in India, the AMR has emerged as a major public health problem. India is home to some of the highest rates of antibiotic resistance among the bacteria that are responsible for the majority of illnesses that occur in the community and in healthcare institutions. There is a significant prevalence of antimicrobial resistance in India, which has led to the country being one of the major users of antimicrobials in the world. The Enterobacteriaceae spp. have been listed on the critical priority list of multidrug-resistant organisms that has been compiled by the World Health Organisation (WHO), and it is imperative that this matter be handled as soon as possible. K. pneumoniae is a significant member of the Entero-bacteriaceae family. It is regarded as one of the opportunistic pathogens that are responsible for a wide range of disorders and are shown an increasing tendency to acquire resistance to antimicrobial treatments.

Therefore, the current investigation focuses on the antibiotic resistance that is present in clinical isolates of Klebsiella pneumoniae that were obtained from a variety of clinical specimens. The synergistic action of the established antimicrobial medicines that have been authorised by the FDA, together with a few more medications, against the clinical isolates of K. pneumoniae that are resistant to multiple treatments.

This research was carried out between the years 2015 and 2020, and the Enterobacteriaceae data that was incorporated encompassed the years 2014 to 2019. All of the clinical isolates of Enterobacteriaceae were obtained from diagnostic laboratories and centres located in the Delhi-National Capital Region (NCR) of India. As a result of the COVID-19 pandemic scenario, we were unable to collect clinical isolates in the year 2020. Enterobacteriaceae species are found to play a significant role in the treatment of hospital-acquired infections. This is mostly due to the high robustness of these bacteria as well as the numerous antibiotic resistance mechanisms they possess. In the realm of public health, K. pneumoniae is one of the clinically relevant infections that has garnered a great amount of worry and concern. Within the scope of this investigation, a total of 14,273 clinical isolates of Enterobacteriaceae were identified as K. pneumoniae, with 3663 of them being authentic. The Enterobacteriaceae spp. were verified in 297 out of 2645 clinical specimens in a research that performed a cross-sectional analysis. The study also found that 16.2% of the clinical specimens had K. pneumoniae, which was the second most isolated pathogen. In this investigation, we discovered clinical isolates of K. pneumoniae at a rate of 25.6%, which is comparable to the findings of another cross-sectional study that showed the incidence of isolation of K. pneumoniae at 24%. Therefore, we are able to assert that K. pneumoniae is one of the organisms that is extended the most commonly in both the community and in the settings of nosocomial organizations.

In clinical microbiology laboratories, the conduct of antimicrobial susceptibility testing (AST) of these bacteria is a crucial duty that must be done after the identification of the pathogen that caused the illness. The purpose of this testing is to determine whether or not the bacteria are susceptible to antimicrobial drugs and to discover any possible drug resistance. In this particular investigation, the phenotypic characterisation of the clinical isolates of K. pneumoniae was accomplished by the use of both automated and broth micro-dilution techniques. According to the results of the antibiotic susceptibility tests performed on these clinical isolates, the development of antimicrobial resistance was observed.

The antimicrobial susceptibility testing that was performed using an automated machine and broth micro-dilution revealed that the ampicillin had the greatest rate of resistance, which ranged from 99.5 to 100%. The source of this resistance may be the inherent resistance that K. pneumoniae possesses to this particular antimicrobial agent. Therefore, K. pneumoniae is naturally resistant to ampicillin and amoxicillin because it generates blaSHV-1, which is encoded on the chromosome or on a plasmid that may be transferred with other bacteria. A hundred percent resistance was found in clinical isolates of K. pneumonia that were comparable to the current investigation.

The monobactam antibiotic aztreonam was shown to have an 85% resistance rate among clinical isolates of the bacteria K. pneumoniae. In addition, we found that the rate of resistance was practically same (88.2%) when we used the broth micro-dilution technique. This incidence of resistance is significantly higher than what was found in a seven-year surveillance study of the antibiotic resistance in K. pneumoniae from 2011 to 2017. The research looked at (9-12%) of the cases. According to a review, 73.3% of the aztreonam that was used in this trial was resistant to the medicine, which is comparable to the proportion of resistance that was found in this particular study

It is common knowledge that antimicrobial medicines such as tetracycline have broad range activity against both Gram-positive and Gram-negative bacteria. On the other hand, due to the widespread use of tetracyclines in clinical operations and feed stock, there has been an ongoing selective pressure directed towards organisms that are resistant to the antibiotics. It has been shown that the prevalence of tetracycline resistance among Enterobacteriaceae in clinical settings is rather high, and the rates of resistance have been significantly increased. According to the findings of the current research, around 71% of the clinical isolates of K. pneumoniae were found to be resistant to the antibiotic. According to Leisy-Azar and Ebadi's investigation, which was conducted against clinical isolates of K. pneumoniae, this resistance rate is significantly higher than the 28 percent that they reported. The advent of this category of antimicrobial resistance as a worldwide issue is also suggested by this.

Objectives

1. To the study of alternative methods for combating the development of antimicrobial resistance.

2. To the study of Characterization of the genotypes of clinical isolates that are resistant to multiple drugs for the purpose of confirming antimicrobial resistance (AMR) in K. pneumoniae at the molecular level.

Bacterial Infection-Control Strategies to Avoid Antimicrobial Resistance

When antibiotics are used excessively, they encourage the development of bacteria that are resistant to them. This presents a rising threat to our ability to treat bacterial illnesses, which is a developing concern. By the year 2050, it is anticipated that antimicrobial-resistant bacterial infections would surpass all other causes of death, resulting in considerable economic losses, a rise in morbidity and mortality, and a burden on the healthcare system in the form of unnecessary costs (Figure 1.1).

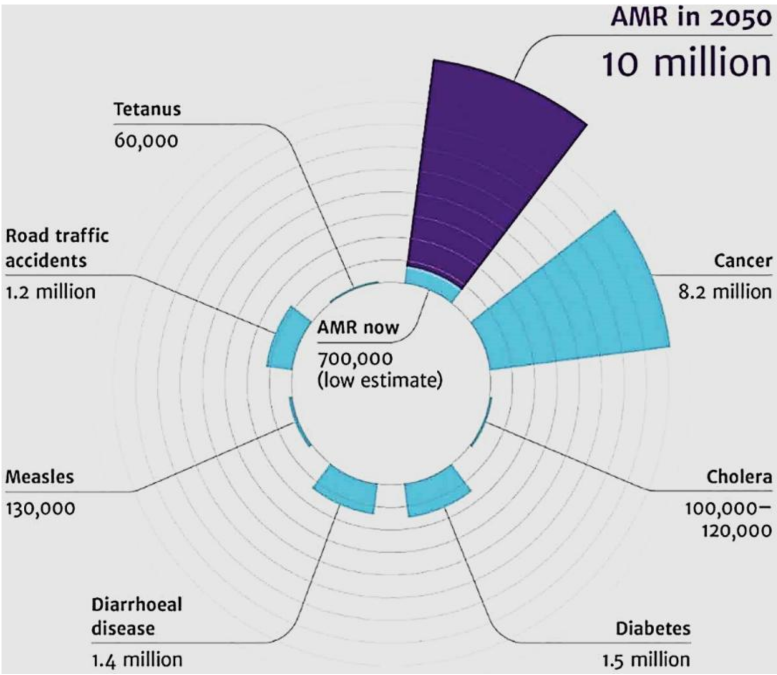

Figure1.1: Disease mortality rates, including those attributable to antibiotic resistance

For a very long time, people have held the belief that the most effective method to prevent this unfavorable prediction from coming true is to develop new antimicrobials that are even more effective than the ones that now exist. On the other hand, the process of developing new antibiotics, obtaining approval for them from regulatory bodies, and finally bringing them down to clinical usage is a very slow one. The pharmaceutical industry is gradually losing interest in the development of novel antibiotics in favor of developing drugs for other diseases that have a rapid return on investment. This is due to the fact that the active lifetime of antibiotics is getting shorter and shorter before the first resistant bacterial strains emerge, and the return on investment is becoming more and more doubtful.

There is a great deal of optimism that developments in nanotechnology will result in emerging strategies for the prevention and management of infections. In light of this, in order to answer the following questions:

(1) Is it feasible to make antibiotic resistance that already exists disappear?

(2) Is there a method to get around the antibiotic resistance that is now prevalent?

(3) Is there a method to stop the emergence of people who are resistant to antibiotics, particularly against emerging infection control tactics that are based on nanotechnology?

As a consequence of this, the healthcare, veterinary, and agricultural sectors have been subjected to an enormous amount of pressure. Within a 'One Health' context, the spread of antimicrobial resistance bacteria from animals that are utilized for food might potentially have severe consequences for the health of both humans and animals. As a result of the worldwide health impact of antimicrobial resistance bacteria and the need for new antibiotics, even so-called "antibiotics of last resort" are losing their effectiveness in clinical settings. This has led to the introduction of innovative strategies to prevent and cure infections caused by multidrug-resistant, extensively drug-resistant, and polydrug-resistant bacteria.

In the following areas, this study aims to thoroughly illustrate several alternative solutions (Figure 1.2):

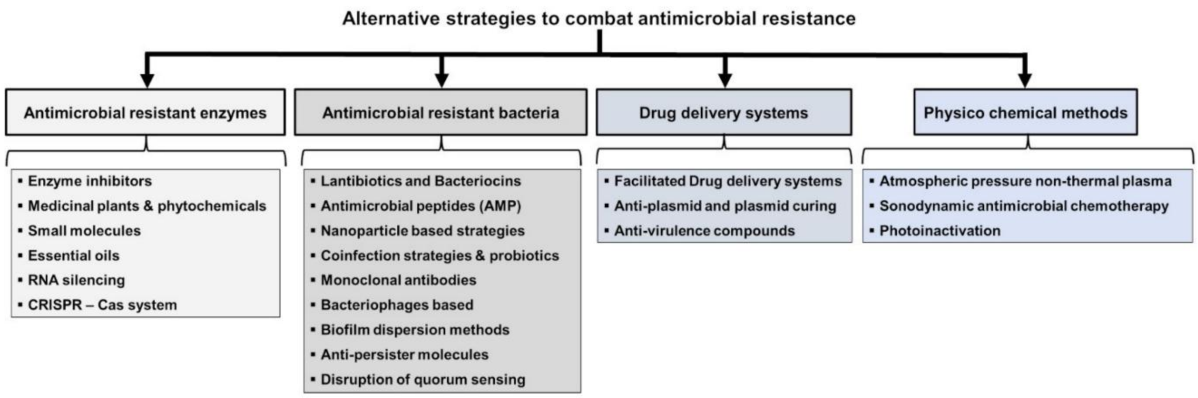

Figure1.2: Types of alternate tactics for battling antibiotic resistance

1. Concentrating on enzymes resistant to antibiotics;

2. Concentrating on microorganisms resistant to antibiotics;

3. Pharmaceutical delivery methods;

4. Physiological-chemical techniques;

5. Non-traditional tactics.

Undoubtedly, one of the most significant challenges that our global community is now confronted with is the growing incidence of bacteria that are resistant to antibiotics. Antimicrobials are at the core of modern medicine because they provide a significant contribution to the treatment of infections, the prevention of infections (also known as prophylaxis) during surgical procedures, and the care of patients who have affected immune systems. The usage of antibiotics by humans increased by a total of 36% between the years 2000 and 2010, with 45% more carbapenems and 13% more polymyxins being used as a last resort. Not only are antimicrobials used for human consumption, but they are also used in the fields of veterinary medicine, aquaculture, and the promotion of development in animals

Novel approaches to infection control

In the process of developing new ways for infection control, novel strategies that are based on nanotechnology are now the focus of considerable research. One may make the case that there are already more novel solutions than are necessary, as a result of the continuous manufacture of a huge number of revolutionary nano-antimicrobials that are highly different from one another. The origins of a number of recently established nanotechnological approaches to the prevention of infections may be traced back to approaches that were first developed for the management of malignancies. Unfortunately, there has been a comparatively less amount of work put into translating these new infection-control approaches for application in clinical settings. The major drivers of this endeavor have been academic interests.

The presentation of an numerous antimicrobials that are based on nanotechnology in Nano-antimicrobials are able to go through pathogenic biofilms because of their small size and the flexibility of their surface. A great number of antimicrobials that are now in use have a tough time penetrating pathogenic biofilms because of the extracellular matrix that is generated by different strains of bacteria. The extracellular matrix protects the inhabitants of biofilms from the host immune system and any antimicrobial attacks that may be launched against them.

MULTIDRUG RESISTANCE GROWING IN ANTIBIOTIC RESISTANCE

In 1945, as he was accepting the Nobel Prize, Sir Alexander Fleming gave a speech in which he warned about the risks associated with excessive use of penicillin and the rise in the development of resistance to the antibiotic. A significant percentage of bacteria already have resistance mechanisms prior to the discovery of antimicrobial drugs. These mechanisms were already in place. As a consequence of the growing use of antibiotics in both animals and people, the prevalence of microorganisms that are resistant to antibiotics has increased.

Antibiotics have the ability to impose a selection pressure on microbial populations; the size of this pressure increases in direct proportion to the number of antibiotics that are used. Antibiotics have been shown to be an effective weapon in the fight against bacterial illnesses ever since they were first introduced more than seventy years ago. However, a significant number of pathogenic organisms have developed resistance to the treatments that were formerly successful against them. This resistance has been passed down through generations. It is becoming more apparent that antimicrobial drugs, which were formerly thought to be helpful against infectious diseases, are becoming less effective against an expanding array of infectious ailments. In recent years, there has been a significant rise in the occurrence of bacterial antibiotic resistance, particularly in livestock systems and healthcare facilities. This is a cause for concern. The danger of antibiotic resistance is increased as a result of this.

CONCLUSION

This study came to the conclusion that, that are resistant to many drugs have developed resistance to at least one antibiotic. There is a possibility that organisms may develop resistance to many drugs if antibiotics are not used appropriately. Several factors have contributed to the development of antibiotic resistance, which has made it more challenging to treat illnesses that are caused by these microorganisms. Clinical professionals may be able to find a solution to the problem of infections caused by multidrug-resistant microorganism through the process of medication repurposing and combination research of the treatments that are already in use another way in which multidrug-resistant strains might emerge is when bacteria go through a biological process that renders them resistant to more than one antibiotic. This may occur when genes that produces resistance to many antibiotics are connected on a chromosome or plasmid, or when a host organism develops with mutations that make it resistant to more than one antibiotic.

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