IMPACT OF MULTIDRUG RESISTANCE BACTERIA ON HUMAN HEALTH

Dr.N.Uma Maheswari Asna M

 PG and Research Department of Microbiology PG and Research Department of Microbiology

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 educational trust women's college (Autonomous) Educational trust women's college (Autonomous)

 Sundarakkottai ,Mannargudi-614016 Sundarakkottai ,Mannargudi-614016

 e-mail id: umasamiamf@gmail.com e-mail id: asnasaaj@gmail.com

 ABSTRACT

 A major global health issue that has been made worse by the lack of innovative classes of antibiotics that have entered clinical use over the past 40 years is the rising incidence of diseases brought on by bacteria that are resistant to several drugs. Antimicrobial drug resistance among different microbial species (infectious agents) has rapidly become a global threat to public health. It results in failure of microbial response to standard treatment due to the pacing advent of new resistance mechanisms and decrease in efficiency of treating common infectious diseases, prolonging illness, increasing healthcare costs, and greatly increasing the risk of death. . As a result of their high levels of multidrug resistance (MDR) and increased morbidity and mortality, nearly all effective infecting agents (such be bacteria, fungi, viruses, and parasites) are referred to as "super bugs." Despite the fact that MDR growth is a natural phenomena, improper antimicrobial medication usage, unsanitary living circumstances, improper food handling, and subpar infection prevention and control procedures all favour the establishment and spread of MDR. Given the importance of MDR, this article underlines its drawbacks and the necessity to comprehend its relevance and how it works to treat microbial infections.

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###  INTRODUCTION

The frequency of microbial illnesses has sharply grown during the past few decades. Resistance has developed among different types of microbes as a result of the ongoing use of antimicrobial medications to treat illnesses. The term "multidrug resistance" (MDR) refers to a microorganism's insensitivity to or resistance to the antimicrobial medications supplied to them (which are structurally unrelated and have diverse molecular targets), notwithstanding prior sensitivity to it. According to the WHO, these resistant microorganisms (such as bacteria, fungi, viruses, and parasites) may fend off an antimicrobial drug's attack, which results in inefficient therapy that causes diseases to continue and spread.. Although the emergence of MDR is a natural occurrence, the large increase in patients with immunocompromised conditions—including HIV infection, diabetes, organ transplant recipients, and patients with severe burns—makes the body a prime target for hospital acquired infectious diseases, which aids in the spread of MDR. Studies from the WHO report have revealed very high rates of antibiotic resistance in bacteria, including Escherichia coli against cephalosporin and fluoroquinolone antibiotics, Klebsiella pneumoniae against cephalosporin and carbapenem antibiotics, Staphylococcus aureus against methicillin, Streptococcus pneumoniae against penicillin, Nontyphoidal Salmonella against fluoroquinolone antibiotics, and Shigella species against fluoroquinolnes.Although the emergence of MDR is a natural occurrence, the large increase in patients with immunocompromised conditions—including HIV infection, diabetes, organ transplant recipients, and patients with severe burns—makes the body a prime target for hospital acquired infectious diseases, which aids in the spread of MDR. Studies from the WHO report have revealed very high rates of antibiotic resistance in bacteria, including Escherichia coli against cephalosporin and fluoroquinolone antibiotics, Klebsiella pneumoniae against cephalosporin and carbapenem antibiotics, Staphylococcus aureus against methicillin, Streptococcus pneumoniae against penicillin, Nontyphoidal Salmonella against fluoroquinolone antibiotics, and Shigella species against fluoroquinolnes. Neisseria gonorrhoeae is resistant to cephalosporin, and Mycobacterium tuberculosis is resistant to rifampicin, isoniazid, and fluoroquinolones, which cause many hospital-acquired infections and common diseases such urinary tract infections, pneumonia, and bloodstream infections. There are just a few antifungal medications available for the treatment of persistent fungal infections. Resistance to drugs such as polyene macrolides (amphotericin B), azole derivatives (ketoconazole, fluconazole, itraconazole, and voriconazole), DNA and RNA synthesis inhibitors (flucytosine), and 1,3-β-glucan synthase inhibitors exists in isolates of Candida spp., Aspergillus spp., Cryptococcus neoformans, Trichosporon beigelii, Scopulariopsis spp. Prolonged drug exposure and nonstop viral replication result in the advent of various resistant strains and persistence of infections despite therapy. This has made antiviral resistance a matter of concern in immunocompromised patients. Immunosuppressed transplant recipients and oncology patients with either cytomegalovirus (CMV) or herpes simplex virus infections experienced the effects of antiviral medication resistance (HSV), Varice The enormous increase in patients with immunocompromised conditions, such as HIV infection, diabetes, organ transplant recipients, and patients with severe burns, makes the body a prime target for hospital acquired infectious diseases, which promotes the spread of MDR. Studies from the WHO report have revealed very high rates of antibiotic resistance in bacteria, including Shigella species against fluoroquinolones, nontyphoidal Salmonella against fluoroquinolones, Escherichia coli against cephalosporin and fluoroquinolone antibiotics, Klebsiella pneumoniae against cephalosporin and carbapenem antibiotics, Staphylococcus aureus against methicillin, and human herpes simplex virus (V (HIV) Plasmodia, Leishmania, and other isolates were examined. The frequency of microbial illnesses has sharply grown over the past few decades. Resistance has developed among different types of microbes as a result of the ongoing use of antimicrobial medications to treat infections. The term "multidrug resistance" (MDR) refers to a microorganism's insensitivity to or resistance to the antimicrobial medications delivered to them (which are structurally unrelated and have diverse molecular targets) notwithstanding prior sensitivity to them. According to the WHO, these resistant microorganisms (such as bacteria, fungi, viruses, and parasites) may fend off attack by antimicrobial medications, which results in inefficient treatment that causes diseases to remain and spread. Despite the fact that the emergence of MDR is a natural phenomenon, an enormous increase in the prevalence of immunocompromised illnesses, such as HIV infection and diabetes, Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae, Nontyphoidal Salmonella, Shigella species, and Neisseria gonorrhoea are just a few examples of the bacteria that are highly resistant to antibiotics such as cephalosporin and fluoroquinolones in people who have undergone organ transplantation and severe burn patients. There are just a few antifungal medications available for the treatment of persistent fungal infections Flucytosine, azole derivatives, 1,3-glucan synthase inhibitors (echinocandins), DNA and RNA synthesis inhibitors (ketoconazole, fluconazole, itraconazole, and voriconazole), and polyene macrolides (amphotericin B) are among the medications that some isolates of Candida spp., Aspergillus spp., Cryptococcus neoformans Long-term medication exposure and continuous viral reproduction lead to the emergence of different resistant strains and the maintenance of infections in spite of treatment. Antiviral resistance has become a worry in immunocompromised people as a result of this. Immunosuppressed transplant recipients and oncology patients with cytomegalovirus (CMV), herpes simplex virus (HSV), varicella-zoster virus (VZV), human immunodeficiency virus (HIV), influenza A virus, hepatitis C (HCV), or hepatitis B virus infections have experienced the effects of antiviral drug resistance (HBV) Antibiotics including chloroquine, pyrimethamine, artemisinin, pentavalent antimonials, miltefosine, paromomycin, and amphotericin B as well as atovaquone and sulfadiazine have been tested against isolates of Plasmodia, Leishmania, Entamoeba, Trichomonas vaginalis, schistosomes, and Toxoplasma gondi Malaria, which is caused by Plasmodium falciparum, is one of the most prominent examples of a condition susceptible to MDR. In many tropical and subtropical areas, the protozoan parasite Entamoeba spp. also causes amoebiasis, a serious public health problem. Schistosomiasis is seen as a hazard to world health on a par with malaria and other chronic illnesses. The importance of MDR, various factors that contributed to its development, issues related to MDR, and potential solutions are all highlighted in this review paper.

ANTIMICROBIAL RESISTANCE

This refers to a microbe's capacity to expand in the presence of a chemical (drug) that would otherwise impede their development or completely eradicate them. When it came to treating infections brought on by such germs, their resistance to antimicrobial medication was mostly successful. Among the microbes that defy medication (bacteria, fungi, viruses and parasite). Antimicrobial medications cannot effectively cure certain germs, and infection sets in instead, increasing the risk of transmitting to others. Due to antimicrobial resistance, it is more difficult to get rid of illnesses from the body since the effectiveness of present treatments decreases. As a result, several infections disorders are more challenging to cure now than they were a few decades ago. The use and abuse of antimicrobial medications, which is one of the causes that has contributed to the creation of drug resistant bacteria, has led to a decrease in the protective efficacy of these treatments as more germs developed a resistance to them. When compared to other isolates of the same species, a bacterium is said to be resistant when it is insensitive to an antimicrobial medication. Despite the commercial introduction of various new medications, resistant infectious germs are becoming more common, especially in individuals who have had extended drug exposure. Antimicrobial medications typically work by either inhibiting a metabolic pathway, such as nucleotide synthesis, which then prevents DNA/RNA synthesis, further protein synthesis, and disruption of the cell membrane, or by competing with the substrate of any enzyme involved in cell wall synthesis, such as chitin synthase. In order to circumvent medications' effects and endure exposure to them, microorganisms have developed a wide range of defence mechanisms. This section will mostly discuss the defence mechanisms that microorganisms evolve to fend against drug-induced death.

CLASSIFICATION OF MDR

 The survival of various microbial strains after receiving the right dosages of medications for a set amount of time and the development of high degrees of resistance in them are both indicators. Along with antimicrobial resistance, other factors contributing to this clinical failure include immune system suppression, a lack of or inadequate medication bioavailability, or an accelerated rate of drug metabolism. Primary or secondary resistance can be used to categorise multiple medication resistance.

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 Figure:1.Classification of MDR

A. Primary resistance

Occurs when the organism has never encountered the target medicine in a specific host, i.e., there is a drug resistance in a patient who has not previously received antitubercular therapy. For instance, people who have not previously had TB therapy may develop primary medication resistance. The spread of drug-resistant strains is understood to be the primary source of drug resistance.

 B. Secondary resistance.

The phrase "acquired resistance" is also used to describe this type of resistance, which only develops in an organism as a result of drug exposure. This can also be described as the evolution of resistance in a patient who has already taken chemotherapy. As an illustration, acquired drug resistance expresses TB isolated from patients who have undergone or are presently receiving anti-tuberculosis medication therapy for at least one month.

 It can also be put into the following categories:

 C.Intrinsic resistance

Intrinsic resistance is a microorganism's natural capacity to withstand the activity of a certain antimicrobial agent due to inherent structural or functional properties that allow tolerance of a specific antibiotic or antimicrobials. This is also known as "insensitivity" since it happens in organisms that have never been vulnerable to that specific medicine. Natural insensitivity can be caused by: • Lack of drug affinity for the bacterial target • Inaccessibility of the drug inside the bacterial cell • Extrusion of the drug by chromosomally encoded active exporters • Innate synthesis of enzymes that inactivate the drug Gram-positive bacteria, for example, to aztreonam (a betalactam), Gram-negative bacteria to vancomycin, anaerobic bacteria to aminoglycosides, and aerobic bacteria to metronidazole.

 D. Extreme resistance

It refers to an organism's capacity to survive the inhibitory effects of at least one or two of the most potent antimicrobial medications (Loeffler and Stevens, 2003). This, also known as XDR, appeared in individuals after they had received first-line treatment, for example, XDR-TB (extensive drug resistant tuberculosis) resistance to fluoroquinolone.

 E. Clinical resistance

Clinical resistance is defined as a situation in which the infecting organism is inhibited by a concentration of an antimicrobial agent that is associated with a high likelihood of therapeutic failure or the reappearance of infections within an organism as a result of impaired host immune function, particularly when the pathogen is inhibited by an antimicrobial concentration that is higher than could be carefully attained with normal methods.

BACTERIAL MULTIDRUG RESISTANE AND MODE OF ACTION

MDR microorganisms are bacteria that have developed resistance to some routinely used antibiotics. There are several varieties of MDR bacteria that may be found in the environment, including water and soil. They cause illnesses in the same way as nonresistant bacteria do. When an infection with multi-drug resistant bacteria develops, the choice of appropriate antibiotic to treat the infection may be significantly more limited. Examples include Psuedomonas aeroginosa, Staphylococcus aureus (MRSA), Escherichia coli, Acinetobacter baumannii, Klebsiella pneumoniae, Mycobacterium tuberculosis, and Neisseria gonorrhoeae. Antibiotic resistance in microorganisms can emerge via four different mechanisms:

A. Drug omission or modification

Enzymatic deactivation, like in penicillin G, occurs in some penicillin-resistant bacteria by the formation of -lactamases. The bacterial cell's protective enzymes will add an acetyl or phosphate group to a particular spot on the antibiotic, reducing its ability to bind to bacterial ribosomes and impair protein synthesis.

 B. Target- or binding site modification

For example, changes to PBP—the penicillin binding target site—in MRSA and other penicillin-resistant bacteria, or changes to the structure of ribosomal protection proteins. These proteins protect the bacterial cell against antibiotics by changing its structure. Changes in protein conformational shape cause these proteins to lose their action, preventing protein synthesis and assisting bacterium growth.

 C.Metabolic pathway modification

For instance, the lack of paraaminobenzoic acid (PABA), a precursor for the production of folic acid and nucleic acids.

 D. Less drug accumulation

By reducing drug permeability or enhancing active drug pumping across the cell membrane. Bacterial susceptibility to a given medication is determined by the balance of antibiotic absorption and elimination. Thus, one technique employed by bacteria to acquire antibiotic resistance is to reduce the quantity of antibiotic that can pass through the bacterial cell membrane.

Viruses with Multidrug Resistance and their Modes of Action

Viruses have developed a variety of resistance mechanisms that allow them to avoid the effects of antimicrobials and antivirals. As a result, many have developed resistance to practically every current therapy. This problem, while not new, is becoming more acute, and it is now clear that a fundamental understanding of the mechanisms that microbes and viruses use to develop resistance is required if we are to gain new insights into ways to combat it. To suppress viral replication, antiviral medicines often target viral DNA polymerase with reverse transcriptase activity.

Resistance to Multiple Drugs Fungi and their Modes of Action

To deal with the antifungal, fungal cells have devised a number of ways. They have learned to change the targets of antifungal medications or, more typically, to boost the efflux of incoming drugs. Fungi's cell wall is critical to their existence. Drugs that inhibit ergosterol production (e.g., polyenes) in fungus, preventing the cell from growing. For example, a decrease in the ergosterol concentration of the fungal plasma membrane) results in lower permeability and drug absorption into the cell. Changes in membrane composition (for example, -1, 3-glucan and lipid content in fungal cell membrane) also result in a lack of active target sites for medications (for example, echinocandins in fungi to bind).

. Mutations in the target's genes generate molecular changes and preserve cellular activity by decreasing sensitivity to inhibition. Another mechanism of MDR has been discovered to be an overexpression of drug target enzymes, which leads to target by pass due to changes in certain metabolic pathways (e.g., azoles and allylamines in fungi), resulting in the production of alternate target molecules and interference in some protein synthesis. Yeast, such as Candida species, can grow resistant to azole formulations over time, necessitating treatment with a new medication class. Because of their tolerance to several antifungal treatments, Scedosporium proflificans infections are virtually always deadly.

 Mechanisms of Antibiotic Resistance Development

In the summer of 2002, the long-awaited "superbug" came. Staphylococcus aureus, a common but potentially lethal bacteria, had developed a novel antibiotic resistance gene. This novel strain was identified from diabetic patients' foot ulcers in Detroit, Michigan, where methicillin resistant (formerly methicillinresistant) S. aureus (MRSA) was well recognised as the hospital's scourge. The newest strain was resistant to vancomycin, one of the few medications that could still control S. aureus. This novel vancomycin resistant S. aureus (VRSA) strain was also resistant to ciprofloxacin, methicillan, and penicillin. Hospital vancomycin-resistant Enterococci (VRE) were isolated from the same patient.



Figure 3:mechanism of MDR

The patient's vancomycin-sensitive S. aureus acquired the vancomycin resistance gene VanA from VRE through conjugation, resulting in the emergence of a new threat to human health. Bacteria typically gain resistance through a number of mechanisms. Unfortunately, a certain type of resistance mechanism is not restricted to a particular class of drug. Two bacteria may use different resistance mechanisms to accept the same chemotherapeutic medication. Antimicrobial resistance can be acquired by susceptible bacteria by genetic mutation or by obtaining antimicrobial resistant genes from other bacteria. This can be performed by a variety of biochemical processes, including mutation, destruction or inactivation, efflux, or genetic transfer of components between bacteria via conjugation, transformation, or transduction

A.Mutation

This is a mutation in the DNA that might occasionally result in a change in the gene product, which is the antimicrobial's target. When a sensitive bacterium comes into touch with an antibiotic at a therapeutic dose, such as fluroquinolones, the antimicrobial can bind to the particular enzymes, in this example, DNA gyrase. The DNA gyrase enzyme is a necessary bacterial enzyme for DNA replication. Fluroquninolones, as a result, prevent bacterial DNA replication. Antimicrobials no longer bind efficiently when spontaneous mutations arise in certain sections of the genes encoding these enzymes. This permits the bacteria to keep replicating its DNA. Pathogens frequently develop resistance simply by inhibiting medication entry. Penicillin G has little effect on many gram negative bacteria. because it cannot penetrate the envelops outer membrane . Genetic mutations that lead to changes in penicillin binding proteins also render a cell resistant. A decrease in permeability can lead to sulfonamide resistance .

B. Destroy or deactivate

Many bacteria have genes that create enzymes that chemically breakdown or deactivate antimicrobials, leaving them useless against bacteria. The antibiotic is either destroyed or changed by enzymatic activity before it can reach the target location and harm the bacterial cell . The degradation of penicillin's beta -lactam ring by the enzyme penicillinase medicines are also rendered inactive by the addition

 This is a DNA mutation that may result in a change in the gene product, which is the antimicrobial's target. When a sensitive bacteria comes into contact with a therapeutic dosage of an antibiotic, such as fluroquinolones, the antimicrobial can bind to the specific enzymes, in this case, DNA gyrase. The DNA gyrase enzyme is a bacterial enzyme required for DNA replication. As a result, fluroquninolones inhibit bacterial DNA replication. When spontaneous mutations occur in certain portions of the genes encoding these enzymes, antimicrobials no longer bind effectively. This allows the bacterium to continue duplicating its DNA. Pathogens frequently build resistance merely by preventing medicines from entering the body.

 Many gram-negative bacteria are unaffected by penicillin G. a hemical group Chioramphenicol, for example, includes two hydroxyl groups that may be acetylated by the enzyme chioramphenicol acyltransferase with actyl CoA as the donor. Aminoglycosides can be altered and deactivated in a variety of ways. Acetylation of amino groups is catalysed by acetyltransferases. Some aminoglycoside modifying enzymes catalyse the addition of hydroxyl groups from phosphates or adenyl groups (addenyltransferases)

 C.Efflux

Active efflux of medicines from the interior of bacterial cells is one of the most prevalent drug resistance mechanisms. These drug-resistant bacteria use energy-driven drug efflux pumps to extrude antimicrobial drugs, lowering their intracellular concentration to sub- or non-inhibitory levels. A channel that actively exports antibacterial and other substances out of the cell is what an efflux pump is. The antibiotic enters the bacteria through a channel known as porin and is subsequently pushed out by the efflux pump. These transport proteins are commonly referred to as multidrug resistant pumps since they are largely non-specific and may pump a wide range of medicines. There are two types of active efflux pumps: primary active transport and secondary active transport Primary active transport employs ATP hydrolysis to actively efflux medications from cells, whereas secondary active transport uses an iron gradient to actively efflux drugs from cells. ATP-driven transporters are also referred to as ABC (ATP Binding Cassette) transporters or P-glycoprotein transporters. Bacteria employ both active transport systems to resist the inhibitory effects of antimicrobial drugs, and they are commonly referred to as efflux pumps . Many are drug/proton antiporters, in which a proton enters the cell and the drug exits. Such mechanisms are seen in E. coil, P. aeruginosa, and S. aureus, among others.

 D. Measures to Reverse Resistance

 Several laboratory and epidemiological studies indicate that various processes are predicted to cause long-term persistence of resistant bacteria. One process is compensatory evolution, where the costs of resistance are ameliorated by additional genetic changes, resulting in the stabilization of resistant bacteria in the population. Even though most resistance is associated with fitness cost, some resistance mutations appear to be gratuitous. The occurrence of such cost-free resistances will also cause irreversibility since the driving force for reversibility is absent. The public should wash raw fruit and vegetables thoroughly to clear off both resistant bacteria and possible antibiotic residues. When they receive prescriptions for antibiotics, they should complete the full cours The resistant bacterium is impacted not only by its capacity to tolerate the antibiotic, but also by its contact with the host and ability to be transmitted between hosts in the primary genetic processes, horizontal gene transfers. Most resistance mechanisms, it has been noted, impart a reduction in bacterial fitness, which can be manifested as lower growth and survival inside and outside of a host, as well as reduced virulence or transmission rate from environment to host or between hosts. Washing hands after each patient visit is an important and simple step that is all too frequently forgotten. Two epidemiological studies, one on erythromycin resistance in Streptococcus pyogenes and the other on penicillin resistance in Streptococcus pneumonia, have been proposed as supporting their resistant versatility.e of therapy (to ensure that all the pathogenic bacteria die) and should not "save" any pills for later use .Customers should also avoid requesting antibiotics for colds and other viral diseases, and instead seek non-antibiotic treatments for mild problems such as acne. They can continue to use antibiotic ointments on minor injuries, but they should think carefully about using hand lotions and other antibacterial-infused items on a regular basis. According to new laboratory discoveries, certain bacteria-fighting compounds included in consumer items can select for germs that are resistant to both antibacterial treatments and antibiotics.

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THE PROBLEMS OF MULTIDRUG RESISTANCE BACTERIA

Resistance to several antimicrobial agents in pathogenic bacteria has emerged as a major worldwide public health problem. Drug-resistant bacterial infections are a significant cause of patient death and morbidity, and developing antibiotic resistance is significantly jeopardising the great medical advances made possible by antibiotics over the last 70 years. For example, in 2020, almost 95,000 people in the United States developed methicillin-resistant Staphylococcus aureus (MRSA) infections, and 19,000 people died from MRSA infections - more than die each year from HIV/AIDS, emphysema, Parkinson's disease, and homicide combined.

While the development of Many fields of medicine will suffer if innovative approaches to combating multi-drug resistant (MDR) pathogens are not developed, including surgery, premature infant care, cancer chemotherapy, critical care, and transplantation medicine, all of which are only possible with the availability of effective antibiotic therapy. Compounding the problem of developing bacterial resistance to already authorised antibiotics is the pharmaceutical industry's lack of investment in antibiotic discovery due to antibiotics' intrinsic poor rate of return when compared to treatments targeting chronic conditions MDR bacteria have been designated as one of the top three threats to human health by the World Health Organization, and the Infectious Disease Society of America has issued a call to action new antibiotics is one approach for the treatment of MDR bacterial infections, the fact remains that only two new classes of antibiotics have been introduced into the clinic over the last two decades, neither of which are significantly active against Gram-negative bacteria invariably develop relapse Daptomycin, for example, was brought into the clinic in 2003, and in less than a year, later the emergence of resistance in patients with Enterococcus faecium and MRSA infections was observed. As a result, alternative approaches to controlling bacterial infections are sorely needed.



 Figure 3:MDR properties

Bacteria and antibiotics

Bacteria have an amazing capacity to adapt to harsh environmental conditions, exemplifying the old natural rule of'survival of the fittest.' The formation of antimicrobial resistant bacteria appears to be an unavoidable side effect of almost every new antibiotic, and it is recognised as a serious issue in the treatment of microbial illnesses in hospitals and the community.

 SIGNIFICANE OF MDR

It has been a long time since antibiotics have been used. According to surveillance in various regions of the world, including Africa, some parts of America, the Eastern Mediterranean Region, Europe, South-East Asia, and the Western Pacific Region, a large number of infectious microorganisms have evolved over time. These organisms are now able to resist the inhibitory effects of these medications in an alarmingly large number of species. An infectious disease (such as a bacterium, a fungus, a virus, or a parasite) that requires a lot of MDR and causes more morbidity and fatalities is referred to as a "super bug" . The fact that deadly diseases including TB, pneumonia, HIV, influenza, malaria, yeast infections, and many more remain significant causes of death today demonstrates MDR as a substantial global danger to public health. Due to MTB's resistance to specific drugs, the likelihood of eradicating tuberculosis has reduced, making it a global problem. According to a 2012 survey, 92 nations have extensively drug resistant TB, with 6% of current cases and 20% of those that have previously received treatment having MDR (XDR-TB). Because the bacterial agent that causes pneumonia has been shown to be resistant to both cephalosporin and carbapenems, due to extended spectrum β-lactamases (ESBL) mediated mechanism, , rendering all forms of therapy with -lactam antibiotics ineffective. Antiretroviral therapy has failed in recent years due to HIV medication resistance, which has resulted in expensive costs and a variety of negative effects. The protozoan parasite that causes malaria had started to develop a resistance to several of its most potent medications, including pyrimethamine, artemisinin, and chloroquine. As a result, new pharmaceuticals have been introduced to replace these outdated, useless ones, raising the cost of healthcare. The evolution of antifungal treatment resistance in invasive yeast infections, such as Candidiasis, has increased morbidity and death globally and added to the economic burden on the world. The failure of bacteria to respond to conventional medications is attributed to antimicrobial resistance (AMR) or MDR. This causes the length of the course of treatment to be extended, which drives up health care costs and exacerbates the predicament of those who cannot afford such charges.

PROBLEMS RELATEDTO MDR

The effectiveness of antimicrobial medications is significantly impacted by antibiotic resistance, which is also associated with high death rates and high medical costs. MDR hinders the ability of illness to be controlled by increasing the risk that resistant infections will spread. The patient's infection time is extended as a result of the treatment's decreasing efficacy. Since the bacteria have developed a resistance to commonly used medications, which has pushed the creation of more expensive treatments, the cost of therapy has grown as a result of MDR. Since the bacteria have developed a resistance to commonly used medications, which has pushed the creation of more expensive treatments, the cost of therapy has grown as a result of MDR. The growth of MDR has been considerably assisted by the success rates of contemporary medical operations like cancer therapy and organ transplantation. The efficiency of antimicrobial agents is also significantly and considerably impacted by variations in the resistance profiles of bacterial and fungal diseases, as well as the level of public cleanliness. Global commerce and tourist expansion boost the possibility for MDR to spread over the world while reducing the export and import of numerous goods that have an impact on the economies of developing nations.

REMEDIES OF MDR

MDR development is a challenging problem that has grown into a terrible international worry. Cooperative efforts are required to reduce the emergence and spread of MDR since diseases that were previously treatable are now among the leading causes of death in this time period. Additionally, implementing antibiotic stewardship, which is defined as coordinated interventions intended to improve and measure the appropriate use of antibiotics, in places that are vulnerable to inappropriate use of antibiotics, is urgently needed. Numerous antimicrobial stewardship programmes (ASPs) are really carried out today to enhance clinical results, increase safety, minimise or stabilise MDR, and optimise antibiotic therapy. The "front-end" and "back-end" of ASP interventions involve limiting the availability of specific antimicrobial drugs and, respectively, simplifying or eliminating the use of broad-spectrum antibiotics. Therefore, in order to contribute to future success, there is an urgent need for support and cooperation at the global, regional, subregional, and national levels.

CONCLUSION

Unarguable facts include the rapid rise in serious systemic infections and the spread of antibiotic-resistant bacteria. The need for novel treatments is constant since existing antibacterial medications are insufficient. In order to regain power over illnesses, numerous awareness campaigns that should facilitate their proper usage must be put into action. Unavoidable natural phenomena like MDR pose a significant threat to human health on a global scale. The MDR must be combated by worldwide cooperation. In order to survive the unfavourable circumstances, pathogens frequently adapt different resistance mechanisms. A deeper understanding of the pathobiology of microbial species will be cultivated together with improved understanding of the molecular mechanisms regulating MDR, which should make it easier to create novel medicines to treat these stubborn infections. Antimicrobial medication development must continue since current options are inadequate.

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