MULTIDRUG RESISTANCE: OVERVIEW

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ABSTRACT
Anti-microbial use and the spread of anti-infection resistance in hospital settings are well-known problems, but anti-toxins and anti-infection resistance as environmental hazards and poisons have received little attention. As a result, the increased number of preventions from a wide range of antimicrobial experts by a variety of living beings is a major worry for modern medicine. Due to the rise of bacteria antibiotic resistance, "antibiotics" have become a threat. Because of their availability and unrestricted access, antibiotics are being used irrationally in people, veterinary medicine, and agriculture, especially in underdeveloped nations.

Keywords: Antibiotics; antimicrobial; resistance; availability

INTRODUCTION
Multidrug resistance (MDR), also known as multi-resistance, is antimicrobial resistance demonstrated by a type of bacterium to at least one antimicrobial drug in three or more antimicrobial categories. MDR in bacteria is achieved by the addition of genes, each of which codes for resistance to a specific agent, on resistance (R) plasmids or transposons, and/or the action of multidrug efflux pumps, each of which may push out even more than one drug type. A bacterium is said to be MDR when it is resistant to more than one antibiotic [1, 2]. MDROs (multidrug-resistant organisms) are bacteria (germs) that have evolved resistance to a variety of antibiotics. Many people's bodies contain these bacteria, which can be found on the skin, in the nose or other moist parts of the body, and secretions. This can occur in two distinct ways i.e. a bacterium could have several resistant strains, each of which imparts antibiotic resistance. Resistance genes are typically stored on plasmids, which are small DNA pieces that can be transferred from one bacterium to another in a single event. Another theory is that a single resistance mechanism gives drug resistance to several antibiotics. More information on plasmids and co-selection may be found here. Pumping the antibiotic out of the cell is one of bacteria's resistance strategies. Such pumps may recognize a large range of chemicals, including many antibiotics, in some cases. In other words, the bacteria use a single pump to release a range of antibiotics. Another term for this is cross-resistance [3, 4].

Antibiotics have been used to treat life-threatening bacterial infections for years, and they have significantly improved human health and longevity. However, a substantial large proportion of antibiotics implement for human therapy and also applied in farm animals including in aquaculture, have led to the recognition of infective bacteria insusceptible to multiple drugs. Antibiotic-resistant strains were once only seen in hospitals, but they are now prevalent throughout the world. By
chemically inactivating antimicrobial agents or generating specific enzymes, bacteria have always been one step ahead. Extensive use of antibiotics is a common global phenomenon in hospitals, animal husbandry, and aquaculture, which raises antibiotic levels in the environment and spread rates, as well as a shortfall of adequate antimicrobial handling, all these factors are accountable for the expansion of antibiotic resistance. In other words, bacteria (Antibiotic-resistant) are flattering more familiar, which measure that there are hardly any antimicrobial medicines are accessible to treat several diseases [5, 6].

It is now known that the widespread manufacturing and usage of antibiotics for medical treatment harms the environment including human health. The huge rise in the frequency of diseases caused by bacteria (drug-resistant) around the world has sparked a surge in interest in this topic. If no new antibiotics are created or found by 2050, it is estimated that there will be no effective antibiotic available. This necessitates the research of alternate antibiotic-resistant disease management strategies. Researchers have been driven to explored and securitized the alternate treatments for MDR infections because of the rising ubiquity of MDR bacteria. This is a threat for which traditional chemotherapies are no longer beneficial, but numerous alternative techniques may be able to help. Recently, scientists still working on nanoparticles (NPs) derived from plant products which may interact with microorganisms, causing modification in terms of its structure and morphology of cells; bacteriophage therapy also developed and act antagonistically where bacteria spread less resistance; combination or mixture of drugs that act on heterogeneous targets in multiple pathways etc. There is a need to look for alternative methods of controlling antibiotic-resistant pathogens, and there are some available [7, 8]. Many research organisations all over the world are actively looking for novel methods.

One of the examples i.e. *Bacillary dysentery* is no longer a major disease in affluent countries, but it continues to be a problem in areas where public health is lacking and has some significant issues. It seems remarkable that bacillary dysentery remains one of the most prevalent infectious diseases in a world where sanitation is generally considered to be good. The rise of antibiotic-resistant pathogenic species is one of the most consequential challenges cladding the healthcare system today. Infections are mainly caused through MDR microorganisms i.e. bacteria are becoming more common and pose a serious threat. This appears to be due to the evolution of drug-resistant bacterial strains. These species were once restricted to the hospital environment, but they can now be found everywhere. The most common gram-positive bacteria are *Staphylococcus aureus*, *Enterococcus faecium*, *Enterococcus faecalis*, and *Streptococcus pneumonia*. Among the gram-negative strains, the most common were *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Antimicrobial resistance is genetically determined in these strains and is most frequently mediated by the acquisition of extra-chromosomal genetic elements via horizontal gene transfer [9-11].

**HISTORY OF MDR**
Alexander Fleming invented penicillin, the very first true antibiotic, in 1928. Antibiotics have since been created to treat acne, bronchitis, conjunctivitis, ear infections, sexually transmitted infections (streptococcal pharyngitis, tonsillitis, upper respiratory tract infection, urinary tract infection, and many other infections). Three major reasons for antibiotic resistance [10-13], according to the ECDC (European Centre for Disease prevention and control) i.e.
• The first instance of antibiotic misuse i.e. overuse of antibiotics to manage viral illnesses. Antibiotics only work on bacterial illnesses and do not effect on viral infections.

• The second sort of antibiotic abuse that leads to antibiotic resistance is incorrectly diagnosed. When the exact bacterium originating the illness is unknown, doctors often give an antibiotic that kills a broad spectrum of germs rather than the specific bacteria linked to the illness.

• Finally, the ECDC points to use improper antibiotic as the third cause.

Some bacteria are naturally resistant to antibiotics, while others develop resistance as a result of genetic alterations brought on by drug exposure. Favourable mutations have a higher chance of surviving and so becoming more frequent throughout time. Because beneficial changes in bacteria are mobilised by experimenting with new and transposons, they can spread swiftly across various bacterial species. As a consequence, a variation that permits a microbe to withstand antibiotic exposure can quickly spread to other bacteria, even bacteria from various organisms. As a result, in order to preserve human health, preventing conditions that enable this scenario is vital. As an outcome, resistance might be acquired or innate. Due to the ease with which resistance-related material can be transmitted between bacterium species, resistance to antibiotics has the potential to spread as well.

ANTIMICROBIAL SUSCEPTIBILITY TESTING (AST)
Medical assistants (clinical laboratory scientists) employ AST to evaluate which antimicrobial treatment is most fortunate and victorious for certain patients. It accommodates in the diagnostic and therapeutic applications offered by hospitals, clinics, and national nosocomial infection preventive and control activities on a broader scale. Researchers have recently had to implement continuous surveillance efforts for resistant strains genetic alterations in bacterial DNA.

On Muller-Hinton agar, AST was implemented to apply the Kirby-Bauer disc diffusion procedure. Ampicillin and Amoxicillin-clavulanate (10 g), Ciprofloxacin (5 g), Cefixime, Nitrofurantoin (300 g), Tetracycline (30 g), Penicillin 10 units, and Norfloxacin (10 g) were used in the AST. After 16–18 hours of incubation at 37 °C, zones of inhibition were sustained and allocated as susceptible or resistant. Intermediate is isolated comparisons between susceptible and resistant were taken into account. Isolates that are resistant to at least three classes are known as MDR bacteria [12-14].

ANTIBIOTIC-RESISTANT BACTERIAL
Biofilms are dense colonies of microorganisms that are resistant to antibiotics and the host defence system due to their refractory structure and durability. The last antibiotic dosage that intercept detectable growth of microorganism after inoculate with media (bacteriological) while keeping inside the extent of anti-microbial medicine clinical prescriptions is known as the minimal inhibitory concentration (MIC). At semi dosages (concentrations underneath the MIC), exposure of bacterial cells continues to expand at a slower amount, and the Least Selective Concentration is established as the lowest antibiotic quantity that promotes the selection or preference of a resistant mutant over wild type cells. For a vast spectrum of bacteria, the MSC is expected to be 1/4 to 1/230 of the MIC values. Bacterial genomes may have mutations or genes that aid in the survival of microorganisms in the treatment of infectious diseases caused by de novo mutated gene or the transmission of resistant strains from other microbes, antibiotic-sensitive microorganisms can become resistant to antibiotics. Antibiotic resistance comes as a result of preference stress as a result of extensive use.
Horizontal gene transfer (HGT) linking the cells of non-identical species or genera can show the antibiotic resistance [11-14].

Some bacteria (resistant) are found surprisingly reporting in the environment and are also important in medicinal settings. The European Antimicrobial Resistance Surveillance Network, an organisation that tracks Gram-negative bacteria resistance trends, has emphasised the desperate requirement to halt the spread of drug resistance in the world. Because of their cell wall characteristics, Gram-negative bacteria are naturally resistant to vancomycin. Furthermore, Klebsiella spp. are ampicillin-resistant, and Pseudomonas aeruginosa strains are typically resistant to tetracycline, chloramphenicol, sulphonamides, and trimethoprim. The World Health Organization (WHO) has designated the genera Pseudomonas and Acinetobacter, as well as those belonging to the Enterobacteriaceae family, as taxa for which new, effective treatments are urgently needed. For four primary reasons, these Gram-negative bacteria are of significant concern as antibiotic resistance agents. To begin with, they produce an extended spectrum of -lactamases (ESBLs), which confer resistance to antimicrobials such as cephalosporins, penicillins, and monobactams, as well as a growing number of carbapenem-resistant strains; all of these are new-generation antibiotics used as "the last line of antibiotic defence" against resistant organisms [14-16].

In short, antibiotic resistance can be acquired in two ways: spontaneously or intentionally (by transfer of resistance genes). Antibiotic resistance originally emerged when Staphylococci came into contact with penicillin, the first commercially produced antibiotic, which created an enzyme (penicillinase) to breakdown it. Bacteria have been transformed into "superbugs," also called as MDR germs, as a result of the ongoing use of many medications. Pseudomonas aeruginosa, Acinetobacter baumannii, E. coli, K. pneumoniae, vancomycin-resistant Enterococci (VRE), methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Staphylococcus aureus (VRSA), vancomycin-resistant Staphylococcus aureus (VRSA), and extensively drug-resistant S. aureus (VRSA) are examples of MDR bacteria that are difficult to treat (XDR) Mycobacterium tuberculosis that causes tuberculosis. Microbes can exhibit resistance by inactivating antibiotics, having limited penetrability and having strong enzymes involved, and transferring resistant genes located on plasmids, transposons, and bacteriophages. Microorganisms have developed a variety of complex methods to tolerate antibiotics and defend themselves from being eliminated by these antimicrobial compounds [8-12]. One of its most triumphant ways is to immobilize the antibacterial factor by chemically change or eliminating it. This is done only by producing enzymes like modifying enzymes in aminoglycoside, which alter amino functional groups and lactamases, which dissolve the linkage in amide group of lactam ring, lactam antibiotics. One more resistance mechanism is vancomycin resistance, which is caused by the presence of an outer barrier that reduces the entry of antimicrobial drugs in Gram-negative bacteria. Another typical resistance method is to stop antibiotics from working by obstructing the target site in various ways, such as protecting (tetracycline and fluoroquinolone resistance) or changing the target site (rifamycin resistance). Within these kinds of mechanisms, there is a staggering amount of variability, and a single strain may have multiple types of resistance [17-18].
CONCLUSION

Although most antibiotics are only found in trace amounts in soil, the recent finding of microbes that use antibiotics as nutrition suggests that some antibiotic breakdown (resistance) genes have an evolutionary basis. Alternative techniques for controlling MDR pathogens have been investigated by numerous research groups. Among them, numerous publications have cited and most promising ones are bacteriocins, phage therapy, essential oils, antibodies, etc. Furthermore, research has focused or studied on the use of quorum-sensing inhibitors as well as nano therapy. Antibodies and bacteriophages have been around since the 1970s, and bacteriocins have been hypothesised since the 1960s. After 1990, essential oils have been explored and projected as a master plan for controlling MDR infections, and recently, quorum sensing inhibitors and nano therapy have also acquired as a feasible method for controlling these resistant strains.

REFERENCES