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The Challenges of Antimicrobial Resistance: Strategies for Global Health and Sustainable Solutions

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Abstract: Antimicrobial resistance (AMR) is one of the highest critical issues causing global health in the 21st century, jeopardizing the chances of efficacy of antibiotics or any other form of antimicrobial agents. Microorganisms like bacteria, viruses, fungi, and parasites develop resistance to drugs that once efficiently cured the infection, making them difficult or even impossible to treat.

This current phenomenon adds up to a grave public health problem that increases morbidity and mortality rates and healthcare costs all around the world. The WHO lists AMR among the ten topmost threats to global public health, thereby needing urgent coordinated efforts among governments, healthcare providers, and the public to curtail its spread. There are several actors in the rise of AMR; principally among them are overuse and misuse of antibiotics in human medicine and agriculture. In healthcare settings, unnecessary prescriptions for antibiotics are written for viral infections, which do not need antimicrobial treatment. Also, patients often do not complete their prescribed courses of antibiotics, allowing resistant strains to survive and multiply. According to a detailed report if current trends are allowed to continue, AMR could kill 10 million people annually by the year 2050, making it more deadly than cancer.

Keywords: Antimicrobial resistance, AMR, Antibiotic resistance, Healthcare, one health approach.

I. INTRODUCTION

Antimicrobial resistance (AMR) is now globally recognized as one of the major threats to health, with serious ramifications on the prevention and treatment of infectious diseases. The extended suffering, increased mortality, and growing burden of these diseases on health care systems arise when microorganisms (including bacteria, fungi, viruses, and parasites) develop resistance to the effects of antimicrobial agents.

That is, except for efforts aimed at curtailing the spread of AMR, scanty endeavours have been made to have resistant pathogens that are still increasing due to the overexploit. of antibiotics in human medicine and agriculture and of the natural evolution and mutation in bacterial populations (Dadgostar, 2019)AMR will thus continue to evolve due to inappropriate prescription practices, over-the-counter availability of medicine in certain regions, and suboptimal adherence to treatment regimens, particularly for bacterial infections. The unrestricted and often prophylactic application of antibiotics to livestock is contributing to the selection of resistant bacterial strains that can spread from animals to humans through contact, ingestion of food products, or environmental exposure (Morrison, 2022) (Palma, 2020)

The big concern with AMR is the horizontal gene transfer ability of bacteria, which can occur by transformation, transduction, and conjugation (Lowy, 2003)These processes allow for the rapid dissemination of resistance among different bacterial species, eventually giving rise to the multidrug-resistant (MDR) strains, which are now rendering the treatment efforts with conventional antibiotics a lot more implausible.

This has been particularly evident in hospital settings, where nosocomial infections due to resistant pathogens, including but not limited to methicillin-resistant, Staphylococcus,aureu (MRSA), carbapenem-resistant Enterobacteriaceae (CRE), and vancomycin-resistant Enterococci (VRE), have posed severe treatment challenges and increased mortality rates (Lowy, 2003)The increasing presence of MDR bacteria in community settings is now raising concern about diminishing effectiveness of available antimicrobial therapies.

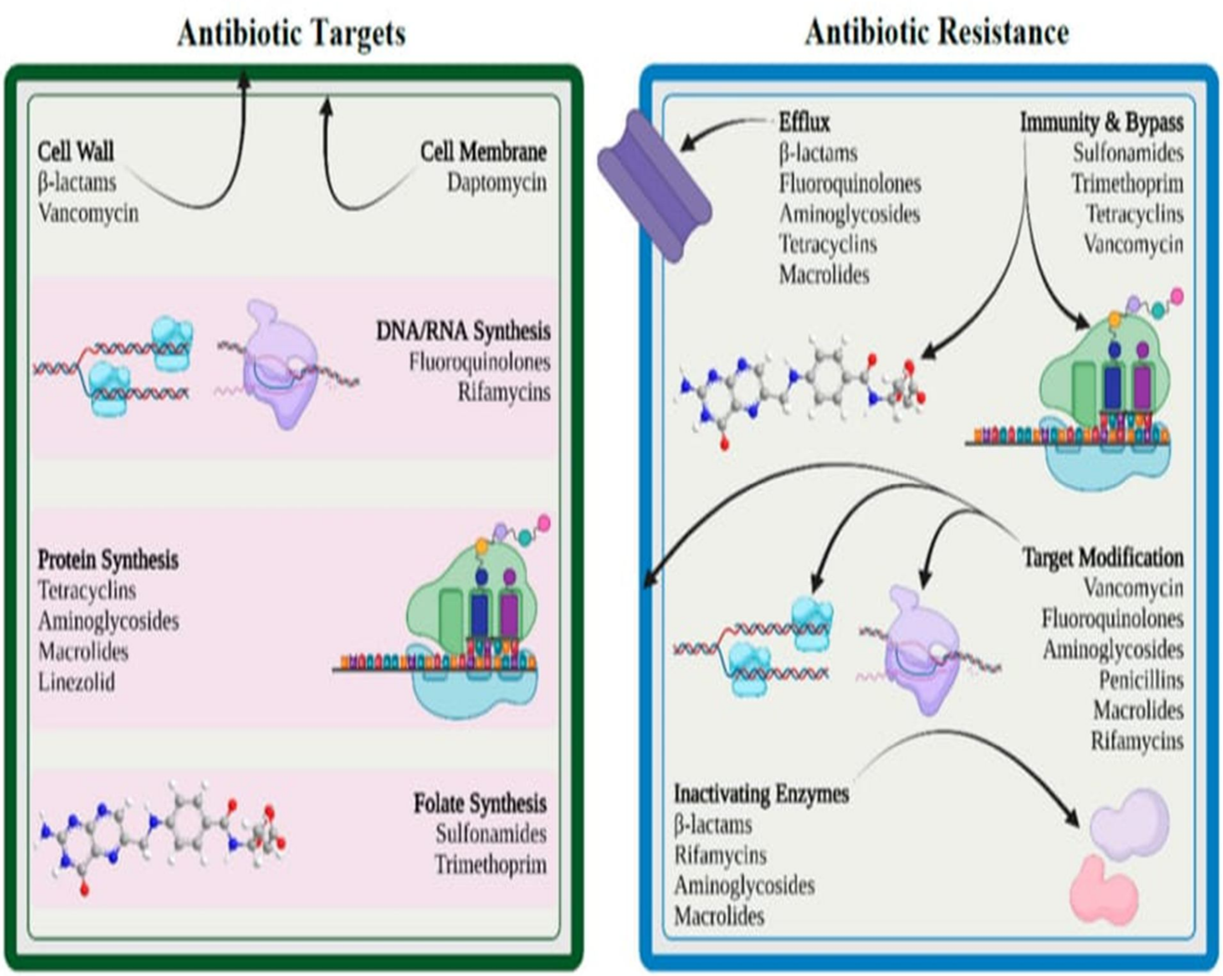

Fig-1 Antibiotic targets and mechanism of drug resistance (Md Salam 2023)

The enormous economic consequence of AMR, as infections attributed to resistant bacteria are associated with prolonged hospitalization, additional diagnostic tests, and use of more expensive treatments of second or third lines (Dadgostar, 2019)AMR lays heavy financial burden upon the health-care systems; it also has implications to productivity on a global scale, as individuals with resistant infections suffer long periods of illness with less participation in the workforce. The World Health Organization has recognized AMR as an urgent priority with the pressing need for new antibiotics, especially against Gram-negatives, which possess unique structural defences such as permeability barriers of outer membrane and efflux pumps in relation to their resistance (Breijyeh, 2020).In spite of pressing demand for new antimicrobial agents, however, the development pipeline for these drugs remains limited, owing largely to unreasonable regulatory requirements, austere nature of drug research-and-development costs, and lack of adequate financial incentives for pharmaceutical companies (Aslam, 2018).Several pharmaceutical companies have left antibiotic research, citing low profit margins and uncertain return on investment as their reasoning, severely aggravating the situation of reduced treatment options.

Among the many drug-resistant pathogens, Staphylococcus aureus exemplifies the hurdles faced by AMR. This opportunistic microorganism demonstrates extreme versatility in acquiring resistant mechanisms against almost all classes of antibiotics, including penicillin's, cephalosporins, and glycopeptides, such as vancomycin, the latter being considered a last resort therapy at one point in time (Lowy, 2003).The ability of S. aureus to survive in a variety of settings, avoid immune clearance, and form biofilms on implanted devices have contributed to it being one of the most common causes of hospital-acquired infections, including infections of the bloodstream, pneumonia, and surgical site infections.

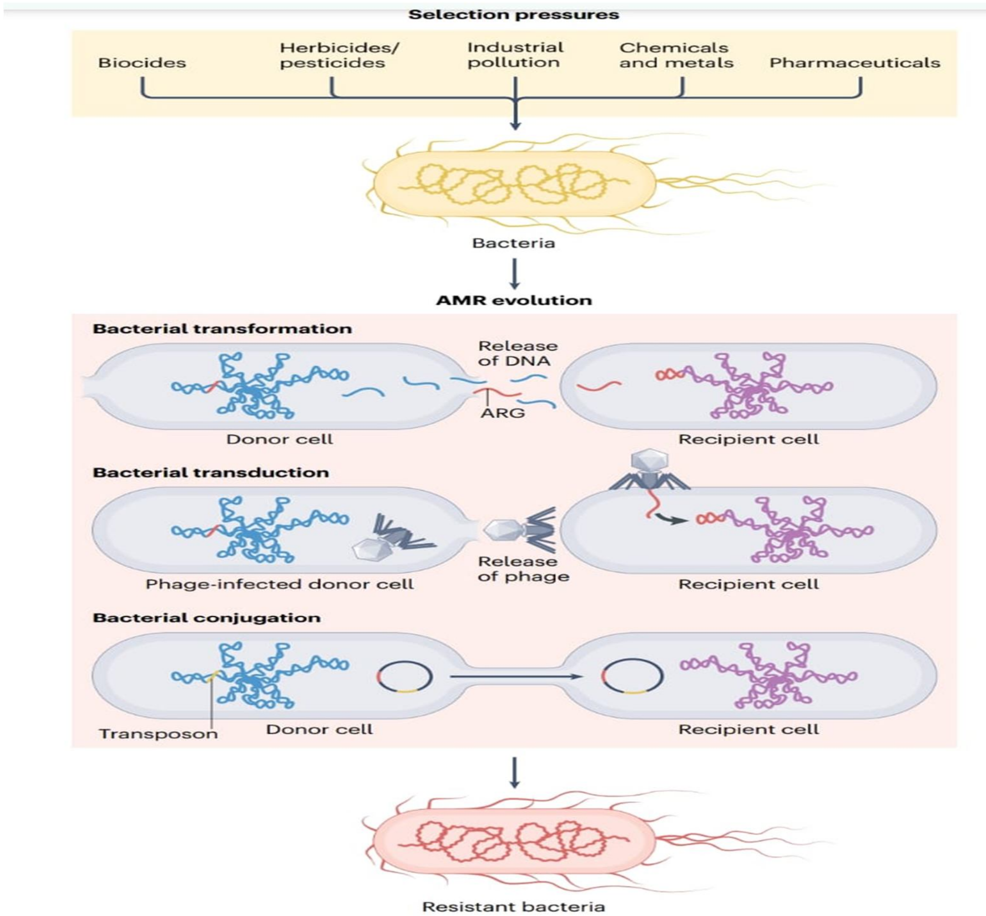

Fig-2 Development of the Antimicrobial resistance (Djordjevic, 2023)

The mortality rates with MRSA infections continue to stay high despite existing antimicrobial therapies; hence an urgent need arises for new treatment options and stringent infection control measures.

AMR is best combated with holistic approaches, such as combining antimicrobial stewardship with an infection prevention strategy and new types of therapeutic intervention development. The domains of antimicrobial stewardship include proper antibiotic use through evidence-based prescribing, minimizing unnecessary exposure to antibiotics, and ensuring adherence to treatment guidelines. Infection prevention measures from good hygiene and sanitation practices to vaccination activities and surveillance systems will play a leading role in limiting the transmission of resistant bacteria within healthcare and into the community. Meanwhile, a growing interest in research on alternative therapies such as bacteriophages, antimicrobial peptides, probiotics, monoclonal antibodies, and vaccines appears promising in the battle against resistant infections.

An all-round approach to AMR called One Health, considers the medical interrelatedness of antimicrobial resistance concerning human, animal, and environmental health. It has paved the way for collaboration between health care providers, veterinarians, policymakers, and researchers in putting together policies to curb antibiotic misuse and limit the spread of resistant microorganisms (Palma, 2020)).The strategy for counteracting the ill effects of AMR and ensuring perpetual effectiveness of life-saving antibiotics includes strengthening global collaboration, raising public awareness, and making investments in the development of new antimicrobial agents and alternative therapies.

Antimicrobial resistance is a complicated public health problem that is growing with each passing day, needing immediate and uninterrupted action. There are increasing resistant bacterial strains from prolonged treatments and some altogether not their options in antibiotic development that stress the urgency of worldwide and interdisciplinary action. Indeed, the more generalized progress of antimicrobial stewardship programs, backed by interventions on infection preventions, innovative research, and exploring One Health paradigms, bets toward minimizing the short-term effects of AMR and make way for future generations to access effective treatment options.

II. GLOBAL EFFECTS AND RAMIFICATIONS OF THE AMR

Antimicrobial resistance (AMR) is the most serious public health challenges today. It has consequences reaching deep into human health, healthcare systems, and the broader economy.

A. AMR as a Global Health Crisis

It blows decades of achievement in medicine into the air. Indeed, the burden of multidrug-resistant pathogen infections, like that of Mycobacterium tuberculosis, Neisseria gonorrhoeae, and Staphylococcus aureus, leaves ever-increasing difficulty in the treatment of infections. By a Data issued by the World Health Organization, AMR is high on its priority agenda, and it will shape and drive action in achieving a concerted global response to this colossal challenge. The burden of antimicrobial resistance does not rest solely on infectious diseases, as it bears complexity to treatment in the non-communicable, such as cancer, and incorporates health service provisions including surgical interventions and organ transplants. Such patients suffering from resistant infections and single-occupancy rooms within Intensive Care Units (ICUs) are more likely to die and have greater invasive medical support. In addition, resistant infections lead to increased hospital readmissions, a major challenge for healthcare providers around the world.

B. Impact on Healthcare Systems

The Antimicrobial Resistance cause a lot of impact on the health care systems. due to which this will create a lot of problems related to the health care facilities that can lead to financial burden, economic burden on the state or the country.

1) Increased Mortality and Morbidity: It is characterized by high rates of death and poor health outcomes. Studies have shown that resistant infections carry a greater risk of severe sepsis, a higher risk of treatment failure, and longer hospital stays. For example, multi-drug-resistant organisms (MDROs) contribute significantly to increased morbidity and mortality among healthcare-associated infections (HAIs).
2) Economic Burden: Economic losses attributable to AMR are grave. Resistance infections may result in long stays in hospital, increased health care expenses, and indirect losses because of decreased productivity. Unless curbed, it is projected that AMR will cause over 10 million deaths each year by 2050 with far-reaching economic ramifications such as a loss of over $100 trillion from a global economic output. This economic burden is further worsened for low- and middle-income countries (LMICs), which are already burdened in their health system.
3) Compromise to Modern Medicine: The major compromises of modern medicine, such as surgery and organ transplantation, along with anticancer treatment, are being threatened by AMR. The complication in managing infections due to resistant pathogens in immunocompromised patients, for example, patients undergoing chemotherapy or organ transplantation, is just one manifestation of AMR. The routine practice of caesarean sections or C-sections, along with a plethora of other surgeries, is now made hazardous in the absence of efficacious antibiotics.

C. Affects Beyond Infectious Diseases.

These impacts talk about the need where the approaches of AMR need to be discussed and for the ones which are going beyond the infectious diseases and the consequences they create for the human being and their well-being.

1) Non-Communicable Diseases: These dynamically created phrases allow the expression of the data held there. Because of the unique manner with which information is delivered, the creation of distinct meanings takes place in the same words. Such phrases would require many revisions before they could be called professional quality. This comes from anywhere in the world. AMR severely affects non-communicable diseases. Take for example patients with diabetes, liver disease, or physical injury; these patients get resistant infections, which further complicate the outcome of their health. The resistive infection in cancer patients leads to treatment delays and complications that reduce prognosis and increase mortality rates.
2) Health Services: An increase in AMR has far-reaching implications for healthcare such as surgery, organ transplantation, and ICUs. Resistant infections often lead to prolonged hospital stays during therapy, allowing high complexity medical care, contributing to the load on healthcare resources, and increasing the overall cost of care. Increased hospital resources are used for infection control measures that add to financial and logistical challenges.

D. Drivers of AMR

The Drivers are the reason due to which the antimicrobial resistance can occur. where each of them has a role to perform but they are not able do the mechanism. few of the Drivers are explained in detail for the overall understanding of the problem and what they are.

1) Overuse and Misuse of Antimicrobials: One of the biggest agents of AMR is with humans and animals-the inappropriate property of antibiotics. Overprescription is tied to humans, while in agriculture, antibiotics are applied as growth promoters. Farming animals and use of antibiotics spur resistant strains, which may transfer to humans through food and environmental exposure.
2) The Famine of New Antimicrobial Agents : Development of antibiotics has slowed in the recent past. New antibiotics have, therefore, become sparse commodities for healthcare systems as well as among international lines in which resistant infections are treated. Resistance gene dissemination is rapid among pathogens, which should already raise concern on the comparably slow development of new antibiotics. New antibiotic inventions face prohibitive cost and regulatory barriers installed through procedures toward their availability, keeping the pipeline shut for novel antimicrobials.
3) Poor Hygiene and Infection Control : Dispensary and poor hygiene contribute tumour resistant pathogens. For example, the spread of Clostridium difficile and Klebsiella pneumoniae in hospitals is usually attributed to lapses in environmental disinfection and hand hygiene. Poor sanitation infrastructure in many LMICs further worsens this spread position of resistant bacteria.

E. Economic and Social Implications

Amr is a microcosm of different this. due to which it will cause problems in the Society and the economy. Because we will see there is a rise in the cost of the products, medical instruments, and equipment.

1) Economic Impact: The economic burden of AMR is extremely high indeed. Direct costs come from prolonged hospitalization, while indirect costs arise from lost productivity. Alone in the EU, resistant infections in HAI account for an estimated 3.2 million cases and 37,000 deaths each year. The World Bank estimates that without effective intervention, AMR could cut up to 3.8% off the world's GDP by 2050.
2) Social Implications: AMR poses a grave disadvantage to the already vulnerable group of people, namely, the immunocompromised and others living among LMICs. In these nations, poor access to clean water, sanitation, and health facilities enhances the transmission of resistant pathogens. Conversely, the communities face a varying degree of barriers in accessing adequate treatment, thereby creating differential health inequities.

F. AMR mitigation strategies

There is a lot of Strategies that are to look unto and frame strategies to overcome this AMR.so that it benefits the people ,the country and the world .the strategies need to friendly and even effective .so that there will be a chance to over the situation and not have any impact due to AMR.

1) Surveillance and monitoring: An uninterrupted surveillance mechanism is imperative for checking the emergence and spread of AMR, and for naming a suitable focal point of action whenever new threats appear. Although the APEC system has made strides in AMR surveillance in Asia, the major gaps still exist in low- and middle-income countries. Enhanced monitoring correlates with strengthening laboratory abilities and implementing standardized reporting systems.
2) Antimicrobial Stewardship: Antimicrobial stewardship programs enhance effective antibiotic use by significantly reducing resistance through the application of interventions. These interventions have included audit and feedback and education-based programs which reduce inappropriate antibiotic uses while improving compliance with guidelines. An ASP should be instituted at every healthcare institution to promote responsible practice in prescribing.
3) Infection Prevention and Control: Environmental disinfection, Hand hygiene, and patient isolation. These are important approaches for stopping the line of resistant organisms from patient to patient in hospitals. To avoid transferring resistant organisms, compliance with infection control measures by healthcare workers must be stringent for patients.
4) Research and Development: Research and development represent the only workable way to find solutions to AMR. These should include the search for novel antimicrobial agents, development of diagnostic tools, and exploration into alternative treatments such as bacteriophage therapy and monoclonal antibodies. Public-private partnerships can help to put innovation on the sufficient path and help the rapid deployment of new treatment options.
5) One Health Approach: Considering human, animal, and universal health, the One Health approach is vital in the global issue of AMR. It means that AMR is a collective problem, and all sectors involved should collaborate to tackle its spread. Strengthening global cooperation on this and taking coordinated policy action along healthcare, agricultural, and environmental fronts will give a head-start on combating AMR. AMR presents an immediate danger to global health, economic stability, and the very sinews of modern medicine. Unless we act with the utmost urgency and coordinated effort, the AMR pandemic will

undoubtedly enter another gear of devastation, resulting in grievous losses in terms of mortality, healthcare costs, and aggravated social and economic inequalities. It is thus essential that all prospective avenues available to hold this disaster through efficient surveillance, antimicrobial stewardship, infection prevention, and research be stepped up to ensure that antimicrobial efficacy is not compromised for generations to come.

III. CAUSES OF ANTIMICROBIAL RESISTANCE

Complex and multifaceted, Antimicrobial Resistance awakens by multiple causes. The causative factors associated with antimicrobial resistance need to be known in detail for the formulation of right strategies against this increasing phenomenon.

A. Environmental Reservoirs of Antimicrobial Resistance

As a rule, the environment serves to harbour a variety of antimicrobial resistance genes (ARGs). Natural ecosystems such as soils and waters harbour innumerable microbial communities bearing resistance determinants even in the absence of human-induced selective pressure.

1) Soil as a Reservoir: Soil has been reported as a rich source of genes an antibiotic might resist. A study of remote Alaskan soils revealed diverse beta-lactamases, including bifunctional beta-lactamases able to confer resistance to beta-lactam antibiotics (D costa, 2006).The catalytic results indicate that soil microbial communities display features of ancient reservoirs of resistance genes even under unperturbed conditions. Thus, the presence of the ARGs in soil makes an urgent case for monitoring and understanding the ecosystem dynamics involved in AMR.
2) Water Systems: Antibiotic-resistant bacteria very easily contaminate the sewage and natural waters. The failure of wastewater treatment facilities has allowed resistant forms of microbes to get into the environment and assist in the further spread of AMR (Baker-Austin, 2006). Studies show that effluent-laden rivers downstream from wastewater treatment plants harbour significant levels of resistant bacteria with implications on human health and the health of aquatic ecosystems. Contamination of these water systems with antibiotics and resistant bacteria raises further public health risks as these pathogens may enter the food chain affecting human populations.
3) Old Resistance Genes: Functional metagenomic studies on ancient soil from the Arctic revealed the existence of resistance genes thousands of years before the anthropogenic use of antibiotics (Baker-Austin, 2006).These genes showed resistance to the modern antibiotics that would have been present at that time. Moreover, these natural reservoirs managed developing AMR. The ever-presence of these genes in the environment only emphasizes that the historical context is critical in understanding the phenomenon of AMR. They also show that the potential for resistance is built into microbial communities and may only get worse when humans interfere with the system.

B. Overuse and Misuse of Antibiotics

The most key factor of driving AMR has been the inappropriate application of antibiotics in human medicine, agriculture, and different sectors by placing resistant microbes' populations under tremendous selective pressure with prominent levels of selection.

1) Human Medicine: The indiscriminate prescribing antibiotics in clinical settings has been a spur for the emergence of resistant pathogens. The overuse of broad-spectrum antibiotics has been associated with the most common resistant organisms, for instance, methicillin resistant Staphylococcus aureus and other strains (Levy, 2002) Evidence shows that 30% of outpatient prescriptions of antibiotics may be unnecessary, adding to the ever-increasing burden of AMR (Fleming-Dutra, 2016)Misdirected antibiotic use does not only affect the individual patient, but also impinge on the broad public health arena, as resistant strains of organisms spread in communities.
2) Agriculture: Extensive antibiotic treatment, fed to livestock, aquaculture, or husbandry selects for the resistant bacteria, which can finally spread to humans by the food chain or even through direct contact. With specific regard for livestock-associated MRSA (LA-MRSA), it has been noted to originate from the veterinary use of antibiotics (Smith, 2009). As far as minimal use of antibiotics for enhancing animal growth is concerned, many countries banned it, although it is still the practice in many other countries where the AMR crisis becomes aggravated. About agricultural practice's use of antibiotics for disease control and growth promotion, public health is now under serious threat, as organisms may develop resistance and enter the food chain.

3) Aquaculture: Intensification of production systems in finfish aquaculture has led to increased bacterial diseases and later overuse of antimicrobials. This is now driving the evolution of resistance mechanisms in aquatic pathogens which create risk for both, fish health and human consumers (Cabello, 2006) Poor regulation of antibiotics in aquaculture results in resistant strains that would pose threat to aquatic and terrestrial ecosystems alike. The aquaculture-human pathway`s by which resistant bacteria travel is through the consumption of contaminated seafood, underlying one health for the futures of humans and the environment.

C. *Transfer Horizontally of Gene*

Horizontal gene transfer is the important mechanism by which resistance genes are spread among bacteria. By this way, resistance determinants can be bought within truly brief time in bacteria even if the determinant has a varied species.

1) Plasmid-Mediated Resistance: Resistant genes are mostly found on plasmids, which are types of mobile genetic elements. For instance, the mcr-1 gene that carries colistin resistance has been found on plasmids in Escherichia coli and Klebsiella pneumoniae isolates from humans, animals, and the environment (Liu, 2016). Plasmid-mediated resistance creates a very rapid mode of dissemination of resistance traits among bacterial populations. Another way of transferring plasmids through bacteria from one species to other leads to increased diversification resulting in a much more complicated control of AMR.
2) Inter Species Transfers: Resistance genes show multi-directional transfer toward varied species of bacteria. On developing Neisseria lactamase, it was found that penicillin resistance developed due to the replacement of a part of the Pena gene with a homologous region stemming from N. flavescens showing interspecies HGT (Harrison, 2013)).These organisms are in a position to exchange genes across themselves and microbial communities as a whole. The resistance gene transmission among species leads to giving birth to new resistant mutant strains which can aggravate the treatment.
3) Biofilm and Gene Exchange: Structured communities are formed by the bacteria called biofilm and their presence in this environment can provide opportunity. for gene exchange on resistance. These communities function as genes reservoirs, protecting the bacteria from antimicrobial agents and, therefore, allowing persistence and diffusion of resistance (Hall-stoodley, 2004)The biofilm-like pattern of living works toward the survival of resistant bacteria in hostile environments, making it all the more complicated to effect treatment. Biofilms form on many surfaces, including medical devices, leading to persistent infections that are difficult to manage.

D. *Evolutionary Adaptation and Biofilm Formation*

Adaptation and evolution are further supported by various survival mechanisms employed by bacteria in the presence of antimicrobials. Such mechanisms include biofilm development, enzymatic degradation of antibiotics, and export of the antibiotic molecules by efflux pumps. For a detailed explanation, see Fig -3

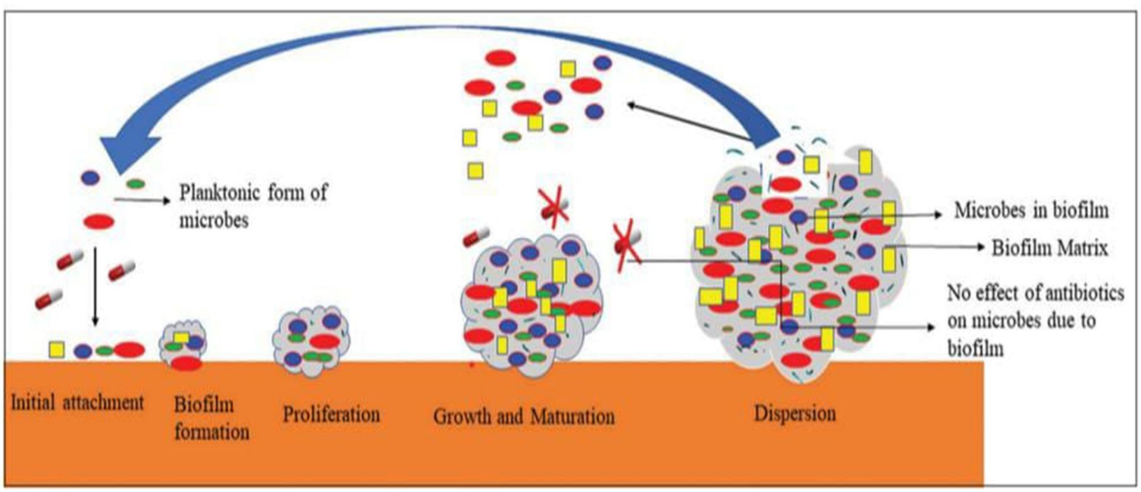

Fig -3 Biofilm formation by microbes (Paneri, 2022)

1) Biofilm Lifestyle: Biofilm is a structured populations of microorganisms embedded in a protective matrix. They decrease antibiotic penetration and serve as a breeding ground for the exchange of resistance genes. Studies have shown that biofilm-adapted bacteria develop resistance mechanisms through pathways distinct from those of planktonic bacteria, such as mutations in efflux pump regulators (Fletcher, 2015)The ability to form biofilms is a significant factor in the persistence of infections and

the development of AMR. Biofilms can also aid in supporting chronic infections since they are difficult for the immune response and antimicrobial treatment to reach.

2) Enzymatic Resistance: Certain bacteria produce enzymes that inactivate antibiotics. As beta-lactamases are capable of degrading beta-lactam antibiotics, aminoglycoside-modifying enzymes confer resistance to aminoglycosides (Bush & Jacoby, 2010)These enzymes are harboured on mobile genetic elements enabling their rapid spread among populations of bacteria. Production of these enzymes is a common mechanism of resistance, constituting a major challenge in clinical settings.
3) Efflux Pumps: Most bacteria have efflux pumps, which pump out antibiotics from the cell. The overexpression of efflux pumps is one of the common forms of resistance mechanism by which it can be controlled and regulated through the acquisition of mutations during evolutionary adaptation within the bacterial species (Li&Nikaido, 2004)Efflux pumps can render multiple classes of antibiotic resistance, thus complicating the treatment strategies. Efflux pumps in certain bacterial hosts can cause "multidrug resistance" in the bacterial population and make the infections difficult to treat.

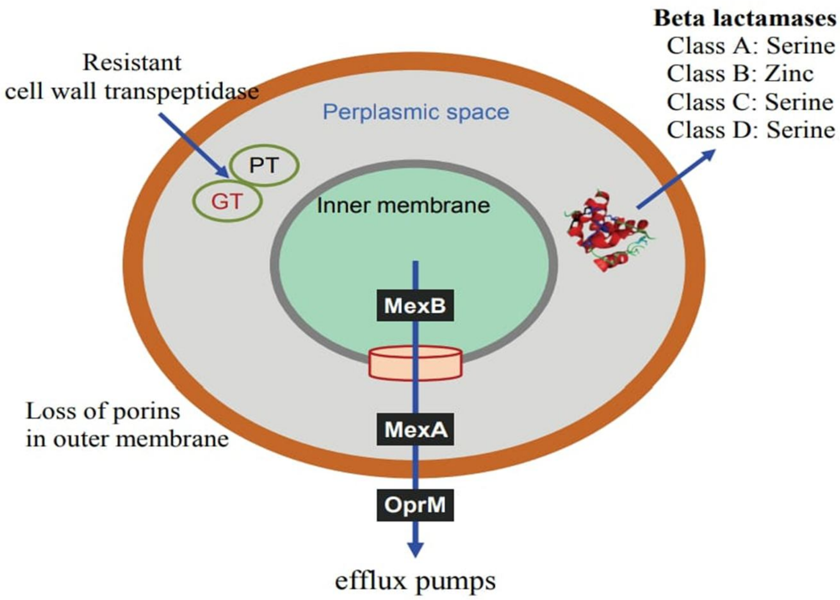

Fig 4 The systematic Diagram of the antibiotic resistance mechanism

E. Global Dissemination and Ecological Pressures

Ecological factors and human activity contribute to the global spread of AMR. All the microbial ecosystems are interconnected so that any gene for resistance can be spread across different environments in a noticeably brief time.

1) Environmental Contamination: Antibiotics, along with resistant bacteria, find their way into the environment through wastewaters, agricultural runoff, and discharge from industries. Once in the environment, persistency and dissemination of the contaminants occur, subjecting different microbial populations to resistances genes (Kummerer, 2009).Strikingly, the presence of antibiotics creates a selective pressure for resistant strains to survive in the environment. Environmental pollution could set up resistant bacteria in natural ecosystems, thereby complicating effort towards the management of AMR.
2) Ecological Flux: The Fluctuations in environment such as resource availability, promote the evolution of resistance. Population bottlenecks that occur in such volatile environments will either fixate or eliminate resistance genes depending on the selective pressures present (Baker-Austin, 2006)One must recognize that the ecological dynamics would be very useful in predicting and managing any spread of AMR.
3) One Health Perspective: The reality of the spread of AMR is that it does not occur in one ecosystem or one species. Genes of resistance flow freely between humans, animals, and the environment, and so the need for a comprehensive approach to AMR. A One Health approach affirms that human, animal, and environmental health are inextricably linked in the global combat against AMR. Cross-cutting collaboration thus strengthens surveillance and intervention programs.

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F. Lack of New Antibiotic Development

The past few decades have seen a slowdown in new antibiotic development, and this has worsened the AMR problem. Hence, existing innovations offer the health systems limited possibilities of treating resistant infections.

1) Decline in Discovery: Fewer new antibiotics have been approved in recent years for clinical use, leaving voids in the treatment of infections caused by resistant pathogens (Ventola, 2015)The decline of discovery for antibiotics is alarming as the few antibiotic options available become less effective against emerging resistant strains. The lack of new antibiotics limits treatment options of patients with resistant infections, which continues to increase morbidity and mortality.
2) Challenges in Development: First, the cost and regulatory hindrances to the research becoming targets for resistant pathogens for urgent need without harming the host microbiome add to the impediments of developing new antibiotics (Laxminarayan, 2013)Although the pharmaceutical industry is viewed as having low returns on investment in antibiotic development, barriers to entry further diminish interest in new drug discovery.

G. Socioeconomic and Cultural Factors Affecting Resistance Development

Socioeconomic and cultural challenges Favor the promotion of AMR. Limited access to health care, coupled with self-medication and the high prevalence of counterfeit drugs, worsen the situation in low- and middle-income countries.

1) Misuse in Developing Countries: Misuse of antibiotics by patients and a weakly regulated pharmaceutical industry are major reasons for the development of resistance in these resource-poor settings (Okeke, 2005)Oftentimes, antibiotics are available without prescriptions and are misused and overused. Resistance in these areas is further aggravated by limited access to quality health care and lack of education.
2) Cultural Practices: Some traditional medicine in certain regions employs antibiotics, or these are employed as growth promoters in agriculture, both of which result in the perpetuation of resistance (Murray, 2016). Cultural attitudes towards antibiotics may affect prescribing practices and potentially propagate AMR. Addressing the cultural dynamics is equally important for the effective design of public health interventions against AMR.

H. Genetic and Ecological Interactions

The work of genetic and ecological interactions within microbial communities is fundamentally central to the establishment and spread of AMR. The common AMR research has not taken any interactions into consideration.

1) Mutualistic Associations: Microbiological communities, such as biofilms, can shield bacteria against antibiotics and allow the interchange of resistance genes. These mutualistic associations highlight the significance of microbial ecology for understanding AMR (Baker, 2018)). The interactions that occur amongst different microbial species may thus affect the dynamics of resistance gene dissemination.
2) Resistance Units (RUs): Resistance Units are the genetic elements conferring resistance and passed on from one bacterium to another. They can be derived from environmental bacteria or from human-animal-food-associated microbiomes, creating a complex resistance dissemination pathway (Baker-Austin, 2006). Knowledge of the genetic-ecological interplay behind the establishment of RUs is pre-requisite for setting up successful interventions against AMR.

I. Wildlife and Food Chain

Wildlife and the food chain function as conduits through which AMR is transmitted. Animals, especially those found in proximity to humans, serve as reservoirs and vectors for resistant bacteria.

1) Livestock-Associated MRSA: The emergence of LA-MRSA in pigs and other livestock has been attributed to the use of antibiotics in agriculture. These resistant pathogens can be passed on to humans via direct contact or contaminated food products (Smith, 2009)The involvement of livestock in the transmission of AMR serves as a reminder for the integrated approach towards resistance. Thus, monitoring and controlling the antibiotic use in agriculture are essential to counteract such risks of transmission to humans.
2) Wildlife as Sentinels: In ecological terms, wildlife can serve as sentinels of environmental contamination, especially in the case of apex predators. A study in the wildlife reserves of Costa Rica determined that cats carried higher amounts of resistance genes as indicators for pollution in the environment at large (Gonzalez, 2018) The monitoring of wildlife shall contribute to understanding the ecological dynamics of AMR and to thereby enter into public health concerns.

J. Climate Change and Ecosystem Disruption

Besides the factors mentioned earlier, climate change or ecosystem disturbance may influence the environment of the AMR. Environmental change might alter, in some way, may further enhance the transfer of resistant genes into microbial communities.

1) Ecosystem Processes: At this point in time, antibiotics in the surrounding environment may very well disrupt processes such as methanogenesis and nitrogen transformation - key stages for the maintenance of Eco balance (Kummerer, 2009)This leads to niches for resistant bacteria. Disruption of microbial gene dynamics may also be influenced by the effect of climatic changes on these communities.
2) Human Impact on Ecosystems: It was found that human activities, by themselves-not forest coverage-are the primary drivers of these ecosystems in terms of the presence of ARGs (Gonzalez, 2018)One of the impacts caused by human activities on natural ecosystems is the increase in the flow of resistance genes through anthropogenic activities such as deforestation and agriculture. It thus becomes relevant to know how human activities have changed ecosystems to form effective strategies against AMR. Antimicrobial resistance is a multifactorial problem caused by a range of factors like environmental reservoirs, overuse and misuse of antibiotics, horizontal gene transfer, evolutionary adaptation, and socioeconomic causes. For that reason, understanding the multifactorial reasons behind AMR is an important participatory strategy at national and international levels. By cross-sector collaboration and promoting responsible antibiotic use, the effects of AMR can be reduced and preservation of antimicrobial effectiveness for the future may happen.

IV. STRATEGIES IN FIGHTING AMR

We need to make certain strategies through which we can overcome the situation, and we need to do certain changes by which there is AMR control and the choice to get away from it. Where we can bring some regulations in the use of the medication, the control on the nod of prescription being given and the other means.

A. Rational Use of Antibiotics

Regulators, health professionals, and patients should cooperate in the rational use of antibiotics.

Regulating Prescriptions: Policies that restrict antibiotic sales without prescriptions.

Public Awareness Campaigns: Raising the awareness of the public of the risks associated with the misuse of antibiotics.

Improve Diagnostic Tools: Prescribe antibiotics only after a right diagnosis is made.

B. Strengthening the Surveillance Systems

Those patterns of antibiotic resistance monitoring will help early detection and response.

National and Global AMR Surveillance Programs: These programs are global. They are backed by organizations like the World Health Organization.

Data sharing & transparency: Helping countries' ability to share AMR data to find trends and devise strategies overall.

C. Eliminate the Cause of Infection and Antibiotic Necessity

Improve hygiene practices: To promote handwashing and sanitation.

Vaccination Programs: Social mobilization for increasing immunization rates to prevent infections.

Hospital Infection Control: Show strict hygiene protocols in health care settings.

D. Research and Development of New Antibiotics

The pharmaceutical industry is at the forefront of combating AMR by making new drugs.

Grants and tax benefits should be given for antibiotic research to incentivize innovation.

Public-private partnerships could bring together governments, researchers, and pharmaceutical companies in the quest for rapid drug development.

Novel therapies: The investigation of alternative treatments like bacteriophage therapy and antimicrobial peptides.

E. Reduction of the use of Antibiotics in Agriculture.

Agricultural antibiotic use is instrumental in antimicrobial resistance.

Countermeasures include the following:

Laws restricting antibiotic use on livestock should restrict their use for purposes of growth promotion.

Promotion of Sustainable Farming Practices. Organic and antibiotic-free farming should be encouraged.

Development of Alternative Treatments. Research into probiotics and vaccines for animal health.

F. Strengthening Global Policies and Cooperation

International organizations, governments, and stakeholders must work together.
WHO Global Action Plan on AMR: It serves to implements global strategies against AMR.
Intergovernmental collaboration: In the fight against AMR, cooperation among countries is necessary to manage threats that extend beyond their borders.
Funding and support: Increased financing for AMR research initiatives and public health programs.

V. ISSUES FACED IN THE FIGHT AGAINST AMR

A. Despite the Progress made, other Challenges still Abound

The Absence of Public Awareness: Many people misuse antibiotics without understanding the risks.
Poor Healthcare Accessibility: Developing countries face bottlenecks in antibiotic regulation and infection control.
Slow Development of Novel Antibiotics: Drug companies are limited by financial and regulatory constraints.
In several nations, antibiotics are routinely administered to livestock not only for infection treatment but also for growth promotion and increased production efficiency (Van Boeckel, 2015) This introduces selection pressure for the emergence of resistant strains, which can be transmitted to humans from the animal either through the food chain, direct contact with farm animals, or environmental contamination. In aquaculture and agriculture, these substances also contribute to the problem by releasing antimicrobial agents into soil and water systems, thus promoting the persistence and transfer of resistance genes amongst microbial populations (woolhouse, 2015)AMR also creates a huge economic burden beyond health considerations. Infections that are resistant lead to longer hospital stays, rising medical expenditures, and a greater need for intensive care (Dadgostar, 2019)The World Bank (2017) examined the global scenario and presented findings that suggest AMR could result in an economic loss of $100 trillion by the year 2050-with low- to middle-income countries facing disproportionate burdens.

B. Global Collaboration- Importance

AMR is a global issue needing international cooperation. The WHO declared in its Global Action Plan on Antimicrobial Resistance in 2015, five important objectives: (1) improving awareness and understanding of AMR, (2) strengthening surveillance and research, (3) reducing infection rates, (4) Reducing the use of antimicrobial medicines, and (5) ensuring sustainable investments in countering AMR (WHO, 2015)Countries are expected to modify it further into national action plans suitable for their specific contexts, ensuring they have coordinated and appropriate responses in place.
In addition to WHO, organizations such as FAO and OIE also work on responsible antibiotic use in agriculture and strengthen One Health initiatives. One Health approach stands at the confluence of human, animal, and environmental health in addressing AMR (Van Boeckel, 2015).Antimicrobial resistance stands as a grave and increasing threat to global health and requires an urgent and multipronged response. Through responsible antibiotic use, strengthened infection control measures, increased public awareness, and fostering international cooperation, the further emergence of AMR can be slowed and the effectiveness of current antimicrobial therapies preserved. Governments, health professionals, scientists, and the public must combine forces to guarantee that effective treatment options stay available to future generations. Without immediate action, AMR could reverse decades of medical progress, turning once-treatable infections into killers again.

C. AMR Strategies

Given the complexity of AMR, a multi-pronged approach is needed to alleviate its effects. One particularly key step includes promoting responsible antibiotic usage through antimicrobial stewardship programs (ASPs) that orient health practitioners on requiring antibiotics only when necessary and in the correct dosage (Howard, 2015)

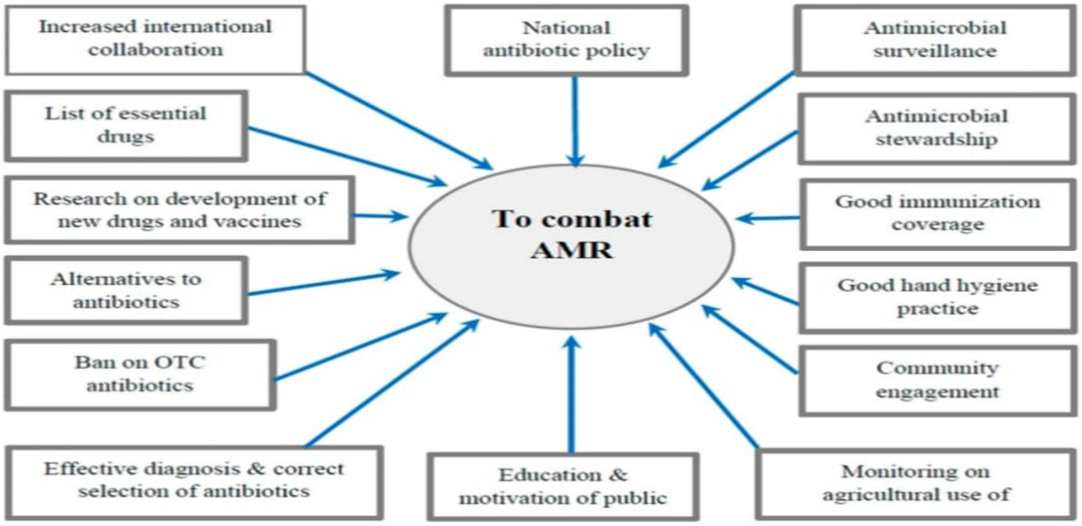

Fig-5 Major innervations to combat AMR (Md Salam2023)

In a similar vein, beneficial use of IPC in hospitals and community settings—for example, improved hand hygiene practices, vaccination programs, and sanitation—can contribute in a significant way to the lessening of antibiotic treatments required (WHO, 2021)). Public awareness campaigns are key role in educating the population and healthcare personnel on the dangers of misuse of antibiotics. Examples of how the European Antibiotic Awareness Day and WHO's World Antimicrobial Awareness Week have raised awareness of AMR and encouraged changes in behaviour are given by (Hutter, 2019)

One more key part in combating AMR trouble is investment into research and development (R&D). The state of the antibiotic pipeline has still been stagnant, given the urgent need for new antimicrobial agents, due to challenges in the scientific, regulatory, and economic realms. The joint efforts of governments and pharmaceutical companies need to create incentives for the development of next-generation antibiotics, alternative therapies (bacteriophage therapy, etc.), and rapid diagnostic tools that can quickly find infections and thereby limit unnecessary use of antibiotics (Ardal, 2020)

VI. THE BROAD IMPACT OF AMR

Consequences of AMR extend well beyond the healthcare sector. According to the WHO, AMR accounts for millions of deaths each year, with projections that by 2050, it could kill up to 10 million per year if not tackled (O Neill, 2016) Moreover, antibiotic resistant infections elevate healthcare expenditure due to lengthened hospitalization, more expensive treatment, and mortality (CDC, 2022). Economic impact of AMR is severe, and it has estimates that globally, if uncontrolled, $100 trillion in economic output will be lost by the year 2050.

A. Important Strategies in Fighting AMR

What we need to address the impending threat of AMR is a wide-ranging approach. Governments will come together with health providers, researchers, and the public in broad-based strategies to intercept. Some of them are key approaches to AMR mitigation:

1) Development of New Antimicrobials and Alternative Therapies

The ongoing decline in development of new antibiotics has worsened the AMR continuum. It is important to encourage pharmaceutical interest into the research of new antimicrobial agents, necessary to counteract resistant strains creeping up. Investments into alternative therapies, such as bacteriophage therapy, antimicrobial peptides, and immunotherapies, are promising avenues for treatment (Czaplewski, 2016) Investment in repurposing current drugs and screening natural products could also provide a more sustainable way of obtaining antimicrobial agents.

2) Advancing Rapid and Accurate Diagnostics

Knowing how to compare diagnoses with speed and accuracy is very essential to ensure that antimicrobials will be used appropriately.

Because of delays in obtaining diagnostics and the resultant unnecessary broad-spectrum antibiotics used, inappropriate resistance development starts appearing. Further advancements in rapid diagnostics - including point-of-care testing, biosensors, and artificial intelligence-based test systems, - are expected to improve targeting treatment while reducing unnecessary antibiotic usage (Belkum, 2020)

3) Strengthening Antibiotic Stewardship Programs

Antibiotic stewardship involves developing policies to ensure that antibiotics are prescribed only when there is a clear sign and then with the correct dosage and duration of prescription. Healthcare systems and hospitals are encouraged to promote evidence-based practices for antibiotic prescribing and implementing antimicrobial stewardship programs to review prescriptions of antibiotics (Dyar, 2017)Training health workers about responsible prescribing habits would significantly reduce the emergence of resistant pathogens.

4) The One Health Approach

Under the umbrella of the One Health framework, human, animal, and environmental health are mutually cognate in their approach to AMR control. Since antimicrobial use in agriculture contributes to human pathogen resistance. Controlling resistant germs might be further aided by reducing environmental pollution with pharmaceutical wastes and increasing sanitation and hygiene.

5) Public Awareness and Education

Public awareness campaign is very crucial in decreasing AMR. Frequently, due to misinformation, antibiotics are misused in self-medication exercises with viral infections, such as the common cold and flu. Awareness-raising through engagement in the community, media space, and in school-based educational programs should focus on responsible usage of antibiotics, such as encouraging the patient to complete prescribed courses and discouraging their procurement through over-the-counter purchases without medical advice (WHO, 2021)

6) Global Surveillance and Policy Implementation

International cooperation is an essential prerequisite for addressing AMR on a global scale. WHO Global Action Plan on AMR promotes improved surveillance systems, better laboratory capacities, and an increased sharing of data between countries (WHO, 2015)National action plans, tailored to the health care and agricultural environments of their respective countries, must be enacted to coordinate the response to AMR threats. Furthermore, such policies should be directed toward fostering the ability of pharmaceutical companies through subsidies and market entry rewards to engage in antimicrobial research.

7) Future Research Directions

Research will have a continuous future direction. Research continues to be truly relevant based on the rapid evolution of resistant pathogens. Future research should be focused on:

a) AI in Drug Discovery: AI-powered drug design has been created to ease the identification of new antibiotics by analysing big datasets and predicting molecular interactions.
b) Phage Therapy: The usage of bacteriophages (viruses that infect bacteria) appears promising for treatment of resistant bacterial infections when applied as an alternative to antibiotics.
c) Nanotechnology in Antimicrobials: Nanoparticles and nanocarriers can improve the delivery of drugs about their efficacy level while reducing the toxicity level under treatment.
d) Vaccination Development: Money spent on vaccines means less reliance on antibiotics because infections can be prevented before they occur.

Addressing AMR would, thus, be a collaborative and continuous effort between governments, healthcare providers, researchers, industries, and the public. It would take an all-inclusive approach that integrates antibiotic stewardship, innovative treatment strategies, rapid diagnostics, and global cooperation in mitigating the threat of AMR. Public awareness and education should also be prioritized to ensure the responsible use of antibiotics and hygiene practices. Consistent funding in research and development will further search for alternative treatments and new antimicrobials. Global society can then implement the above measures to keep the efficacy of antimicrobial therapies while securing a healthier future for generations to come.

VII. STUDY CASES AND SUCCESS STORIES

Sweden is among the countries recognized as having been initiative-taking and effective against AMR. Such strategies have included strong rules, public awareness campaigns, and serious surveillance programs which translate into successful reductions in both antibiotic usage and dissemination of resistant bacteria. This case study highlights the multi-faceted approaches that Sweden has built into its fundamental policies, collaborative measures, and some measurable outcomes.

A. Early Recognition and Policy Development

Sweden's commitment to AMR for several decades can be traced back to the beginning of dealing with AMR. In 1986, Sweden became the first country to ban antimicrobials against growth promotion. This landmark decision was taken precisely on the concerns of possible antibiotic residues in the meat and the ultimate rebound effect on public health. The ban indeed addressed consumer concerns, but it also set the stage for antibiotic usage to become a national agenda from then on.

In 1995, the Swedish Strategic Program Against Antibiotic Resistance (Strama) was proven as a voluntary network of different stakeholders from human and veterinary medicine, public health, and environment. The main purpose of Strama was to coordinate efforts to check and control antibiotic resistance within the country. It has by now turned into the cornerstone of the AMR strategy in Sweden and serves as a platform for member collaboration and data sharing.

In Sweden, AMR measures are in the deep One Health spirit, considering the multifaceted characteristics of human health, animal health, and environmental health. It is ensured that this Multi perspective is mounted to address the multiplicity in AMR transmission processes. Some key elements include:

1) Surveillance and Monitoring: The country has put in place a comprehensive surveillance system that watches antibiotic sales and resistance patterns in both the human and veterinary sectors. Analyses of consumption and resistance trends are published annually in the Swedres-Svarm report, which is jointly published by the authorities of the Public Health Agency of Sweden and the National Veterinary Institute.
2) Regulatory Measures: Sweden's regulatory measures concerning antibiotic prescription go much beyond the ban imposed in 1986. All antibiotics must be prescribed, and in animals, they can only be used for therapeutic purposes under the supervision of a veterinarian. These regulations have contributed significantly to the control of indiscriminate use of antibiotics.
3) Environmental Implications: The environment's role in AMR transmission has been acknowledged in contribution to the establishment of monitoring of antibiotic residues in water sources along with green pharmacy initiatives by the Swedish agencies. The above-mentioned aim would also include reduction of emissions from production as well as the introduction of sustainable waste management practices.
4) Collaborative Endeavours Along with Public Participation: Collaboration is a hallmark of all antimicrobial resistance (AMR) initiatives in Sweden. There is continuous communication among government agencies, health stakeholders, farmers, and food safety agencies in seeking proper use of antibiotics. Campaigns such as these manage to create awareness on AMR and effect a culture change into more sensible antibiotic usage. This collaboration is what the new "Antibiotic Smart Sweden" is about. Initiated in 2019, this project aims to integrate antibiotic stewardship into all areas, among healthcare, education, and agriculture. Creating such criteria and partnerships, the initiative also aims to target an "antibiotic smart" society.
5) Measurable Outcomes: The outcomes of Sweden's all-inclusive and far-reaching measures are observable and measurable. Among European countries, Sweden has one of the least levels of antibiotic resistance. AMR accounted for only 581 deaths in Sweden in 2019, which amounts to the lowest age-standardized mortality rate due to AMR, among the 204 countries surveyed. Antibiotic usage in veterinary medicine has diminished immensely. Total sales of all antibiotics for use in animals from 1984 to 2018 have decreased from 53.4 tons to 10,042 kg of active ingredient. Such decline is a testimony to the functioning of very stringent regulations and measures for disease prevention in animal husbandry.
6) The Challenges and future directions: Particularly due to globalization, there are still challenges met in the negotiations against AMR. The imminent risk whereby travelling and trade put resistant strains in contact with destinations that harbour higher AMR problems stays. Persistent public awareness campaigns and creation of new antibiotics are also pressing issues. Sweden's ambition is to keep a leading role in fighting AMR issues internationally. The updated Swedish Strategy to Combat Antibiotic Resistance (2024-2025) emphasizes that international collaboration, research, and innovation to counter new threats will remain in focus. Sweden indeed offers a model for other countries in combating AMR by its multifaceted diplomatic and collaborative efforts. Via a sound setting of early policies, a steadfast orientation in One Health, and public involvement from all fronts, Sweden made considerable achievements in controlling antibiotic resistance. Thus, supporting these achievements and expanding upon them would depend on continued adaptation and global collaboration.

B. Case Study 2: The Netherlands' Successful Decrease In The Use Of Agricultural Antibiotics Pollution

AMR is going to become one of the major global issues concerning antimicrobial resistance, further compounded by the application of excessive antibiotics in agriculture. The Netherlands has shown its leadership position among nations trying to reduce antibiotic usage in livestock, as it has done by about 60% from 2009 to 2019, without adversely affecting the overall health and productivity of animals. This case study analyses the deprived strategies along with the influence the government regulation and education of farmers had in assessing the effectivity of such measures.

1) Background on Antibiotic Use in Dutch Agriculture

Before 2009, the Netherlands had one of the highest rates of antibiotic use in livestock in Europe. Concerns about AMR development and the transmission of resistant bacteria to humans were raised due to a heavy reliance on antibiotics, especially in the intensive farming sectors such as poultry, dairy, and pig farming. Studies showed that resistant bacteria from farm animals could reach humans through food, direct contact, and environmental contamination. On recognition of the threat, the Dutch government, along with agricultural organizations, launched a national strategy to limit antibiotic usage in food-producing animals.

a) Government Regulations and Policy Changes

The Dutch government set several tight policies and regulations for driving antibiotic reduction: Mandatory.

Reduction Targets: - In 2009, the government set a 20% reduction target by 2011, a 50% reduction by 2013, and later extended it to 60% by 2019. These goals are legally enforced.

Ban on Preventive Antimicrobial Usage: - Farmers did not have use of antibiotics for routine pretreatment. The only time they are allowed to use it is when the treatment was for bacterial infections in animals.

Restrictions to Veterinary prescription: - Farmers had free access to the antibiotic for their farm animals before the reforms. The new policy mandates veterinary Prescription before every use of antibiotics. The continued restricted sales for the veterinarians have also cut financial benefits from overprescribing.

Surveillance and Data Reporting: - The Netherlands was set up as a veterinary Medicines Authority to watch the use of antibiotics. Every farmer, then, had to give some data to check the use of antibiotics.

b) Farmers Education and Awareness Program

It being acknowledged that the role of farmers in this whole matter was crucial, in bringing the Dutch government, universities and industry organizations together to enlighten livestock producers. Major initiatives include:

Training Programs on Animal health and Biosecurity: -Farmers would be trained to improve hygiene, disease prevention, and housing conditions which would reduce the prevalence of infections.

Best Practices for Alternative Treatments: -Farmers would be encouraged to rely on vaccination programs, probiotics, and feed additives instead of antibiotics in boosting the immune response of animals.

Financial and Support Incentives: - Farmers were financially rewarded for effective reduction of antibiotic use. They could also be offered low-interest loans for improvements in their farms that directly helped animal welfare.

c) Farm Management Practices Enhanced

Farm management practices that proved best practices in the reduction of antibiotic use include as follows:

Better Nutrition and Feed Quality: Providing a good feed feature with essential nutrients to animals enhances their immunity.

Hygiene and Biosecurity Measures: -On the farm, strict hygiene protocols have included disinfection of equipment, control of access to the farm and separation of sick animals.

Selective Breeding for Disease Resistance: -The Dutch farmers focused their activity on breeding animals with better disease resistance and thereby minimized infection incidence.

d) Outcomes and Impact of the Reduction in Antibiotics.

From 2009 to 2019, the Netherlands cut down antibiotic use in livestock by over 60%. This success came with several major outcomes:

Decrease of Antibiotic-Resistant Bacteria: -There was a marked decrease in resistant bacteria in farm animals and meat products according to studies.

Concurrently Stable Animal Health and Productivity: -Due to the framework that developed over time aiming at health improvement without antibiotics, productivity levels in Dutch farms remained high despite the reduced antibiotic use.

International Recognition and Impact: -The Netherlands served as a global role model for decreased antibiotic use in agriculture, favouring policy-change in Germany, Denmark, and the EU.

Reduced Human Opportunities of Exposure to Antibiotic-Resistant Bacteria: -The reduced AMR in livestock had the benefit of reducing its chance to be transmitted to humans and, thus, protect public health.

2) Challenges and Learning Experiences

The different challenges and lessons can be learnt in this because of which it will help to control and overcome the future infections and Burdens. The following are the different challenges and learning that we get from this AMR and this experience will help in all the future.

a) Challenges faced.

- Early Resistance from Farmers and Veterinarians: -Some farmers complained about losing production if practices were altered to what they feel were traditional systems. Veterinarians complained because sales of antibiotics decreased, and earnings were then lost.
- Continuous Monitoring Needs: - Continuous and rigid monitoring was necessary to ensure compliance.
- Cost of alternative strategies: - The construction of better housing, high biosecurity, and vaccination needed high upfront investments that small farmers found difficult to prepare for.

b) The lessons for other countries are listed below:

Government Commitment Is Important: Strong law and enforcement help the changes.

- Resistance Can Be Lessen through Education and Cooperation: Farmers will be encouraged to embrace new methods when training and incentives are provided.
- Alternatives to Disease Prevention Work: Good hygiene, vaccination, and nutrition can only help in reducing reliance on antibiotics.
- The Dutch approach is a positive example illustrating how government policy, education, and farm management improvements can dramatically reduce dependence on antibiotics in agriculture while keeping productivity. Their model offers helpful lessons for other countries in the same battle against antimicrobial resistance in the food chain.

Describing this case study, the multifaceted approach uses regulation, education, and innovation for reducing antibiotic use in livestock ensuring food safety and public health.

VIII. CONCLUSION

AMR has been considered as the greatest threat in global health issues and the way it has high relevance risk factors to make impacts on population health, economy, and effectiveness of medical treatment. Microorganisms like bacteria, viruses, fungi, and parasites can undergo mutations that help them develop resistance against antimicrobial agents, causing the infection to become more difficult to treat. Such a scenario would be brought about through excessive and inappropriate use of antimicrobials in human medicine, in veterinarians' practices, and in agriculture. In this make-believe world, where there is no immediate and effective countermeasure against AMR, it will create a reality where a routine infection may not be treatable and becomes life-threatening, a medical procedure becomes riskier, and there will be an increased economic burden due to extended hospital stays and decreased productivity of the workforce

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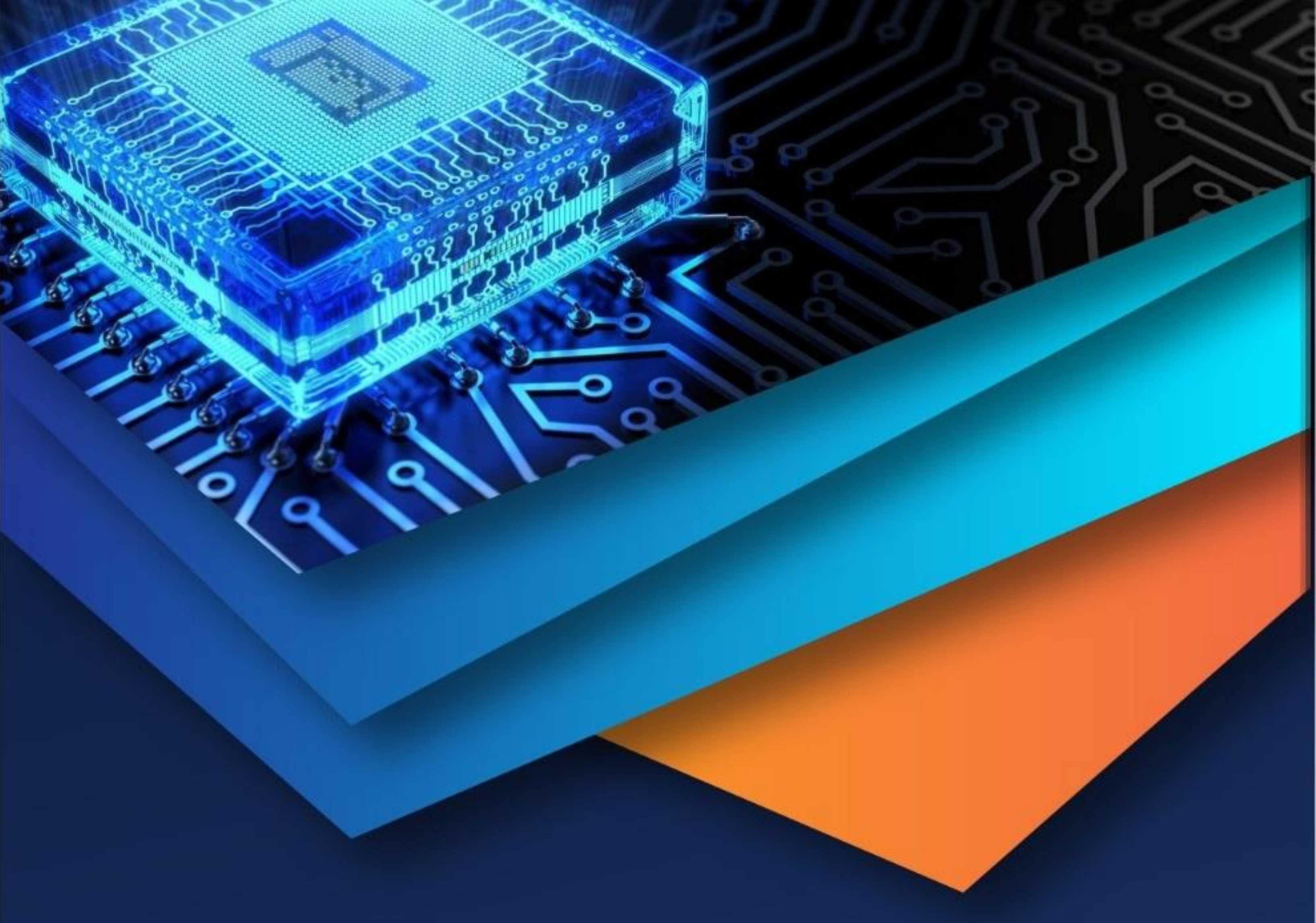

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