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Antimicrobial resistance: Understanding the mechanism and strategies for prevention and control

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ABSTRACT

Antimicrobial resistance (AMR) is a growing public health concern globally, with the threat of a post-antibiotic era, where common infections can become fatal, a very plausible reality. Despite ongoing efforts to control AMR, both mortality and expenses have increased. To combat this threat, a thorough understanding of the mechanisms and the driver behind this issue needs to be known. The key mechanisms of resistance are modification or destruction of antimicrobials, reduction of access to the target, and alteration of the target. These mechanisms may be present in the microorganisms naturally or may have been acquired from other microorganisms. As AMR jeopardizes the successful prevention and treatment of many infectious diseases, this article looks at the causes of AMR, along with the possible mechanisms of resistance development, and suggests control strategies to deal with the problem conclusively.

INTRODUCTION

One of the major public health issues of the twenty-first century is antimicrobial resistance (AMR), which poses a threat to the efficient prevention and treatment of an expanding number of infections caused by bacteria, parasites, viruses, and fungi that are no longer susceptible to the conventional medications used to treat them [1]. It has taken a drastic form, proving to be very challenging for healthcare professionals and patients worldwide alike. Playing a major role in the spreading of antimicrobial-resistant genes (ARGs), in both hospital and non-hospital environments, this phenomenon primarily developed due to the overuse and misuse of antimicrobial agents by patients mostly [2]. The antimicrobial resistome is an aftermath of the ARG reservoir formed due to the collective contributions of anthropogenic factors and environmental microorganisms [3].

In developing countries, such as Bangladesh, the occurrence of AMR is increasing day by day. This is mainly attributed to the fact that antimicrobial agents are used in a wide variety of things, starting from animals, poultry, agriculture, and in the treatment of disease patients [3]. Antimicrobial agents and drugs have been used for decades to treat infections by pathogenic microorganisms, namely bacteria, viruses, fungi, etc. However, over the course of evolution, these microbes have attained resistant genes, and can thus survive antimicrobial treatment [4]. This is not a very well-received idea by healthcare professionals as it can prove to be harmful to the patients. The phenomenon of antimicrobial resistance has skyrocketed in developing countries, mainly because of the ease of availability of these drugs over the counter [5]. In Bangladesh, there have been

countless reports of cases where the patient reports showed shreds of evidence of resistance to a large number of antimicrobials and antibiotics used. All these combined have provoked an evolutionary response in the pathogenic microorganisms to develop and acquire ARGs. The following table shows some of the common classes of antibiotics, their year of discovery, the year in which AMR was first observed in them, the mechanism of resistance employed along with an example from each class.

Table 1. Some common antibiotics classes with their year of discovery, year of noted resistance, mechanism of resistance, and examples.

Class of Antibiotics	YOD	YOR	Resistance Mechanisms	Examples	Ref.
β-lactams	1928	1945	Cleavage by β-lactamases, altered penicillin-binding proteins	Penicillin, Cephalosporin	[6,7]
Aminoglycosides	1943	1946	Enzymatic modification, efflux pump	Streptomycin	[8,9]
Tetracyclines	1944	1950	Mainly efflux pumps	Tigecycline	[10,11]
Quinolones	1961	1968	Efflux pumps, target modifications	Ciprofloxacin	[12,13]
Lipopeptides	1986	1987	Modification of the cell wall and cell membrane permeability	Daptomycin	[14,15]
Glycopeptides	1953	1960	Efflux pumps, altered cell wall permeability	Vancomycin	[16,17]
Phenicols	1946	1950	Reduced membrane permeability, mutation in the ribosomal subunit	Chloramphenicol	[18,19]

*YOD- Year of Discovery, YOR- Year of Noted Resistance

There are several reasons for the sudden surge of antimicrobial resistance that is becoming a global threat, including in developing countries. Among these causes of resistance are included inadequate public health infrastructures, lack of proper knowledge and education, lack of awareness, contamination, agricultural applications, microbial mutations, and of course, overuse of antimicrobial agents for even the slightest of inconveniences [6]. This paper focuses on the origin of antimicrobial resistance, the threat it poses to developing nations, the mechanisms by which these resistant microbes are acquiring the ARGs and developing AMR, and lastly, discussions about the potential control strategies trying to prevent global AMR.

CAUSES OF ANTIMICROBIAL RESISTANCE

Antimicrobial resistance is primarily controlled by adaptive evolution [7]. The main reasons that lead to the development of antimicrobial resistance are primarily the ease of accessibility of broad-spectrum antibiotic usage for any minor infections without consulting the professionals, along with their indiscriminate usage in farms and poultry, which lead to the microbes developing ARGs that can be easily and rapidly transferred from generations to generations [5]. In particular, developing countries were found to be more vulnerable to such instances including Bangladesh, due to poorly surveilled healthcare facilities, poor sanitation, extensive use and misuse of antibiotics and prophylactics in agriculture, poultry as well as aquaculture industry, along with unmonitored and unhygienic agriculture, aquaculture, and livestock food production processes [8]. The combined result of all these irregularities culminates in the spreading of antibiotics, antibiotic residues, as well as ARGs, and antibiotic-resistant bacteria (ARBs) into the environment [9]. ARGs may develop through genetic recombination induced by mutations, antibiotic pressure, and the immune response of the patients. These genes can transfer through horizontal gene transfer (HGT), which acts as the selective pressure and favors the microbes containing the gene more than the ones that

do not [10]. There are several causes of antimicrobial resistance. Some of them have been outlined as follows:

Mutations

Microorganisms create a world where millions of them can live together in a commensal manner, sometimes living in symbiosis as well. Through mutations, recombination, and horizontal gene transfers, the genetic diversity of the pathogenic bacteria is increasing, providing them with a greater chance of developing AMR [11]. A genetic mutation in one or a few of them is not an uncommon occurrence. Some can have DNA repair mechanisms that can rectify the problems. Other times, these mutations can favor them and give them a selective advantage that allows them to survive environments that are normally unfavorable to others. These mutations, when occurring in an immense number of organisms altogether in a population, can give rise to phenomena such as antibiotic resistance, for example. These resistant genes are then quickly transferred from generation to generation due to the rapid multiplication of microorganisms, and eventually develop an entirely separate population containing the mutated gene, giving rise to a new phenotype [6]. Microbes can quickly adapt to their changes, and thus these ARGs can spread over generations very rapidly. Another reason is the low fitness cost of these ARGs for the host microbes, leading to ready transfer of them between plasmids and between bacteria; due to this low maintenance cost, these ARGs can evolve more efficiently in response to previously effective forms of the same antibiotics [12]. Such a phenomenon has been observed in the emergence and development of tigecycline and a few tetracycline resistance genes [13].

Mutations can also occur through the microbe's acquiring transposons, also known as jumping genes [4]. "Transposable elements" or "transposons" are segments of DNA that have the ability to move from one location to another within the genome, including within the same chromosome or even between different chromosomes. Transposable elements can carry genes for antimicrobial resistance and other traits, and their movement can contribute to the spread of these traits within a population. The process of transposition refers to the movement of transposable elements within the genome, which can occur either through a "cut-and-paste" mechanism, in which the transposon is excised from one location and reinserted into another, or a "copy-and-paste" mechanism, in which the transposon is duplicated, and the copy is inserted into a new location [14,15]. This transposition can also occur between the chromosomal DNA and plasmid DNA in bacteria. Movement of these transposons can change the length of the chromosome, changing the resulting DNA sequence, ultimately giving rise to the antimicrobial resistance phenomenon in the microorganism, thereby making the organism resistant to antimicrobial treatment [4]. One other method of introducing mutations is the acquisition of integrins, found in plasmids, chromosomes, and transposons, which can integrate into the genome using their integrase, cause gene expression using their promoter, and also contains a gene that allows integration of small pieces of DNA called gene cassettes [16].

Moreover, ARGs for several different antibiotics can be naturally assembled on the same mobile genetic element, as evolution would favor this coexistence, particularly in the anticipatory event of antibiotic exposure, giving a rise to multi-resistance phenotype. Notably, this occurrence takes place naturally, independent of the frequency or use of antibiotics, as has been observed in clinical isolates [17]. The increasing use of antimicrobials on a global scale is only adding fuel to this multi-resistance issue, encouraging multidrug resistance as well [18].

In order to correct genetic errors accumulated in the genes of bacteria, the evolutionary process uses both vertical and horizontal gene transfer. Vertical gene transfer involves the transfer of resistant genes to progeny, reducing antibiotic affinity, which gives them a selective advantage for survival [19]. Horizontal gene transfer (HGT) also plays a prominent role in the accession of AMR, highlighting the amazing adaptive capabilities of microbes, especially bacteria since this process can happen between the same as well as different bacteria taxa. During HGT, ARGs from one microbe retained in their plasmids can be transferred and taken up by others from the environment such as from the microbiota community in the soil or even the gastrointestinal microbiome [20]. HGT has the ability to transfer ARGs, and AMR as a consequence, through human, environmental, and veterinary pathogens.

Poor drug quality

It is not uncommon for retail pharmacies and local vendors in underdeveloped or developing countries to be selling outdated, adulterated, and unfit drugs [5]. The ease of availability and misuse of antibiotics can contribute to the development of antimicrobial resistance (AMR) in microorganisms. When antibiotics are overused or used improperly, the bacteria targeted by the drugs can adapt and become resistant to their effects, making them less effective in treating infections [21,22]. Environmental conditions, such as temperature, humidity, and light can significantly affect the stability and shelf life of drugs. Exposure to unsuitable environmental conditions can lead to chemical reactions, physical changes, and microbial growth, which can all degrade the quality and potency of drugs [23,24]. Furthermore, some of the drugs do not even contain the appropriate amount of the active substance, which is hidden from the patients. This means that the patients are unknowingly consuming less than the required dosage, hence allowing for antimicrobial organisms to thrive in such conditions [25]. This can lead to unresponsiveness of the patients to the first line of drugs in case of infections (e.g., urinary tract infection, wound infections, etc.), increasing the risk of fatality, lengthened hospitalization period, and higher costs. Observations from various hospitals in the capital of Bangladesh have demonstrated this occurrence as patients showed little or no sensitivity to commonly administered antibiotics such as amoxicillin, ampicillin, ciprofloxacin, and amoxiclav [26].

Healthcare discrepancies

The healthcare infrastructure is quite underdeveloped in countries like Bangladesh, Somalia, etc. Inappropriate and exaggerated usage of antimicrobials for any minor infections, such as prescribing antibiotics for viral infections or undiagnosed conditions, can cause the development of unnecessary antibiotic-resistant microbes. Moreover, prescribing broad-spectrum antimicrobials in situations where the specificity of antimicrobial action is needed can also lead to antimicrobial resistance [27, 28]. Furthermore, underdeveloped countries like Bangladesh lack the necessary laws and regulations required for proper drug distribution. Additionally, there is also malpractice and difference in practice regimes of healthcare professionals in different countries, leading to different or wrong drug doses, prescriptions, etc. [5, 29]. Doctors or practitioners sometimes suggest antimicrobials just by judging the symptoms, previous experience, and local epidemiology, rather than waiting for confirmed test results. Albeit this saves the time spent waiting for test results, in several cases, this approach fails to affect any useful outcome for the patients [6]. There also lies the huge factor that in such countries, especially in the rural areas, the people do not have

enough money required for the purchase proper drugs. Local pharmacies employ people who do not have the proper knowledge about the drugs in store, as well as their benefits, side-effects, and storage conditions, and easily give a certain drug to the patient without checking proper prescriptions. As per a study conducted by observing infected patients in tertiary hospitals in Dhaka, a significant presence of multiple-drug resistant (MDR) pathogens was found, specifically in infected patients suffering from acute respiratory infections, diarrhea, typhoid fever, and wound infections [30]. These reflect the effects of misuse and overuse of antimicrobial drugs, and the resulting increase in AMR in hospital settings [5].

Patients' negligence

A common tendency in people, typically those not well-educated on the matter, is to insist on going for antibiotic treatment for as simple minor illnesses as fever or the flu, without even consulting a practitioner, and even go as far as not completing the full course of the antibiotic dosage just because they start to feel somewhat better than before. Patients even tend to miss doses of antibiotics and use them improperly due to their inadequate knowledge of the harmful effects of alcohol consumption during antibiotic treatment [5]. These kinds of behavior promote AMR, and these people need to be educated about the immense risks they are putting themselves, and the general population into.

Agricultural and pharmaceutical dissemination

The issue of using antimicrobial agents like pesticides, insecticides, and fungicides on agricultural lands and products, as well as their dissemination into the environment, is significant. These treatments may be useful for the crops, momentarily, helping to achieve a greater yield. In the long run, however, these compounds can build up and accumulate in the crops and other agricultural products, which can then transfer to humans upon consumption. [31, 32]. A prominent way of AMR and ARG dissemination from the food animals, besides consumption, is through urine and fecal expulsion onto soil and surface waters, along with their application as manure for fertilizer use in farming [33].

Antibiotics are used in animals to treat their diseases and used to promote their growth and development [34]. Accumulation of these antibiotics in animals and then consumption of these by humans can lead to the transfer of the ARGs to humans, resulting in increased AMR. For instance, tetracycline is one of the most used antibiotics in the treatment of domestic animals, and resistance to it has been found to prevail in various sample sources such as food, wildlife, domestic animals, and even in the environment [35]. Studies in African countries have also shown the presence of multidrug-resistant genes in meat and agricultural products meant for human consumption [36,37]. These findings suggest the harboring and transfer of the ARGs from these food products to humans in Africa and other developing countries.

Moreover, most livestock animals are exposed to low doses of antimicrobials for long periods in the form of mass medications, which stimulates the development of conditions ideal for the growth, selection, and spread of resistant microbes, both between and within animals and humans alike [38]. Other studies in rural Bangladesh have shown that farmers prefer cheaper local pharmacists and village doctors as their go-to option for animal health treatment. These people often do not have the required training for proper animal care and end up suggesting remedies that depend on the

herbal treatment that may contain additional unknown compounds that result in antimicrobial resistance. Altogether, these factors lead to an increased incidence of AMR [39]. A comprehensive pathway demonstrating the route of ARGs and ARBs through the ecosystem, using the agricultural medium, and finally reaching are shown in Figure 1.

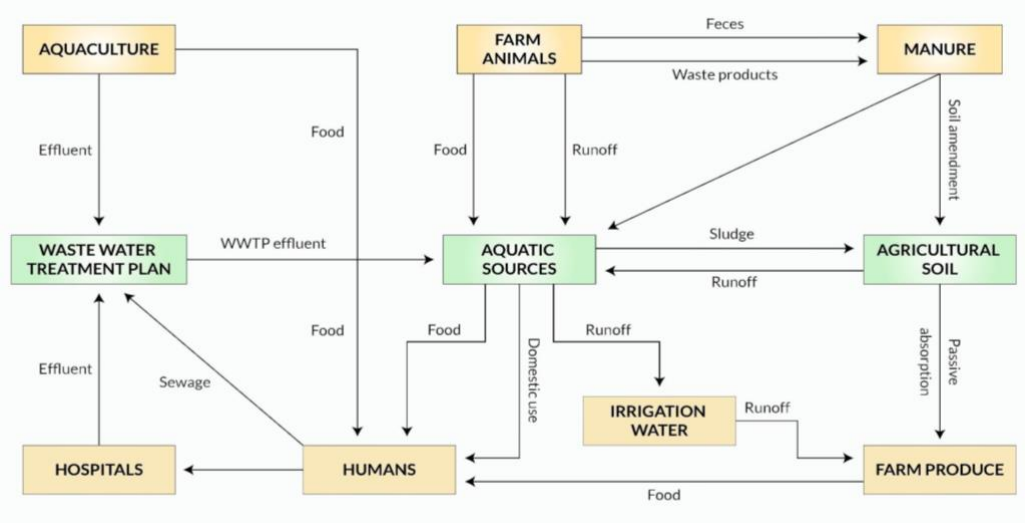

Figure 1. Flowchart showing the plausible transmission routes of ARGs and ARBs through the environment and reaching humans involving the agricultural context. This flowchart is a simplified representation of the complex transmission pathways of ARGs and ARBs in the agricultural context. The actual transmission routes may vary depending on several factors, including the type of antibiotic used, the mode of administration, the type of animal or crop, and the environmental conditions.

In addition, some pharmaceuticals dispose of antibiotics in the sewerage system irresponsibly, which eventually find their way into the river system and enable microbes to develop into "superbugs" over time as the resistance strains get time to mutate and evolve in that antibiotic-rich environment [40]. Hospital effluents and untreated wastewater also contribute to this effect equally, particularly in a low-resource environment [41].

MECHANISMS OF ANTIMICROBIAL RESISTANCE

The first naturally produced antibiotics are estimated to have emerged more than 40 million years ago, which indicates that antimicrobial resistance is a similarly old phenomenon [42]. Microbes have developed several mechanisms that help them become resistant to antimicrobials. Silent ARGs are harbored in the genomes of many bacterial species inherently, which are not expressed in an antibiotic-free environment due to lack of selection pressure. This infers that there are many hidden niches of genetic pools containing these potential ARGs, and the environment acts as a reservoir of AMR [3]. Once a resistant microbe arises it gains a competitive advantage over non-resistant variants and quickly rises in number.

With regards to the origin, resistance can be of two types: intrinsic and acquired (Figure 2). The former is a natural trait shared by microbes ubiquitously, regardless of the exposure to previous antimicrobial compounds, and independent of HGT, so that resistance to a particular antimicrobial compound or family of compounds arises without any need of mutation or acquisition of any new resistance genes [43]. An example of this would be the resistance to most β-lactam antibiotics by *Pseudomonas aeruginosa*. The latter, acquired resistance, consists of all the other mechanisms by which

microbes can obtain ARGs such as chromosomal mutations and all forms of HGT [44]. Prolonged or repeated use of antimicrobials, even in low doses, can result in the selection of high-level resistance in successive microbial generations, enhancing their ability to acquire resistance to other forms of antimicrobial agents as well [45].

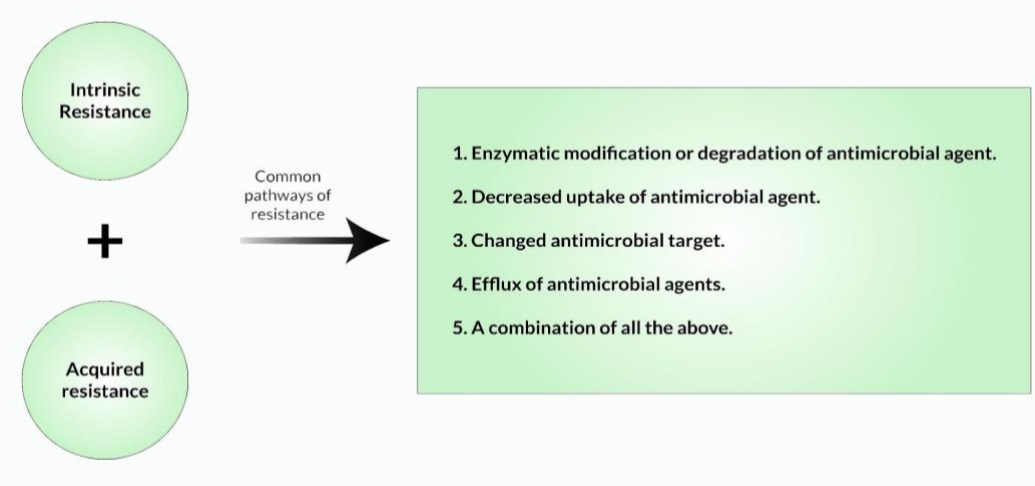

Figure 2. Antimicrobial resistance (AMR) can arise through different pathways. This figure provides an overview of the common pathways involved in the origin of AMR. These include: (1) Enzymatic modification or degradation of antimicrobial agent, (2) Decreased uptake of antimicrobial agent, (3) Changed antimicrobial target, (4) Efflux of antimicrobial agents, and (5) A combination of all above. Addressing this problem requires a coordinated effort across different sectors, including human and veterinary medicine, agriculture, and environmental health.

Understanding the mechanisms by which AMR arises is key to developing ways to fight against it. AMR mechanisms include various modes of action such as complete obstruction of antibiotic entry into cells, premature removal of antibiotics from cells, antibiotic degradation, alteration of antibiotic-targeted cells, a reduced influx of antimicrobial drugs into cells due to change in permeability of porins in cellular outer membranes, as well as efflux pumps and plasma translocases in certain bacteria [46]. An outline of the main mechanisms for antimicrobial resistance is given below (Figure 3).

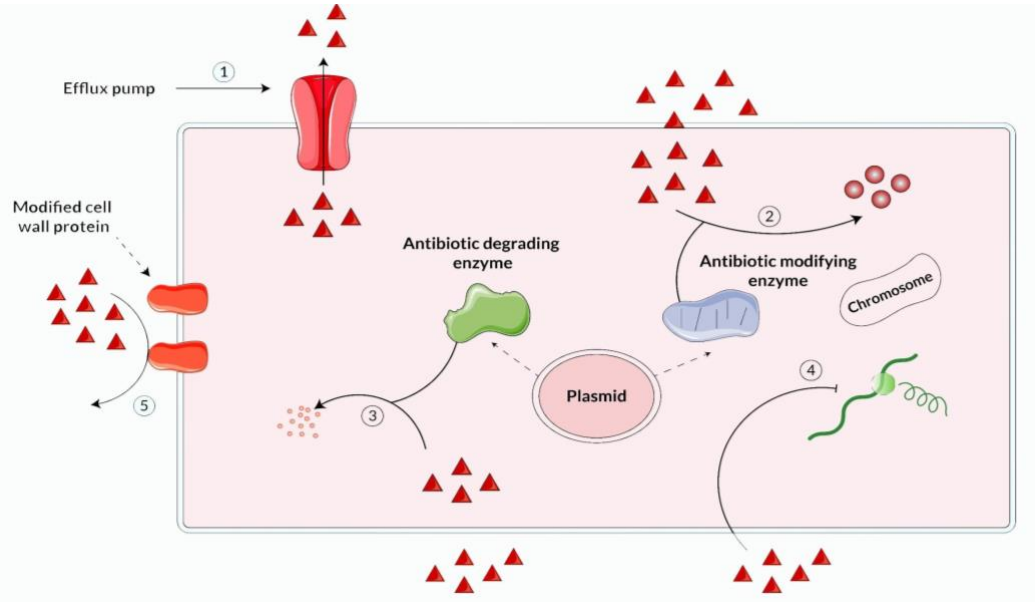

Figure 3. Schematic representation of the Main mechanisms of antimicrobial resistance. Antimicrobial resistance can occur through various mechanisms, including enzymatic inactivation of the antimicrobial

agent, Modification of the antimicrobial target, Reduced permeability of the bacterial cell membrane, Efflux pumps that pump the antimicrobial agent out of the bacterial cell. This figure summarizes the major mechanisms of antimicrobial resistance and can be used as a reference for understanding how resistance can occur and potentially be addressed.

Modification or destruction of antimicrobials

Bacteria can produce enzymes that modify drugs, hindering or preventing the chemical from binding to the target site, rendering the drug to be ineffective. This is achieved through mechanisms such as phosphorylation (chloramphenicols, aminoglycosides, and macrolides), acetylation (aminoglycosides, chloramphenicols), adenylation (aminoglycosides and lincosamides), glycosylation (macrolides) and hydroxylation (tetracycline and tigecycline) [47]. Some microorganisms have enzymes called beta-lactamases that can cleave the beta-lactam ring of certain antibiotics such as penicillins, cephalosporins, and carbapenems, rendering them inactive. This is a common mechanism of resistance among bacteria. Similarly, macrolide antibiotics can be inactivated by bacterial enzymes called esterases or phosphotransferases. These enzymes break down the macrolide structure, rendering the antibiotic ineffective against the bacteria [48-50].

Reduction of access to the target

Bacteria achieve this by decreasing permeability to drugs or enhancing the removal of drugs that have entered the cell. Gram-negative bacteria have a natural protective outer membrane that hinders the entry of hydrophilic drugs such as β-lactams, tetracyclines, and fluoroquinolones [51].Resista nce to β-lactams can be further enhanced by differential expression of porins which reduce the intake of the drug into the periplasm [52].

Bacteria can also be resistant to a drug without being impermeable to it. This is achieved by pumping out the drug (tetracycline, ciprofloxacin) from the periplasm [53]. Also known as efflux, this mechanism can play a vital role in both intrinsic and acquired AMR can be of two types: drug-specific and multidrug. For drug-specific efflux pumps to function, the mechanisms are encoded by the acquired mobile genetic elements mentioned previously whereas multi-specific mechanisms are typically encoded by the chromosome and are a consequence of mutation in the regulatory genes [54]. This mechanism is specifically the most common bacterial AMR mechanism involved in intrinsic resistance [55].

Alteration of target

The target of the drugs can be altered through mutations, modified by enzymes, or replaced. Mutation of rRNA nucleotides can affect the conformation of the drug-binding site, providing resistance to most ribosome-targeting antibiotics which interact exclusively with rRNA [56]. Enzymes such as rRNA methyltransferases can modify specific sites on rRNA, which can reduce the affinity of drugs that target those sites. This can result in the development of antibiotic resistance in bacteria, as the modified rRNA can no longer bind to the antibiotic effectively, rendering the drug ineffective in treating the infection [57-60]. By replacing a target, bacteria can perform an important cellular function without inhibition of the metabolic pathway by the antibiotic. Vancomycin and β-lactam resistance are achievable in this way [61].

CONTROL STRATEGIES TO AVOID ANTIMICROBIAL RESISTANCE

The problem of AMR is concerning as it leads to treatment-failures, greater rates of morbidity and mortality, as well as increased costs in the health sector. Particularly in developing countries, the lack of awareness of proper antibiotic use poses a high risk of giving rise to multiple drug-resistant pathogens, making all available antimicrobials ineffective in fighting the infections. Most pharmaceutical companies do not consider the development of new antimicrobials to be financially lucrative, as they speculate resistance to new drugs will also develop with time regardless. As a result, these companies choose to develop drugs for chronic diseases such as diabetes as this allows them to sell a large number of drugs to each affected person [62]. Although there is no easy and fast way to deal with AMR, rethinking designing new antimicrobial agents, or looking for natural inhibitory substances, must be explored and considered. For example, several phytochemicals have shown their potential as antimicrobial agents acting as antibiotic reversal agents; these have the ability to be propitious substitutes to antibiotics to resist the shrinking pool of conventional antibiotics [63]. Besides, the primary focus at the moment should be on preventing resistance from emerging in the first place or stopping the spread of resistant microbes to other people [45].

Hygiene and sanitation

Mitigating the spread of existing populations is an important step in controlling antimicrobial-resistant microbes. The overcrowding and poor sanitation issues prevalent in developing countries are increasing the circulation and spread of pathogenic microbes. Transmission of all types of pathogens is assisted through human-contact, water, food, and vectors. Bacteria can spread from human to human directly through contact or indirectly through sneezing, coughing, etc.

This spread of resistant microbes can be reduced by improving sanitation and basic hygiene practices among the population [64]. Good hygiene practices such as washing hands, and sneezing/coughing into tissues or the elbow will limit the spread and reduce the risk of becoming a carrier of resistant microbes. Infection rate can be reduced significantly even in hospitals, where the spread of MDR pathogens is highest, by simply increasing the handwashing rate among caregivers [65]. The use of alcohol-based hand-rubs and alcohol for scrubbing in such cases can effectively alleviate AMR in such settings by degerming quickly [66]. Resistant bacteria have been found in water sources and effluents from treatment plants, which can come into contact with humans and re-infect new hosts. This can be prevented by proper treatment of wastewater before being released into waterways [67].

Veterinary medicine

Antimicrobial resistance in microbial species that are pathogenic to humans may rise from animals as many human drugs can be interchangeably used for veterinary practices. Most antimicrobials used for veterinary medicine belong to the same class as human medicine. These antimicrobials also have veterinary uses other than fighting infections. Until recently, 70% of the antibiotics administered to food animals were to promote growth [68]. This involves feeding a low concentration of antibiotics over a long period, a type of procedure that greatly facilitates the enrichment of resistant populations [69].

New methods to control infections in food animals are required to prevent the emergence of antimicrobial resistance in food animals. Utilizing enzymes, probiotics, and acids to improve animals' health shows great benefits. By utilizing these methods, the use of antibiotics as growth promoters can be phased out [70, 71]. We can use bacteriophages, antimicrobial peptides, and bacteriocins as substitutes for antibiotics to fight infections, further reducing their usage [72].

Vaccination

One method of avoiding facilitating antimicrobial resistance in microbes is by not using them in the first place. Vaccines train the immune system in recognizing pathogens so that they can mount an effective and rapid immune response if the pathogen is encountered [73]. Even members of the population who cannot be vaccinated are protected through a phenomenon known as herd immunity. This reduces the prevalence of the pathogen in the population. As the body's immune system can fight the microbes on its own the need to use antimicrobials is reduced. Even antimicrobial-resistant strains are seen to become less prevalent with the use of vaccines [74,75]. Even viral vaccines have been shown to reduce the prescription and consumption of antibiotics. This effect is seen because antibiotics are often prescribed wrongly for viral diseases even in developed countries. As vaccines can prevent the disease from taking hold medications, including antimicrobials are not needed by the patient [76].

Education

Antimicrobials are one of the most important drugs that are needed in developing countries as infections are the leading cause of death [77]. However, they are often prescribed without proper oversight from health professionals and are even readily available without prescriptions [78]. Inappropriate use of antimicrobials needs to be controlled in both hospitals and communities. This is especially hard in developing countries as they lack adequate pharmacological surveillance systems.

Health-care professionals need to be trained to identify and prescribe the correct dosage and drugs and to recognize when antimicrobials are not needed at all. They need to be informed of up-to-date trends in AMR within the population they are practicing in. The practice of rotating and restricting the prescription of antibiotics must be implemented strictly. The capacity to do AMR testing on patient's needs to be increased so that reliance on broad-spectrum antibiotics is reduced. Legal consequences need to be in place for wrongful prescriptions and intentionally prescribing multiple antibiotics due to financial incentives from pharmaceuticals [79].

The general population needs to be educated about the threat of AMR in a language they can understand. Media professionals need to be trained to convey scientific information in an easy-to-understand manner to carry out campaigns such as those conducted for HIV/AIDS and Tuberculosis which help to raise similar awareness about AMR [80].

Government officials need to realize the severity of going back to a pre-antimicrobial state and address the dispensation of drugs without prescriptions in a strict manner. Implementing educational programs teaching the proper use of antimicrobial drugs to doctors, pharmacists, and the populace is the most efficient technique in the worldwide battle against MDR microbes [4, 81].

NATIONAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE

AMR is a complex issue that requires a multi-faceted approach involving not just the scientific and medical communities, but also policymakers, industry stakeholders, and the general public (Figure 4). A policy framework can help to prioritize research areas, allocate funding and resources, and establish guidelines for the responsible use of antibiotics. Furthermore, a policy framework can facilitate international collaboration and coordination, as AMR is a global issue that requires a global response. This can involve sharing data and research findings, as well as establishing joint initiatives to address common challenges. A dedicated policy framework can provide a roadmap for AMR research and help to ensure that efforts are focused and coordinated towards achieving the common goal of combatting AMR.

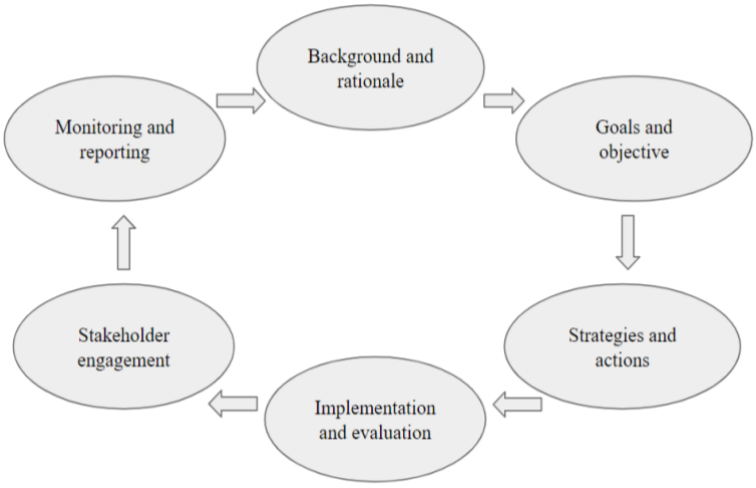

Figure 4. Policy framework of antimicrobial resistance.

CONCLUSION

Antimicrobial resistance is a growing concern worldwide that needs immediate attention. There are several reasons that contribute to the increased AMR phenomenon, namely microbial genetic mutations, healthcare and patient negligence, lack of awareness, agricultural applications, overuse of antibiotics and other antimicrobial drugs, etc. These incidents are most seen in under-developed or developing countries, such as Bangladesh, where there is a lack of resources. AMR can occur through numerous mechanisms such as modification of the antimicrobial itself, modification of the target and reducing access to the target. Additionally, suggestions for strategies to control the threat of AMR in Bangladesh have also been focused on here, which include maintenance of proper sanitation and hygiene, judicious use of food animals, and education of the population. In conclusion, it is the utmost responsibility of all citizens to be self-aware and make others around them aware of the dangers of antimicrobial resistance, and the risks it presents to future generations, along with refraining from any actions that lead to the development of AMR. Only then, the hope for a better and healthy world to live in can be effectively realized.

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AUTHOR CONTRIBUTIONS

This work was a collaboration among all the authors. MHA designed the outlines of the manuscript. MHA, RAIR and MMR wrote the initial draft of the manuscript and MFM revised the whole manuscript. All authors read and approved the final submitted version of the manuscript.

CONFLICTS OF INTEREST

There is no conflict of interest among the authors.

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