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Review Article

Practical Approaches for Combating Antibiotic-Resistant Bacteria and Genes in Wastewater Within Developing Countries

Sunil Pandey*, [1], Jennifer L salerno[1], Shyam Prakash Dumre[2]

Abstract

Antibiotic resistance is a significant public health challenge that necessitates a com-prehensive approach to maintain antibiotic effectiveness. In developing countries, in-adequate treatment infrastructure has led to wastewater being a potential source of antibiotic-resistant bacteria (ARB) and genes which give rise to antibiotic resistance, referred to in this paper as antibiotic-resistant genes (ARGs). This article reviews cur-rent strategies to address ARGs and ARB in wastewater in developing countries. Our review emphasizes the importance of enhancing wastewater treatment infrastructure to effectively remove ARB and ARGs and reduce their release into the environment. Additionally, it addresses the need for monitoring and surveillance to track the pres-ence and dissemination of ARB and ARGs in wastewater. We also discuss potential ob-stacles and challenges to implementing these approaches and the need for further re-search to assess their real-world effectiveness. Overall, this review underscores the need for a comprehensive strategy to combat ARB and ARGs in wastewater in devel-oping countries to safeguard public health.

Keywords: Antibiotic resistance, Wastewater, Developing countries

Introduction

This review elaborates on potential methods to reduce the levels of antibi-otic-resistant bacteria (ARB) and antibiotic-resistant genes (ARGs), which give rise to antibiotic resistance, in wastewater in underdeveloped nations. ARGS are defined as a mutation in a bacterial chromosome that leads to resistance to a particular antibiotic and are dangerous to public health and to the environment (1). At the same time, drug-resistant pathogens themselves, which include bacteria and viruses, are spread-ing in wastewater and are also causing significant impacts on water quality, public health, animal health, and food safety (2, 3). Developing countries are more vulnerable to these potential threats than developed countries because of geographical and socio-economic factors (4). One effective strategy to reduce the risk these threats pose could be to improve water treatment plants in developing countries to remove antibiotic residues, thereby reducing the entry of these resistant genes and bacteria into essential water sources.

In addition, the importance of detecting parasites resistant to disinfectants or treatments in wastewater cannot be overstated for several reasons. First, early detec-tion of resistant parasites aids in safeguarding public health by identifying potential risks and enabling prompt interventions to mitigate infection spread (4, 55). Second, consistent monitoring of resistance in wastewater facilitates the development of im-proved disinfection techniques

Affiliation:

[1]George Mason University, Fairfax VA 22030

[2]Tribhuvan University, Kathmandu Nepal 44600

***Corresponding author:**
Sunil Pandey, George Mason University, Fairfax VA 22030.

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and treatment approaches to counter resistance (4, 55-56). Third, identifying resistant parasites in wastewater can guide the establishment of targeted regulations and policies for industries that contribute to this issue, thereby reducing the release of resistant parasites into the environment (57). Lastly, the early detection of resistant parasites supports global efforts in tracking and understanding the emergence and dissemination of resistance, promoting international cooperation to tackle this escalating problem (57). In this paper we are focused on bacteria rather than parasites.

Resistance can lead to treatment failures and the spread of antibiotic-resistant in-fections, which can be challenging to treat and have serious consequences, including increased morbidity and mortality (3-4). The World Health Organization (WHO) has identified antibiotic resistance as one of the biggest threats to global health (57). Ap-proximately 700,000 deaths worldwide are caused by antibiotic-resistant infections each year. One potential source of ARB is wastewater, which can harbor high levels of antibiotics, ARB and ARGs. In developing countries, where wastewater treatment in-frastructure is often inadequate, untreated sewage can be released into the environ-ment, spreading ARBs and ARGs. Common ARGs found in wastewater include genes conferring resistance to tetracyclines (such as tetA and tetB), beta-lactams (such as blaCTX-M, blaKPC, blaTEM, blaSHV, blaAMPC, and blaTEM), and sulfonamides (such as sul1 and sul2) (38-39). In addition, common ARBs found in wastewater treatment plants include the Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Enterococcus species. These bacteria can harbor various ARGs, including those that confer resistance to tetracyclines, beta-lactams, sulfonamides, and multiple classes of antibiotics (such as the multidrug resistance gene, mecA) (39-40). This is a significant issue in nations that are still growing and developing, as these countries often have limited access to effective antibiotics and may be highly vulnerable to the negative impacts of antibiotic-resistant infections. Developing nations are especially vulnerable due to their limited resources, weak infrastructure, and often underdeveloped political and social institutions. These countries typically struggle to respond effectively to cri-ses such as natural disasters, economic shocks, or public health emergencies. Addition-ally, they face challenges in addressing long-term issues like poverty, inequality, and environmental degradation, which can exacerbate their vulnerability to external shocks.

Given the urgent need to mitigate the rise of antibiotic-resistance in vulnerable nations, this review article summarizes current knowledge on strategies to combat an-tibiotic resistance in wastewater in developing countries. We focus on three main are-as: first, improving wastewater treatment infrastructure to effectively remove antibi-otics, ARB and ARGs from water sources. Second, implementing measures to reduce the release of antibiotics into the environment, and third, monitoring and surveillance to track the presence and spread of ARB in wastewater. We also discuss the potential challenges and barriers to implementing these strategies and the need for further re-search to determine their effectiveness. Our review highlights the need for a compre-hensive approach to address antibiotic resistance in wastewater in developing coun-tries and underscores the importance of addressing this issue to protect public health.

Materials and Methods

This review article's materials and methods section describes the process the au-thors followed to identify and review relevant studies on strategies to combat antibi-otic resistance in wastewater in developing countries. Specifically, we conducted a comprehensive literature search using several electronic databases (PubMed, Google Scholar, Science Direct, and Elsevier) and identified 58 studies that met our inclusion criteria. These studies were published between 2010 and 2022 and were written in English. We used a combination of keywords such as "antibiotic resistance," "wastewater," "developing countries," "treatment," "prevention," and "surveillance" to identify relevant studies. In addition to the electronic database search, we manually searched reference lists of relevant articles to identify additional studies. Once we had identified the relevant studies, we reviewed and analyzed them to extract information on strategies to combat antibiotic resistance in wastewater in de-veloping countries. This information was organized according to its relevance to the three main areas outlined in the introduction: improving wastewater treatment infra-structure, implementing measures to reduce the release of antibiotics into the envi-ronment, and monitoring and surveillance of ARB in wastewater. For each of these ar-eas, the authors have summarized the current state of knowledge, including existing strategies and interventions and potential challenges and barriers to implementation. Our review aims to provide a comprehensive overview of current knowledge on strat-egies to combat antibiotic resistance in wastewater in developing countries and to identify areas in need of further research.

Culture-based methods in detecting antibiotic resistance involve growing bacteria from wastewater samples on agar plates containing various antibiotics. The bacteria that grow in certain antibiotics are resistant to those antibiotics. This method can be time-consuming and may only detect some ARGs or ARB present in a wastewater sample. Other methods, such as molecular biology-based methods including polymer-ase chain reaction (PCR) and quantitative PCR (qPCR), can detect specific ARGs in wastewater samples. These methods can be more sensitive and specific than cul-ture-based methods but require specific reagents, equipment, and trained personnel. Results obtained on the presence of

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ARGs by molecular techniques do not have to cor-respond to the expressed phenotype. Metagenomics approaches such as next-generation sequencing (NGS) can also identify the resistance gene and the bacteria that harbor it. Unlike the aforementioned techniques, metagenomics can give a complete picture of the resistance profile of the wastewater (40). Among the 43 articles reviewed, several methods for identifying ARGs in wastewater were found, including PCR and real-time qPCR. It is important to note that the essential materials used in PCR and real-time qPCR are DNA molecules, thermostable DNA polymerase or DNA replicate enzymes, primers labeled with fluo-rescent or non-radioactive markers, 5-ATP, magnesium chloride (MgCl2), and one mM Dithiothreitol (DTT) (6). Among these, all PCR, real-time qPCR, and metagenomics methods are best for analyzing scientific samples as these techniques can be used to check the presence or absence of different types of genes in biological samples or even determine their levels in samples. However, researchers must understand the various factors like time, temperature,season, humidity and light exposure can influence the results. These days real-time qPCR has become an essential tool in modern microbiol-ogy because it has high sensitivity, specificity, and speed in detecting and quantifying nucleic acids. It allows for rapid identification and measurement of microorganisms, including pathogens, in clinical, environmental, and research settings. Real-time qPCR offers the advantage of monitoring the amplification process in real-time, providing quantitative data and reducing the risk of contamination associated with post-amplification procedures. The technique also allows for multiplexing, enabling the simultaneous detection of multiple targets in a single reaction. This combination of features has led to the widespread adoption of real-time qPCR in areas such as diag-nostics, epidemiology, food safety, and microbial ecology.

Results

Our review results find several ARBS and ARGs that have been detected in wastewater treatment plants. One example is Escherichia coli, which is frequently found in mammals' guts and is often used as a marker for fecal contamination of water sources. Strains of E. coli that are resistant to antibiotics such as ampicillin, tetracy-cline, and sulfonamides have been discovered in wastewater treatment facilities in developing countries (39-40). Another common bacterium found in wastewater is Klebsiella pneumonia, a bacterium which can cause respiratory, urinary tract, and bloodstream infections. K. pneumoniae is known to resist multiple antibiotics, including carbapenems, a group of last-line defense antibiotics used in cases of antibiotic re-sistance. This resistant strain has been isolated from wastewater treatment plants. A third bacterium found in wastewater is Pseudomonas aeruginosa, which can cause a wide range of infections and is known to be resistant to multiple antibiotics, including aminoglycosides, cephalosporins, and fluoroquinolones. The resistant strain of P. aeru-ginosa has also been isolated from wastewater treatment plants.

ARGs have also been commonly found in wastewater treatment plants. For exam-ple, blaCTX-M is a gene that confers resistance to cephalosporins, a group of antibiotics widely used to treat bacterial infections. Specifically, blaCTX-M is a type of be-ta-lactamase enzyme that can break down and inactivate these antibiotics, rendering them ineffective in treating conditions caused by bacteria carrying this resistance gene. As a result, infections caused by blaCTX-M-producing bacteria can be challenging to treat and may require alternative antibiotics or combination therapy to achieve effec-tive treatment outcomes. The drug group typically used to combat infections where blaCTX-M has given rise to resistance are beta-lactam antibiotics, such as cephalo-sporins, penicillin, and carbapenems. These antibiotics commonly treat many bacterial infections, including urinary tract infections, pneumonia, sepsis, and intra-abdominal infections. Several other genes also give rise to resistance. qnr is a gene that confers resistance to fluoroquinolones, a class of drugs utilized to cure various bacterial infections such as urinary tract infections (UTI), respiratory tract infections, and gastrointestinal in-fections. sul1, sul2, and sul3 confer resistance to sulfonamides, a group of antibiotics used to treat bacterial infections like urinary tract infections, ear infections, and res-piratory tract infections. ermB, ermC, and ermF are genes that can resist erythromycin used to treat conditions like respiratory tract infections, skin infections, and sexually transmitted infections (40-41).

Table 1: List of ARB and ARGs in wastewater treatment plants.

Bacteria	Gene(s)	References
Escherichia coli	blaCTX-M, qnrS, tetA, sul1	(39-42)
Pseudomonas aeruginosa	blaIMP, sul1, tetA, catB3	(39,41)
Klebsiella pneumoniae	blaCTX-M, blaKPC, mcr-1	-43
Acinetobacter baumannii	blaOXA-23, blaOXA-24, blaOXA-58	(42-43)
Salmonella enterica	blaTEM, blaSHV, tetA	-38
Staphylococcus aureus	mecA, ermB, tetK	(38-41)

These are only some of the most frequently observed cases, with many other genes responsible for antibiotic resistance having been found in wastewater, and new genes continually being discovered. It is also important to note that the presence of ARGs in wastewater does not necessarily mean that the corresponding resistance will be found in all bacteria in the wastewater. Instead, the presence of these genes serves as an in-dicator of the potential for the development of antibiotic

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resistance in the environ-ment. To tackle this issue, there are several points below which can serve as a focus for reducing the presence of ARB and ARGs in wastewater.

Improving wastewater treatment infrastructure

Adequate wastewater treatment is critical for reducing the levels of ARB and ARGs in wastewater and thus protecting public health. However, in developing coun-tries, wastewater treatment infrastructure needs to be improved to reduce the release of untreated wastewater into the environment. The combination of centralized and decentralized wastewater treatment offers several advantages for reducing the pres-ence of ARB and ARGs. Firstly, decentralized treatment systems can provide localized treatment, reducing the transport of untreated wastewater and associated pollutants. Secondly, decentralized systems often employ natural treatment processes such as constructed wetlands, which have been shown to effectively reduce ARB and ARG levels. On the other hand, centralized systems can employ advanced treatment tech-nologies such as membrane bioreactors and ozone disinfection, which have been shown to effectively remove ARBs and ARGs. Moreover, centralized systems can treat more significant volumes of wastewater, making them suitable for managing wastewater from multiple sources.

Recent studies have demonstrated the effectiveness of combining centralized and decentralized wastewater treatment for reducing levels of ARB and ARGs. For exam-ple, a study conducted by (48) in China found that combining centralized and decen-tralized treatment reduced the abundance of ARGs in wastewater by 59.3% and the diversity of ARB by 56.7%. Another study by (49) in the United States found that the combination of centralized and decentralized treatment reduced the relative abun-dance of ARGs by up to 80% in the effluent from a wastewater treatment plant. For several reasons, developing countries often need more centralized and decen-tralized wastewater treatment systems. Firstly, more infrastructure and financial re-sources are required to make investing in wastewater treatment facilities easier for developing countries. Secondly, the lack of trained personnel and technical expertise can hinder the development and operation of wastewater treatment facilities in de-veloping countries. This can result in inadequate or ineffective treatment, releasing ARB and ARGs into the environment. In addition, a lack of awareness and political will can also contribute to the need for improved wastewater treatment facilities in developing countries. In many cases, wastewater treatment is not prioritized due to competing resource demands and a lack of understanding about the importance of proper wastewater management.This combination of a lack of infrastructure and trained personnel has resulted in a situation where untreated or poorly treated wastewater is usually discharged into nearby water bodies, leading to environmental pollution and health hazards. According to a World Bank Report from March 2020, around 80% of the wastewater generated in developing countries is discharged into the environment without adequate treatment. This untreated wastewater contains high levels of pathogens, nutrients, and chemicals, leading to environmental degradation and public health risks (50).

Overall, the need for centralized and decentralized wastewater treatment systems in developing countries is a significant challenge that must be addressed urgently. Im-proving access to safe and reliable wastewater treatment facilities can reduce envi-ronmental pollution, protect public health, and promote sustainable development. One approach to enhancing wastewater treatment infrastructure is the implementation of centralized treatment systems. These systems involve collecting, treating, and dis-charging wastewater at a central location, and they are effective at removing antibiot-ics, ARB and ARGs from wastewater (9). However, the construction and maintenance of centralized treatment systems can be expensive, and there may be challenges in se-curing funding and overcoming logistical barriers to implementation (10). Another approach is using decentralized treatment systems, which are smaller and more locally based. Decentralized systems can be more cost-effective and easier to implement, es-pecially in areas with limited infrastructure (10). One example of a decentralized treatment system is constructed wetlands, which use natural processes to remove con-taminants from wastewater (11). However, decentralized systems may be less effective than centralized systems at removing antibiotics, ARB and ARGs (10-11). Both centralized and decentralized wastewater treatment offer a promising ap-proach to reducing the presence of ARB and ARGs in wastewater. By combining both approaches, the strengths of each treatment method can be leveraged, thus providing a more resilient and effective system for managing wastewater. While improved infrastructure is a critical approach for reducing the presence of ARB and ARGs in wastewater in developing countries, other approaches are key to maximally reducing antibiotic resistance. Methods that target the reduction of the re-lease of antibiotics into the environment are another important strategy for combating antibiotic resistance in wastewater in developing countries. Several approaches can be taken to achieve this, including:

Reducing unnecessary antibiotic use

Overuse and misuse of antibiotics are significant contributors to the development of antibiotic resistance (12). Efforts to reduce unnecessary antibiotic use, such as by implementing prescribing guidelines and patient education, can help reduce the levels of antibiotics in wastewater. One such approach is Antimicrobial Stewardship Programs (ASPs). First and foremost, ASPs promote the judicious use

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of antimicrobials, reducing the likelihood of overuse and misuse, which are vital contributors to the development of antibiotic re-sistance (58). Secondly, ASPs help improve patient outcomes by prescribing appropri-ate and targeted antimicrobial therapy, decreasing the risk of treatment failure and adverse effects (11,58).

Improving the disposal of antibiotics

Proper disposal of antibiotics is also essential to prevent their release into the en-vironment. Improvement can be achieved by implementing programs to collect and safely dispose of expired or unused antibiotics (12).

Regulating the discharge of antibiotics from point sources

Point sources, such as hospitals and pharmaceutical manufacturing facilities, can significantly contribute to the levels of antibiotics in wastewater (9). Regulations that limit the discharge of antibiotics from these sources help reduce their release into the environment.

Monitoring and surveillance:

Effective monitoring and surveillance systems are essential for tracking the pres-ence and spread of ARB in wastewater in developing countries. The information col-lected by such systems can identify potential outbreaks and inform public health in-terventions. There are several approaches to monitoring and surveillance of Arb and ARGs in wastewater, including:

Routine monitoring

Regular monitoring of wastewater can provide valuable information on the levels of antibiotics and ARB present. This can be done using monitoring systems installed at wastewater treatment plants (10).

Targeted monitoring

Targeted monitoring can focus on specific antibiotics or ARB of concern (10,11). This can be useful for identifying emerging trends or hotspots of antibiotic resistance.

Why Antibiotic Resistance is a Global Problem:

Results suggest that pathogens isolated from various sources such as food pro-cessing industries, the pharmaceutical industry, livestock farms, sewage systems, and nature have been found to resist aminoglycoside antibiotics (13,14). Several reports in-dicate that resistance gene transfer is standard across global regions with a higher presence in developing countries in continents such as Africa and South Asia (15). Antibiotic resistance is a global problem, so this topic is of widespread importance (14-16). Modern illnesses lead to the large-scale use of antibiotics. The excessive use of antibiotics is due to the overuse of these medications, which has increased the inci-dence of antibiotic-resistant bacterial strains. Many of these strains are pathogenic, in-creasing the threat of them causing epidemics globally (17). Spontaneous growth mechanisms drive antibiotic resistance, and so are not nec-essarily caused by deliberate actions by humans. Yet it is indisputable that antibiotic resistance is a major public health threat related to many aspects of human activity: lifestyle choices, social conditions, economic development, and agricultural production (16-17). However, in many situations, people can unknowingly contribute to the spread of antibiotic-resistant pathogens through various measures, including (as men-tioned) the overuse and misuse of antibiotics, poor hygiene practices, consuming con-taminated food and water, and not completing prescribed courses of antibiotics. It is essential to be aware of these actions and take steps to minimize the spread of ARB.

Recently, scientists researched detecting genes and bacteria in wastewater treat-ment. The new findings show that ARB and ARGs were prevalent in wastewater across the globe (18). Observation shows that the country's waste management systems, rules, and regulations are essential in influencing the prevalence of ARGs in wastewater (20-22). Further results show that Nepal detected a few genes which can be traced back to humans hosted in hospital settings and animal sources as they discuss their envi-ronmental impacts (15). Russia had a comparatively lower amount of ARGs detected than other European countries (23). In contrast, Hungary mainly had agricultural sources and medical facilities as their main contributors to the total amount of ARB. Below are the problems underdeveloped countries face when it comes to antibiotic re-sistance:

Laboratory infrastructure: Underdeveloped countries often need more laboratory infrastructure for detecting ARB and ARGs, such as PCR machines and sequencing platforms, which are more widely available in developing countries (Smith et al., 2014).

Access to antibiotics: In underdeveloped countries, access to antibiotics may be limited or non-existent, while in developing countries, antibiotics may be more readily available, but often without prescription or regulation, leading to overuse and misuse (51).

Clinical practices: Clinical practices in underdeveloped countries are often subop-timal due to a lack of resources and training, resulting in the overuse of antibiotics and the spread of ARB (52).

Disease burden: The disease burden in underdeveloped countries is often domi-nated by infectious diseases, including those caused by ARB, whereas in developing countries, the disease burden is more diverse, with non-communicable conditions also playing a significant role (53).

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Surveillance systems: Developing countries are more likely to have established surveillance systems for tracking antibiotic resistance, while underdeveloped countries often lack these systems (52-53).

Data quality: Data on antibiotic resistance in underdeveloped countries may be of poor quality due to a lack of infrastructure and resources. In contrast, in developing countries, the quality of data is generally better but still imperfect (54).

Research capacity: Developing countries often have more research capacity and expertise in antibiotic resistance than underdeveloped countries, although both are typically limited (52, 54).

Resource allocation: Developing countries may be better able to allocate resources to combat antibiotic resistance, while underdeveloped countries often need more fi-nancial and political support to address this issue (54).

In summary, while there are some similarities in the challenges faced by under-developed and developing countries in detecting ARB and ARGs, there are also signif-icant differences as described above. Understanding these differences can guide efforts to improve the detection and management of antibiotic resistance in different settings.

Strategies to Combat Antibiotic Resistance

The research undertaken by this study collated numerous strategies to combat ARB and ARGs in wastewater, including sludge screening by toxicology, epidemiology, genetic analysis, and sterility (14, 17). Furthermore, ARB and ARGs must be monitored closely to determine whether they are increasing in wastewater, how much they are increasing, and what potential problems this could cause. In this case, it is also neces-sary to identify and provide information about known sources of resistance (4). This procedure will also help to reduce infections through the inappropriate use of antibi-otics. Researchers can help to identify sources of antibiotic resistance in the environ-ment, such as contaminated water sources, soil, and food animals. This can be done by reporting any unusual or concerning observations, such as changes in water quality or fish die-offs, to the appropriate authorities. In addition, they can help to raise aware-ness about antibiotic resistance by sharing information with others, including family members, friends, and healthcare providers. This helps ensure that all stakeholders are informed about the risks associated with antibiotic resistance and that they are taking appropriate steps to prevent its spread. Overall, identifying and providing information about known sources of antibiotic resistance is an essential step in combating this global public health threat. By working together and taking collective action, we can all help to slow the spread of ARB and preserve the effectiveness of these life-saving drugs.

Table 2: Comparison of developing and developed world in detecting genes and bacte-ria in wastewater treatment.

Developing Countries	Developed Countries
The study suggested that existing wastewater treatment processes in developing countries must be improved to combat ARB and ARGs in wastewater.	Developed countries have made great strides to improve the efficiency of municipal wastewater discharge treatment and promote a cleaner environment (23).
The study also suggested that testing a new bacterial species may be required to meet the complete defense against multidrug-resistant organisms (7).	In contrast to developing countries, rich nations have built treatment facilities to deal with the problem of spotting ARB and ARGs in wastewater treatment (51).
There are challenges in developing countries, such as the high cost of operation and poor awareness among citizens to prevent and manage potential risks (13).	Developed nations destroy bacteria before releasing wastewater into the environment using chlorine, UV light, or both. This makes their cities safer to live in (4, 5).

In addition, developed countries generally have higher levels of awareness and education about the importance of detecting genes and bacteria in wastewater treat-ment and the risks associated with antibiotic resistance. In contrast, developing coun-tries may have lower awareness and education. Partially as a result of this gap in awareness and education, there is a significant difference in the prevalence and diver-sity of ARB and ARGs in developed and developing countries (46).

Prevalence

Studies have shown that the prevalence of ARB and ARGs is generally higher in developing countries than in developed countries. This discrepancy is likely due to various factors, such as higher levels of antibiotic use and inadequate wastewater treatment infrastructure in developing countries (43).

Diversity

ARB and ARG diversity are generally higher in developing countries. This trend can be attributed to a combination of factors, such as greater exposure to different sources of antibiotics, including those used in agriculture and aquaculture, and a greater diversity of bacterial populations in developing countries. Moreover, the genetic diversity of bacterial populations in developing countries may contribute to the greater variety of ARB and ARGs observed in these regions. The high prevalence of mobile genetic elements, such as plasmids and transposons, in de-veloping countries' bacterial populations, may also facilitate the spread of ARGs (44, 47). Overall, the higher diversity of ARB and ARGs in developing countries highlights the need for a global approach to addressing this issue. Efforts should focus on im-proving the appropriate use of antibiotics, developing alternative

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strategies to reduce the need for antibiotics, and promoting sustainable agriculture and aquaculture prac-tices that reduce the use of antibiotics. (44, 47).

Antibiotic resistance mechanisms

Multidrug-resistant strains of bacteria are prevalent in developed countries and can carry many resistance genes. In contrast, developing countries tend to have a higher prevalence of resistant strains, each taking fewer resistant genes. This differ-ence in resistance patterns may be due to differences in antibiotic usage, healthcare practices, and the genetic diversity of bacterial populations. In developed countries, antibiotics are often overused and misused, leading to the selection of multi-drug-resistant strains. In contrast, in developing countries, resistance may arise from the spread of multiple resistant strains, each with a different set of resistance genes. This highlights the importance of global efforts to combat antibiotic resistance, in-cluding the appropriate use of antibiotics, the development of alternative therapies, and the promotion of sustainable agriculture and aquaculture practices (43-44). Overall, understanding the differences in resistance patterns between developed and developing countries can help to guide efforts to address the global public health threat of antibiotic resistance.

Type of resistance

Developed countries often resist broad-spectrum antibiotics such as beta-lactams, fluoroquinolones, and erythromycin. Developing countries often resist drugs such as tetracyclines and sulfonamides, commonly used in agriculture and aquaculture, and have less access to newer, more expensive antibiotics (45-46). It is vital to note that these are general trends, and significant variations can exist within and between countries. A combination of approaches is likely most effective in combating antibiotic re-sistance in wastewater in developing countries. Additional studies are necessary to es-tablish the best combination of the methods mentioned above for reducing the pres-ence of ARB and ARGs in wastewater and to identify potential obstacles or hurdles to their execution.

Discussion

The results of our review suggest that a multifaceted approach is needed to effec-tively combat antibiotic resistance in wastewater in developing countries. Improving wastewater treatment infrastructure, implementing measures to reduce the release of antibiotics into the environment, and monitoring and surveillance are all essential strategies that can help to address this issue. Improving wastewater treatment infra-structure is critical for removing antibiotics, ARB and ARGs from wastewater and protecting public health. While centralized treatment systems effectively remove these contaminants, they can be expensive and challenging to implement in specific settings. Decentralized treatment systems, such as constructed wetlands, can be more cost-effective and easier to implement. However, they may be less effective at remov-ing antibiotics and ARB and thus need improving. Reducing the release of antibiotics into the environment is another important strategy for combating antibiotic resistance in wastewater. Efforts to reduce unnecessary antibiotic use and improve the disposal of antibiotics can reduce the levels of these substances in the environment. In addition, regulating the discharge of antibiotics from point sources, such as hospitals and phar-maceutical manufacturing facilities, can also help to reduce their release into the en-vironment. Effective monitoring and surveillance systems are essential for tracking the presence and spread of ARB and ARGs in wastewater. This information can identify potential outbreaks and inform public health interventions. Routine and targeted monitoring can provide valuable information on the levels of antibiotics, ARB, and ARGs in wastewater. Surveillance of outbreaks can help identify the source and extent of an epidemic and also inform public health interventions. Overall, our review high-lights the need for a comprehensive approach to addressing antibiotic resistance in wastewater in developing countries. Improving wastewater treatment infrastructure, reducing the release of antibiotics into the environment, and implementing effective monitoring and surveillance systems are all essential strategies that can help to protect public health and address this growing global health concern.

Conclusion

In summary, antibiotic resistance poses a significant public health challenge that calls for a comprehensive response. One key contributor to the emergence of ARB is inadequately treated wastewater in developing nations, which can introduce substan-tial amounts of antibiotics and ARB into the environment. This review underscores the urgency of enhancing wastewater treatment infrastructure, instituting measures to curb the discharge of antibiotics into the environment and employing monitoring and surveillance to track the existence and dissemination of ARB in wastewater. Addition-ally, we touched upon the possible obstacles and hindrances in executing these strate-gies and emphasized the necessity for further research to evaluate antibiotic resistance in developing countries. In short, a comprehensive approach is needed to address antibiotic resistance in wastewater in developing countries and to protect public health. This approach should involve a combination of strategies, including improving wastewater treatment infra-structure, reducing the release of antibiotics into the environment, and implementing effective monitoring and surveillance systems. By working together, we can help re-duce the threat of antibiotic resistance and protect the health of communities world-wide.

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