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Antibiotic Resistance in Domestic Wastewater: Addressing Treatment Inefficiencies and the Imperative for Sanitation System Enhancement

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Abstract

The increasing detection of antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs) in domestic wastewater represents a pressing global environmental and public health challenge. Wastewater treatment plants (WWTPs), while designed to remove conventional pollutants, are increasingly recognized as reservoirs and hotspots for the persistence and horizontal gene transfer (HGT) of ARGs among microbial communities. This study aims to explore the mechanisms underlying bacterial antibiotic resistance, evaluate the limitations of conventional treatment processes –particularly disinfection methods such as chlorination – in effectively removing ARB and ARGs, and assess the implications for sanitation management in Indonesia. A systematic literature review (mini-review format) was conducted to synthesize recent findings on ARB/ARGs presence in WWTPs and the performance of existing treatment technologies. Results show that ARGs can persist even after disinfection, especially in extracellular forms, and that chlorination may, in some cases, promote ARGs release through cell lysis. Furthermore, several resistant strains demonstrate tolerance to standard chlorine doses. In Indonesia, where domestic wastewater treatment coverage and compliance remain inadequate, the uncontrolled discharge of partially treated or untreated wastewater exacerbates the spread of antibiotic resistance in aquatic environments. This study concludes that existing treatment systems are insufficient to address antibiotic resistance risks and emphasizes the urgent need for improved sanitation infrastructure, monitoring, and targeted treatment technologies.

Keywords: ARB, ARGs, disinfection, sanitation, WWTP.

INTRODUCTION

Since their discovery over a century ago, antimicrobial agents – including antibiotics, antifungals, antivirals, and antiparasitics – have significantly extended average life expectancy. The first antibiotic, Salvarsan, was introduced in 1910. In just over 100 years, antibiotics have transformed modern medicine and contributed to an increase in average human lifespan by approximately 23 years. The discovery of penicillin in 1928 marked the beginning of the golden age of antibiotic discovery, which peaked in the mid-1950s (Hutchings, Truman, & Wilkinson, 2019). Among all antimicrobials, antibiotics are the most widely recognized and essential, primarily used to treat bacterial infections. Other types of antimicrobials combat viral and parasitic diseases such as AIDS and malaria (The World Bank, 2017). These essential medicines save millions of lives every day (WHO, 2024). Global data from 2000 to 2015 show that daily antibiotic consumption increased from approximately 21.1 billion to 34.8 billion tons (Zhu, Su, Lai, Zhang, & Liu, 2021), reflecting a consistent rise in global antibiotic use.

However, the very importance of antimicrobials in saving human and animal lives is now being undermined by the emergence of antimicrobial resistance (AMR) – a phenomenon in which bacteria, viruses, fungi, and parasites no longer respond to the antimicrobial agents designed to eliminate them (WHO, 2024). AMR arises through adaptive evolutionary changes in pathogens, enabling them to survive exposure to previously effective treatments (The World Bank, 2017). As a result, antibiotics and other antimicrobials become ineffective, leaving humans and animals vulnerable to untreatable infections. Pathogens survive and proliferate, patients become sicker and may die, healthcare costs rise, and disease transmission continues unabated (The World Bank, 2017; WHO, 2024).

Murray et al. (2022) developed a predictive statistical model estimating the global mortality associated with AMR in 2019. Based on this model, it is estimated that 4.95 million (range: 3.62–6.57 million) deaths were associated with bacterial AMR that year, of which 1.27 million (95% uncertainty interval: 0.911–1.71 million) were directly attributable to bacterial AMR. Regionally, the highest all-age mortality rate due to AMR was recorded in Western Sub-Saharan Africa, with 27.3 deaths per 100,000 population (20.9–35.3), while the lowest was in Australasia, with 6.5 deaths (4.3–9.4) per 100,000. Lower respiratory infections accounted for more than 1.5 million AMR-associated deaths in 2019, making it the most burdensome infection syndrome. Six leading pathogens – *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* – were responsible for 929,000 (660,000–1.27 million) AMR-attributable deaths and 3.57 million (2.62–4.78 million) AMR-associated deaths in 2019. According to WHO (2024), AMR is currently responsible for 1.3 million deaths annually and contributes to an estimated 5 million deaths each year.

Furthermore, Jonas et al. (2017) argue that the economic burden of AMR will disproportionately affect low-income countries, exacerbating global economic inequality. This disparity stems from higher infectious disease prevalence and a greater reliance on labor income in countries with lower per capita incomes. The impact of AMR on poverty is particularly alarming. Under a high-impact AMR scenario, an additional 24 million people could be pushed into extreme poverty by 2030, with the majority residing in low-income countries. Looking ahead, WHO (2024) forecasts that AMR will pose a substantial threat to global economic stability, with annual costs potentially reaching up to US$3.4 trillion by 2030 and pushing 28 million people into poverty by 2050.

Antimicrobial resistance is a natural process that occurs over time through genetic changes in pathogens, including spontaneous mutations or the acquisition of antibiotic resistance genes (ARGs)(Quirós et al., 2014). However, its emergence and spread have been greatly accelerated by human activities, particularly the misuse and overuse of antimicrobial agents for the treatment, prevention, and control of infections in humans, animals, and plants. Such misuse is a major driver in the development of drug-resistant pathogens (WHO, 2023).

The use of antimicrobials significantly impacts the human gut microbiome, transforming it into a critical reservoir for AMR. Once colonized by resistant genes, commensal organisms can serve as major contributors to the dissemination of resistance due to microbial community interactions (Brinkac, Voorhies, Gomez, & Nelson, 2017; Penders, Stobberingh, Savelkoul, & Wolffs, 2013). Research has demonstrated that antimicrobial resistance is present in the human gut flora. For instance, a study published in Antimicrobial Agents and Chemotherapy examined resistance to seven antimicrobial agents in aerobic gram-negative gut flora from over 600 individuals, including hospital patients and members of the general public. The results revealed that 62.5% of stool samples from individuals with no recent antibiotic use still contained at least 10% of organisms resistant to at least one antibiotic. Moreover, approximately 40% of the samples exhibited resistance to multiple antibiotics at similar levels (Levy, Marshall, Schluederberg, Rowse, & Davis, 1988).

Another study analyzed clusters of ARGs derived from bacteriophage DNA isolated from the feces of 80 healthy individuals—46 females and 34 males, aged 6 months to 102 years—who visited a hospital in Barcelona, Spain over a six-month period. The study found that 70% of the samples tested positive for one or more ARGs in phage DNA (Quirós et al., 2014). In a separate study published by Karkman, Pärnänen, and Larsson (2019) metagenomic analysis of untreated wastewater was conducted to characterize bacterial resistomes at 79 locations across 60 countries. The study concluded that the presence of resistance genes could largely be attributed to fecal pollution, with no strong evidence of selective pressure occurring in the environment. In Indonesia, a domestic study conducted by researchers at Airlangga University further confirmed the presence of AMR in human feces. Fecal samples collected from residents in East Java revealed that nearly all contained bacteria resistant to commonly used antibiotics, including tetracyclines, beta-lactams, macrolides, and even vancomycin—a last-resort antibiotic for treating severe infections. Alarmingly, ARGs were also detected in Gram-negative bacteria, which are typically more difficult to treat due to their robust cell wall structure (Wibowo, 2024).

These findings collectively indicate that microorganisms in the human digestive system have adapted to antibiotic exposure and that the human gut microbiota may serve as a significant reservoir for antimicrobial resistance genes. This reservoir has the potential to spread into the environment via fecal contamination. Therefore, monitoring and controlling the spread of AMR through effective hygiene and sanitation practices is critically important.

Domestic wastewater must be treated prior to discharge into the environment to prevent negative impacts on ecosystems and human health. The primary goal of wastewater treatment is to remove or reduce harmful substances such as organic matter, excess nutrients, heavy metals, pathogenic microorganisms, and toxic chemical compounds that can contaminate water, soil, and air. If discharged without adequate treatment, domestic wastewater can lead to water source contamination, eutrophication, disease transmission, and disruption of ecological balance. Therefore, wastewater treatment is an essential step to ensure that effluent released into the environment meets safe quality standards.

Typical domestic wastewater treatment plants (WWTPs) employ a series of treatment units designed to progressively remove contaminants from wastewater. These generally include preliminary treatment, primary treatment, secondary treatment, tertiary treatment, sludge treatment, and effluent discharge. Preliminary treatment removes large materials and grit through screening and grit chambers. Bar screens remove materials such as plastics and fabrics, while grit chambers allow heavier solids like sand and gravel to settle. During the primary treatment stage, wastewater flows into primary sedimentation tanks where solids settle at the bottom as sludge, and lighter materials like oil and grease float to the surface and are removed. Secondary treatment involves biological processes using microorganisms to break down organic matter. Common methods include activated sludge systems, trickling filters, or sequencing batch reactors. The wastewater is then transferred to secondary settling tanks to allow suspended solids and microorganisms to settle as sludge. The tertiary treatment stage involves advanced processes to remove nutrients such as nitrogen and phosphorus, including filtration, disinfection, and chemical treatment. Techniques such as sand filtration, UV irradiation, or chlorination help ensure the treated water meets environmental quality standards. The sludge treatment phase processes sludge collected from the primary and secondary treatments through thickening, anaerobic digestion, or drying to reduce its volume and prepare it for disposal or reuse (Burton et al., 2013; Davis, 2019; Qasim & Zhu, 2018).

The final stage, effluent discharge, involves releasing the treated water—now free of harmful contaminants—into rivers, lakes, or other water bodies, or reusing it for irrigation, industrial processes, or groundwater recharge. The criteria used to ensure the treated wastewater is safe for discharge are referred to as effluent quality standards. In Indonesia, these are defined under the Regulation of the Minister of Environment and Forestry No. P.68/MENLHK/SETJEN/KUM.1/8/2016 on Domestic Wastewater Quality Standards, which sets the microbiological quality parameter as total coliform at a maximum of 3,000/100 mL. Total coliform is a general indicator of microbial water quality. Other commonly used indicators include *Escherichia coli* (*E. coli*), *Clostridium perfringens*, and *coliphages* (Pepper, Gerba, & Gentry, 2014).

However, such indicators do not account for the presence of antibiotic-resistant microorganisms (ARMs) or antibiotic-resistant bacteria (ARB). If the effectiveness of WWTPs is measured solely by the reduction of total coliforms or *E. coli*, it is likely that these organisms can be adequately removed. But what about ARB? Can they be effectively eliminated during wastewater treatment so that effluent is safe for environmental discharge? Therefore, this study aims to assess the effectiveness of WWTP treatment units in removing ARB as the ultimate goal for WWTPs is to serve as a major barrier to the environmental release of ARB. Several studies have examined the presence of antibiotic resistance genes (ARGs) in WWTP units, as well as the persistence of ARB or ARGs throughout the treatment process. However, these studies have been conducted separately. Consequently, the present research seeks to compare and integrate these findings to evaluate the overall performance of domestic wastewater treatment systems in removing ARB and ARGs in a more comprehensive manner.

Material and Method

The method employed in this study is a literature review. A literature review, as a research method, is generally defined as a systematic way to collect and synthesize previous studies. By integrating findings and perspectives from various empirical sources, literature reviews can offer strong answers to research questions (Snyder, 2019). More specifically, this study adopts a systematic literature review in the form of a mini-review. A systematic literature review is a critical evaluation of past research studies that address the research question of interest (Onwuegbuzie & Frels, 2016). This method aims to provide a focused and productive review to answer a specific research question, rather than broadly discussing a topic area (Gough, Oliver, & Thomas, 2012). The mini-review approach, as described by Elfar (2014), is intended to summarize the most prominent concepts related to the effectiveness of wastewater treatment plant (WWTP) units in removing antibiotic-resistant microorganisms (ARMs). It highlights the most relevant and recent findings. The concise format of a mini review, compared to a full review, facilitates easier understanding of the literature and identifies areas for future research development (Collins, ND; Elfar, 2014). Importantly, as noted by Booth, Papaioannou, & Sutton (2012), the goal of this approach is to produce a reliable synthesis of research that can provide credible answers to the objectives of this study, while also identifying gaps in current knowledge that require further investigation.

RESULTS AND DISCUSSION

Results

Bacteria can become resistant to antibiotics through two main mechanisms: intrinsic resistance and acquired resistance. Bacteria may develop intrinsic resistance to certain antibiotics due to their inherent structural and/or functional characteristics that prevent the antibiotics from acting effectively (Jian et al., 2021). D’Costa et al. (2011) published an article titled “Antibiotic resistance is ancient”, revealing the presence of resistance traits in bacteria extracted from 30,000-year-old permafrost sediments. Furthermore, Bhullar et al. (2012) discovered bacteria resistant to 14 commercially available antibiotics, isolated from a cave that had remained geologically isolated for over 4 million years. These findings provide compelling evidence that resistance is a natural and ancient bacterial trait.

Intrinsic resistance encompasses several mechanisms: the active efflux of certain antibiotics after entering the bacterial cell via porins, and the inability of some antibiotics to penetrate the outer membrane, thus preventing them from reaching their target site (Jian et al., 2021). In addition to these functional traits, intrinsic resistance can involve other strategies. First, bacteria may reduce intracellular antibiotic concentrations by limiting antibiotic uptake (poor osmosis) or actively pumping them out. Second, bacteria can alter antibiotic targets through genetic mutations or posttranslational modifications of target proteins. Third, bacteria may inactivate antibiotics by degrading them (via hydrolysis) or chemically modifying their structure to render them ineffective (Jian et al., 2021).

Beyond intrinsic mechanisms, bacteria can also acquire resistance. Bacteria that already carry antibiotic resistance genes (ARGs) can transfer these genes to other bacteria that initially lack them. Pathogenic bacteria can acquire ARGs through plasmid exchange at the genetic level, leading to robust resistance. Plasmids carrying ARGs, integrons (In), and transposons (Tn) can be horizontally transferred among strains of the same or different species (Jian et al., 2021; G. Liu, Thomsen, & Olsen, 2022). Horizontal gene transfer (HGT) refers to the movement of genetic material between bacteria through three main processes: transformation (uptake of free DNA from the environment), conjugation (direct cell-to-cell transfer), and transduction (transfer via bacteriophages or bacterial viruses) (Burmeister, 2015). While many resistance genes evolved naturally in the environment long before human influence (Bhullar et al., 2012; D'Costa et al., 2011), they now spread rapidly among human pathogens (Burmeister, 2015). Even after resistant bacterial strains die, ARGs remain in the environment for extended periods, protected by DNA-associated enzymes such as deoxynucleotidases (Jian et al., 2021).

The presence of HGT mechanisms facilitates the spread of ARGs in microbe-rich environments, such as the human gut or wastewater treatment plants (WWTPs). WWTPs are known to be ARG reservoirs and are considered hotspots for HGT among bacterial communities (Cai, Sun, Li, & An, 2021; Che et al., 2019; Gao et al., 2024; Uluseker et al., 2021; Yin et al., 2019). A study by Yin et al. (2019) even demonstrated a positive correlation between mean cell residence time (MCRT) in activated sludge units and the abundance of ARGs. Activated sludge systems are commonly used in WWTPs to treat organic waste from both domestic and industrial sources. Consequently, if ARGs are not effectively removed in activated sludge units of WWTPs, they may persist in the environment through the discharge of treated effluent.

The presence of ARB and ARGs have been identified in both the influent and effluent of wastewater treatment plants (WWTPs) globally. The efficiency of ARG removal varies across different stages of treatment – primary, secondary, and tertiary – and also depends on whether the ARGs are present in intracellular or extracellular forms (Drane, Sheehan, Whelan, Ariel, & Kinobe, 2024). ARB and ARGs in WWTP can also present at the same time with antibiotics (Mutuku, Gazdag, & Melegh, 2022; Wang, Chu, Wojnárovits, & Takács, 2020). Therefore, both antibiotics, ARB and ARG exist equally in WWTP. The results of research conducted by Wang et al. (2020) showed the presence of antibiotics and ARB and ARG in WWTP. The study reviewed and assessed the occurrence of antibiotics in wastewater treatment plants (WWTPs) across different periods (1999–2009 and 2010–2019) and regions (Europe, America, Asia, and Africa). Macrolides (clarithromycin, erythromycin, azithromycin, roxithromycin), sulfonamides (sulfamethoxazole), trimethoprim, quinolones (ofloxacin, ciprofloxacin, norfloxacin), and tetracyclines (tetracycline) were the most frequently detected antibiotics, while common ARGs included bla (blaCTXM, blaTEM), sul (sul1, sul2), tet (tetO, tetQ, tetW), and ermB genes. A positive correlation between antibiotic concentrations and ARGs abundance was observed, except for β-lactam antibiotics and bla genes, where bla genes persisted despite the hydrolysis of β-lactam antibiotics. Overall, antibiotic levels were lower in Asian countries during 2010–2019 compared to higher levels in North America and Europe during 1999–2009. In secondary treatment effluent, trimethoprim showed the highest median concentration (138 ng/L), while other antibiotics were typically below 80 ng/L, and ARG abundances ranged from 2.9 to 4.6 logs.

Further, the review shows a strong link between certain antibiotics and their corresponding ARGs in WWTPs, especially for quinolones, sulfonamides, macrolides, and tetracyclines. While β-lactam antibiotics are often removed due to hydrolysis, bla genes remain detectable. Higher antibiotic consumption in some European countries is associated with greater ARG abundance in WWTPs. Although WWTPs can remove a large portion of organic pollutants, antibiotic removal is less effective, similar to total nitrogen removal rates. Biological treatment does not significantly increase ARGs or ARB, but measurable levels of antibiotics, ARGs, and ARB still exist in treated wastewater (Wang et al., 2020).

Wastewater contains various types of human pathogens associated with waterborne diseases. Disinfection is a primary mechanism used to inactivate and destroy pathogenic organisms in wastewater and is one of the essential steps in wastewater treatment and reuse. Disinfection methods are broadly categorized into three main types: (1) chemical, (2) physical, and (3) radiation-based techniques (Qasim & Zhu, 2018). While chemical and physical processes have been successfully used to disinfect liquid waste, disinfection using gamma radiation has been studied for a long time but remains impractical for wastewater applications. According to Davis (2019), commonly used disinfectants include chlorine (free, combined, and chlorine dioxide), ozone, and ultraviolet irradiation. Studies by Han et al. (2016) and Kalli et al. (2023) show that chlorination is a widely used disinfection technique in wastewater treatment plants (WWTPs) to inactivate or kill pathogens. However, standard disinfection methods such as chlorination and UV irradiation have shown limited effectiveness in removing antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs), with ARGs being more resistant to treatment than ARB. In some cases, disinfection may even promote resistance (Wang et al., 2020). As a result, effluent discharge remains a concern due to the continued release of antibiotics and ARGs into the environment.

A study conducted in China investigated the behavior of nine antibiotic-resistant bacteria and two types of ARGs in wastewater treated with varying doses of chlorine (Yuan, Guo, & Yang, 2015). Water samples were collected from the effluent of a biological aerated filter (BAF) in a WWTP in Shanghai. The WWTP employed a treatment train consisting of a primary sedimentation tank (PST), followed by an anaerobic-anoxic-oxic (A2/O) process, a secondary sedimentation tank (SST), BAF, and finally, a disinfection unit. The hydraulic retention time (HRT) of the A2/O process was 7.5 hours, and the BAF operated at a loading rate of 0.35 kg NH_3-N/(m^3·day) with a 1-hour HRT. Chlorine concentrations applied to the BAF effluent were 0, 15, 30, 60, 150, and 300 mg Cl_2·min/L. The study found that chlorination effectively inactivated most ARB, with complete inactivation achieved at the lowest dose (15 mg Cl_2·min/L) in many cases. However, bacteria resistant to sulfadiazine and erythromycin exhibited tolerance even at 60 mg Cl_2·min/L. Quantitative real-time PCR analysis revealed that chlorination only slightly reduced the levels of erythromycin and tetracycline resistance genes, with overall removal efficiencies of 0.42 ± 0.12 log and 0.10 ± 0.02 log, respectively. Moreover, approximately 40% of erythromycin resistance genes and 80% of tetracycline resistance genes were unaffected by chlorination. The study concluded that bacterial tolerance to chlorine and the specific characteristics of resistance genes based on antibiotic type are key factors influencing the effectiveness of ARG elimination through chlorination.

Another study showed the effects of three disinfection methods—ultraviolet (UV), chlorination, and ozone—on ARG levels in secondary effluents. UV treatment showed an exponential decrease in ARGs abundance with higher doses (R^2 = 0.68–0.92), while chlorination (0–5 mg/L for 30 minutes) showed a linear reduction (R^2 = 0.77–0.99). Ozone at 2 mg/L achieved effective ARGs removal but further increases in concentration had little additional effect. DNase I experiments revealed that UV and ozone treatments caused bacterial apoptosis, releasing free ARGs into the water (Zheng et al., 2017). These findings improve understanding of ARG behavior during wastewater disinfection.

Liu (2024) studied further about ARGs by observed it over a year at a full-scale treatment and reclamation facility. Evidently, ARGs in wastewater existed both within cells (inARGs) and as free extracellular DNA (exARGs) in which exDNA is a major reservoir of ARGs fraction. The release of exARGs from cells can increase due to treatments like chlorination that damage bacterial cells. Free extracellular DNA or exARGs comprised of dissolved (Dis-exARGs) and particle-adsorbed forms (Ads-exARGs). Ads-exARGs made up as much as 30% of total ARGs in raw sewage. Chlorination, both at low and high doses, increased Dis-exARGs and Ads-exARGs. Differences in ARGs behavior reflected varying bacterial resistance to chlorine, and some opportunistic pathogens co-occurred with ARGs. The findings suggest that higher chlorine doses are needed for effective inARGs and exARGs removal. Chlorination, whether at low or high doses, raised the proportion of exARGs, although their removal varied depending on the ARGs type and bacterial host. Laboratory tests indicated that exARGs degrade faster at low chlorine exposure (CT), while inARGs are removed more efficiently at higher CT levels. Both full-scale and lab-scale results emphasized that CT values above 43 mg Cl_2·min/L are needed to achieve over 2-log reductions of ARGs. Optimizing chlorination conditions is therefore essential to effectively eliminate inARGs and exARGs, helping to reduce the risk of ARGs spread in the environment.

Discussion

Wastewater treatment plants receive wastewater containing a wide array of pollutants, including antibiotics and chemicals from various sources. These facilities harbor large and diverse microbial communities and offer a conducive environment for the proliferation and spread of AR (Uluseker et al., 2021). The presence of ARB and ARGs have been identified in both the influent and effluent of WWTPs globally (Drane et al., 2024). Furthermore, ARB and ARGs often coexist with antibiotics in these environments (Mutuku et al., 2022; Wang et al., 2020).

Although WWTPs are intended to remove water quality parameters that pose risks to the environment, rendering treated wastewater safe for discharge, numerous studies have shown that these facilities also act as reservoirs of ARB and hotspots for horizontal gene transfer (HGT) among bacterial communities (Cai et al., 2021; Che et al., 2019; Gao et al., 2024; Uluseker et al., 2021; Yin et al., 2019). In fact, ARB populations tend to increase in WWTPs compared to raw water sources. A study by Yin et al. (2019) demonstrated that the mean cell residence time (MCRT) in activated sludge units positively correlates with ARG abundance—longer MCRT leads to higher ARG concentrations

ARGs in wastewater can exist both intracellularly (inARGs) and as free extracellular DNA (exARGs), with the latter further divided into dissolved (Dis-exARGs) and particle-adsorbed forms (Ads-exARGs). Extracellular DNA constitutes a significant portion of the ARG pool. Treatments such as chlorination can damage bacterial cells, leading to increased release of exARGs into the environment (M. Liu & Kasuga, 2024). This release can result in a higher overall abundance of ARGs within WWTPs. The efficiency of ARG removal differs across treatment stages – primary, secondary, and tertiary – and depends on whether the ARGs are intracellular or extracellular (Drane et al., 2024).

While WWTPs are effective at removing a significant portion of organic pollutants, they are less efficient at removing antibiotics, and measurable levels of antibiotics, ARGs, and ARB persist in treated effluent (Wang et al., 2020). The inactivation of ARB and ARGs is influenced by treatment type and operating parameters, with ARGs proving more resistant to treatment and posing risks of environmental dissemination (Kalli et al., 2023; M. Liu & Kasuga, 2024).

Bacterial tolerance to chlorine and the characteristics of resistance genes based on antibiotic type are two key factors that influence the effectiveness of the chlorination process (Yuan et al., 2015). Based on chlorine dose, in general – the higher the chlorine dose, the greater its effectiveness in inactivating resistant bacteria. However, this effectiveness is not always linear, as some bacteria exhibit tolerance to certain chlorine concentrations. For instance, most antibiotic-resistant bacteria were eliminated at a dose of 15 mg Cl_2 min/L, but bacteria resistant to sulfadiazine and erythromycin remained viable up to 60 mg Cl_2 min/L, indicating varying bacterial tolerance to chlorine Based on antibiotic type, the type of antibiotic to which resistance is developed also affects elimination efficiency. Bacteria resistant to erythromycin and sulfadiazine demonstrated higher tolerance to chlorination compared to those resistant to other antibiotics. Furthermore, resistance genes for erythromycin and tetracycline were only slightly reduced by chlorination, suggesting that the targeted antibiotic type also plays a role in determining the success of resistance gene removal. As WWTPs are not designed to remove these antibiotic resistance determinants from wastewater, and as a result, they are present in treated effluent, leading to environmental and public health concerns regarding wastewater disposal and reuse (Kalli et al., 2023), Liu (2024) proposed higher doses of chlorination as a prerequisite for the effective removal of both within cells and free extracellular ARGs.

These findings underscore that conventional disinfection methods such as chlorination are insufficient to control ARB and ARGs. The implications of their presence in the environment still require further investigation, and control technologies need continued development. In the Indonesian context, where domestic wastewater is often poorly treated in both quality and coverage, the presence of ARB represents a more severe challenge. Although Indonesia has regulations mandating the treatment of domestic wastewater and has established effluent quality standards, implementation remains inadequate. Untreated or partially treated domestic wastewater (i.e., not meeting standards) continues to be discharged into the environment. Greater attention is urgently needed to improve Indonesia’s sanitation governance.

CONCLUSION

Findings from various studies indicate that chlorination, the most commonly used disinfection method in WWTPs, is insufficient for controlling ARB. Greater attention is required to address the risks posed by ARGs present in post-chlorinated effluent. Moreover, the absence of a standardized regulatory framework governing acceptable antibiotic concentrations hampers the ability to monitor environmental water quality. The current practice of relying solely on E. coli or total coliform counts as water quality indicators is inadequate. Consequently, the indiscriminate discharge of antimicrobials – often at biologically active concentrations – into urban wastewater treatment systems remains widespread. These antimicrobials exert selective pressure on bacterial populations, fostering the development of resistance with significant implications for public health.

From a technological standpoint, there is still a considerable gap in treatment approaches that needs further investigation. It is essential to integrate innovative technologies into routine operations to ensure both sustainability and effectiveness. Future research should prioritize the development of advanced removal technologies, particularly those targeting frequently detected antibiotics and associated ARGs. Advanced treatment processes, such as ozonation, activated carbon adsorption, and nanofiltration, offer improved removal performance, although their efficiency is influenced by the characteristics of the wastewater matrix. Since complete elimination of antibiotics and ARGs using current methods remains unfeasible, reducing antibiotic use and implementing routine WWTP monitoring are crucial steps in managing environmental risks.

In Indonesia, where WWTPs are still rarely employed to treat domestic wastewater, sanitation remains a critical public health challenge. A significant portion of the population still lacks access to safe and adequate sanitation services. While many households have access to basic sanitation, only a small fraction is categorized as safely managed – meaning human waste is safely treated and disposed of. As a result, a considerable number of households continue to rely on sanitation practices that pollute the environment and pose serious health risks. This lack of access contributes to persistent open defecation, environmental contamination, and elevated disease risk, especially among children. The presence of ARB further exacerbates sanitation-related challenges.

Improving Indonesia's sanitation infrastructure has thus become an urgent necessity. Such improvement requires a comprehensive approach encompassing: (1) adequate regulation and enforcement; (2) infrastructure development, including public latrines, wastewater treatment systems, and improved waste management; (3) behavior change, through public awareness campaigns emphasizing hygiene and sanitation practices; (4) community involvement in the planning and implementation of sanitation programs; and (5) partnerships among government agencies, the private sector, donor institutions, and international organizations. Addressing these issues is essential to improving the country's sanitation conditions and curbing the spread of ARB.

REFERENCES

Bhullar, K., Waglechner, N., Pawlowski, A., Koteva, K., Banks, E. D., Johnston, M. D., . . . Wright, G. D. (2012). Antibiotic resistance is prevalent in an isolated cave microbiome. *PLOS ONE, 7*(4), e34953. doi:10.1371/journal.pone.0034953

Booth, A., Papaioannou, D., & Sutton, A. (2012). *Systematic Approaches to a Successful Literature Review*: SAGE Publications.

Brinkac, L., Voorhies, A., Gomez, A., & Nelson, K. E. (2017). The Threat of Antimicrobial Resistance on the Human Microbiome. *Microb Ecol, 74*(4), 1001-1008. doi:10.1007/s00248-017-0985-z

Burmeister, A. R. (2015). Horizontal Gene Transfer. *Evolution, Medicine, and Public Health, 2015*(1), 193-194. doi:10.1093/emph/eov018 %J Evolution, Medicine, and Public Health

Burton, F. L., Tchobanoglous, G., Tsuchihashi, R., Stensel, H. D., Metcalf, & Eddy, I. (2013). *Wastewater Engineering: Treatment and Resource Recovery*: McGraw-Hill Education.

Cai, Y., Sun, T., Li, G., & An, T. (2021). Traditional and Emerging Water Disinfection Technologies Challenging the Control of Antibiotic-Resistant Bacteria and Antibiotic Resistance Genes. *ACS ES&T Engineering, 1*(7), 1046-1064. doi:10.1021/acsestengg.1c00110

Che, Y., Xia, Y., Liu, L., Li, A.-D., Yang, Y., & Zhang, T. (2019). Mobile antibiotic resistome in wastewater treatment plants revealed by Nanopore metagenomic sequencing. *Microbiome, 7*(1), 44. doi:10.1186/s40168-019-0663-0

Collins, L. (ND). Mini Literature Review: A new type of literature review article. Retrieved from https://www.emeraldgrouppublishing.com/archived/products/journals/call_for_papers.htm%3Fid%3D5730

D'Costa, V. M., King, C. E., Kalan, L., Morar, M., Sung, W. W. L., Schwarz, C., . . . Wright, G. D. (2011). Antibiotic resistance is ancient. *Nature, 477*(7365), 457-461. doi:10.1038/nature10388

Davis, M. L. (2019). *Water and Wastewater Engineering: Design Principles and Practice, Second Edition*: McGraw Hill LLC.

Drane, K., Sheehan, M., Whelan, A., Ariel, E., & Kinobe, R. (2024). The Role of Wastewater Treatment Plants in Dissemination of Antibiotic Resistance: Source, Measurement, Removal and Risk Assessment. *13*(7), 668.

Elfar, J. C. (2014). Introduction to mini-review. *Geriatr Orthop Surg Rehabil, 5*(2), 36. doi:10.1177/2151458514536969

Gao, X., Xu, L., Zhong, T., Song, X., Zhang, H., Liu, X., & Jiang, Y. (2024). The proliferation of antibiotic resistance genes (ARGs) and microbial communities in industrial wastewater treatment plant treating N,N-dimethylformamide (DMF) by AAO process. *PLOS ONE, 19*(4), e0299740. doi:10.1371/journal.pone.0299740

Gough, D., Oliver, S., & Thomas, J. (2012). *An Introduction to Systematic Reviews*: SAGE Publications.

Han, C., Lalley, J., Namboodiri, D., Cromer, K., & Nadagouda, M. N. (2016). Titanium dioxide-based antibacterial surfaces for water treatment. *Current Opinion in Chemical Engineering, 11*, 46-51. doi:https://doi.org/10.1016/j.coche.2015.11.007

Hutchings, M. I., Truman, A. W., & Wilkinson, B. (2019). Antibiotics: past, present and future. *Curr Opin Microbiol, 51*, 72-80. doi:10.1016/j.mib.2019.10.008

Jian, Z., Zeng, L., Xu, T., Sun, S., Yan, S., Yang, L., . . . Dou, T. (2021). Antibiotic resistance genes in bacteria: Occurrence, spread, and control. *61*(12), 1049-1070. doi:https://doi.org/10.1002/jobm.202100201

Kalli, M., Noutsopoulos, C., & Mamais, D. (2023). The Fate and Occurrence of Antibiotic-Resistant Bacteria and Antibiotic Resistance Genes during Advanced Wastewater Treatment and Disinfection: A Review. *15*(11), 2084.

Karkman, A., Pärnänen, K., & Larsson, D. G. J. (2019). Fecal pollution can explain antibiotic resistance gene abundances in anthropogenically impacted environments. *Nature Communications, 10*(1), 80. doi:10.1038/s41467-018-07992-3

Levy, S. B., Marshall, B., Schluederberg, S., Rowse, D., & Davis, J. (1988). High frequency of antimicrobial resistance in human fecal flora. *Antimicrob Agents Chemother, 32*(12), 1801-1806. doi:10.1128/aac.32.12.1801

Liu, G., Thomsen, L. E., & Olsen, J. E. (2022). Antimicrobial-induced horizontal transfer of antimicrobial resistance genes in bacteria: a mini-review. *J Antimicrob Chemother, 77*(3), 556-567. doi:10.1093/jac/dkab450

Liu, M., & Kasuga, I. (2024). Impact of chlorine disinfection on intracellular and extracellular antimicrobial resistance genes in wastewater treatment and water reclamation. *Science of The Total Environment, 949*, 175046. doi:https://doi.org/10.1016/j.scitotenv.2024.175046

Murray, C. J. L., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., . . . Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet, 399*(10325), 629-655. doi:10.1016/S0140-6736(21)02724-0

Mutuku, C., Gazdag, Z., & Melegh, S. (2022). Occurrence of antibiotics and bacterial resistance genes in wastewater: resistance mechanisms and antimicrobial resistance control approaches. *World Journal of Microbiology and Biotechnology, 38*(9), 152. doi:10.1007/s11274-022-03334-0

Onwuegbuzie, A. J., & Frels, R. (2016). *Seven Steps to a Comprehensive Literature Review: A Multimodal and Cultural Approach*: SAGE Publications.

Penders, J., Stobberingh, E. E., Savelkoul, P. H., & Wolffs, P. (2013). The human microbiome as a reservoir of antimicrobial resistance. *4*. doi:10.3389/fmicb.2013.00087

Pepper, I. L., Gerba, C. P., & Gentry, T. J. (2014). *Environmental Microbiology*: Academic Press.

Qasim, S. R., & Zhu, G. (2018). *Wastewater Treatment and Reuse: Theory and Design Examples*: Taylor & Francis, CRC Press.

Quirós, P., Colomer-Lluch, M., Martínez-Castillo, A., Miró, E., Argente, M., Jofre, J., . . . Muniesa, M. (2014). Antibiotic Resistance Genes in the Bacteriophage DNA Fraction of Human Fecal Samples. *Antimicrobial Agents and Chemotherapy, 58*(1), 606-609. doi:10.1128/aac.01684-13

Snyder, H. (2019). Literature review as a research methodology: An overview and guidelines. *Journal of Business Research, 104*, 333-339. doi:https://doi.org/10.1016/j.jbusres.2019.07.039

The World Bank. (2017). *Drug-Resistant Infections: A Threat to Our Economic Future - Executive Summary*. Washington, USA: World Bank Group.

Uluseker, C., Kaster, K. M., Thorsen, K., Basiry, D., Shobana, S., Jain, M., . . . Pala-Ozkok, I. (2021). A Review on Occurrence and Spread of Antibiotic Resistance in Wastewaters and in Wastewater Treatment Plants: Mechanisms and Perspectives. *12*. doi:10.3389/fmicb.2021.717809

Wang, J., Chu, L., Wojnárovits, L., & Takács, E. (2020). Occurrence and fate of antibiotics, antibiotic resistant genes (ARGs) and antibiotic resistant bacteria (ARB) in municipal wastewater treatment plant: An overview. *Science of The Total Environment, 744*, 140997. doi:https://doi.org/10.1016/j.scitotenv.2020.140997

WHO. (2023). Antimicrobial resistance. Retrieved from https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

WHO. (2024). Antimicrobial resistance (AMR) is invisible. I am not. Retrieved from https://www.who.int/campaigns/world-amr-awareness-week/2024/amr-is-invisible-i-am-not

Wibowo, A. T. (2024, Juli 18, 2024). Bahaya Resistensi Antibiotik Pada Saluran Pencernaan Manusia Indonesia. Retrieved from https://unair.ac.id/bahaya-resistensi-antibiotik-pada-saluran-pencernaan-manusia-indonesia/

Yin, X., Deng, Y., Ma, L., Wang, Y., Chan, L. Y. L., & Zhang, T. (2019). Exploration of the antibiotic resistome in a wastewater treatment plant by a nine-year longitudinal metagenomic study. *Environment International, 133*, 105270. doi:https://doi.org/10.1016/j.envint.2019.105270

Yuan, Q.-B., Guo, M.-T., & Yang, J. (2015). Fate of Antibiotic Resistant Bacteria and Genes during Wastewater Chlorination: Implication for Antibiotic Resistance Control. *PLOS ONE, 10*(3), e0119403. doi:10.1371/journal.pone.0119403

Zheng, J., Su, C., Zhou, J., Xu, L., Qian, Y., & Chen, H. (2017). Effects and mechanisms of ultraviolet, chlorination, and ozone disinfection on antibiotic resistance genes in secondary effluents of municipal wastewater treatment plants. *Chemical Engineering Journal*, *317*, 309-316. doi:https://doi.org/10.1016/j.cej.2017.02.076

Zhu, T.-t., Su, Z.-x., Lai, W.-x., Zhang, Y.-b., & Liu, Y.-w. (2021). Insights into the fate and removal of antibiotics and antibiotic resistance genes using biological wastewater treatment technology. *Science of The Total Environment*, *776*, 145906. doi:https://doi.org/10.1016/j.scitotenv.2021.145906