Review

Emergence Of Antibiotic Residues And Antibiotic-resistant Bacteria In Hospital Wastewater: A Potential Dissemination Pathway Into The Environment: A Review

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Sylvain GODREUIL

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Review

Emergence of Antibiotic Residues and Antibiotic-Resistant Bacteria in Hospital Wastewater: A Potential Dissemination Pathway into the Environment: A Review

Wilfried Blandin Evoung Chandja [1,*], Richard Onanga [1], Pierre Philippe Mbehang Nguema [2], Romeo Wenceslas Lendamba [3], Yann Mouanga-Ndzime [1], Jacques François Mavoungou [2] and Sylvain Godreuil [4]

[1] Laboratory of Bacteriology, Interdisciplinary Medical Research Centre of Franceville (CIRMF), Franceville, P.O. Box 769, Gabon
[2] Microbiology Laboratory, Research Institute of Tropical Ecology (IRET), Libreville P.O. Box 13354, Gabon
[3] Clinical Operations Department, Medical Research Centre of Lambaréné (CERMEL), P.O. Box. 242, Lambaréné, Gabon
[4] Laboratory of Bacteriology, Montpellier University Hospital Centre, UMR MIVEGEC (IRD, CNRS, University of Montpellier), 34295 Montpellier, France
* Correspondence: evoungblandin@gmail.com

Abstract Medicinal activities carried out within hospitals lead to a high consumption of antibiotics and subsequently result in a high excretion rate of antibiotic residues. These antibiotics consumed in human medicine are not fully absorbed by the body and are often discharged into the environment as biological waste from infected human patients. The significant water consumption in hospitals and the pharmaceutical impact on wastewater from healthcare facilities facilitate the emergence and spread of antibiotic-resistant bacteria and antibiotic-resistant genes in the environment. Hospital effluents could be doubly involved in the dissemination of antibiotic molecules and multidrug-resistant bacteria in various ecosystems. The objective of this study is to characterize hospital effluents by assessing antibiotic concentrations and the diversity of antibiotic-resistant bacteria in these hospital wastewaters and within the environment (aquatic environments; rivers), as well as to inventory the bacteria present and those carrying antibiotic resistance in both hospital wastewater and the environment

Keywords: hospital effluents; antibiotic resistance; bacteria; environment

Introduction

The effluents generated by hospital activities can pose a potential danger both to humans and the environment due to the nature and quantity of specific substances and microorganisms they carry (pharmaceutical residues, chemicals, and multidrug-resistant pathogenic bacteria). These effluents are discharged into the municipal sewer system without prior treatment, similar to conventional urban wastewater [1].

On average, in healthcare facilities, the antibiotic consumption of a hospitalized patient is about ten times higher than the average consumption per capita in households [2]. Furthermore, the significant use of antibiotics in hospitals exerts selective pressure that promotes the emergence of multidrug-resistant bacteria, including extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-EB) [3]. These multidrug-resistant bacteria are then eliminated in wastewater as antibiotic-resistant fecal bacteria (ARFB) and liquid waste [2,4,5]. In developing countries, wastewater treatment before discharge into the environment presents a major challenge due to a lack of resources, unplanned urbanization, and limited industrialization [6].

It is in this context that communal and hospital wastewater plays a key role in the dissemination of antibiotic-resistant bacteria (ARB), such as ESBL-EB [3–7]. Hospital effluents contribute to the

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contamination of various ecosystems, affecting the habitats of certain animals (small rodents, aquatic animals, etc.) [8]. Multidrug-resistant microorganisms carried in these contaminated waters can induce the transfer and dissemination of antibiotic resistance genes (ARGs) to other bacteria, especially pathogenic bacteria, posing a significant health risk to surrounding populations [9,10]. This is a global public health problem, highlighting the importance of a literature review on antibiotic-resistant bacteria (ARB) isolated from hospital wastewater. This literature review will consist of drawing up a list of antibiotic residues and bacteria carrying antibiotic resistance, present both in hospital wastewater and in the environment.

Materials and Methods

Relevant articles on the subject were searched in Google Scholar, PubMed, and CrossRef databases. Articles or other scientific publications primarily addressing the following keywords were considered: "antibiotic residues in hospital sewage ", "bacterial resistance to antibiotics in hospital wastewater", "hospital wastewater risks for human health", "hospital wastewater risks for the environment", and "ESBL in hospital effluents" (Figure 1). The documents included in this study were published between 2002 and 2022. To obtain articles more easily for this study, each keyword was directly associated with the name of a country. The objective was to identify recent trends in the microbiology (bacteriology) of hospital wastewater, and its risks to human health, and aquatic ecosystems.

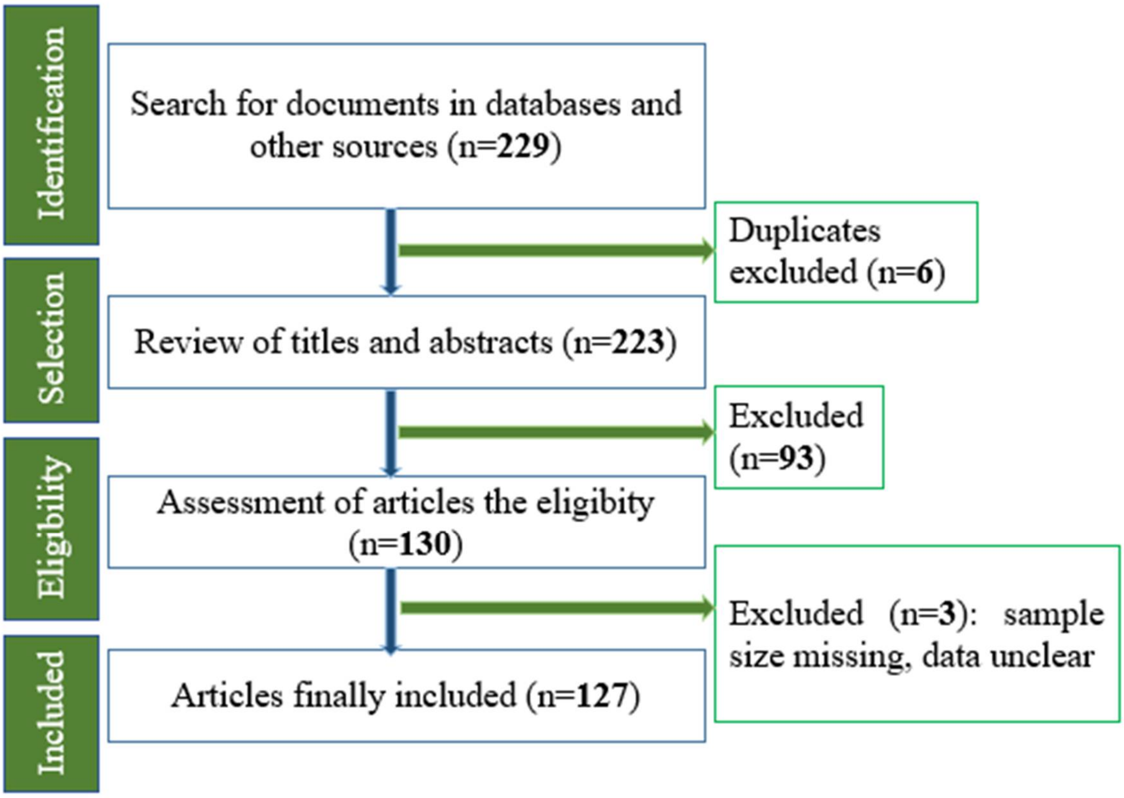

Figure 1. Flowchart of the process for selecting included studies.

Hospital Waste Disposal

Hospitals are significant consumers of water. While the per capita daily water consumption in domestic settings ranges from 150 to 200 litres, the average water consumption in hospitals has increased from 400 to 1200 litres per day, and the production of liquid waste is estimated at 1 cubic meter per day per active bed [27–29]. Additionally, special waters used by the hospital, such as distilled water for irrigation, wound cleaning, tissue rinsing, or surgical equipment humidification, add to this water consumption [30]. The quantity of wastewater discharged by hospitals is estimated at 1000 litres per day in America [27,31,32].

In Africa, the situation regarding the disposal and treatment of liquid waste is dire [18]. Liquid waste generated by hospitals is continuously discharged into natural water reservoirs without any prior treatment, leading to the vulnerability of local flora and fauna in these natural environments [33,34].

Antibiotics and Antibiotic-Resistant Bacteria in Hospital Wastewater

Origins of Antibiotics Found in Wastewater

Medical activities carried out within hospitals generally lead to high antibiotic consumption and a high excretion rate of antibiotic residues [10,11,76]. This consumption is believed to be the main source of antibiotic resistance in some patients and the environment, but it is difficult to assess [12,13]. Indeed, after ingestion, antibiotics undergo chemical modifications, and the resulting metabolites can be more or less toxic and may also have different, even antagonistic properties compared to the initial medication [14]. Most of these antibiotics consumed in human and veterinary medicine are not fully absorbed by the body and are often released into the environment as biological waste (blood, urine, pus, etc.) from infected human and animal patients [15–18].

Furthermore, the portion of unused medications eliminated through wastewater discharge points can constitute a potential source of ecosystem pollution [19,20].

Additionally, healthcare facilities' discharges present a unique situation due to the number of patients treated, and the quantity and variety of drugs used, including anticancer drugs, anaesthetics, antibiotics, diagnostic products, contrast agents, or radioactive materials [21,22]. In the external environment of hospitals, the quantitative and qualitative evolution of antibiotic and microorganism contamination occurs according to the gradient of anthropogenic activities [23–25] (Figures 2 and 3).

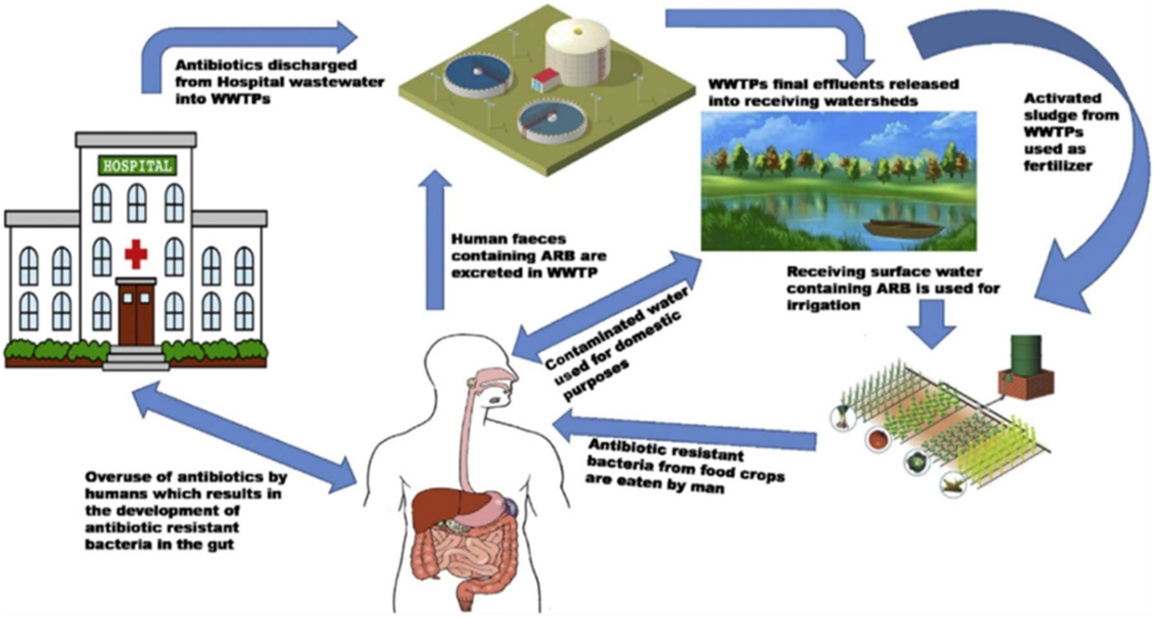

Figure 2. Schematic diagram illustrating the process of spread of antibiotic-resistant bacteria. [26].

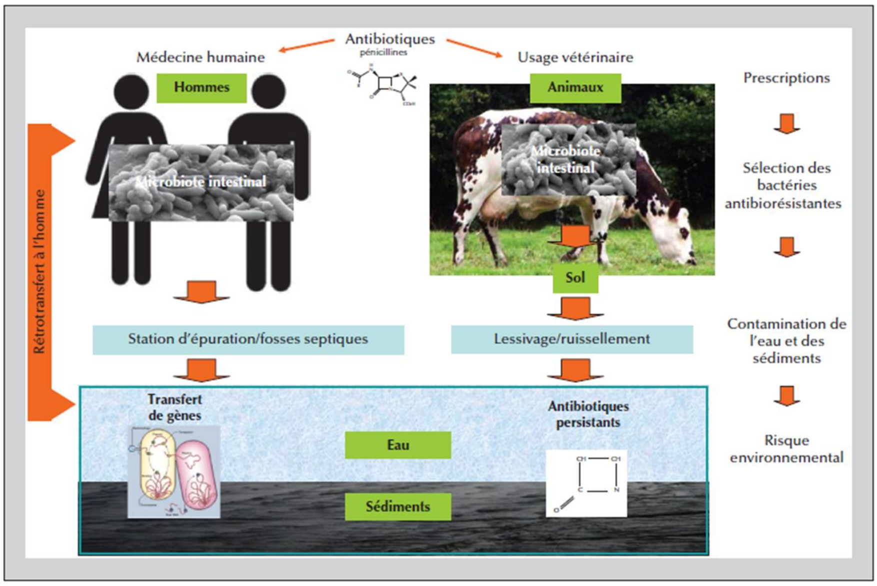

Figure 3. Circulation of antibiotic-resistant microorganisms and antibiotics within the four major ecosystems: humans and animals undergoing antibiotic treatment, soil, and water [57].

Antibiotics in Hospital Wastewater and Their Dissemination in the Environment

Antibiotics are essential drugs used to combat bacterial infections in both human and veterinary medicine [113]. The intensive use of antibiotics in both of these medical fields has two serious consequences for environmental impact: the presence of residues of active molecules and the increase in the selection of resistant bacteria. The most commonly used antibiotic families in hospitals are beta-lactams (penicillin and cephalosporins), sulfonamides, tetracyclines (doxycycline, oxytetracycline), quinolones/fluoroquinolones (nalidixic acid, ciprofloxacin, ofloxacin, etc.) [71,72]. Antibiotics prescribed in human and veterinary medicine, along with antimicrobial resistance bacteria (AMRB), are released into the environment through urine and faeces [25]. Four antibiotics have been detected and quantified, with three of them regularly found in hospital effluents. These include amoxicillin (0.066 ± 0.08 µg/l), erythromycin (0.04 ± 0.0 µg/l), sulfamethoxazole + trimethoprim (0.06 ± 0.21 / 0.08 ± 0.006 µg/l), and metronidazole (0.02 ± 0.0 µg/l). Amoxicillin and sulfamethoxazole were detected and quantified at both points, while erythromycin and metronidazole were only found at the "G" Point of Bamako Teaching Hospital [73]. Treated effluents from wastewater treatment plants (WWTPs) and soil runoff or leaching are the main sources of water and sediment contamination [114].

Table 1. Average concentrations measured in urban effluents (UWw) and hospital effluents (HWw) for commonly found pharmaceutical compounds [74].

Antibiotics	Concentration in HWw (µg L^{-1})	Concentration in UWw (µg L^{-1})
Ciprofloxacin	0,03-125	0,01-5,88
Clarithromycin	0,2-3	0,1-4,8
Coprofloxacin	0,85-2	
Doxycycline	0,1-6,7	
Erythromycin	27-83	0,04-2,7
Lincomycin	0,3-2	
Metronidazole	0,1-90	
Norfloxacin	0,029-44	0,01-0,96
Ofloxacin	0,353-35,5	0,01-31,70
Oxytetracycline	0,01-3,75	
Penicillin G	0,85-5,2	0,03
Sulfamethoxazole	0,04-83	0,01-6,0
Tetracycline	0,01-4,2	0,01-1,30
Trimethoprim	0,01-15	0,02-7,90

Quantification of Antibiotic Residues Encountered in Samples from Certain Rivers Worldwide

In the study conducted by Dong Li et al. in China, the resistance rate to doxycycline (DOX) has consistently been the lowest (1.5% to 83.1%) among tetracyclines (1.5% to 95.2%) in the three water samples from the Xiao River. The resistance prevalence rate was lower for cefotaxime (CTX) (1.5% to 71.2%) than for ampicillin (AMP) (24.6% to 93.1%), both of which are beta-lactams [56].

According to a study conducted on irrigation water samples in Burkina Faso, the antibiogram showed that non-typhoid Salmonella was resistant to tetracycline (66.67%, 38/57), followed by ampicillin (66.67%, 38/57), amoxicillin + clavulanic acid, and amoxicillin (30%, 17/57) [75]. A Gabones study highlighted among the 35 coliforms found in 27 samples of river and stream waters, resistance to antibiotics for ampicillin (91%, 32/35), cefotaxime (3%, 1/35), and cotrimoxazole (9%, 3/35). No resistance was detected against ciprofloxacin, imipenem, meropenem, and ertapenem in these waters [64].

The concentrations of antibiotic residues found in wastewater range from nanograms per litre to micrograms per litre [77]. In rivers, the range of antibiotic concentrations varies from a few nanograms to a few tens of nanograms per litre [78]. Among the main sources of surface water contamination, domestic effluents are primarily mentioned, as well as hospital effluents, and pharmaceutical manufacturing and packaging facilities [79].

Table 2. Minimum Inhibitory Concentration (MIC) of 12 antibiotics on bacterial isolates isolated from WW, WTP, and RW [37].

Activity against the Isolates				
Antibiotics	**Resistance Prevalence (%)**	**MIC (mg L^{-1})**		
		Rank	50%	90%
Ampicillin (AMP)	100	64 to ≥ 1024	1024	1024
Amoxicillin (AMO)	100	1 to ≥ 1024	1024	1024
Streptomycin Sulfate (STR)	92.3	1 to ≥ 1024	128	52
Trimethoprim (TRI)	98	8 to ≥ 1024	1024	1024
Chloramphenicol (CHL)	100	256 to ≥ 1024	1024	1024
Sulfonamide (SUL)	100	512 ≥ 1024	1024	1024
Tetracycline (OXY)	90.6	2 to ≥ 512	128	256
Oxytetracycline (OXY)	90.6	1 to ≥ 1024	256	512
Nalidixic Acid (NAL)	73.6	1 to ≥ 1024	512	1024
Erythromycin (ERY)	92.5	4 to ≥ 1024	128	512
Spiramycin (SPIRA)	90.6	2 to ≥ 1024	512	1024
Kanamycin (KAN)	54.7	1 to ≥ 1024	128	1024

WW, wastewater effluent; WTP, wastewater treatment plant; RW, river water; 50%, MIC50; 90%, MIC90. MICs for each antibiotic for all isolates tested in WW, WTP, and RW, representing the MICs required for the inhibition of 50% and 90% of bacterial strains, respectively.

Bacteria Found in Hospital Wastewater

Wastewater typically contains 10^7 to 10^8 bacterial organisms per litre, with a concentration of pathogenic bacteria on the order of 10^4 organisms per litre [35]. The most common bacteria found in hospital wastewater can be those originating from biological waste (faeces, urine, surgical instruments, etc.) of hospitalized patients (*Acinetobacter* spp., *Klebsiella pneumoniae, Proteus mirabilis, Enterobacter* spp., *Bacillus* spp., *Salmonella* spp., *Shigella* spp., and *Staphylococcus aureus*, among others), or bacteria responsible for nosocomial infections (*Escherichia coli, Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas* spp., etc.). Pathogenic bacteria such as *Salmonella*, especially *Salmonella typhi* and *paratyphi* species, are generally more prevalent in hospital-origin urban wastewater and can be harmful to human health while potentially harbouring antibiotic resistance genes (ARGs) [36,37]. The concentrations of identified bacteria are 10 times higher in hospital effluents than in community wastewater [16,37,38].

Table 3. Main bacteria found in bathing waters ([39,40]).

Pathogenic species	**Load of bacteria detected in 100 ml water effluent**	**Estimated minimal infecting Dosis**
Campylobacter spp.	10^4-10^5	1.10^3
Clostridium perfringens	6.10^4-8.10^4	10^3-10^5 spores

Escherichia coli	10^4-10^7	10^6-10^7 ; 10-10^2
Entérocoques intestinaux	$4.7.10^3$-10^8	60-10^2
Salmonella spp.	0.2-8.10^3	10^4-1010
Vibrio spp.	ND	1.10^6
Shigella spp.	0.1-10^3	10-10^4

Haut du formulaire ; NA = not applicable.

Bacteria Isolated in Community Wastewater and Rivers

In developing countries, poverty and a lack of awareness about health risks lead populations to use wastewater as their primary choice for irrigating vegetable gardens [58]. These practices expose vegetable growers to health risks and also lead to the introduction of various contaminants from these waters into the food chain [59]. In most African countries, there are numerous issues related to the quantity and quality of hospital wastewater. In Burkina Faso, Somda et al. reported that hospital wastewater was responsible for the contamination of certain lettuces and other garden products, as they were contaminated with certain antibiotics and bacteria (Salmonella paratyphi B and Salmonella spp.) generated by hospital activities, and these various impacts were identified in the surrounding water bodies [60]. Furthermore, it has been reported in some countries like Benin, Morocco, and Kenya, that hospital wastewater is discharged into community septic tanks due to inappropriate drainage systems [61–63].

In Gabon, studies conducted by Jonas Ehrhardt et al. [64] and Yala et al. [65] have shown a high population of enterobacteria in the rivers bordering certain provinces of Gabon. In the first study, they were able to isolate *Citrobacter freundii* (25.9%, 7/27), *Enterobacter* spp (25.9%, 7/27), Escherichia coli (3.7%, 1/27), *Klebsiella pneumoniae* (22.2%, 6/27), *Kluyvera ascorbata* (3.7%, 1/27), *Leclercia adecarboxylata* (3.7%, 1/27), *Pantoea dispersa* (3.7%, 1/27), *Serratia marcescens* (37%, 10/27), and *Yokenella regensburgei* (3.7%, 1/27). This corresponds to an overall contamination rate of 13.5% by coliforms. Additionally, a strain of *Klebsiella pneumoniae* producing extended-spectrum beta-lactamase (ESBL) was found in one of the collected samples [64] (Table 3). In the second study, the authors were able to isolate the following enterobacteria*:* *Enterobacter sakazakii* (9.67%, 3/31), Escherichia coli (6.45%, 2/31), *Enterobacter cloacae* (3.2%, 1/31), *Klebsiella ozaenae* (3.2%, 1/31), and *Klebsiella pneumoniae* (3.2%, 1/31) [65].

Table 4. Transmission of pathogenic bacteria between household effluents and environmental effluents.

country	Source	Host (s)	Reference
Benin	Urban wastewater	*Eschérichia coli,*	[66]
RC	Household Wastewater	*Escherichia coli, Salmonella* spp., *Shigella* spp., *Klebsiella* spp., *Enterobacter aerogenes, Enterobacter cloacae , Arizona* spp., *Proteus* spp.	[67]
Gabon	River	*Citrobacter freundii, Enterobacter* sp, *Escherichia coli, Klebsiella pneumoniae, Kluyvera ascorbata, Leclercia adecarboxylata, Pantoea dispersa; Serratia marcescens; and Yokenella regensburgei, Salmonella enterica*	[64]
Tunisia	Urban wastewater	*Escherichia coli, Salmonella* spp.	[68]
Ethiopia	Hospital sewage	*Klebsiella* spp., *P. aeruginosa*	[69]
DRC	River	*Escherichia coli*	[70]

RC: Republic of Congo, DRC: Democratic Republic of Congo.

In estuarine environments or rivers, antibiotic-resistant bacteria and the most stable drug molecules settle in the mudflats [23]. The sediments then become an environment in which subinhibitory concentrations of antibiotic molecules (or their metabolites) can be reached. Potential transfer of resistance genes to native species, followed by retrotransfer to pathogenic strains for humans, is possible, although the probability is low [25].

The Bacteria Isolated from Both Hospital Effluents and Rivers

The number of microorganisms can multiply by a thousand in river waters after urban waste discharge and stagnant waters provide a favourable environment for the development of bacterial biofilms conducive to the contamination of numerous ecosystems [41–43]. However, antibiotic-resistant bacteria naturally exist in many water sources, even in geographical areas without significant antibiotic selection pressure [44].

Table 5. List of Bacteria found in hospital wastewater and some rivers in Africa.

Species	Country	Water source	Reference
Pseudomonas aeruginosa, salmonella spp.	Ivory Coast	Hospital sewage	[38]
Escherichia coli	DRC	Hospital sewage, river	[45]
Klebsiella spp.	South Africa	Hospital sewage	[46]
Salmonella spp., *Pseudomonas* spp, and *Escherichia coli*	Burkina Faso	Hospital sewage	[47]
Klebsiella pneumoniae, Aeromonas spp. and *Escherichia coli*	Benin	Hospital sewage	[48]
Escherichia coli, Enterococcus faecium, Enterobacter cloacae and *Pseudomonas aeruginosa, Acinetobacter townrii*	Benin & Burkina Faso	Hospital sewage	[49]
E. coli, Klebsiella spp., *Salmonella* spp, *Shigella* spp., *Citrobacter* spp.; *Bacillus* spp., *Proteus* spp.	Ethiopia	Hospital sewage	[50]
Klebsiella spp., *Pseudomonas* spp., *E. coli, Citrobacter* spp.,	Ethiopia	Hospital sewage	[51]

DRC: Democratic Republic of Congo.

Antibiotic-Resistant Bacteria Found in Rivers Surrounding Hospitals

Microbial pollutants can also serve as indicators of water quality [52]. Untreated effluents generated by hospital activities can significantly contribute to the spread of microbial pollutants in the environment, particularly multidrug-resistant bacteria (MDR) originating from patient pathological products [53,54]. MDR from effluents primarily stem from either colonized patient biological fluids [15,16] or horizontal transfer of resistance genes between multidrug-resistant infectious strains and environmental strains [55].

In China, a study by Zhang L et al. (2020) demonstrated that the most frequently identified bacteria in the river water receiving hospital effluents were *E. coli* (37.9%, 25/66), followed by *K. pneumoniae* (16.7%, 11/66) and *Acinetobacter* spp. (16.7%, 11/66), but the resistant strains identified in the effluent samples were dominated by *Pseudomonas* spp. (29.4%, 5/17), *Acinetobacter* spp. (29.4%, 5/17), and *E. coli* (23.5%, 4/17). In another study, researchers characterized bacterial populations in surface waters (Xiao River) receiving effluents from an oxytetracycline (OTC) production plant. In upstream river water, only *Stenotrophomonas maltophilia* isolates showed a significantly higher prevalence of resistance compared to *Pseudomonas fragi*, *Pseudomonas fluorescens*, *Bacillus cereus*, and *Pseudomonas putida* (paired Wilcoxon test, all 'p' values were < 0.009) [56].

In France, the multidisciplinary FLASH project (Fate of Antibiotics, Gene and Antibiotic-Resistant Bacteria Fluxes in Surface Hydrosystems) aimed to study the relationship between antibiotic prescription (both veterinary and human use), antibiotic resistance, and antibiotic molecules in water on the scale of a rural hydrological continuum and a hospital continuum discharging into a Seine tributary (the Risle). The study's results show the presence of antibiotic-resistant strains of *E. coli* and *Enterococcus* spp. circulating in these waters. This antibiotic resistance selection pressure results from both medical prescriptions in human clinics and veterinary clinics [23].

Antibiotic-Resistant Bacteria (Gram-Negative Bacilli) in Water

Compared with Enterobacterales, few published reports have documented the isolation of class A carbapenemase-producing glucose-non-fermenting Gram-negative bacteria (GNB) from aqueous ecosystems, KPC (*Klebsiella pneumoniae* carbapenemase), KPC-2-, GES variants (for Guiana extended spectrum). The GES-5 enzyme has been detected in *K. pneumoniae* isolated from stream water [60] , in *R. ornithinolytica* and *Citrobacter* sp. Recovered from river water [57,59], in *Enterobacter* spp. isolates obtained from seawater [25,48], in *Citrobacter* spp., *E. coli, K. pneumoniae, K. oxytoca* and *E. cloacae* obtained from hospital sewage [53,61,62], in *E. cloacae* complex, in *K. pneumoniae* and in *R. ornithinolytica* isolated from wastewater treatment plants (WWTPs) [53,57,63], and GES-16 producing *Acinetobacter* spp. and *Aeromonas* spp. isolates were recovered from WWTPs, hospital sewage, and river and seawater samples in the USA, Brazil and China [118–120,122,123,125]. In addition, the GES-31 carbapenemase was first described in an *Aeromonas punctata* isolate recovered from a Brazilian river [121] de Araujo et al. and Xu et al. have reported the isolation of KPC-2-producing *Aeromonas hydrophila* from rivers in Brazil and China, respectively [121,127]. Recently, KPC-2-producing *A. hydrophilia* and *Aeromonas caviae* were recovered from river water and WWTP effluents [124,126].

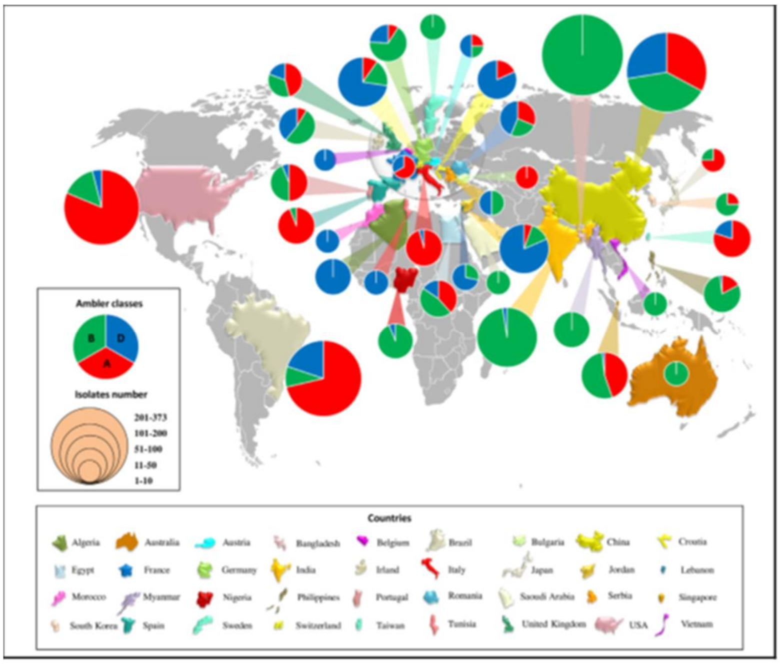

Figure 4. Worldwide distribution of carbapenemase-producing Gram-negative bacteria in aquatic environments [117].

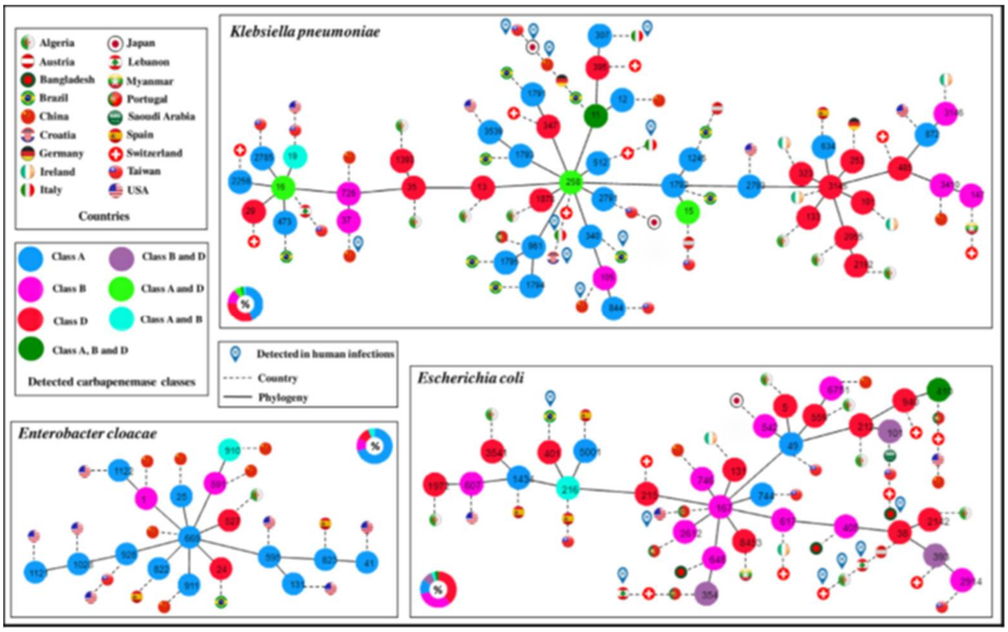

Figure 5. Multilocus sequence typing (MLST) data set generated using PHYLOViZ Online, indicating the sequence types (STs) of carbapenemase-producing *Klebsiella pneumoniae*, *Escherichia coli* and *Enterobacter cloacae* detected in aquatic environments with the respective carbapenemase class and geographical area [117].

Characterization of ESBLs in Wastewater

Numerous studies have found significant quantities of bacteria producing extended-spectrum beta-lactamases (ESBL-producing *E. coli*) in community and hospital effluents, as well as in bathing waters, with more ESBL-producing *E. coli* in hospital wastewater than in community wastewater [3]. This can be explained, in part, by a higher frequency and density of carriage among hospitalized patients compared to healthy community carriers [82]. On the other hand, the high consumption of antibiotics in hospitals leads to their elimination in the form of compounds that are still active in wastewater. These compounds exert a selection pressure that favours resistant bacteria, including extended spectrum β-lactamases (ESBLs) [93]. These enzymes that hydrolyze broad-spectrum penicillins and cephalosporins were initially derived from narrow-spectrum plasmidic penicillinases and were mainly found in hospital strains of *Klebsiella pneumoniae* [80,81] and *Klebsiella oxytoca* [37].

Table 6. Bacteria capable of producing ESBLs encountered in effluents (Hospitals and rivers).

Country	Source	Host	ESBLs	Reference
Ghana	River waters	*Escherichia coli*	P, *E. coli*	[83]
South Africa	Sewage	*Escherichia coli*	P, *E. coli*	[84]
Burkina Faso	Sewage	*Klebsiella oxytoca, Serratia* spp, *Citrobacter* spp,	P, *Klebsiella oxytoca*	[85]
Cameroun	Well water	*E. Coli, Salmonella* spp, *P. aeroginosa, Klebsiella pneumoniae et Bulkholderia cepaceae*	P, *E. coli*	[86]
Ivory Coast	Hospital sewage	*E. coli, K. pneumoniae, P. aeruginosa et Acinetobacter baumanii*	P, *Acinetobacter baumanii*	[115]
Nigeria	Hospital sewage	*E. coli, Klebsiella pneumoniae, E. coli, K. pneumoniae*	P, *E. coli & K. pneumoniae*	[87]
Ethiopia	Sewage	*E.coli, Salmonella, Klebsiella pneumonia, Enterobacter aerogenes, Citrobacter,*	P, *K. pneumonia & E. coli*	[88]

Klebsiella oxytoca and Enterobacter cloacae,

P: Positive at ESBL.

Characterization of Antibiotic Resistance Genes in Bacteria Isolated from Wastewater

In South Africa, for Fadare F. T et al., among the 31 bacterial species isolated in this study, genes encoding for beta-lactamases were detected in 20 species (64.5%, 20/31), while resistance genes to other antibiotic families were detected in 27 species (87.1%, 27/31). The most commonly detected beta-lactam resistance genes belonged to the *bla*CTX-M group (including groups 1, 2, and 3), which were detected in isolates at a rate of 51.6% (16/31) [18]. In China, on the other hand, other authors were able to determine (66.3%, 69/104) the *bla*CTX-M-type gene in water samples [7]. In the same study by Fadare F. T, they showed that the most frequently detected resistance genes to other antibiotic families were CatII (79.2%, 19/24) (acting against Phenicol), followed by the tetA gene (46.7%, 14/30) (against Tetracyclines). The frequencies of other non-beta-lactam genes include sulI and sulII (35.5%, 11/31) (against Sulfamides), tetB (23.3%, 7/30), aadA (12.9%, 4/31) (against Aminoglycosides), tetC (10%, 3/30), and tetD (3.3%, 1/30) [18].

The Fate of Hospital Antibiotics in Natural Environments

The danger of pharmaceutical substances in the environment lies in the fact that they can behave from a physico-chemical perspective like substances secreted by the host organism, thus retaining their effectiveness [89]. They can also substitute for molecules or bind to specific receptors within the recipient organism. Furthermore, these substances may follow the path of bioaccumulation of antibiotics in organisms and affect ecosystem functioning [90].

Also, the low concentrations of drugs and their metabolites, generally lower than those encountered in therapy, do not allow for an accurate estimation of the actual presence of these substances in the environment [116].

Fecal bacteria and chemical contaminants associated with suspended matter in the water column settle in the mudflats, and sediment accumulation zones [92]. In these sediments, it has been shown that antibiotics persist for more than 30 years, at concentrations reaching 32 mg/kg for quinolones, 15 mg/kg for sulfamides, and 20 mg/kg for nalidixic acid [92]. The risk associated with certain antibiotics such as doxycycline, oxytetracycline, and levofloxacin lies in their elimination by the organism in an active form (bioactive molecules), potentially dangerous for the environment [91-116.].

Risk of Contaminated Water in Aquatic Animals

Aquatic environments constitute important reservoirs of antibiotic-resistance genes. They also serve as a vehicle through which antibiotic-resistance genes (ARGs) or antibiotic-resistant bacteria (ARB) can be disseminated from one ecosystem to another [100]. The effects of these anthropogenic inputs on the bacterial flora of the aquatic environment are still poorly understood. However, the genomes of aquatic bacteria are particularly rich in mobile genetic elements involved in the selection and dissemination of resistance genes [101]. For example, qnrA and qnrS, plasmidic resistance genes to quinolones, have been mobilized from the genomes of *Shewanella algae* and *Vibrio splendidus* [102].

The bioaccumulation of antibiotics in wild fish species has been observed by Valdés et al. [103]. Erythromycin was the most commonly observed antibiotic in the crustacean *Fenneropenaeus penicillatus* at the adult stage, at concentrations ranging from 2,498 to 15,090 ng/g^{-1} [104]. When the aquatic environment receives inputs from animal or anthropogenic sources, the number and type of bacteria present can render the water unfit for human and animal use [105,106].

Consequences of Contamination Related to Hospital Wastewater

Most diseases resulting from contact with wastewater are caused by pathogenic germs such as bacteria. These pathogens can cause severe illnesses, especially in particularly vulnerable groups (children, the elderly, and individuals with weakened immune systems), and workers in contact with such waters, such as sewage workers and wastewater treatment plant employees [91].

Consuming Untreated Water Can Lead to Waterborne Illnesses

Therefore, water, vital for existence, can also be a source of water-related diseases [107]. According to the World Health Organization (WHO), 361,000 children under the age of 5 die each year from diarrheal diseases due to inadequate access to clean water and sanitation [108]. Human health is seriously affected by water-related diseases, as well as by pollution from chemical discharges into water from various human activities. According to UNICEF, 60% of child mortality worldwide is due to infectious or parasitic diseases, mostly related to water pollution [109–111]. Moreover, if measures are not taken to combat antibiotic resistance, it is estimated that by 2050, antibiotic-resistant bacteria could be responsible for the deaths of 10 million people annually worldwide, including 390,000 people in Europe. Global economic losses would amount to 100.000 billion euros [112].

Conclusions

This review has demonstrated the potential relationship between hospital effluents and environmental contamination by antibiotic-resistant bacteria. Therefore, it is essential to consider the entire chain of the issue to study prevention measures effectively. The genetic diversity of naturally occurring bacteria in the environment makes them a natural reservoir of resistance genes. The spread of antibiotic-resistant bacteria and their genes in hospital wastewater could, in turn, worsen their presence in the environment. Further studies are needed to assess the impact of antibiotic-resistant bacteria and their genes in watercourses. Ensuring the good quality of water before discharge helps maintain a minimally or non-polluted environment while ensuring the health of the population.

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