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REVIEW

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Global distribution of antimicrobial resistance genes in aquaculture

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Abstract

Aquaculture has rapidly developed into one of the most fast-expanding food industries, providing an essential source of protein for humanity worldwide. The rapid growth of the aquaculture industry is closely associated with the crucial role of antimicrobials in the prevention and treatment of animal diseases. Nevertheless, the irrational utilization of antimicrobials gives rise to the emergence of pathogen resistance, which poses a potential threat to human health and environmental sustainability. This issue has garnered considerable attention from international organizations and has escalated into a global public health crisis that requires urgent intervention. This paper undertakes a review of the sources of antimicrobial resistance in aquaculture, drawing on data from Microbial Browser for Identification of Genetic and Genomic Elements (MicroBIGG-E) and related literature. The characteristics and distribution patterns of drug resistance genes in pathogenic bacteria of diseased aquatic animals and food-borne bacteria of contaminated aquatic products were elaborated in detail. The emergence of resistant aquatic bacteria is not solely attributable to the utilization of antimicrobials in aquaculture, but rather is closely related to human social activities. Diverse antimicrobial resistance genes related to tetracyclines, aminoglycosides, β-lactams, quinolones, sulfonamides, and amphenicols that coexist in foodborne pathogens might contribute to multidrug resistance in aquaculture. This review also evaluates the potential risks of antimicrobial resistance in aquaculture with respect to human health, food safety, and ecological balance. Government entities, research institutions, and private companies are adopting proactive measures and initiating specific strategies to alleviate the dissemination of antimicrobial resistance, thereby enhancing human and animal health as well as ecological sustainability.

Keywords Aquaculture, Antimicrobials, Pathogen, Aquatic products, Resistance genes, Distribution

Introduction

Aquaculture represents one of the most promising sectors within global food production [1]. In 2022, global aquaculture production increased to 185 million tons [2]. However, the global aquaculture industry is encountering sustainability challenges, such as environmental impacts, disease control, market instability, and extreme weather events. The transition from semi-intensive to intensive farming practices, alongside the application of antimicrobial agents for disease management, are pivotal factors contributing to the increase in aquaculture yield. In aquaculture environments, antimicrobials are frequently present at concentrations lower than those for therapeutic purposes. This not only enhances the selection pressure

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for resistant bacteria in animals or the environment to screen out resistant bacteria, but might also facilitate the transfer of resistance genes among different species of bacteria within aquatic ecosystems. It is now well documented that antimicrobial resistance genes (ARGs) and antimicrobial-resistant bacteria (ARB) migrate from aquatic environments to terrestrial ecosystems, potentially posing risks to human and animal health [3].

Antimicrobial resistance (AMR) occurs as a result of natural selection; however, the heavy use of antimicrobials and other influencing factors of modern human life, accelerate the evolution of "silent" or "precursor" resistance genes within bacteria. In addition to a small number of bacteria with natural resistance to certain drugs, the majority of bacteria develop resistance mainly through changes in target sites, reduction of bacterial outer membrane permeability, acquisition of active efflux systems, and production of inactivated enzymes [4]. These resistance mechanisms do not exist independently; instead, the level of bacterial resistance is determined by their combined effects. Genes that confer resistance spread from environmental bacteria via mobile genetic elements and are subsequently transferred to humans and animals, leading to increased abundance, diversity, and mobility of resistant bacteria [5].

Recently, the matter of AMR has drawn the attention of international organizations to jointly tackle the global public health crisis. The United Nations Environment Programme (UNEP) lists ARGs as the first of six novel environmental pollutants. In 2022, to address a variety of health threats, the World Health Organization (WHO), World Organization for Animal Health (WOAH), Food and Agriculture Organization of the United Nations (FAO), and UNEP co-issued the "One Health" Joint Action Plan. It focuses on zoonotic epidemics, food safety risks, AMR, and the environment, with the aims of improving human, animal, plant, and environmental health while promoting sustainable development [6]. Within the framework of the "One Health" notion, the problem of AMR in aquaculture should also be considered of great importance. In this review, we aim to present the sources of AMR in aquaculture, detailing the characteristics and distribution patterns of ARGs in diseased aquatic animals and contaminated aquatic products, both domestically and internationally. We also describe some of the strategies that have been implemented, and offer additional recommendations to alleviate the emergence of AMR among aquatic bacterial populations.

Sources of AMR in aquaculture

Antimicrobials used in aquaculture

Since the sulfonamides were introduced for disease control in the 1940s, significant progress has been made in preventing and treating bacterial diseases in fish [7]. By the 1950s, other antimicrobial agents in addition to the sulfonamides, including tetracyclines, quinolones, and aminoglycosides had become widely utilized for treating infection and preventing diseases [8]. Despite the use of oral feeding and immersion as the most effective administration methods, the researchers estimated that about 70–80% of antimicrobials are not absorbed by fish and are eventually excreted into aquatic ecosystems via urine or feces [9–11]. The irrational utilization of antimicrobials will not only have an impact on the microorganisms within the animal body and the environment, but also exert huge antibiotic pressure on the microorganisms, leading to the rapid development and dissemination of AMR within the bacterial community [12]. Previous studies have also reported large-scale epidemic infections caused by pathogens resistant to different classes of antibiotics [13–15]. The issue of resistance in aquaculture has also drawn the attention of international organizations. In 2006, a joint meeting of WHO, FAO, and WOAH was held to evaluate the consequences related to utilitation of antimicrobials agents in aquaculture, highlighting the necessity of paying attention to the potential risk of ARGs spreading from aquatic animals to humans [16].

Wastewater from urban rivers

Traditional aquaculture ponds are open water bodies with nearby rivers as the primary source of water. Consequently, urban rivers are considered as important reservoirs for ARB and ARGs in aquaculture. With the acceleration of urbanization and industrialization, large quantities of wastewater from pharmaceutical factories, hospitals, and farms are discharged into urban rivers, which then become the main carrier for the spread of ARGs and ARB [12, 17–19]. Aiming to evaluate AMR in China's Pearl River, Gao et al. [18] utilized metagenomics to analyze global microbiome data, revealing that the types of ARGs and ARB in the water and sediment of the Pearl River were more diverse than those in other countries. Discharge of wastewater from sewage treatment plants and landfills drives the epidemic of riverine bacterial resistance, and the levels of resistance among bacterial groups are highly correlated with human and animal sources. Das Manas et al. [19] conducted a metagenomic analysis of the surface water and sediments of Indian rivers. Their results indicated that ARB in the environment mainly originated from *Enterobacteriaceae*, which showed multidrug resistance to fluoroquinolones, sulfonamides, β-lactams, tetracyclines, aminoglycosides, and other drugs. Using isolates from aquatic animals and aquacultural environments, several studies have also identified clinically significant genes that confer resistance to various drugs, including extended-spectrum β-lactamases (ESBLs) [20–22], carbapenem (bla_{NDM}) [23–25], colistin (*mcr*) [26, 27], tigecycline (*tet*[X]) [28, 29], vancomycin (*vanA*) [30, 31], and linezolid (*optrA*) [32, 33]. Although these types of resistance genes are frequently found in patient and hospital wastewater, there is concern about their potential spread through rivers to nearby ponds. The aquaculture environment may act as a reservoir and transmission vector for clinically significant resistant pathogens, thereby increasing the threat to public health.

Sewage from livestock and poultry farms

In addition to the direct administration of antimicrobials, integrated fish farming constitutes another critical source of AMR in aquaculture. From the 1990s to the beginning of this century, a farming model based on multi-utilization of livestock, poultry, and aquaculture resources was popular in South China, South and Southeast Asia, and Africa, with examples including integrated pig-fish and duck/goose-fish farms [34–37]. Farmers typically constructed pig houses or duck/goose sheds near ponds, utilizing the waste from the livestock and poultry as organic fertilizer for fish cultivation [37]. By saving breeding space and feed costs, this production mode increased the economic benefits of breeding and was among the most economically efficient aquaculture models in the era of low breeding density and limited antibiotic use [37]. However, the expansion of large-scale livestock and poultry farming has gradually exposed the shortcomings of this model. Livestock and poultry feces contain antibiotics excreted through metabolism, as well as ARB carrying various ARGs. Untreated fecal matter that is discharged directly into ponds may affect the microbial community of aquatic animals and aquaculture water bodies, potentially polluting the ecological environment [12]. In a previous study [38], we found that *Aeromonas* isolated from livestock/poultry-fish integrated farms were exhibited significantly higher resistance to 13 antibiotics than those isolated from non-integrated farms. Furthermore, we identified class I integrons carrying diverse gene cassettes in resistant *Aeromonas* isolates from livestock-fish integrated farms, implying that antibiotic usage in livestock farming contributes to the dissemination of multidrug resistance in aquaculture [34]. Since the enactment of China's most stringent environmental protection legislation in 2017 [39], small-scale pig farms in rural areas have been effectively prohibited, and integrated pig-fish farming has gradually decreased. However, integrated waterfowl-fish farming is still common in the Pearl River Delta region of Guangdong province. The potential influence of ARB and resistance gene pollution caused by this model requires more attention. The study revealed that total relative abundance of ARG subtypes in the samples of duck-fish integrated farms were significantly higher than those of freshwater single farms, where Enterobacteriaceae was the main host source of ARG [40–42].

Foodborne pathogen contamination of aquatic products

Foodborne pathogens can contaminate aquatic products during havesting, transportation, processing, storage, sales and other processes, thereby becoming the source of the dissemination of various bacterial diseases, and posing a potential threat to human health and safety [43]. Consuming undercooked aquatic products can readily lead to food-borne poisoning, resulting in diarrhea, vomiting and fever. Hence, aquatic foods are among the products that give rise to foodborne bacterial diseases worldwide [44]. Bacteria commonly present in aquatic food including fresh aquatic animals and processed products can be classified into three categories: bacteria that naturally coexist along with freshwater or marine aquatic animals (e.g., *Aeromonas* spp. and *Vibrio* spp.); environmental bacteria that exist with frozen foods (e.g., *Listeria monocytogenes*); and commensal or opportunistic pathogenic bacteria that naturally inhabit in intestines of humans or animals (e.g., *Escherichia coli, Salmonella enterica*, *Klebsiella pneumoniae, Campylobacter jejuni*, and *Staphylococcus aureus*) [44]. The occurrence of AMR foodborne pathogens in aquatic products has steadily increased worldwide in recent years [32, 43–45]. The growing prevalence of *S. enterica* and *E. coli* strains exhibiting resistance to "last-resort" antibiotics, such as imipenem, polymyxin B, and tigecycline, is of great concern [25, 26, 28, 44, 46].

Briefly, apart from the use of antimicrobial agents in aquaculture, AMR of aquatic bacteria is also closely related to human social activities involving families, hospitals, pharmaceutical factories, and the farming, processing, and transportation of livestock and poultry [12, 47]. Antimicrobial agents are extensively utilized in human and veterinary medicine, and then introduced into the environment via human and animal excretion or inadequately treated pharmaceutical waste [12]. The environment can facilitate the colonization and infection of hosts by ARB, contributing to the evolution and dissemination of both ARB and ARGs [47].

Distribution of ARB and ARGs in aquaculture

Current situation

The intricate origins of AMR in aquaculture highlight the diversity and complexity of ARGs. The majority of ARGs found in human clinical and terrestrial animal isolates can also be identified in aquatic animals and processed (frozen, dried, smoked, etc.) aquatic products [25, 32]. To achieve a comprehensive understanding of the genetic information of human clinical, animal, and foodborne pathogens worldwide, the National Center for Biotechnology Information (NCBI) has developed the Microbial Browser for Identification of Genetic and Genomic Elements (MicroBIGG-E) (https://www.ncbi.nlm.nih.gov/pathogens/microbigge/) [48]. Featuring all bacterial isolates and three categories of genes (AMR, stress response, and virulence), this tool has become essential for utilizing bacterial genomics to explore and compare the global distribution and origin information of various genes, and to comprehend the spread of AMR worldwide [49]. For this review, we used the following terms to search MicroBIGG-E for host sources of pathogenic bacteria: "fish," "shrimp/prawn," "crab," and "shellfish/clam" as keywords, and "AMR" as filter words. We found that, by 30th December 2024, 23,165 contigs related to drug resistance of aquatic animals and products from 75 countries and regions had been uploaded, of which 9689 contigs (1977 isolates) were from fish, 8923 contigs (1620 isolates) were from shrimp, 1925 contigs (263 isolates) were from crabs, and 2448 contigs (519 isolates) were from shellfish.

Distribution of ARB in aquaculture

To examine the different host bacteria carrying ARGs in various types of aquatic products, records were selected through keyword searches of MicroBIGG-E. The results showed that 4379 pathogenetic bacteria covering 58 bacterial taxa were identified in aquatic animals and products. The predominant bacterial genera carrying ARGs in different aquatic hosts are shown in Fig. 1. Overall, the records uploaded to MicroBIGG-E were mainly associated with *Vibrio* spp. (1896 isolates, 43.3%) and *Salmonella* spp. (1382 isolates, 31.6%). Resistant isolates of *Vibrio* spp. were mainly obtained from shellfish and shrimp, accounting for 409 isolates (78.8%) and 855 isolates (52.8%), respectively. The predominant resistant strains isolated from fish were *Salmonella* spp. and *Vibrio* spp., with 716 isolates (36.2%) and 574 isolates (29.0%), respectively, while those isolated from crab were *Salmonella* spp. and *Listeria* spp., with 71 isolates (27.0%) and 64 isolates (34.3%), respectively. The higher number of resistance records related to *Vibrio* spp. in the database is due to the natural coexistence of this species with aquatic animals in aquatic environments, especially sea and brackish water [50]. In contrast, *Salmonella* spp. do not naturally inhabit aquatic environments. The high detection rate of salmonella in aquatic products could potentially be ascribed to the contamination of offshore waters by human domestic sewage and poor sanitary conditions in the aquatic products market. [44].

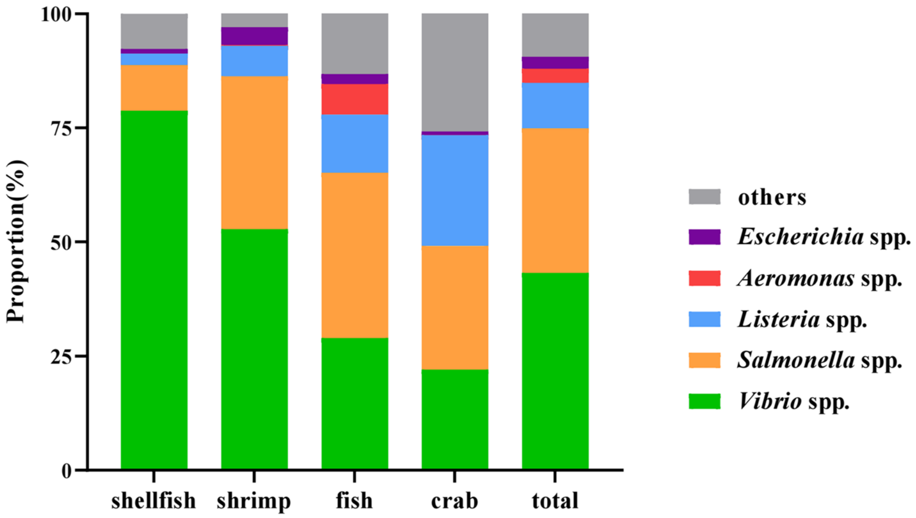

Fig. 1 Analysis of the primary hosts of antimicrobial resistance genes (ARGs) across various aquatic animals and products based on data from Microbial Browser for Identification of Genetic and Genomic Elements (MicroBIGG-E)

Occurrence of ARGs in pathogens from diseased aquatic animals

The growing prevalence of resistant bacterial pathogens constitutes a significant challenge for aquaculture, restricting the attempts to control diseases in aquatic animals [51]. To effectively manage quatic pathogens, it is vitally important that we understand the occurrence and distribution of their ARGs. The majority of bacterial infections affecting aquatic animals are attributed to *Vibrio* spp., *Aeromonas* spp., *Streptococcus* spp., *Edwardsiella piscicida*, *Photobacterium damselae*, and *Yersinia ruckeri* [52]. After filtering for "isolation source," we were able to analyze a total of 3699 isolates of the aforementioned fish and shrimp pathogens for genotypic resistance determinants. Although the genomic sequences from MicroBIGG-E were limited, we found that these pathogens had diverse types of ARGs, with the number varying from 1 to 13 types of ARGs in one strain. Table 1 presents examples of ARGs identified in typical aquatic pathogens from diseased animals. Comparing different pathogenic species, the majority of strains of *Aeromonas* spp., *Vibrio parahaemolyticus*, and *P. damselae* were found to carry more than three classes of ARGs, making them prone to contributing to multidrug resistance.

It is well documented that the genus *Aeromonas* demonstrates resistance to several antimicrobials, suggesting that certain drugs might be ineffective in controlling infections caused by some *Aeromonas* species [22, 34].

Table 1 Examples of antimicrobial resistance genes (ARGs) identified in typical aquatic pathogens from diseased animals

Host (species)	Pathogen	Genotype	Number of resistance genes carrying	Isolation source	Location	Collection year	Assembly No.
fish	*Aeromonas salmonicida*	*aadA7*, *ampC*, *aph(3")-Ib*, *aph(6)-Id*, $bla_{\text{CMY-2}}$, bla_{OXA}, *cphA*, *floR*, *mcr-3*, *sul1*, *sul2*, *tet(A)*, *vat*	13	sick fish	Canada: New Brunswick	2004	GCA_000786805.1
fish	*Aeromonas dhakensis*	ampC, bla_{OXA}, *cphA*, *floR3*, *mcr-3*, *qnrS2*, *sul1*, *sul2*, *dfrA1*, *tet(A)*, *vat*	11	kidney, liver	Vietnam	2018	GCA_031915045.1
fish	*Aeromonas veronii*	aadA1, bla_{OXA}, *catB3*, *cphA*, *dfrB4*, *sul1*, *tet(A)*, *vat*	8	kidney, liver	Vietnam	2019	GCA_031914865.1
Fish (*Cyprinus carpio*)	*Aeromonas hydrophila*	bla_{OXA}, *cepH*, *cphA1*, *mcr-3*, *mph(A)*, *tet*(E)	6	liver	USA: LA	2019	GCA_021356275.1
Fish (Tiger grouper)	*Vibrio vulnificus*	*varG*, *catB*, *tet*(35), *tet*(34)	4	diseased fish	Thailand: Songkhla	2012	GCA_039833915.1
Fish (*Epinephelus fuscoguttatus*)	*Vibrio alginolyticus*	bla_{CARB}, *catC*, *tet*(35), *tet*(34)	4	diseased fish	Thailand: Southern part, Karabi province	2013	GCA_026962575.1
freshwater fish	*Vibrio harveyi*	bla_{VHH}, *tet*(35), *tet*(34)	3	brain	USA: Florida	2019	GCA_028991555.1
Shrimp (*Penaeus vannamei*)	*Vibrio parahaemolyticus*	$bla_{\text{CARB-18}}$, $bla_{\text{CTX-M-14}}$, *catC*, *sul2*, *tet*(34), *tet*(35), *tet*(E)	7	hepatopancreas	China: Guangdong	2022	GCA_027277845.1
Shrimp (*P. vannamei*)	*V. harveyi*	bla_{VHH}, *tet*(35), *tet*(34)	3	diseased shrimp lesion	Mexico	2005	GCA_000259935.1
fish	*Photobacterium damselae*	*bla*, *catA2*, *qnrS*, *aar-3*, *aadA16*, *sul1*, *sul2*, *dfrA27*, *tet*(M), *tet*(B)	10	/	China: Qingdao, Shandong	2009	GCA_030169025.1
Fish (*Channa* spp.)	*Edwardsiella. piscicida*	*ampC*, *mph(A)*, *catA1*, *catA2*, *sul1*, *drfA12*, *tet*(D)	7	/	/	2019	GCA_030340645.1
Fish (*Salmo salar*)	*Yersinia ruckeri*	bla_{YRC}	1	/	Australia: Tasmania	2014	GCA_001883155.1
Fish (*Oreochromis* spp.)	*Streptococcus agalactiae*	*tet*(M)	1	fish organ	Malaysia: Kuala Lipis	2009	GCA_041728555.1

According to the MicroBIGG-E database, over 90% of *Aeromonas* isolates from diseased fishes, including *Aeromonas dhakensis*, *Aeromonas hydrophila*, *Aeromonas veronii,* and *Aeromonas salmonicida*, possess ARGs for aminoglycosides, β-lactams, tetracyclines, and trimethoprim. β-lactam resistance genes with diverse genotypes and subtypes are highly prevalent in *Aeromonas* strains, and include *oxa, cmy, aqu, mox, cphA*, and *ampC*; some of these are regarded as ESBL genes. The production of ESBLs by aquatic pathogens may represent failed actions of cephalosporins [53]. Interestingly, we also found that only *Aeromonas* strains carried *mcr-3*, which encodes a phosphoethanolamine transferase and contributes to colistin resistance. In a previous study, Guo et al. reported that the non-mobile colistin resistance (NMCR) determinants NMCR-3, NMCR-4, and NMCR-5 located on the chromosomes of *Aeromonas* are the progenitors of *mcr-3*, *mcr-5*, and *mcr-7* [54]. *Aeromonas* spp. are extensively distributed in freshwater environments and freshwater aquatic animals, indicating that aquaculture may facilitate the emergence and dissemination of novel colistin resistance mechanisms in aquatic and terrestrial animals, thereby posing a potential threat to public health and food safety [54, 55].

Another of the most common bacterial diseases that affect various marine fish, shrimps, and shellfish is vibriosis. Several species of the Vibrionaceae, including *V. parahaemolyticus*, *Vibrio harveyi*, *Vibrio vulnificus*, and *Vibrio alginolyticus*, cause this disease [56]. The frequent identification of resistant *Vibrio* strains has caused substantial economic losses to farmers around the world. Unexpectedly, apart from *V. parahaemolyticus*, other species of *Vibrio* were found to carry only a few genotypes of ARGs. Tetracycline resistance genes are the predominant class identified in *Vibrio* strains, among which *tet*(34) and *tet*(35) are the main genotypes. These genes may enhance the activity of efflux pumps, protect ribosomes and facilitate the inactivation of microbial enzymes in these microorganisms [57]. The *catC* gene, a member of the chloramphenicol acetyltransferase (CAT) family, is located on the *V. parahaemolyticus* chromosome, where it confers intrinsic resistance to chloramphenicol [58]. We found that over 90% of isolates of *V. alginolyticus* also harbored *catC*, which was absent in *V. harveyi* and *V. vulnificus*.

Occurrence of ARGs in foodborne pathogens in aquatic products

Aquatic products are irreplaceable components of the human diet. Given the aforementioned sources of AMR in aquatic products, resistant foodborne pathogens such as *E. coli*, *S. enterica*, *C. jejuni*, *S. aureus*, *L. monocytogenes*, and *Clostridum botulinum* pose an alarming global and widespread threat to public health [59]. Over the past decades, the incidence of resistant foodborne pathogens has been constantly increasing worldwide [43, 44, 59]. In addition, foodborne pathogens that are resistant to several clinically significant antimicrobials designated for the treatment of multiple drug resistance, such as extended-spectrum cephalosporins, fluoroquinolones, polymyxins B, tigecycline, vancomycin, and linezolid, have also been identified in aquatic products in several countries worldwide, which should draw more attention and concern. [28, 60–62]. Based on MicroBIGG-E data, the resistant foodborne pathogens from aquatic products possess diverse types of ARGs, with the number ranging from 1 to 26 types in a single strain. Table 2 details some of the most frequently detected ARGs alongside their respective antibiotic classes, including tetracyclines, aminoglycosides, β-lactams, quinolones, sulfonamides, and amphenicols. Strains of the Enterobacteriaceae, including *E. coli*, *S. enterica* and *K. pneumoniae*, carry more diverse genotypes compared with other species, suggesting that *Enterobacteriaceae* may constitute a major reservoir of ARGs.

To illustrate the occurrence and distribution of clinically significant ARGs in aquatic products, we utilized the MicroBIGG-E database and literature searches of Elsevier's ScienceDirect, PubMed, and Wiley Online Library. Table 3 outlines the main clinically significant ARGs that were identified in aquatic products. In 2009, Indian scientists first reported the identification of the NDM-1 gene from a patient. This gene encoded a carbapenem enzyme that hydrolyzed most β-lactam [63], and has since been reported worldwide, particularly in *Enterobacteriaceae* from various sources. While more than 60 subtypes of NDM enzymes have been documented, only NDM-1 and NDM-5 have been detected in aquatic products (Table 3). In addition to Enterobacteriaceae [21, 25, 64], NDM-1 has been reported in *Vibrio* spp. [65, 66] and *Aeromonas* spp. [22, 45], whereas NDM-5 is mainly identified in *E. coli* [20, 46] and *K. pneumoniae* [24, 67] (Table 3). Some reports of aquatic products identified as carrying *bla*$_{\text{NDM-1}}$ and sold in supermarkets in Australia [66], the USA [25], Canada [64], France [23], and Japan [62] were mainly found to originate from Southeast Asia, suggesting that this ARG has been widely spread through global trading.

In 2016, Chinese scientist Liu YY reported a new colistin resistance gene *mcr-1*, which was located on the plasmid in commensal *E. coli* from food animals [72]. Its transferability has made it difficult to treat clinical infections of colistin-resistant *E. coli.* In the MicroBIGG-E database and recent literature on colistin-resistant bacteria from aquatic products, *mcr-3* was mainly identified in *Aeromonas* spp., whereas *mcr-1* was mainly reported in

Table 2 Examples of ARGs identified in typical foodborne pathogens from aquatic products

Host	Foodborne-pathogen	Genotype	Number of resistance genes carrying	Isolation source	Location	Collection year	Assembly No.
fish	*Escherichia coli*	*aac(3)-IId*, *aadA1*, *aadA2*, *aadA5*, *bla*$_{\text{EC}}$, *blaTEM-1*, *cmlA1*, *sul3*, *drfA12*, *dfrA17*, *estT*, *floR*, *lun(F)*, *oqxA*, *oqxB*, *qnrS1*, *tet*(A), *tet*(X4)	18	/	China: Guangdong	2021	GCA_032285135.1
shrimp	*E. coli*	*aadA1*, *aadA2*, *aph(3’)-Ia*, *bla*$_{\text{EC}}$, *bla*$_{\text{SHV}}$, *bla*$_{\text{TEM-1}}$, *cmlA1*, *floR*, *dfrA12*, *dfrA17*, *estT*, *lnu(F)*, *qnrS1*, *sul3*, *tet*(A), *tet*(M), *tet*(X4)	17	/	China: Guangdong	2021	GCA_032286305.1
shellfish	*E. coli*	*aac(6’)-Ib4*, *aadA1*, *aph(3”)-Ib*, *aph(3’)-XV*, *aph(6)-Id*, *bla*$_{\text{ACC-1}}$, *bla*$_{\text{EC}}$, *bla*$_{\text{SHV-12}}$, *bla*$_{\text{VIM-1}}$, *catB2*, *dfrA14*, *sul1*, *sul2*, *mph(A)*, *qnrS1*	15	/	Italy	2016	GCA_002776495.1
crab	*E. coli*	*rmtB1*, *aadA1*, *aadA2*, *bla*$_{\text{CTX-M-55}}$, *bla*$_{\text{EC}}$, *bla*$_{\text{TEM-1}}$, *cmlA1*, *dfrA12*, *sul3*, *qnrB7*, *tet*(A)	11	/	India: Cochin	2017	GCA_017813585.1
fish	*Klebsiella pneumoniae*	*aac(3)-IId*, *aadA16*, *aph(3’)-Ia*, *aph(3’)-Ib*, *aph(6)-Ic*, *aph(6)-Id*, *arr-3*, *bla*$_{\text{CTX-M-3}}$, *bla*$_{\text{DHA-1}}$, *bla*$_{\text{SHV-1}}$, *bla*$_{\text{TEM-1}}$, *ble*, *dfrA27*, *sul1*, *sul2*, *floR*, *fosA*, *fosA3*, *mph(A)*, *oqxA*, *oqxB19*, *qnrB4*, *qnrB91*, *qnrS1*, *aac(6’)-Ib-cr5*, *tet*(A)	26	/	China: Shandong	2019	GCA_028863925.1
shrimp	*K. pneumoniae*	*aph(3’)-Ia*, *aph(3”)-Ib*, *aph(6)-Id*, *bla*$_{\text{LAP-2}}$, *bla*$_{\text{SHV-1}}$, *floR*, *fosA*, *oqxA*, *oqxB*, *qnrS1*, *sul2*, *tet*(A)	12	/	China: Shenzhen	2023	GCA_037198215.1
crab	*K. pneumoniae*	*aac(6’)-Ib3*, *aph(3’)-Ia*, *bla*$_{\text{CTX-M-2}}$, *bla*$_{\text{KPC-2}}$, *bla*$_{\text{OXA-2}}$, *bla*$_{\text{SHV-11}}$, *catA1*, *fosA*, *mph(A)*, *oqxA*, *oqxB*, *sul1*	12	/	Brazil: Sao Vicente	2017	GCA_013002785.1
shellfish	*K. pneumoniae*	*bla*$_{\text{SHV-60}}$, *fosA*, *oqxA10*, *oqxB19*	4	/	India: Cochin	2019	GCA_017814795.1
fish	*Salmonella enterica*	*aac(3)-IVa*, *aadA1*, *aadA2*, *aph(3’)-Ia*, *aph(4’)-Ia*, *arr-3*, *bla*$_{\text{OXA-1}}$, *ble*$_{\text{O,}}$ *catB3*, *cmlA1*, *dfrA12*, *sul1*, *sul2*, *sul3*, *floR*, *aac(6’)-Ib-cr*, *oqxA*, *oqxB*, *tet*(B)	19	frozen eel fish	USA	2015	GCA_005899085.1
shellfish	*S. enterica*	*aac(3)-IVa*, *aadA1*, *aadA2*, *aph(3’)-Ia*, *aph(4)-Ia*, *arr-3*, *bla*$_{\text{OXA-1}}$, *ble*$_{\text{O}}$, *catB3*, *cmlA1*, *floR*, *aac(6’)-Ib-cr5*, *oqxA*, *oqxB*, *sul1*, *sul2*, *sul3*, *tet*(B)	18	/	China: Shanghai	2012	GCA_044318665.1
shrimp	*S. enterica*	*aadA1*, *aadA2*, *aph(3’)-Ia*, *bla*$_{\text{TEM-1}}$, *dfrA12*, *sul2*, *sul3*, *cmlA1*, *floR*, *qnrB19*, *tet*(A), *tet*(M)	12	frozen shrimp	Ecuador	2022	GCA_024423175.1

Table 2 (continued)

Host	Foodborne-pathogen	Genotype	Number of resistance genes carrying	Isolation source	Location	Collection year	Assembly No.
crab	*S. enterica*	*aac(3)-IVa*, *aadA1*, *aph(3')-Ia*, *aph(4)-Ia*, *dfrA14*, *floR*, *sul1*, *tet*(A)	8	crab meat jumbo lump	USA	2018	GCA_004224865.1
fish	*V. parahaemolyticus*	*aph(3")-Ib*, *aph(6)-Id*, *blaCARB-18*, *catC*, *sul2*, *tet*(34), *tet*(35), *tet*(59)	8	freshwater food	China	2020	GCA_045007075.1
shrimp	*V. parahaemolyticus*	*ant(2")-Ia*, *aph(3')-Ia*, *aph(3")-Ib*, *aph(6)-Id*, *arr-2*, *bla*$_{\text{CARB-18}}$, *bla*$_{\text{VEB-1}}$, *catC*, *floR*, *dfrA31*, *ere(A)*, *qnrVC1*, *sul2*, *tet*(34), *tet*(35), *tet*(C)	16	/	Indonesia	2020	GCA_023313035.1
shellfish	*V. parahaemolyticus*	*aph(3")-Ib*, *aph(6)-Id*, *bla*$_{\text{CARB-18}}$, *bla*$_{\text{GMA-1}}$, *catC*, *dfrA46*, *sul2*, *floR*, *qnrVC6*, *tet*(34), *tet*(35), *tet*(B), *tet*(M)	13	/	China: Liaoning	2015	GCA_028472865.1
crab	*V. parahaemolyticus*	*aph(3")-Ib*, *aph(6)-Id*, *bla*$_{\text{CARB-18}}$, *bla*$_{\text{CTX-M-15}}$, *catC*, *dfrA23*, *dfrA46*, *sul2*, *qnrVC6*, *tet*(34), *tet*(35), *tet*(A)	12	/	Germany	2017	GCA_020741135.1
fish	*Vibrio vulnificus*	*catB, floR*, *sul2*, *tet*(34), *tet*(35), *tet*(59), *varG*	7	freshwater fish	China: Shanghai	2018	GCA_032050495.1
shrimp	*Staphylococcus aureus*	*aph(2")-Ia*, *ant(6)-Ia*, *aph(3')-IIIa*, *dfrG*, *fosB*, *mecA*, *mepA*, *mph(C)*, *msr(A), sat4, tet*(38)	11	/	India: Alappuzha, Kerala	2019	GCA_024668545.2
crab	*S. aureus*	*ant(6)-Ia*, *aph(3')-IIIa*, *fosB*, *mecA*, *mecR1*, *mepA*, *mph(C)*, *msr*, *sat4*, *tet*(38)	10	fresh crab meat	USA: MD	2024	GCA_044400285.1
fish	*S. aureus*	*ant(6)-Ia*, *aph(3')-IIIa*, *erm(C)*, *fexA*, *fosY*, *mepA*, *sat4*, *tet*(38), *tet*(K)	9	/	China	2024	GCA_041923585.1
fish	*Listeria monocytogenes*	*fosX*, *vga(G)*, *tet*(M)	3	smoked fish dip cajun style	USA: Florida	2005	GCA_004572115.1
shellfish	*L. monocytogenes*	*fosX, vga(G)*, *tet*(M)	3	/	USA: RI	2014	GCA_004445175.1
crab	*L. monocytogenes*	*fosX*, *vga(G)*, *tet*(M)	3	jonah crab meat	USA: RI	2014	PDT000034733.3
shrimp	*L. monocytogenes*	*fosX*, *vga(G)*	2	frozen raw shrimp	Indonesia	2020	GCA_016434905.1
shrimp	*Campylobacter jejuni*	*aph(3')-I*, *bla*$_{\text{CMY-65}}$, *bla*$_{\text{GIL}}$, *catA*	4	/	USA: MO	2019	GCA_022967615.1
shellfish	*C. jejuni*	*bla*$_{\text{OXA-184}}$, *tet*(O)	2	/	France	2017	GCA_032797205.1
fish	*Clostridum botulinum*	*bla, catA, cfr, cplR, fosX, lsa*	6	retail fish market	India: Kerala, Cochin	2004	GCA_003017225.1

E. coli [69, 73], and *mcr-9.1* [27] and *mcr-10* (GenBank Accession No. NZ_JADOZA010000047.1) were also found in enterobacteria (Table 3). Studies have revealed that diverse subtypes of the MCR family might originate from precursor genes on the chromosomes of bacteria, such as *Moraxella* spp. [68], *Aeromonas* spp. [74], and *Shewanella* spp. [75], implying that certain aquatic pathogens are intrinsically resistant to colistin and contribute to the dissemination of colistin resistance through the aquaculture sector [75, 76].

The emergence and widespread dissemination of Tet(X4)-degrading enzymes and a novel efflux pump have attracted much attention in recent years [28, 70]. The *tet*(X4) gene, which is located on a plasmid and confers high levels of tigecycline resistance, was first detected in animal samples in 2019 [77]. Since then,

Table 3 Occurrence and distribution of clinically significant ARGs in aquatic animals and products

Classes of ARGs	Genotypes	Resistant phenotype	Pathogen	Host	Isolation sources	Prevalence	Collection date	Location	GenBank No. /References
β-lactams	*bla*$_{NDM-1}$	All β-lactams with the exception of aztreonam and β-inhibitors	*E. coli*	*Mastacembelus*	intestines	/	2020.03	Vietnam: Hanoi	NZ_AP026939.1
			A. veronii	*Channa striata*	intestines	/	2020.03	Vietnam: Hanoi	NZ_AP027937.1
			V. fluvialis	*Solenidae*	/	/	2022.08	China: Shandong	NZ_CP126305.1
			V. parahaemolyticus	a shelled shrimp tail (imported from Vietnam to France)	/	/	2016.01	France	PETB00000000/ [23]
			V. cholerae	shrimps (supermarkets)	/	/	2023	China: Shenzhen	NZ_JBBFAW010000010.1
			V. alginolyticus	shrimps (supermarkets)	/	13/1363, 0.95%	2016.12	China: Shenzhen	GCA_020223695.1/ [65]
			V. alginolyticus	cooked prawns (imported from Thailand)	/	/	2021	Australia: Melbourne	GCF_026639325.1/ [24]
			Citrobacter braakii, Providencia rettgeri	frozen retail shrimp (imported from Vietnam purchased at a grocery store in USA)	whole shrimps	/	2022	USA: Ohio	CP114802, CP114797/ [25]
			K. pneumoniae	*Ruditapes decussatus* (markets)	/	2/18, 11.1% (selective media)	2016.03	Tunisia: Gabes	[21]
			A. sobria, Acinetobacter baumanii	frozen shrimps (imported from Asia sold in supermarkets in USA)	/	2/948, 0.2%	2019	USA: New York	[45]
			A. veronii, *A. hydrophila,* *Aeromonas enteropelogenes*	river fish (supermarkets)	intestines	7/83, 8.4% (selective media)	2020.03	Vietnam: Ho Chi Minh	[22]
			Escherichia cloacae	Bivalve mollusks (retail seafood products imported from Vietnam)	/	2/101, 2% (selective media)	2019–2014	Canada	[64]
			E. cloacae	*Penaeus monodon* (imported from Vietnam)	/	3/117, 2.6% (selective media)	2020	Japan	BPMY01000001.1/ [62]
	bla$_{NDM-5}$		*E. coli*	*Otolithes cuvieri* (retail markets)	/	1/19, 5.3%	2016	India: Mumbai	KJ576638/ [20]
			E. coli	fish	/	/	2021	Bangladesh: Dhaka	DAQNEZ010000074.1
			E. coli, C. freundii	*Ctenopharyngodon idella* (supermarkets)	intestines	7/196, 3.6% (selective media)	2019.01	China: Guangzhou	NZ_CP054192.1/ [46]
			E. coli	*Procambarus clarkii*	/	/	2020	China	NZ_CP084057.1
			K. pneumoniae	wild-caught fish (fishmarkets)	a fragment of liver, kidney and spleen	/	/	Djibouti	[24]
			K. pneumoniae	*Hypophthalmichthys molitrix* (farms), *Labeo rohita* (farms, markets)	Intestinal swabs	4/18, 22.2% (selective media)	2020–2021	India: Uttar Pradesh	[67]

Table 3 (continued)

Classes of ARGs	Genotypes	Resistant phenotype	Pathogen	Host	Isolation sources	Prevalence	Collection date	Location	GenBank No. /References
Colistin	*mcr-1*	Polycolistin B	*S. enterica serovar Rissen*	raw mussel (production area)	/	1/19, 5.3%	2012–2016	Spain: Galicia	[26]
			E. coli	*Oncorhynchus mykiss* (farms)	intestines	5/5, 100% (selective media)	2019	Lebanon: Bekaa	SAMN14127928/ [68]
			E. coli	fish (supermarkets)	flesh, gills and intestine	4/257, 1.6%	2012–2016	China: Guangzhou/ Hangzhou/Nanjing	[59]
			E. coli		intestines	58/63, 92.1% (selective media)	2019–2020	Vietnam: Ho Chi Minh/ Can Tho	[69]
	mcr-3		*E. coli*	*C. striata*, *C. fuscus* (markets)	intestines	5/63, 7.9% (selective media)	2019–2020	Vietnam: Ho Chi Minh/ Can Tho	[69]
	mcr-9.1		*Enterobacter ludwigii*	*Sparus aurata* (a land tank from a fish multi-trophic farming)	muscle	/	2018.03	Portugal	NZ_JABRPH010000155.1/ [27]
			S. enterica subsp. *enterica serovar Typhimurium*	frozen crawfish	whole shrimps	/	2011.07	China	AAEDLY010000064
	mcr-10		*Enterobacter hormaechei*	fish	/	/	2018	Germany	NZ_JADOZA010000047.1
Tetracyclines	*tet*(X4)	tigecycline	*E. coli*	shrimps (markets)	fecal swab	1/29, 3.4% (selective media)	2023	China: Shenzhen	NG_065852.1/ [29]
			E. coli, *C. freundii*	fish, shrimps, crabs, shellfish (markets)	/	9/73, 12.3% (selective media)	2021.07–2022.09	China: Guangzhou	SAMN36775957-SAMN36775966/ [28]
	tmexCD-toprJ		*A. veronii*, *A. hydrophila*	fish	intestines	7/80, 8.8%	2019.05–2021.04	China: Zhejiang	[70]
	tmexC2D2.2-toprJ2		*A. hydrophila*	fish (markets)	muscle	1/45, 2.2% (selective media)	2021.12	China: Guangzhou	[71]
	tmexCD2-toprJ1		*Pseudomonas putida*	shrimp	/	/	2023.10	China: Huzhou	NZ_JBFNXZ010000012
Glycopeptides	*vanA*	high level resistance to vancomycin and teicoplanin	*Enterococcus faecium*, *Enterococcus faecalis*, *Enterococcus durans*	*S. aurata* (natural marine ecosystem)	faeces	7/118, 5.9% (selective media)	2007	Portugal	[30]
			E. faecalis, *E. gallinarum*	tilapia, shrimps (supermarkets)	/	20/54, 37%	2023.06–2023.12	Egypt	[33]
	vanB		*E. faecalis*, *Enterococcus gallinarum*	tilapia, shrimps (supermarkets)	/	17/54, 31.5%	2023.06–2023.12	Egypt	[33]
Oxazolidinones	*optrA*	linezolid	*S. agalactiae*	tilapia (supermarkets)	sliced fish	/	2015	Singapore	DASIHH010000019.1
			E. faecalis	catfish	/	/	2020	USA: Los Angeles	AAXDOC010000037.1
			E. faecium, *E. faecalis*, *E. durans*	fish	/	/	2022	China	NZ_JARPTN010000027.1NZ_JARQEZ010000006.1
			S. aureus, *Staphylococcus lentus*, *Staphylococcus haemolyticus*	*Gadidae* (salted and seasoned seafoods)	fillets (muscle and skin tissues)	44/311, 14.1%	/	Italy	[32]

tet(X4) has been identified in food-borne *Enterobacteriaceae* from humans and terrestrial animals. Recently, it was reported in a strain of *E. coli* isolated from the intestines of commercial shrimp sold in a local seafood market in China [29], suggesting that aquatic products may be contaminated with tigecycline-resistant food-borne bacteria. In Gram-negative bacteria, resistance to tigecycline can also be caused by overexpression of efflux pump genes. In 2020, Chinese scientists first reported a novel plasmid-mediated efflux pump gene cluster, namely TMexCD1-TOprJ1, in *K. pneumoniae* of chicken-origin [78]. Subsequently, six variants of the cluster were detected in a variety of important pathogens of humans, terrestrial animals, food, and sewage [79]. However, the cluster was found to be less prevalent in aquatic animals than in, with current reports limited to *Aeromonas* isolated from fish [70, 71] and *Pseudomonas putida* isolated from shrimp (GenBank Accession No. NZ_JBFNXZ010000012) (Table 2).

Vancomycin and linezolid are typically employed in clinical settings to treat severe infections caused by multidrug-resistant Gram-positive bacteria. To date, nine genotypes of the vancomycin resistance gene (*van*) family have been identified in *Enterococcus* from different sources [80]. Among them, *vanA* and *vanB* are prevalent in *Enterococcus* isolated from the intestinal tract of aquatic animals [33] (Table 3).

Linezolid belongs to the oxazolidinone class, which was first introduced to China in 2007 and is regarded as the last resort for treating serious infections [81]. In 2015, Wang et al. [82] first reported the *optrA* gene in *Enterococcus* isolated from animals and humans in China. This gene belongs to the adenosine triphosphate-binding box transporter superfamily effector system and mediates multiple drug resistance. In our search of the MicroBIGG-E database, *optrA* was detected in 10 strains of *Streptococcus agalactiae* from tilapia fillets sold in Singapore supermarkets in 2015 (GenBank Accession No. DASIHH010000019.1). This gene has also been detected in *Enterococcus* and *Staphylococcus* isolated from aquatic products worldwide in recent years [32, 33].

With the extensive application of antibiotics, the aforementioned clinically significant ARGs are carried by pathogen-infected patients, but can also be detected in food animals and the natural environment, suggesting that these ARGs have been widely disseminated. Although the detection rate of these newly discovered ARGs remains low in food animals and the environment, most could be easily transferred to other microorganisms via plasmids, and possibly through the food chain, thereby increasing the threat to human health [53, 75, 83, 84]. Further research concerning the possible carriage of such ARGs by aquatic animals is necessary, and should emphasize the genomic relatedness of aquatic foodborne pathogens and the factors influencing bacterial contamination of aquatic environments and products.

Solutions and strategies to mitigate resistance in aquaculture

AMR poses a public health challenge for populations worldwide. Government entities, scientific research institutions, and private enterprises have started moving forward with plans to mitigate the risks of AMR to crucial aquaculture industries and to protect human and animal health. Below, we outline three main approaches that have been taken in China specifically.

1) In terms of government actions, legislative measures, such as the regulation of antibiotics and the development of guidelines for their rational use in aquaculture, have been initiated to strengthen the supervision of antibiotic management. National surveillance to monitor the prevalence of AMR of aquatic pathogens has been carried out since 2015, covering 16 provinces. Activities to enhance public awareness of AMR and promote the rational use of antimicrobials have also been undertaken through publicity and educational campaigns.
2) In scientific research institutes and universities, the prevalence, mechanisms, and transmission of AMR in aquaculture have been studied, aiming to comprehend the epidemiological characteristics and trends of AMR in different regions. Novel, rapid, and precise diagnostic technologies have been employed for the prevention and control of animal diseases. In addition, to reduce the usage of antibiotics, research is underway to develop multiple green and safe alternatives to antimicrobials, such as vaccines, Chinese herbal medicines, microecological preparations, bacteriophages, and enzyme preparations. Furthermore, it is crucial that we create effective technologies to alleviate the selective pressure on bacteria to develop antimicrobial resistance (including ARGs), within both living organisms and environmental cultures.
3) Regarding aquaculture enterprises, good aquaculture and biosecurity practices are needed for safe, high-quality aquatic products. Regular, strict hygienic practices are also indispensable for reducing contamination and transmission of pathogens. Furthermore, enhanced water quality health management is crucial for increasing aquaculture production and profitability.

Conclusions

This review focused on the sources of AMR and the occurrence and distribution of ARGs from diseased aquatic animals and contaminated aquatic products. Antimicrobial use and other human activities have contributed to the development and spread of ARB and ARGs. Following increased understanding and awareness of AMR in aquaculture, government entities, research institutions, private enterprises, farmers, and other stakeholders are taking action to mitigate the transmission of AMR, thereby enhancing human and animal health as well as ecological sustainability.

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Authors' contributions

Y.D. and A.T. contributed to the conception and design of the work. Y.D. drafted the manuscript. F.Z., F.W., H.G., Y.L., and Z.H. substantively revised the manuscript. All authors read and approved the final version of the manuscript.

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Data availability

All of the data supporting the conclusions of this article are included within the article.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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