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ORIGINAL ARTICLE

Use and impact of veterinary drugs, antimicrobials, and supplements in fish health management

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ABSTRACT

Objective: The study was carried out to investigate the use and impact of veterinary drugs, antimicrobials, and supplements in commercial aquaculture for fish health management measures in three selected areas of Mymensingh, Bangladesh.

Materials and Methods: Data collection was conducted through questionnaire interviews with owners of 50 fish farms and 25 drug shop owners from Trishal, Fulpur, Tarakanda, and Sadar Upazila of Mymensingh district.

Results: A total of 15 trade-named veterinary antibiotics and six categories of other compounds were identified in this study. Antibiotics were found as the most used veterinary drugs (80.85%), followed by disinfectants, nutritional supplements, saline, ammonia removal agents, probiotics, and pesticides. These veterinary compounds' performances for fish health management were found to vary (10%–60%) significantly.

Conclusion: This study's findings urge the necessity to produce and approve effective aqua drugs and treatments to ensure farmed fish and public health.

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Introduction

Aquaculture expansion and intensification have become popular in Bangladesh. This farming trend has raised the frequent use of various drugs and chemicals in aquaculture for health management in some regions [1]. Farmers usually apply these to protect their farmed animals susceptible to multiple diseases and health problems [2,3]. Intensive fish farming to achieve greater productivity can lead to greater susceptibility to infections due to viruses, bacteria, fungi, and parasites. But the uncontrolled and inappropriate application of aqua drugs against diseases poses potential risks toward microbial resistance, which will eventually affect both the production system and environment [4]. This is because infectious diseases essentially require some measures to control the outbreak, whereas non-infectious diseases cannot always be cured by medications [5].

Various fishes' diseases are essential components for successful fish health management and increased production [6,7]. Prevention of infection in fish can be ensured through water quality management, nutrition, and sanitation. However, various drugs and chemicals have been used for centuries as the essential ingredients in successful aquaculture. These are important for aquatic animals' health management, pond construction and preparation purposes, soil–water quality maintenance, aquatic productivity, fish transportation, feed preparation, artificial reproduction, and fish processing [8].

Veterinary drugs are mainly approved for animals or poultry in Bangladesh. Considering fish as an aquatic animal, several drugs are used in aquaculture. These drugs are administered as medicated via feed, and some via immersion. However, fishes do not metabolize antibiotics effectively, and the majority of the administered dose is excreted [9–13]. Ultimately, veterinary drugs and antimicrobials in food animal production have become a primary global concern [14]. Antimicrobial resistance (AMR) in cultured fish has resulted from the continuous use of

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antibiotics in aquaculture. Eventually, it is increasing the possibility of AMR-related factors' transfer to the whole environment. Countries with climate change issues have the highest chance of AMR risks, including human health hazards with varied bioavailability in aquatic systems depending on their environmental impacts. Consequently, sustainable solutions to minimize this antibiotic usage with increased system resilience have recently become a significant concern [15,16].

The administration of drugs to aquatic animals is considerably more challenging than terrestrial animals. It depends on risk factors like drug residues, which may vary depending on the animal's age, feeding, disease status, and excretion [17]. In Asian countries, fish farms integrated with animal houses and agricultural land are commonly practiced, leading to environmental contamination with drug residues in foods and AMR [18]. It can also be a source of environmental pollution because of different disease treatments, inappropriate disposal of aqua-medicine and drugs, and manufacturing processes [19,20]. It may create toxicity in farmed species [21], and the misuse of veterinary drugs can pose negative impacts on food safety, followed by the global fish food trade. For example, chloramphenicol has been shown to have harmful human health concerns and has been banned by reducing this drug's availability for fish [22].

The above-mentioned concerns have brought about the evolution and profound changes in the development and use of veterinary drugs in aquaculture. Since there are only a few approved aquaculture drugs, fish farmers have chosen veterinary drugs, knowing little about their effectiveness. It is therefore essential to identify and understand the impact of veterinary drugs before their application. Considering the emerging above-mentioned issues, this study was conducted to determine the use and effect of veterinary drugs, antimicrobials, and supplements on fish.

Materials and Methods

The study was carried out at Trishal, Tarakanda, Fulpur, and Mymensingh Sadar in the Mymensingh district, where most aquaculture farms are located. A total of 50 commercial fish farmers (Mymensingh Sadar-15, Tarakanda-12, Trishal-14, and Fulpur-9) and 25 drug shops (Mymensingh Sadar-9, Tarakanda-4, Trishal-8, and Fulpur-4) were surveyed. A separate questionnaire was prepared for farmers and drug sellers to collect the data. A questionnaire interview was carried out with open and close-ended questions. The farmers mainly focused on general farm details, drug usage, fish health, disease treatment, and recovery from disease. The drug sellers' questions were about the available veterinary drugs, their use, dose and dosage, companies or source (drug or chemical providers), and disease recovery rate after application. The collected data were coded, summarized, and processed in Microsoft Excel for analysis after eliminating possible errors and inconsistencies.

Results

Use of veterinary drugs by farmers

The application of veterinary drugs for fish health management was a common phenomenon in the study areas. Farmers were reported with irresponsible and frequent use of such drugs without approval and not knowing its effects on fish health. About 70% of the interviewed fish farmers were found to use veterinary drugs. It was evident that they had difficulties in applying medications due to a lack of appropriate knowledge. In this study, 58% of the farmers could not follow appropriate doses. In comparison, only 42% used proper drug and the correct drug dose in their farms for fish health management purposes (Fig. 1a and b).

Types of veterinary drugs

According to the drug sellers, antibiotics and six categories of other compounds, including nutritional supplements,

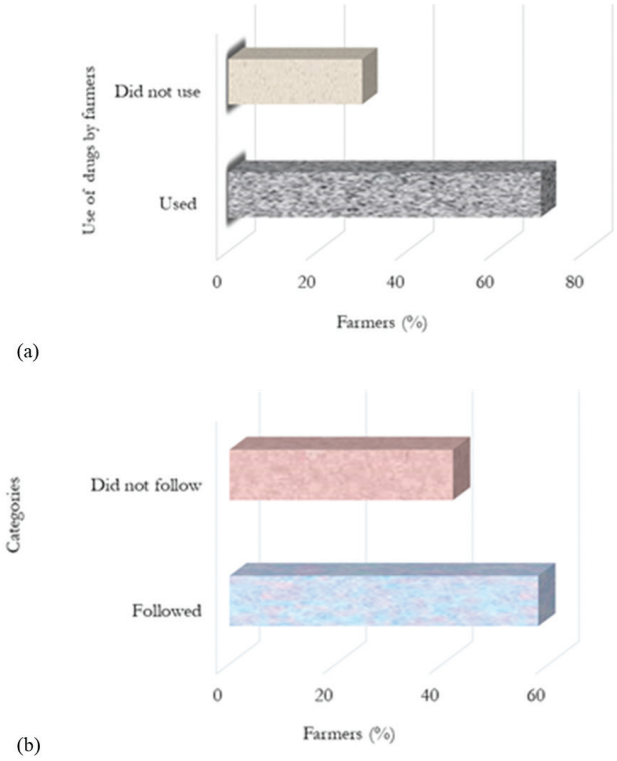

Figure 1. (a) Use of veterinary drugs (%) and (b) appropriate dose maintenance by the farmers (%).

disinfectants, saline, ammonia removal, probiotics, and pesticides, were administered by the fish farmers in this study. Antibiotics were the most used drugs (80.85%) mentioned by the farmers, followed by 6.38% disinfectants and nutritional supplements. The rest was mentioned at the same rate (4.25%) of saline usage, ammonia removal agents, probiotics, and pesticides (Fig. 2).

Use of antibiotics

Antibiotics (six different groups based on active ingredients) were mainly used by the farmers to treat diseased fish, and were generally applied orally by mixing with feed or pond water. Oxytetracycline (25.59%) and amoxicillin (25.05%) were found to be the most sold antibiotics, followed by Ciprofloxacin (17.79%), Sulfadiazine (14.68%), and some other antibiotics like Chlortetracycline (6.37%) and Azithromycin (5.26%) with a lower selling rate (Fig. 3).

A summary of the most widely used veterinary antibiotics used for fish health management in the study areas is given in Table 1. Altogether 15 trade-named antibiotics were reported from the shops provided by seven drug-supplying companies, including Renata Animal Health Ltd., ACI Animal Health Ltd., Novartis Animal Health Ltd., Eon Animal Health Ltd., Navana Pharma. Ltd, Acme Laboratories Ltd., and SK + F. Five antibiotics, including Renamycin, Aquamycin, Oxysentin, Oxy doxy-F, and Oxy-D-vet, were found under the Oxytetracycline group. The active ingredients of such antibiotics were mainly Oxytetracycline. Farmers applied these antibiotics in fish feed following varying doses according to the fish's body weight (Table 1). The amoxicillin group was found as a broad-spectrum antibiotic against both Gram-positive and Gram-negative bacteria in fish. Amoxicillin was used as a reasonably effective drug by farmers against streptococcal infection in fish. Two antibiotics, namely Acimox and Renamox, with the active ingredient of Amoxicillin Trihydrate, were found under the group Amoxicillin. Renaflox, Cipro-plus, and Ciprocin-Vet were the three antibiotics under the Ciprofloxacin group. Renaflox was recorded as the most used Ciprofloxacin by the fish farmers in this study. However, it was mentioned at the product level that it is only approved for veterinary purposes rather than aquaculture. Ciprofloxacin hydrogen chloride and United States Pharmacopeia (USP) were the active ingredients in Ciprofloxacin. The farmers also used three Sulfadiazine drugs (Eskatrim-vet, Micronid, and Ati-vet) in a wide range of water doses. A combination of Sulphadiazine, Trimethoprim and Erythromycin was found as the active ingredients in Sulfadiazine antibiotics. Chlortetracycline named Captor with Chlortetracycline and Hydrochloride British Pharmacopoeia (BP) 45% as active ingredients were found in the drug shops. Azin-vet was the only antibiotic under the Azithromycin group that the farmers found to use at a significantly lower dose (20 mg/kg body weight of fish) against bacterial diseases (Table 1).

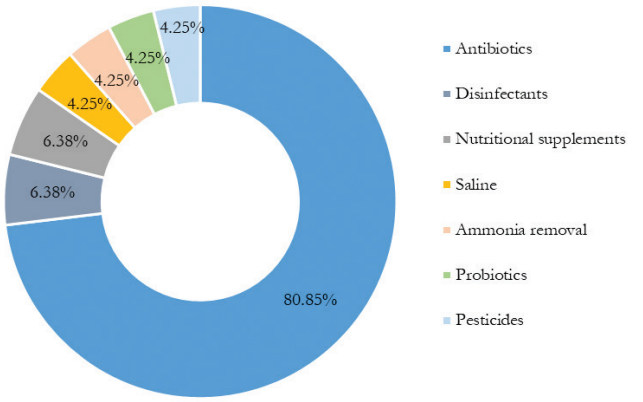

Figure 2. Veterinary drugs used in the study areas.

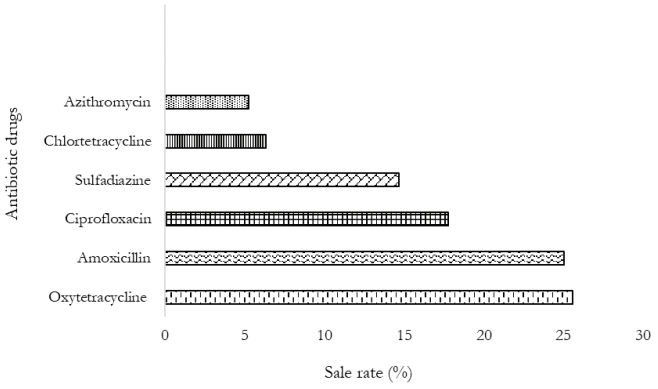

Figure 3. Antibiotics with selling rates (%) used by farmers.

Compounds other than antibiotics

Six categories of other compounds, including nutritional supplements, disinfectants, saline, ammonia removal, probiotics, and pesticides, were found to used by the farmers for fish health management in this study (Table 2). Six different companies were found to supply these products. Virocid, Provin vet, and Timsen were listed as disinfectants. The farmers used vitamins (E-vet plus, Lisovit and Vitex-British Columbia) to enhance fish immunity. The vitamin B complex, vitamin C, vitamin E, and selenium supplements were the active ingredients in vitamin supplements. Electrolyte and vitamin were active ingredients in salines. Farmers were using saline for fish during transportation. However, according to the drug sellers, it is generally used in poultry for diarrhea and dehydration to maintain electrolyte and body physiological saline balance. Bio-aqua and Yucca were found as the ammonia remover used to control and reduce the harmful gas (NH_3, CH_3, and H_2S) in ponds. The extract of *Yucca Schiigera* was the active ingredient in the ammonia remover. Farmers also mentioned that they

Table 1. Veterinary antibiotics found in this study.

Antibiotics (group)	Trade name	Active ingredients	Sources	Dose
Oxytetracycline	Renamycin	Oxytetracycline Hydrochloride USP	Renata Animal Health Ltd.	50 mg/kg body wt.
	Aquamycin	Oxytetracycline + Hydrochloride	ACI Animal Health Ltd.	40 mg/kg body wt.
	Oxysentin	Oxytetracycline + HCL BP	Novartis Animal Health Ltd.	1–2 gm/kg feed for 5–7 days
	Oxy doxy-F	Oxytetracycline + Hydrochloride 20%	ACI Animal Health Ltd.	0.25 gm/kg body wt. for 2 times/day
	Oxy-D-Vet	Oxytetracycline 20% + Doxyclyclin 10%	Eon Animal Health Ltd.	5–10 gm/kg body wt.
Amoxicillin	Acimox	Amoxicillin Trihydrate BP	Navana Pharma. Ltd.	40 mg/kg body wt. for 5–10 days
	Renamox	Amoxicillin Trihydrate 300 mg/gm	Renata Pharmaceuticals Ltd.	1 gm/kg feed for 5–7 days
Ciprofloxacin	Renaflox	Ciprofloxacin HCL USP	Renata Pharmaceuticals Ltd.	1.5–2.5 gm/kg feed
	Cipro-plus	Ciprofloxacin 5.50 mg	Novartis Animal Health Ltd	2–4 gm/kg feed
	Ciprocin-Vet	Ciprofloxacin HCL USP	Novartis Animal Health Ltd.	2–3 gm/kg feed
Sulfadiazine	Eskatrim-Vet	Sulphadiazine + Trimethoprim	SK+F	0.1 ml/l water for 2–3 days
	Micronid	Erythromycin, Sulphadiazine + Trimethoprim	Renata Pharmaceuticals Ltd.	0.5–1 gm/l water
	Ati-vet	Sulfadiazine + Trimethoprim	Acme Laboratories Ltd.	0.1 ml/l water, for 2–3 days
Chlortetracycline	Captor	Chlortetracycline Hydrochloride BP 45%	Novartis Animal Health Ltd.	2.5–3.5 gm/kg feed, for 3–5 days
Azithromycin	Azin-Vet	Azithromycin USP	Acme Laboratories Ltd.	20 mg/kg body wt., for 3–5 days

Table 2. Listed compounds other than antibiotics.

Compounds	Trade name	Active ingredients	Sources	Dose
Disinfectants	Virocid	Didecyldimethylammonium chloride, alcohol	ACI Animal Health Ltd.	7 ml/l
	Provin vet	Providon iodine	AV Agro Ltd.	3–4 ml/l
	Timsen	N-alkyl dimethyl benzyl ammonium chloride	Eon Animal Health Ltd.	0.5 gm/m^2
Nutritional supplements	Vitax-BC	Premix of vitamin B complex and vitamin C	Eon Animal Health Ltd.	0.04 gm/kg feed
	E-vet plus	Vitamin E and selenium supplement	Acme Laboratories Ltd.	1 ml/l water for 3 days
Salines	Osmosaline	Electrolyte with vit-A	Eon Animal Health Ltd.	0.1 gm/l
	Oralyte	Electrolyte with vit-A	AV Agro Ltd.	1.25 gm/l
Ammonia remover	Bio-aqua	Extract of *Yucca schiigera*	Acme Laboratories Ltd.	1–2 ml/kg feed
	Yuka	Extract of *Y. schiigera* that contains saponin and glycocomponent	AV Agro Ltd.	0.002 ml/m^2
Probiotics	Cleantec-100	*Lactobacillus plantarum* *Lactobacillus bulgaricus* *Lactobacillus acidophilus* *Steptococcus thermophylus*	SOMA	0.01 gm/kg feed
	PRO400X	*L. bulgaricus* *L. acidophilus* *S. thermophylus* *Candida pintolopesii*	ACI Animal Health Ltd.	80 gm/kg feed
Pesticides	Energy	800 gm sulphur/kg	Eon Agro Industries	0.17 gm/m^2
	Sumithion	Organo phosphorus	Setu Corporation Ltd.	0.05 ml/m^2

use probiotics (Cleantec-100 and PRO400X) to ensure better immunity and fish growth. Pesticides (Energy and Sumithion) were also used for pest management. The dose for all the above-mentioned compounds was significantly varied (Table 2) depending on the application mode, either in feed or in water for a certain period.

Impact of drugs in fish health management

To know the impact of antibiotics, farmers were asked about the effectiveness of antibiotics in disease treatment of some clinically infected fish, including Rui (*Labeo rohita*), Catla (*Gibelion catla*), Mrigal (*Cirrhinus cirrhosus*), Silver carp

Table 3. Effects of antibiotics in disease treatment.

Species	Clinical signs	Antibiotics	Effectiveness	Disease recovery (%)
Rui, Catla, Mrigal, Pangas, Tilapia	Red spots on body surface, lesions on body surface	Oxy-D-vet	Yes	60
		Renamycin	Limited	30
		Oxysentin	Limited	20
		Eskatrim-vet	Limited	20
		Micronid	Limited	10
		Captor	Limited	20
Catla, Rui, Tilapia, Silver carp	Pop-eyes and abdomen distention	Aquamycin	Yes	50
		Acimox	Yes	50
		Renamox	Limited	10
Tilapia, shing, pabda, gulsha	Reddish and yellowish ulcer on the base of fins and body surface	Ati-vet	Yes	60
		Eskatrim vet	Limited	30
		Renamox	Yes	40
		Azin-vet	Limited	20
		Oxy doxy-F	Limited	20
		Oxy-D-vet	Limited	30
		Ciprocin-vet	Yes	60
Pangas, Catla, Mrigal	Tail, fin, and lower abdominal side rot	Captor	Yes	40

(*Hypophthalmichthys molitrix*), Pangus (*Pangasianodon hypophthalmus*), Shing (*Heteropneustes fossilis*), Pabda (*Ompok bimaculatus*), Gulsha (*Mystus cavasius*), and Tilapia (*Oreochromis niloticus*).

Major clinical signs recorded in fish were red spots and lesions on the body, pop-eyes, abdomen distension, ulcers on the tail, and tail, fin, and lower abdominal side rot. Red spots and lesions on the body were treated with antibiotics such as Oxy-D-vet, Renamycin, Oxysentin, Eskatrim-vet, Micronid, and Captor. The disease recovery rate was remarkably high in only Oxy-D-vet (60%), whereas the rest had a highly varied disease recovery rate (10%–30%). Pop-eyes and abdomen distension were found commonly in Catla, Rui, Tilapia, and Silver carp. Aquamycin and Acimox resulted in a reasonable recovery rate (50%) and low recovery (10%) by Renamox. Reddish and yellowish ulcers on the fin base and body surface in Tilapia, Shing, Pabda, and Gulsha were treated with antibiotics. Ati-vet and Ciprocin-vet had about 60% disease recovery. Fin and tail rot, abdominal side rot in Pangus, Catla, and Mrigal; Chlortetracycline antibiotic, namely Captor, resulted in 40% disease recovery as an effective drug against fish disease in this study (Table 3).

The fish farmers used disinfectants as an easy and practical (50%–60%) control against a wide range of pathogens. Provin Vet and Timsen were found as 60% useful. Salines and Ammonia removers also had 50%–60% effectiveness as a treatment. Probiotics were resulted in 40%–50% effectiveness, according to the farmers. Among two pesticides, Sumithion was more effective (60%) than energy (50%) against fish argulus. Nutritional supplements as vitamins were mostly supplied to breed fish for healthy egg production. In this study, the nutritional supplements' effectiveness ranged from 40% to 60% (Table 4).

Table 4. Effectiveness of compounds other than antibiotics.

Compounds	Trade name	Effectiveness (%)
Disinfectants	Virocid	50
	Provin vet	60
	Timsen	60
Saline	Osmosaline	60
	Oralyte	60
Ammonia remover	Bio-aqua	60
	Yucca	50
Probiotics	Cleantec-100	40
	PRO400X	50
Pesticides	Energy	40
	Sumithion	60
Nutritional supplement	Vitax-BC	60
	Lisovit	40
	E-vet plus	50

Discussion

The interviewed farmers were found to use a wide range of veterinary drugs in aquaculture without maintaining the recommended dose, withdrawal period, and proper

application methods. Recently, poultry and veterinary drugs were widely used to produce fish. This is the most common scenario to use these drugs either in animal husbandry or in aquaculture. Consequently, environmental contamination has become a concern in recent years [23]. Aquaculture farmers cannot consistently maintain the recommended dose due to lack of knowledge, and the indiscriminate use of drugs may lead to profound biodiversity loss of aquatic organisms [24]. Different types of aqua drugs and chemicals are widely used in Bangladesh's aquaculture depending on farmers' demand and market availability [25]. However, minimal information is available regarding the list of approved drugs for aquaculture. A complicated licensing procedure may be the main obstacle for drug approval in aquaculture. Six different antibiotic categories were identified with respective active ingredients in this study with varied disease recovery of their farmed fish. But most of the farmers of this study had limited knowledge about the appropriate dose of drugs and their withdrawal periods, as previously reported [26].

Farmers mentioned that Oxytetracycline and Sulfadiazine had been reported as widely used antibiotics for treating diseases like vibriosis and ulcerative diseases in aquaculture [27,28]. On the contrary, some antibiotics are used as prophylactics and growth promoters. The commonly used chemicals in fish health management included lime, salt, potassium permanganate, sumithion, melathion, formalin, bleaching powder, virex, Aquakleen, and malachite green [29,30]. However, it is not always a good management practice to apply these chemicals.

The farmers mentioned that Tilapia, Shing, Pabda, Gulsha, Rui, Catla, Mrigal, Pangus, and Silver carp showed red spot at the base of fins that gradually turned to an ulcer, red spot on the body surface, lesion on the body surface, pop-eyes, abdomen distention, milky white areas on fins or tails, a reddish and yellowish ulcer on the base of fins, and tail, fin and lower abdominal side rot. According to the farmers, veterinary drugs and chemicals had minimal satisfactory effects, and therefore, drugs could not always correctly cure the disease. However, most of the farmers frequently used these drugs and chemicals without knowing their effectiveness against disease and fish health management. A large number of fish farmers did not properly maintain the appropriate dose in using drugs. After using veterinary drugs, fish disease recovery was found to vary from 10% to 60%, and farmers were not so satisfied. The majority of the farmers used drugs without receiving any prescription from experts. There is a lack of prescribing authorized personnel in the study areas. But according to the Aquaculture Medicinal Products' guidelines of the Department of Fisheries, it is mandatory to receive a prescription from the authorized person before using antibiotics and any other drugs [31].

Veterinary drugs in animal-derived food can generate drug residues and consumer health hazards [32]. The AMR can cause global health risks by directly consuming farm fish or disseminating AMR in the environment through horizontal gene transfer [33]. Moreover, farm animals are considered an essential source of bacteria containing AMR genes, although antimicrobials in aquaculture. However, these compounds are still applied in animal production units and are transmitted to humans mainly during animal-originated food products [34].

Several factors can influence the residue issue in animal products. Drug's properties and their pharmacokinetic characteristics, physicochemical, or biological processes of animals and their products can be mentioned among those drivers. Improper drug usage and failure to maintain the withdrawal period are the most common practices for drug residues. Some prominent public health issues related to drug residue might be the development of AMR, hypersensitivity-derived reaction, carcinogenicity, mutagenicity, teratogenicity, and disruption of intestinal flora [35].

Antibiotic resistance can spread via both vertical and horizontal gene transfer. This resistance depends on the drug uptake, modification of the target drug, drug inactivation, and active efflux of a drug. The highest concentration of antibiotics is usually found in intense anthropogenic pressures, animal husbandry, and aquaculture [36]. Aquaculture systems are highly complex and dynamic, and it is influenced by environmental, biological, cultural, and socio-economic and human behavioral factors. Therefore, indiscriminate antibiotic usage in aquaculture increases gradually to treat or prevent disease and increase productivity. However, these antibiotics are often used to compensate for management and husbandry deficiencies. Besides, proper monitoring of antibiotic usage and resistance often lack in aquaculture practices. Similarly, aquaculture systems expose waste water into the river and take water from it, which may bring people into contact with antibiotic residues and resistant bacteria [37].

Consequently, the AMR situation has become an alarming issue in aquaculture due to the use of antibiotics common for human treatments and the lack of investment in developing new effective antimicrobials [38]. Aquaculture is a significant food production industry in Bangladesh, posing a substantial risk to global AMR dissemination. Thus, effective AMR awareness campaigns for aquaculture communities in Bangladesh are essentially required to change antibiotic use in the coming days [39,40]. Ultimately, safe and effective veterinary drugs need to be available for aquaculture production systems [41]. However, the present study's main limitation was the used drugs' effectiveness data derived only from the farmers' experiences. Further clinical trial in fish under the laboratory condition is required to understand better the drug

efficacy mechanism and direct or indirect impacts of drugs on fish health management.

Conclusion

The use of unapproved veterinary drugs in commercial fish farming paves the way to create potential hazards like antimicrobial residue and AMR. The unwise use of veterinary drugs in this research and its positive and/or negative effects consequently affected the overall fish disease management strategy and the food safety aspect for the consumers. It may also negatively impact the ultimate export quality, and the buyers may reject products. Farmers will experience massive economic loss every year if appropriate and effective drugs are not used in aquaculture. This study's findings will help to create a roadmap for the responsible use of veterinary drugs in aquaculture practices and safeguard public health and combat AMR.

List of abbreviations

AMR = Antimicrobial resistance, mg = Milligram, gm = Gram, kg = Kilogram, ml = Millilitre, L = Liter, wt. = Weight, m^2 = Meter square, % = Percentage, Ltd. = Limited, USP = United States Pharmacopeia, BP = British Pharmacopoeia.

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Conflict of interest

The authors declare that they have no conflict of interest.

Authors' contributions

Md. Ali Reza Faruk: design, formulation, supervision of research, and reviewing the manuscript. Hajera Khatun Shorna: carried out the fieldwork, collection, data analysis, and writing of the document. Ishrat Zahan Anka: data analysis and reviewing of the manuscript.

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