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Current scenario of antibiotic-resistance in Indian aquaculture

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Abstract
Antimicrobial or antibiotic resistance (AMR) as we all know is the ability of a pathogen to survive exposure to an antimicrobial agent that was previously an effective treatment. The AMR has been a growing threat to the health of humans and animals alike and has been identified as a major risk factor by the World Health Organization (WHO). Humans and animals have succumbed to antimicrobial-resistant pathogens and have led to nearly 1 million deaths worldwide. Fishes and other aquacultured species have also been affected by the growing threat of AMR. The current study aimed at providing a brief of the current scenario of AMR in Indian aquaculture.

Keywords: AMR, aquaculture, India, antimicrobials

Introduction

Aquaculture, an exponentially growing sector of the world population has kept fish productivity at an optimum level to meet the protein requirement. There are huge advances in fish culture practices from extensive to intensive. But to conquer this intensification lots of stress has been provided to the cultured animal as well as in the environment which made them prone to infectious diseases. That's why to combat these diseases, many remedial measures have been taken among them, antibiotics are one. Various broad-spectrum antibiotics are the most widely getting used as therapeutic as well as prophylactic measures against bacterial fish infections. The global annual production of antibiotics is estimated to be as high as 100–200 thousand tons, with more than one billion tons having been produced since 1940 (Wang and Tang, 2010; Czekalski *et al*., 2014) [54, 9]. Antibiotics are mainly drugs of natural or synthetic derivations that can destroy or inhibit the growth of micro-organisms through various aspects (Serrano, 2005). The use of these antibiotics as a therapeutic agent is the most useful method for the treatment of any infectious bacterial diseases including in the fisheries and aquaculture sector. The success in the use of any antibiotic in aquaculture is compromised due to the emergence of antimicrobial resistance in bacteria. Antibiotic resistance continues to pose a considerable public health hazard in terms of death and economic losses. Some Health authorities of some countries including India have also formulated action plans for its suppression. In these controversies against AMR, it is important to understand the contribution by the entire following four spheres as humans, animals, environment, and food. In aquaculture, the antimicrobials are mostly administered either through medicated feed or by adding them directly to the pond water. Both the methods may result in heavy use of antimicrobial agents and provide a strong selective pressure in the aquatic animals, as well as in the exposed environments (Le and Munekage, 2004).

This review study incorporates all the spheres of the One Health concept from the Indian perspective. India has one of the highest rates of resistance to antimicrobial agents used both in humans and food animals. The environment, especially the aquatic environment, has also reported the presence of resistant organisms or their genes. Specific socio-economic and cultural factors prevalent in India make the containment of resistance more challenging. Injudicious use of antimicrobials and inadequate treatment of wastewaters are important drivers of AMR in India. Exertions to fight AMR have been initiated by the Indian health authorities but are still at introductory stages. In aquaculture, numerous bacterial diseases routinely encountered, which affect successful production, are mainly due to organisms such as *Aeromonas hydrophila, A. salmonicida, Vibrio anguillarum, V. harveyi, Flavobacterium psychrophilum, Edwardsiella tarda, Citrobacter freundii, Pseudomonas fluorescens* and

Yersinia ruckeri; rarely by Gram-positive ones such as *Streptococcus* and *Staphylococcus*; and also by acid-fast *Mycobacterium* spp. (Sørum 2006) [48]. Among these, the most prevalent reported bacterial pathogen in freshwater aquaculture is *Aeromonas hydrophila* (Watts *et al.,* 2017) [56]. The consumption of such infected cultured fishes poses public health threats including humans. This incidence administers farmers to use antibiotics frequently in the aquaculture system. Concomitant with the rise in antibiotic administration in aquaculture as a part of therapy and prophylaxis, there has been an emergence of antimicrobial resistance (AMR) among bacterial fish pathogens. Many cultured fishes such as carp, salmon, tilapia, catfish, and crustaceans like shrimps worldwide have been reported to possess antimicrobial-resistant pathogens (Watts *et al.,* 2017) [56]. The unceasing use of antibiotics for improving bacterial diseases in aquaculture has led to "pseudo-durability" and their omnipresence in the environment, which has caused the development of selective pressure on the microbial community. Antimicrobial-resistant bacteria formed under selective pressure can develop into an environmental pool of antibiotic-resistant genes. Aquaculture systems and fish farms have been observed as the 'hotspots for AMR genes' and hence the assessment of resistome, the AMR gene collection in aquaculture, is an important topic of research worldwide (Watts *et al*., 2017) [56]. Recently, Brunton *et al*.,(2019) [3] performed a detailed survey on the identification of hotspots for antimicrobial resistance, emergence, and selection in aquaculture systems through a system thinking approach. Increased frequency of severe infections and treatment failures had been reported in humans due to the consequences of the transfer of antimicrobial resistance from aquaculture to humans through the consumption of aquaculture products (Watts *et al.,* 2017) [56].

Factors that Cause AMR

1. Increase in AMR is related to the amount of the antibiotic prescribed, number of doses missed, and inappropriate and unregulated use of antibiotics which happen maybe because sometimes farmers in the aquaculture sector use antibiotics which are not safe and approved by any authority (Pechere, 2001; Arnold and Straus, 2005) [40, 1]
2. Lower antibiotic concentrations, less than the recommended dose (Ventola, 2015) [52] used for a longer duration also contribute to the increase in the AMR.
3. Inappropriate use of antibiotics and chemicals in animal husbandries and aquaculture is led to the emergence and spread of antibiotic-resistant microbes (Prestinaci *et al*., 2016) [41].
4. Resistance towards antibiotics sometimes is also natural. The responsible genes that gain resistance are called environmental resistors. These genes may be transferrable from non-pathogenic to pathogenic microbiomes which may lead to antibiotic resistance (Wright, 2010) [57]
5. Drugs administered in the fish feed also persist in the aquatic ecosystem for a longer period. In addition, sometimes fishes do not metabolize antimicrobials with effectiveness. It has been observed that about 70–80% of active antibiotics and their metabolites are suspended in water and can spread throughout the water so, the practice of using these antibiotics in fish production units has serious environmental consequences, as it may result in selection pressure in many ecosystems (Romero *et al*., 2012; Burridge *et al*., 2010) [42, 4].
6. The sediments and watercourses also demonstrate a high percentage of antibiotic-resistant bacteria and can serve as sources of antibiotic-resistant bacterial genes for fish pathogens. Furthermore, it has been found that resistant bacteria from aquaculture may be transferred to terrestrial animals and as well as in the human environment and are capable of transferring their resistance genes to opportunistic animal or human pathogens (Liliana, 2020) [29].
7. Furthermore, the antimicrobials applied in aquaculture are mostly applied as a metaphylaxis to entire populations containing healthy, sick, and carrier individuals and at doses that are usually higher than those used in terrestrial animal farming. Florfenicol, oxytetracycline, sulfadimethoxine, and ormetoprim are authorized for use in aquaculture in the USA (Romero *et al*., 2012) [42], while florfenicol oxytetracycline, erythromycin, sarafloxacin, sulphonamides, trimethoprim, and ormetoprim are used with authorization in most European countries (Kümmerer, 2009) [26]. China has reported the highest production and as well as the use of antibiotics until 2010 (Yang *et al*., 2010) [59], at which time, the country was also accounted for 67%of the total worldwide aquaculture and was the largest exporter country for fish and fishery products (FAO, 2018) [15]. Furthermore, China does not require veterinary prescriptions for the use of antibiotics in animals (Maron, 2013) [30]. China is followed by India (where antibiotics sales and usage are not yet regulated), which accounting for8% of total worldwide aquaculture production (ECDPC, 2018) [13].

Advance and distribution strategy of antimicrobial resistance

The development and spread of antimicrobial resistance due to the use of antimicrobial agents recklessly in both humans as well as in animals have become a worldwide public health hazard (Heuer *et al.,* 2009) [19]. Unrestricted as well as abuse of therapeutics doesn't allow the more susceptible bacteria to survive and adjust to the low drug concentration and develop resistance (Levy, 1998) [28]. If antimicrobial resistance developed in one ecological niche, that can spread to another such as the use of antimicrobials in aquaculture which can lead to the occurrence of antimicrobial resistance in humans as well as in another environment (Aich *et al*., 2018). Bacteria can get resistant genes by different means and transfer them to a new pathogen with the help of various mobile genetic materials, like plasmids and transposable elements (Romero *et al.,* 2012) [42]. Viruses can also transfer resistance genes rarely by extracting genes from one bacteria and injecting it into a new microorganism (Levy, 1998) [28].

There are various pros and cons of using antibiotics but major issues relyon unregulated use. We should find other safer ways of preventing and treating fish disease outbreaks.

Several alternative methods which can be used are:

- Probiotics, prebiotics, and synbiotics
- Immunostimulants
- Bacteriophage therapy
- Vaccine
- RNA interference
- Quorum sensing inhibition

Probiotics, prebiotics, and synbiotics

Various types of feed additives are used in the aquaculture sector to intensify fish production, which also includes probiotics and prebiotics, having beneficial effects on the host and used in aquaculture as prophylactics to boost disease-resistant ability, they are also beneficial as supplements, to improve growth increasing the size and weight gain, and in some cases, act as as a substitute of antimicrobial compounds in a primary infection (Irianto and Austin, 2002) [20] as well as to stimulate immunity response of the host. Both probiotics and prebiotics have received widespread attention, showing the better production, health safety, and disease resistance of aquatic animals (Dimitroglou *et al.*, 2011) [12]. When probiotics and prebiotics are used combinedly on an animal so that the probiotic bacteria can proliferate vigorously with the help of the prebiotics, this system is known as the synbiotic. Probiotics interact with the immune cells such as mononuclear phagocytes (monocytes, macrophages) and polymorphonuclear leukocytes (neutrophils), natural killer (NK) cells, to enhance innate immune responses. Some probiotics can increase the number of erythrocytes, granulocytes, macrophages, and lymphocytes in various fishes (Irianto and Austin, 2002; Kim *et al.*, 2006; Kumar *et al.*, 2008; Nayak *et al.*, 2007) [20, 22, 25, 34]. There is a report of an increase in the different innate immune system upon administration/intake of probiotics (Sharifuzzaman and Austin, 2009) [45], (Sakai *et al.*, 1995), Probiotics such as *L. rhamnosus*, *E. faecium* and *B. subtilis* are found to stimulate the pro-inflammatory cytokines such as IL-1b1 and TGF b in the spleen and head kidney of the *O. mykiss* (Panigrahi *et al.*, 2007) [36], Sharifuzzaman and Austin (2009) [45] also reported significant higher anti-protease activity in *O. mykiss* with in two weeks of the completion of probiotic species *Kocuria*. There are numerous numbers of prebiotics are available for use and they are broadly classified into two categories i.e. oligosaccharides and polysaccharides. The immunomodulatory activity of prebiotics is mediated by straight interactions with their receptors, like b-glucan receptors and dectin-1 receptors that are expressed on macrophages (Brown *et al.*, 2002) [2]. The ligand-receptor interaction uplifted the activity of signal transduction molecules, such as NF-kB, that stimulate immune cells (Yadav *et al.*, 2002). The prebiotics also helps by giving direct nutrition providence to probiotic bacterias. Some of the examples for such oligosaccharides include Fructooligosaccharides (FOS), Mannan oligosaccharide (MOS), Immunogen® (a commercial product containing two prebiotics, MOS and b-glucan), Galactooligosaccharide (GOS), Arabinoxylan-oligosaccharide (AXOS), etc. Examples of polysaccharides are Inulin, b-glucan, chitin/chitosan, etc.

Immunostimulants

Immunostimulants mainly work on the activation of the white blood cells which plays amajor role in the fish defense mechanism. It might be chemical, drug, or sometimes naturally occurring compounds that elevate the nonspecific defense mechanisms or the specific immune response of the host and may be given alone to activate non-specific defense mechanisms as well as increasing a specific immune response. Such substances may also, but not compulsory, render animals more resistant to infectious diseases and reduce the risk of disease outbreaks if applied before situations known to result in stress and impaired general body performance (e.g. handling, change in temperature and adverse environmental condition, weaning of larvae to supplementary feeds) or before the expected increase in exposure to pathogens and parasites (e.g. spring and autumn bloom formation in the marine environment and high stocking density). The chemical property of different immunostimulants available is structural elements of bacteria (lipopolysaccharides (LPS), lipopeptides, capsular glycoproteins, and muramylpeptides). Various β-1,3-glucan products from bacteria (Curdlan) and mycelial fungi (Krestin, Lentinan, Schizophyllan, Scleroglucan, SSG, VitaStim) β -1,3/1,6-glucans from the cell wall of baker's yeast (MacroGard, Betafectin), Complex carbohydrate structures (glycans) from various biological sources including seaweed Peptides present in extracts of certain animals or made by enzymatic hydrolysis of fish protein Nucleotides, and Synthetic products (Bestatin, muramylpeptides, FK-156, FK-565, Levamisole). Immunostimulants have many health benefits like it reduces the fish mortality rate due to the opportunistic pathogens also prevents different bacterial, viral, or parasitic diseases, which enhances the diseases resistance of the young fishes by elevating the non-specific immune system mechanism and it can also increase the efficacy of other antimicrobials such as vaccines.β-1,3/1,6-Glucans have proved to stimulate the biological activity of shrimp hemocytes and to improve growth, survival rate, and feed conversion efficacy under experimental conditions (Sung *et al.*, 1994; Song and Hsieh, 1994; Sung *et al.*, 1996) [51, 47, 50].

Bacteriophage therapy

Considering the negative impact of antibiotics and other chemotherapeutics, biological control of pathogens would be a very useful strategy to combat bacterial diseases. Historically, these are discovered by Twort (1915) and Dâ€™ Herelle (1917) during the pre-antibiotic era. Now it has been proved that phage therapy declines the bacterial population below the threshold number to a level where the host defense can take care of the remaining bacteria. There are two types of bacteriophage reproduction that occurs in the bacteriophages: (1) Lytic and (2) Lysogenic, in the lytic cycle the virus attaches to a host cell and injects their nucleic acid into the cell, directing the host to produce numerous off springs. Commonly, the replication of phage in the bacterial cell occurs including five steps: adsorption, penetration of genetic material, replication, maturation, and lysis. Phage control for disease caused by *Pseudomonas plecoglossicida* in *Plecoglossus altivelis* was demonstrated by Park *et al.*, 2000 [38]**.** Park and Nakai (2003) [37], reported the efficacy of Bacteriophage control of *Pseudomonas plecoglossicida* infection in ayu (*Plecoglossus altivelis*)**.** Karunasagar *et al.*, 2005 showed the efficacy of bacteriophages against luminous bacterial disease control in shrimp hatcheries by reducing the number of *V. harveyi* counts in water and larvae and tremendously improved larval survival. Bacteriophages can be administered to the fishes by different routes i.e. through the water bath, oral, injection, etc. There is a need for further investigations regarding the possibilities for using phages as an alternative to antibiotic treatment of different fish diseases in aquaculture.

Vaccine

Prevention is always better than cure. So, the prevention and control of fish diseases in Aquaculture are at high priority in the aquaculture industry. Unlike treating human or other animal diseases, few drugs are available for controlling diseases in fish. Therefore, to control different diseases in aquaculture and fish farms relies on a combination of better management practices and the use of the few approved and commercially available drugs and vaccines for the prevention of infections. The immune system is to protect the fish from bacteria, viruses, or any foreign antigen. Fish immunology has a more recent history than human and veterinary animals' immunology but the techniques used are the same. However, methods and routes of administration vaccines to fish differ and vary upon species, pathogen, temperature, and environment (Anderson, 1974). The ideal vaccine formulated for the fisheries sector is the polyvalent vaccine, which protects simultaneously against the majority of the fish pathogens to which a particular fish species is susceptible (Busch, 1997). Depending upon fish species and temperature, vaccination must be performed within a certain minimum period before the risk of their exposure to pathogens (Aich *et al*., 2018). Fishes are mostly immunized by three routes, are intraperitoneal injection (IP), immersion in a diluted vaccine solution (short or long bath), or oral administration of the vaccine (Komar *et al.,* 2004) [23]. First commercially available fish bacterial vaccine was against enteric red mouth disease causes by *Yersinia ruckeri* and *vibriosis* commercialized in the USA in the late 1970s (Evelyn *et al.,* 1997). The first viral vaccine for fish was produced by a Czechoslovakian company (Bioveta) in 1982. The vaccine was against a carp rhabdovirus, causing spring viremia of carp (SVC) in salmonids, and was based on two inactivated strains of SVC virus emulsified in oil and administered by injection. Currently, there are only 14 licensed fish vaccines in the U.S., including 11 killed bacterial, 1 killed viral, and 2 live attenuated bacterial prophylactics (Aich *et al*., 2018). Among the new generation vaccines like recombinant vaccines are emerging which are showing better results in many experimental conditions and also have the power to be the next-generation vaccine for the future. Some report of recombinant vaccines which are licensed, spread in different countries are infectious hematopoietic necrosis virus (IHNV) form recombinant G protein, licensed in Canada; spring viremia of carp virus (SVCV) from recombinant G protein in a baculovirus expression system, licensed in Belgium; infectious salmon anemia virus (ISAV) from recombinant hemagglutinin esterase protein, licensed in Chile; infectious pancreatic necrosis virus (IPNV) from VP2 and VP3 capsid proteins and VP2 protein (Trivalent SRS/ IPNV/Vibrio) licensed in Canada and Chile, respectively (Dhar *et al.,* 2014) [11]. The aquaculture industry is growing very rapidly and the use of vaccination to prevent fish diseases will play a major role in the future. There are many hurdles in the development of a vaccine for the aquatic environment in case of high pathogenic variation, cost-effectiveness, lack of knowledge about fish immunity, a problem associated with vaccine administration, etc. But many types of research in vaccine development are showing hope for effective vaccine discovery which may lead to a better future for vaccine generation.

RNA interference

The occurrence of RNA interference (RNAi) was first described in the late 1980s and has since evolved into a powerful laboratory technique for potent and specific gene silencing (Caplen *et al.,* 2004, Leung and Whittaker 2005) [6, 27]. Turning off the expression of a gene is possible at two steps 1. Transcriptional gene silencing and 2. Post-transcriptional gene silencing. There are main 3 broad stages in the development of an RNAi-based therapy: design, synthesis, and delivery. The post-transcriptional activity of the RNAi machinery to degrade cytoplasmic RNA in a sequence-specific method is the key to its antiviral function in invertebrates. For effective RNAi treatment identification of a target, a gene is very important. The RNAi technology is becoming very much focused in terms of treatment of viral diseases and mainly the shrimp diseases as we know that shrimps don't contain adaptive immunity so vaccination to the shrimps is not possible. RNAi-based vaccines experimentally showed good results in controlling diseases like WSSV, YHV, IHHNV, etc. (Aich*et al*., 2018). Different researches are needed before the commercialization of the technology and RNAi technology which is having a very promising future in the field of therapy.

Quorum sensing inhibition

Quorum sensing is a mechanism in which bacterial populations as whole coordinate gene expressions in response to their population density by producing, releasing, and recognizing small signal molecules called autoinducers (Suga and Smith 2003, Defoirdt *et al.*, 2004) [49, 10]. Quorum sensing mostly controls various phenotypes such as biofilm accumulation (Merritt *et al.*, 2003, Parsek and Greenberg 2005) [32, 39], bioluminescence (Waters and Bassler 2005, Bodman *et al.*, 2008) [55, 53], virulence factors (Mellbye and Schuster, 2011) [31], and swarming (Shrout *et al.*, 2006) which have been shown its role towards bacterial virulence. Since virulence traits of bacteria are controlled by quorum sensing, disruption of quorum sensing has been suggested as a new treatment strategy to control pathogenic bacteria (Finch *et al.*, 1998) [16] in the field of aquaculture and animal husbandry. Quorum quenching (QQ), the disruption of Quorum sensing, can be performed by small antagonists molecules (Givskovm *et al.*, 1996) [18] or signal degrading enzymes (Roy *et al.*, 2011) [43]. The Quorum quenching enzymes produced by microorganisms were classified into three major types according to their enzymatic mechanisms: AHL lactonase (lactone hydrolysis), AHL acylase (amide hydrolysis), and AHL oxidase and reductase (oxidoreduction). Still, this Quorum quenching of bacteria is in the experimental stage but if we can use it in a holistic approach then it can be a great candidate treatment method in the aquaculture industry in respect of the field of Fish disease and treatment methods.

Approved antibiotics in India

All the antibiotics that are in anthropogenic or veterinary use do not apply to aquaculture. The USFDA (United States Food and Drug Administration) is responsible to approve the antimicrobials that can be used in aquaculture. In India, authorities like MPEDA and CAA also play a major role in categorizing and approving the safety of antibiotics for aquacultural aspects.

The list below denotes all the approved antibiotics that can be used in aquaculture:

Approved antibiotics	Action regarding disease aspects	Route of administration at the proper dosage
Chloramine-T	For the control of mortality in freshwater-reared salmonids due to bacterial gill disease and columnaris associated with *Flavobacterium* spp.	Immersion (20 mg/L for 60 minutes every alternated day as many as 3 times)
Oxytetracycline hydrochloride (Terramycin343; Oxymarine^{TM})	Used in finfish fry and fingerlings.	Immersion (200-700 mg/L water for 2-6 hours)
Oxytetracyclinedihydrate (Terramycin®)	1. For the control of gaffkemia caused by *Aerococcus viridans*. 2. For the control of mortality in freshwater-reared salmonids due to cold water disease associated with *Flavobacterium psychrophilum*. 3. For the control of mortality in freshwater-reared *Oncorhynchus mykiss* due to columnaris associated with *Flavobacterium columnare*.	2.50-3.75 g/100 lb fish
Florfenicol (Aquaflor®)	1. For the control of mortality in catfish due to enteric septicemia of catfish associated with *Edwardsiella ictaluri*. 2. For the control of mortality in freshwater-reared salmonids due to cold water disease associated with *Flavobacterium psychrophilum*. 3. For the control of mortality in freshwater-reared salmonids due to furunculosis associated with *Aeromonas salmonicida*. 4. For the control of mortality due to columnaris disease associated with *Flavobacterium columnare* in freshwater-reared finfish and for the control of mortality due to streptococcal septicemia associated with *Streptococcus iniae* in freshwater-reared warmwater finfish.	Medicated Feeds (10 mg/kg fish/day for 10 days)
Sulfadimethoxine/ormetoprim (Romet-30 ®)	1. For the control of furunculosis in salmonids (trout and salmon) caused by *Aeromonas salmonicida*. 2. For the control of bacterial infections in catfish caused by *Edwardsiella ictaluri* (enteric septicemia of catfish).	Medicated feeds (50 mg/kg fish BW for 5 days consecutively)
Sulfamerazine fish grade	Not currently marketed	NA

Antimicrobial-resistant pathogens in aquaculture

Antimicrobial resistance was present in 11,274 numbers of different bacterial isolates from aquatic raised animals and the aquacultural environment (a total of 130,426 antimicrobial resistance patterns to individual antibiotics) (Reverter *et al.*, 2020). An important aspect to highlight that, Instead of best efforts in gathering a global database regarding AMR, aquaculture-derived MAR indices might be limited by the unclear report of AMR among different countries. Twenty-eight countries out of the40 studied displayed MAR indices higher than 0.2, a threshold considered to be an indication of high-risk antibiotic contamination (Krumperman, 1983) [24].

The list below indicates the AMR pathogens that are associated with the common diseases in Indian aquaculture condition:

Diseases in aquaculture	AMR pathogen isolated
Fish	
1. MAS (Motile *Aeromonas* Septicemia)	*Aeromonas* spp.
2. Dropsy	*Aeromonas* spp., *Pseudomonas* spp.
3. Columnaris	*Flavobacterium columnare*
4. Bacterial Gill Disease	*Flavobacterium branchiophilum,*
5. Vibriosis	*Vibrio anguillarum, V. parahaemolyticus*
6. Eye disease	*Aeromonas* spp., *Staphylococcus* spp.
7. Red mouth	*Yersinia ruckeri*
8. Piscine tuberculosis	*Mycobacterium* spp.
9. Edwardsiellosis	*Edwardsiella tarda*
10. Enteric septicemia of catfish	*Edwardsiella ictaluri*
Shrimp	
1. Vibriosis	*Vibrio anguillarum, V. parahaemolyticus, V. harveyi*
2. Brown spot/Blackspot shell disease	*Pseudomonas* spp., *Aeromonas* spp.

(**Source:** Sorum, 2006; Watts *et al.*, 2017; Miller and Harbottle, 2018) [56]

Common antibiotics that are used by Indian fish-farmer communities

Antibiotics	Approved/banned
1. chloramphenicol	Banned
2. ciprofloxacin	Banned
3. Oxytetracycline	Approved
4. Furazolidone	Banned
5. Streptomycin/Neomycin	Banned
6. Erythromycin	Banned
7. Sulfanomides	Approved
8. Trimethoprim	Banned but can be used in mixture with sulfanomides

(**Source:** Watts *et al.*, 2017; Sorum, 2006) [56]

The perspective of farmers towards the use of antibiotics in aquaculture

1. Most farmers are poor and cannot afford the proper biosecurity measures required for proper prophylaxis.
2. About 80% of the seed stocks are being brought from different states and most of the time antibiotics are being applied to reduce mortality rates during transportation.
3. Most antibiotic use is not being supervised properly by trained government personnel and their usage is based generally on previous experience by farmers.
4. Inspection by MPEDA is generally restricted towards species meant for exports and not for those which are traveling to retail markets nationwide.
5. Although surveys occur nationwide enquiring about antibiotic usage, farmers feel unsafe to expose the correct numbers and names in fear of fines being imposed by the government.

Key steps in the regulation of AMR in India

Year, action was taken	Implementation details
2011	Adoption of the “Jaipur Declaration on Antimicrobial Resistance” by India’s health minister along with the health ministers of all member states of the WHO South-East Asia Region. They agreed to, among other things, institute measures to combat AMR, develop national antibiotic policy, regulate use of antimicrobial agents, promote behavioural change in prescribers and communities, build capacity for efficient surveillance of AMR, and strengthen diagnostic facilities.
2012	The “National Programme on Containment of Antimicrobial Resistance” was launched under the 12th five-year plan (2012–2017). AMR surveillance work started in 10 laboratories. A few guidelines were developed (national treatment guidelines for antimicrobial use, guideline on infection control). A national Infection control policy is being finalized. An International Conference on AMR was organized in February 2016.
2016	A workshop “Combating Antimicrobial Resistance: A Public Health Challenge and Priority” was jointly organized by the Government of India and the WHO. The “Medicines with the Red Line” media campaign was launched.
2017	The national network of veterinary laboratories for antimicrobial resistance (AMR) was established (the Indian Network for Fishery and Animals Antimicrobial Resistance (INFAAR)) http://www.fao.org/india/news/detail-events/en/c/853974/
2017	A national action plan on AMR was adopted.
2017	Antibiotic Residue limits in meat were released by the Food Safety and Standards Authority of India (FSSAI)
2018	Kerala adopted the sub-national State Action Plan https://www.reactgroup.org/news-and-views/news-and-opinions/year-2018/keralaindia-launch-of-the-1st-sub-national-action-plan-on-amr/
2019	Kerala adopted the sub national State Action Plan https://www.reactgroup.org/news-and-views/news-and-opinions/year-2018/keralaindia- launch-of-the-1st-sub-national-action-plan-on-amr/

Source: Mutua *et al*., 2020, Antimicrobial Resistance and Infection Control

Conclusion

Farmers who are involved in both finfish and shellfish aquaculture have been made to understand ten basic points for safer antibiotic-smart aquaculture. Antibiotic resistance will not be eliminated so easily as the huge scale use of antibiotics has already piled up a large number of AMR pathogens in the aquatic environment. However, we can be antibiotic-smart and prevent the risks of AMR if we follow the points mentioned below:

1. Antibiotics should be used only after contacting government-trained personnel.
2. Antibiotics should not be used as a growth promoter.
3. Antibiotics should not be used to prevent diseases, it should be used only as a means of treatment for diseased species only when necessary.
4. Every antibiotic has its withdrawal period and should be maintained strictly.
5. The feed should be antibiotic-free until and unless required and told by government personnel.
6. The farm should be clean and free of surrounding waste disposal in the cultured environment.
7. Any waste generated within the farm should not be disposed of in the cultured area.
8. Accurate labeling should be made of all the products which have antibiotics in them.
9. Never procure antibiotics without prescription or before contacting any trained government personnel.
10. All the farmers should know what diseases they can be infected from the pathogens in the aquaculture environment and the risks of AMR pathogens.

Although, most farmers in India are uneducated and cannot understand the meaning of AMR and the risks it thrives, a lot of projects have been set up by different authorities to make the farmers understand and make them antibiotic-smart. Antibiotic resistance will not be removed completely in a few months or years to come, rather we can decrease the consequences of AMR by using them judiciously and safely. The “One-Health” strategy by WHO also targets the problems of AMR in aquaculture and also focusing on how it can be successfully reduced. Alternatives like probiotics, vitamin-mineral mixtures, herbs have become popular in recent days as the major havoc the AMR has been dealing with. Proper vaccination (restricted to some species only) is also an excellent way to reduce antibiotic usage. India being the hub of carp aquaculture, needs more monitoring and surveying to check the antibiotic usage as problems like huge population, massive areas under culture, and darkness of education, most farmers reside in. It is noteworthy that the health of aquacultured species and humans are interlinked.

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