Antimicrobial resistance and its containment in Kerala

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Contents

ABBREVIATIONS

ABR	Antibiotic resistance
ADDL	Avian Disease Diagnostic Laboratory
AMR	Antimicrobial Resistance
ASP	Antibiotic Stewardship Program
BMP	Better Management Practice
BSI	Blood Stream Infection
CAUTI	Catheter Associated Urinary Tract Infection
CDIO	Chief Disease Investigation Office
CLABSI	Central Line Associated Blood Stream Infection
CLSI	Clinical Laboratory Standards Institute
CSO	Civil Society Organization
DIO	Disease Investigation Officer Laboratory
DVC	District Veterinary Centre
ESBL	Extended Spectrum β-lactamase
GAP-AMR	Global Plan on Antimicrobial Resistance
GMC	Government Medical College
GVP	Good Pharmacovigilance Practice
HAI	Healthcare Associated Infection
HICC	Hospital Infection Control Committee
KSPCB	Kerala State Pollution Control Board
MDG	Millennium Development Goal
MSF	Médecins Sans Frontières
NAP-AMR	National Action Plan on Antimicrobial Resistance
NCDC	National Centre for Disease Control
NSQ	Not of Standard Quality
OTC	Over The Counter
RDDL	Regional Disease Diagnostic Laboratories
RGCB	Rajiv Gandhi Centre for Biotechnology
RP	Rinder Pest Eradication Laboratory
RTI	Respiratory Tract Infection
SAP-AMR	State Action Plan on AMR

SDG	Sustainable Development Goal
SLMAP	State Laboratory for Livestock, Marine and Agriculture Products
SSI	Surgical Site Infection
SSTI	Skin and Soft Tissue Infection
STP	Sewage Treatment Plant
UTI	Urinary Tract Infection
VAP	Ventilator Associated Pneumonia
WAAW	World Antibiotic Awareness Week
WHO	World Health Organization

EXECUTIVE SUMMARY

Antimicrobial Resistance (AMR) is a global public health problem. There are many drivers of antibiotic resistance, the most dangerous trend amongst AMR, which include inappropriate use of antibiotics in humans; antibiotic use for growth promotion and disease prevention in animals, horticulture and fisheries; use of animal manure in soil; inadequate treatment of effluents from healthcare facilities and farms, etc.

The Government of Kerala is committed to take suitable action to address antimicrobial resistance in the state involving all stakeholders to develop and implement a State Action Plan on AMR, aligned with the National and Global Action Plan on Antimicrobial Resistance (NAP-AMR) for AMR containment. Inter-sectoral collaboration and a One Health Approach are crucial and integrated in the government's approach.

Creating awareness on AMR among cross sectoral stakeholders is important for AMR containment. Awareness classes are held at all government medical colleges in Kerala for faculty and students. The focus of these classes is to emphasize the importance of rational antibiotic use, infection control practices and need to follow institutional antibiotic policy.

Strengthening laboratory capacity and AMR surveillance systems are also essential for assessing baseline AMR burden and providing evidence based information for action. Kerala has initiated AMR surveillance programme in government hospitals. Since food of animal origin also represents the major route of human exposure to foodborne pathogens, AMR surveillance in animals is as critical as it is in human health, which is also done in three laboratories of the Animal Husbandry Department in the state.

Currently, all Government Medical Colleges (GMC) in Kerala and the General Hospital Ernakulam conduct surveillance of infections of public health importance namely blood stream infection (BSI), skin and soft tissue infection (SSTI), respiratory tract infection (RTI), and urinary tract infection (UTI) as well as tracks six pathogens of public health importance (*Acinetobacter* spp., *E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterococcus* spp.). As a part of next steps, Health Department plans to expand its AMR surveillance to district level in order to get more community data, and conduct a community based study.

Application of good Infection Prevention Control (IPC) measures across human health, animal health and agriculture also helps to prevent infections and limit use of antibiotics. Steps are taken to tackle AMR at

all government medical colleges in Kerala and include scaling up of infection control program to prevent spread of antibiotic resistant organisms. Application of good IPC measures to animal husbandry is important to reduce antimicrobial residues in environment. Kerala State Pollution Control Board recommends adherence to good farm management practices for infection control among flock, issuance of improved biosecurity guidelines by Central Poultry Development Organisation for farm implementation and promotion of antibiotic alternatives (such as vaccination).

Kerala is considered as a consumer state for pharmaceuticals with a total consumption of drugs in the state at around 20,000 crores per annum, with antibiotics making up 20% of the total drugs consumed annually in the state. Poultry farmers in Kerala also use a variety of antibiotics either as growth promoters or for controlling infections. Many prescription medications used for human and animal health ultimately find their way into the environment and can affect the health and behaviour of wildlife. Drugs Control Department has a very significant role to play by way of regulatory action for optimization in use of antibiotics and taking action towards prevention of their 'over-the-counter' (OTC) sale. GMC Thiruvananthapuram has also initiated Antibiotic Stewardship Program (ASP) to ensure the right drug gets prescribed at the right time, in the right dose, for right duration and for the right patient, at all government medical colleges in Kerala.

The importance of research and innovations cannot be over emphasized. As the world is running out of effective antibiotics to fight even simple infections, alternate strategies and new molecules need to be discovered at the earliest. Research is also underway to establish the role of phytochemicals and natural antimicrobial substances as a means to fight antibacterial resistance. Rajiv Gandhi Centre for Biotechnology (RGCB), Trivandrum, Kerala (www.rgcb.res.in), a premier national research institute, is exclusively devoted to research in molecular biology and biotechnology.

Various challenges in development and implementation of Kerala State Action Plan on AMR may include human resources, role of anthropogenic activities in contaminating the natural water bodies, OTC sale of antibiotics, absence of antibiotic residue control program, and traceability problems with food of animal origin. However, despite these challenges the Government of Kerala is extremely committed and supportive of activities and proposals of all relevant stakeholders. Besides, strong collaborations and commitment of stakeholders across human health, animal health, food/agriculture and environment gives a positive direction to success ahead.

BACKGROUND

Introduction

Antimicrobial Resistance (AMR) is the ability of micro-organisms (bacteria, viruses, parasites, fungi) to resist the effect of antimicrobial drugs. AMR, including antibiotic resistance (ABR or drug resistance in bacteria), is the most urgent drug resistance trend and one of the biggest threats to global health, food security and development today.

AMR burden

Estimates have revealed that AMR killed 700,000 people worldwide in 2014 and is predicted to target 10 Million for 2050 (1). Low-middle income countries are most affected owing to high burden of infections and weak public health systems. The need of the hour is to intervene in a timely manner and prevent vulnerability to gains achieved by the Millennium Development Goals (MDGs).

Antibiotic consumption

Globally over 63, 000 tonnes of antibiotics were globally used in livestock in 2010, with 3% of consumption occurring in India (2). India is ranked among the first five countries with a high antibiotic consumption in livestock. Oxytetracycline is a USFDA approved antibiotic and is widely used drug in aquaculture. It has a withdrawal period of six to ten days in various organs of *Penaeus vannamei* at a temperature of 28°C and like other tetracyclines gets excreted by glomerular filtration.

Kerala is considered as a consumer state for pharmaceuticals with a total consumption of drugs in the state at around 20,000 crores per annum, and antibiotics making up 20% of the total drugs consumed annually in the state. According to the National Drug Survey, 10% drugs from government sources and 2% drugs from retail outlets are Not of Standard Quality' (NSQ).

Drivers of AMR

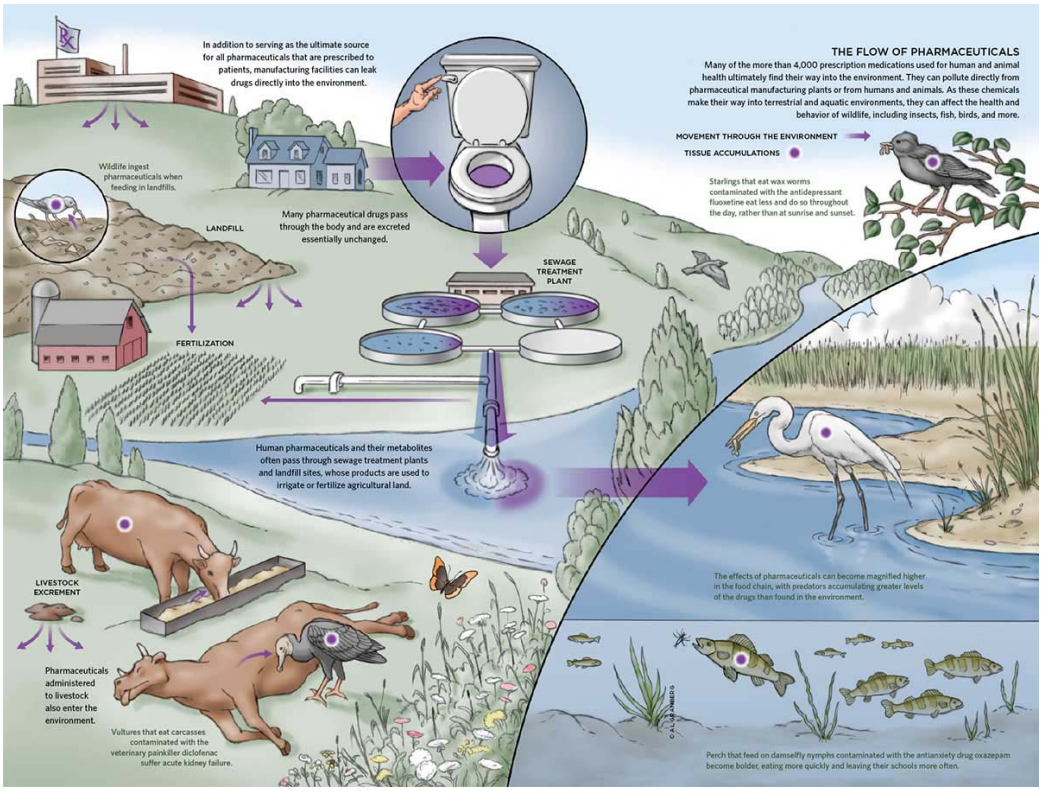
Evolution of resistant strains is a natural phenomenon and resistant traits can be genetically exchanged through generations of bacteria; however, overuse/misuse of antibiotics accelerates this problem.

Major drivers of antibiotic resistance include inappropriate use of antibiotics in human; antibiotic use for growth promotion and disease prevention in animals and horticulture; and use of animal manure in soil. Poultry farmers in Kerala use a variety of antibiotics either as growth promoters or for controlling infections. Most farmers are unaware of withdrawal periods of antibiotics (commonly 7-10 days) and adverse effect of antibiotic residues in products. Many of these drugs are administered without any

consultation with veterinarians. The use of animal manure increases the soil content of antibiotic resistant genes (3).

India stands second after China in aquaculture production – 4.88 million metric tonnes (2014 data) and exported 9.8 million metric tonnes earning 30,213 crore as foreign exchange (FAO, 2016). Kerala contributes 14% of the total marine product exported from the country and exported 159,141 metric tonnes of sea foods valued at Rs.5008.54 crores in 2016. Aquaculture is a source of food production (animal protein), and plays an important role for economy and livelihood in Kerala. Drugs fed to fishes are metabolised in liver/hepato-pancreas, or excreted as it is, either through kidney or faecal matter. Environmental temperature and salinity of the water also affects the accumulation of antibiotics in marine life.

Waste containing non-metabolised antibiotic residues, along with organic matter creates conditions conducive for proliferation of drug-resistant bacteria in sewage treatment plants (STPs). In most of the developing countries including India, more than 70 percent of the urban sewerage does not pass through treatment plants suggesting the role of anthropogenic activities in contaminating the natural water bodies with antibiotic residues and antibiotic resistant microbes. Additionally, over the counter sale of antibiotic is a common practice in India which is complicating the process of regulating the medical use of antibiotics.



The flow of antibiotics (4)

Consequences

Various sources for antibiotics in water bodies can be hospitals, households, municipal sewage treatment plants, animal farms, land application of animal wastes and slaughter houses. Antibiotics can also pollute directly from pharmaceutical manufacturing plants. Many of the more than 4,000 prescription medications used for human and animal health ultimately find their way into the environment. As these chemicals make their way into terrestrial and aquatic environments, they can affect the health and behaviour of wildlife, including insects, fish, birds, and more (3).

Scientists around the world have provided strong evidence that antibiotic use in food producing animals can harm public health as it allows antibiotic resistant bacteria to thrive while susceptible bacteria are suppressed or die. Resistant bacteria can be transmitted from food producing animals to humans through the food supply and cause infections in humans. Infections caused by resistant bacteria can result in adverse health consequences in man. Use of antibiotics and chemotherapeutics also has a negative impact in marine life including immunosuppression, drug resistance as well as bioaccumulation in tissues and environment. Other effects of antibiotics on environment include rapid spread of resistant bacteria and deterioration in environment quality.

AMR impacts progress towards achieving various Sustainable Development Goals (SDGs) as can be seen below:

- Rate of AMR is high in the poor owing to poor affordability of drugs and poor infection control practices (SDG 1: No Poverty)
- Untreatable infections in animals threaten food production and safety (SDG 2: Zero Hunger)
- Medications and antimicrobial use is a core component of health systems (SDG 3: Good Health and Well-Being)
- Antibiotic residues (hospital, pharma & agriculture) contaminate water/environment (SDG 6: Clean Water and Sanitation)
- According to World Bank simulations on high-AMR scenario, an economic cost of $ 120 Trillion is projected by 2050 to attain decent work and economic growth (SDG 8: Decent Work and Economic Growth)
- It is important to balance access, innovation and conservation of antimicrobials (SDG 12: Responsible Consumption and Production)
- Restricting antimicrobial usage requires a multi-stakeholder partnership (SDG 17: Partnerships For The Goals)

Global and national efforts

Improved management of the use of antimicrobials in food animals, particularly reducing those critically important for human medicine, is an important step towards preserving the benefits of antimicrobials for people. Since 2005, WHO has produced a regularly updated list of all antimicrobials currently used for human medicine (mostly also used in veterinary medicine), grouped into 3 categories based on their

importance to human medicine. The list is intended to assist in managing antimicrobial resistance, ensuring that all antimicrobials, especially critically important antimicrobials, are used prudently both in human and veterinary medicine. Currently, 5th revision is the most recent version (5).

The World Health Organization (WHO) developed and endorsed the Global Action Plan on AMR (GAP-AMR) in 2015. Five strategic priorities included in the GAP-AMR are as follows:

1. Improve awareness and understanding of AMR through effective communication, education and training
2. Strengthen knowledge and evidence through surveillance
3. Reduce the incidence of infection through effective infection prevention and control
4. Optimize the use of antimicrobial agents in health, animals and food
5. Promote investments for AMR activities, research and innovations.

India's National Plan on Antimicrobial Resistance (NAP-AMR) has been developed on similar lines as the GAP-AMR and with inclusion of a sixth strategic priority on commitment and collaborations. The six strategic priorities of NAP-AMR and the corresponding focus areas are listed as follows:

1. Improve awareness and understanding of AMR through effective communication, education and training
    a. Communication, IEC resources – to raise awareness amongst all stakeholders, including policy makers, general public and farmers
    b. Education and training – to improve the knowledge and behaviour of professionals
2. Strengthen knowledge and evidence through surveillance
    a. Strengthen laboratories – in human, animal, food and environment sectors – for evidence-informed policy-making
    b. Surveillance of antimicrobial resistance – in human, animal/food and environment sectors – for evidence-informed policy-making
3. Reduce the incidence of infection through effective infection prevention and control
    a. Healthcare – to reduce the burden of infection
    b. Animal health/food – to reduce spread of AMR and antimicrobials through animals and food
    c. Community and community environment – to reduce the spread of AMR and antimicrobials in the community and environment
4. Optimize the use of antimicrobial agents in health, animals and food
    a. Regulations, access and surveillance of antimicrobial use – to ensure rational use without affecting access to antimicrobials
    b. Antimicrobial stewardship in healthcare – to optimise use of antimicrobials in humans
    c. Animal health, agriculture – to optimise use of antimicrobials in animal and food sectors

5. Promote investments for AMR activities, research and innovations
    a. New medicines and diagnostics – to ensure availability of effective diagnostics and drugs to treat infections
    b. Innovations – to develop alternative approaches to manage infectious diseases
    c. Financing – to ensure sustainable resources for containment of AMR
6. Strengthen India's leadership on AMR
    a. International collaborations – to ensure India's contributions towards global efforts to contain AMR
    b. National collaborations – to facilitate collaborations among vertical disease control programmes and national stakeholders
    c. State level collaborations – to ensure action at the ground level against AMR

Global and national campaigns to create AMR awareness include the 'World Antibiotic Awareness Week (WAAW)' in November and the Global 'Hand Hygiene' Day in May every year. The theme for WAAW in 2017 is '*Seek advice from a qualified healthcare professional before taking antibiotics*'.

Similar to the alignment of NAP-AMR to GAP-AMR, State Action Plan on AMR (SAP-AMR) should also align with NAP-AMR. However, it is imperative to simultaneously reflect the local situation, priorities and needs; and take cognizance of local structures, capacity and constraints. It is critical to have an inter-sectoral collaboration, prioritise actions, build on existing activities/success stories, foster individual behaviour change and continually monitor progress towards a successful program implementation.

AWARENESS AND UNDERSTANDING OF AMR

It is important to create awareness on AMR among cross sectoral stakeholders as well as improve their understanding on AMR prevention and control measures.

Human health

To improve the understanding on AMR in human health, awareness classes are held at all government medical colleges in Kerala for faculty and students. The focus of these classes is to emphasize the importance of rational antibiotic use, infection control practices and need to follow institutional antibiotic policy. State Drug Control Department also suggests conducting classes for pharmacists and various awareness programmes for pharmaceutical distributors regarding sale of antibiotics and the complications following its overuse.

Animal/food sector

Scientists around the world have provided strong evidence that antibiotic use in food producing animals can harm public health. Most farmers are unaware of withdrawal periods of antibiotics (commonly 7-10 days) and adverse effect of antibiotic residues in products. Many of these drugs are administered without any consultation with veterinarians.

To improve the understanding on AMR and its control in animals and agriculture, Department of Animal Husbandry, Dairy and Fisheries has played an active role. According to an Advisory issued by Department of Animal Husbandry Dairy and Fisheries, Government of India (2014), farmers, para-veterinarians and poultry entrepreneurs must be educated on the use of antibiotics; ill effects of indiscriminate use; and withdrawal period. The Department has proposed conducting awareness training for all veterinary surgeons on AMR issues, with a minimum of one program in every district.

Department of Fisheries, Government of Kerala also conducts training programmes to enhance farmers' awareness on Better Management Practices (BMPs) and on responsible use of drugs/chemicals in aquaculture. They also conduct awareness campaigns for instilling the need to follow good aquaculture practices and responsible and prudent use of safe veterinary drugs. Besides, demonstration farms have also been introduced to farmers, which successfully showcase effective production through improved BMPs, devoid of antimicrobials.

Environment sector

Many of the more than 4,000 prescription medications used for human and animal health ultimately find their way into the environment. As these chemicals make their way into terrestrial and aquatic environments, they can affect the health and behaviour of wildlife, including insects, fish, birds, and more (4).-

Kerala State Pollution Control Board (KSPCB) recommends training on judicious use of antibiotics in food animal production to reduce spread of antibiotic resistance from farms.

Role of civil society organizations (CSOs)

ReAct, a civil society organization, is one of the first international independent networks to articulate the complex nature of antibiotic resistance and its drivers. ReAct started off its action in Kerala in early 2017 with an aim to engage all sectors and everyone from the public sector to civil society. The focus for 2017 has been on engaging and sensitizing stakeholders across health, agriculture, environment, economic and development sectors, by way of workshops, personal interactions and booths. The Asia-Pacific node of ReAct is at CMC Vellore, India.

Two workshops have been conducted by ReAct towards engaging cross sectoral stakeholders and create awareness on AMR in 2017. Other proposed activities by ReAct are workshops targeting grass-root CSOs and media, antibiotic stewardship in secondary level hospitals, piloting collaborative network with universities and other educational institutions, developing a framework for 'Antibiotic-Smart' communities and map challenges in implementation, globalizing campaign for antibiotic safe procurement practices for quick service restaurants (like KFC) as well as initiating conversation for a State Action Plan on AMR.

Kerala has a strong network of Panchayat Raj institutions who take an active interest in public health. Involving them in AMR activities would reap high dividends especially in raising awareness in the community in rational use of antibiotics.

LABORATORIES AND SURVEILLANCE

AMR surveillance is essential for assessing the AMR burden and for providing the information for action in support of local, national & global strategies. Kerala has initiated AMR Surveillance Program in government hospitals. Food of animal origin also represents the major route of human exposure to foodborne pathogens. AMR surveillance and monitoring of drug resistant infections in animals is critical for control of AMR, and the Animal Husbandry department has initiated activities for detection of AMR. It is necessary to collect the data systematically and aggregate the data to yield estimates of AMR over time across the sectors.

Human health

Under the 'National Program on Containment of AMR' with NCDC as a national focal point, the current National AMR surveillance network includes 10 laboratories and five more are proposed for inclusion in 2017-18. Government Medical College (GMC) Thiruvananthapuram, has been identified as one of the proposed laboratories, and has signed a memorandum of understanding with National Centre for Disease Control (NCDC). As part of the National AMR surveillance network, GMC Thiruvananthapuram will feed its laboratory results & clinical information using the latest version of WHONET and prepare antibiograms in accordance to the Clinical Laboratory Standards Institute guidelines (CLSI). This would help to monitor resistance trends, reveal emergence of potential novel resistance and aid clinicians in empiric treatment of infections. The laboratory would also share its internal quality control records for AST, send 1% of bacterial isolates on quarterly basis to NCDC for external quality control testing, conduct molecular characterization of vancomycin, carbapenem & colistin resistant isolates, share HAIs surveillance data, share antimicrobial usage data of the hospital and preserve isolates for future need.

Currently, based on 'National Policy for Control of AMR 2011' & 'NAP-AMR 2017-21', GMC Thiruvananthapuram conducts surveillance for infections of public health importance namely blood stream infection (BSI), skin and soft tissue infection (SSTI), respiratory tract infection (RTI), and urinary tract infection (UTI) as well as tracks six pathogens of public health importance (*Acinetobacter* spp., *E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterococcus* spp.). The participating institutions included in the surveillance initiative include:

- Government Medical College Thiruvananthapuram (coordinator)
- Government Medical College Kozhikode
- Government Medical College Thrissur
- Government Medical College Kottayam
- Government Medical College Alappuzha
- Government Medical College Ernakulum

- Government Medical College Manjeri
- State Public Health Lab
- Government Hospital Ernakulum

GMC Thiruvananthapuram conducted a microbiological study on samples collected from the seven government colleges/ hospitals during Jan 2017-Aug 2017. The most frequent infection of public health importance identified was SSTI (4913), followed by UTI (2704), BSI (1579) & RTI (1482). A total of 10,628 isolates were identified, out of which ESBL production and carbapenem resistance was found in *E. coli* (59.5%, 22.8% respectively), *Klebsiella* spp. (51.3%, 31.5% respectively), *Pseudomonas aeruginosa* (52.5%, 39.35% respectively) and *Acinetobacter* spp. (49.3%, 43.7% respectively). At a national level, ESBL production and carbapenem resistance has been reported in *E. coli* (61%, 11.5% respectively), *Klebsiella* spp. (51%, 51% respectively), *Pseudomonas aeruginosa* (65%, 42% respectively) and *Acinetobacter* spp. (60%, 69.6% respectively). Colistin resistance was reported in *E. coli* (3.1%) and *Klebsiella* spp. (3.2%). In addition, the analysis also reported 44.1% strains of *Staphylococcus aureus* as methicillin resistant while no strain of *Enterococcus* spp. was vancomycin resistant. At a national level, 47% strains of *Staphylococcus aureus* are reported as methicillin resistant while 12% of *Enterococcus* spp. were vancomycin resistant.

As a part of next steps, GMC Thiruvananthapuram plans to expand its AMR surveillance to district level in order to get more community data, and conduct a community based study (already been approved for health services institutions by State Public Health Lab), in partnership with Rajiv Gandhi Centre. Surveillance system would be developed in stages and incorporate a 'One Heath' approach (currently the surveillance is limited to human health) in order to strengthen AMR surveillance across animals, food & environment.

Clinical isolates studied at Rajiv Gandhi Centre for Biotechnology (RGCB), Trivandrum, Kerala, have consistently shown resistance to cotrimoxazole, trimethoprim, nalidixic acid and streptomycin. Majority (~70%) of the strains demonstrated an intermediate resistance to ampicillin and erythromycin. In another study conducted at RGCB, out of 109 clinical strains of *Acinetobacter* spp., a majority were resistant to penicillin (95.4%), ceftriaxone (94.5%), ceftazidime (94.5%), cefepime (87.2%), gentamicin (86.3%) and tetracycline (81.6%). RGCB in association with Department of Surgery, MCH, Trivandrum conducted resistance profiling of predominant bacterial isolates from chronic diabetic ulcer patients (2014-15) and most isolates of *Pseudomonas* sp., *Proteus* sp., *Enterococcus* sp. and *Staphylococcus* sp., were found to be multi drug resistant. Yet another study conducted in association with SK Hospital, Trivandrum on antibiogram profiling of *Lactobacillus* sp. isolated from infant faeces, showed intrinsic bacterial resistance to vancomycin and metronidazole.

Animal/food sector

Food of animal origin represents the major route of human exposure to foodborne pathogens. AMR surveillance and monitoring of ABR infections in animals is critical for control of AMR.

Laboratory testing methodology for identification of bacterial pathogens in food and food animals includes:

- Bacterial culture and isolate identification
- Characterization of isolates
- Standardized antimicrobial susceptibility testing
- Quality control
- Recommended antimicrobials for surveillance

The Animal Husbandry Department of Kerala is actively involved towards control of AMR in the state. Under the 'Antibiotic Residue Monitoring Programme in Kerala' being implemented by State Laboratory for livestock, marine and agriculture products, major groups of antibiotics covered include those belonging to tetracycline, fluroquinolone and sulphonamide groups. According to a State Laboratory Ernakulum report on antibiotic residue monitoring conducted between April –Sep 2017, of 53 farm samples (broiler poultry from animal farms) tested, resistance was seen in sulphonamide group (12 samples), tetracycline group (8 samples), and fluoroquinolone group (1 sample). Sulphonamides, tetracyclines and fluoroquinolones are commonly used as feed additives or as therapeutics in broiler poultry production. In another study, antibiotic sensitivity testing conducted on 108 samples at Avian Disease Diagnosis Lab Thiruvilla, showed resistance to newer antibiotics like cephalosporins and enrofloxacin.

Currently, 'One Health' approach to AMR surveillance is not established in Kerala. Limited data is available on prevalence of AMR among bacteria associated with livestock & food of animal origin in Kerala. Comprehensive and current information on resistance among these bacteria is required to guide policy decisions as AMR is a global public health priority.

To provide data for estimation of prevalence of AMR bacteria in food and food animals AMR, an integrated veterinary surveillance programme for Kerala has been proposed. The aim of such a program is to develop strategies to keep clinically relevant veterinary resistance to a minimum, with an understanding that antibiotic surveillance has the potential to play a role as a clinical tool which will help farmers and veterinarians to implement best practice and responsible use of antibiotics. The data generated from the programme can be compared with data from international AMR surveys. Apart from surveillance of antimicrobial resistance, the programme also aims at surveillance of antimicrobial use.

Laboratory testing methodology for the surveillance programme includes bacterial culture, isolate identification, standardized antimicrobial susceptibility testing, quality control, use of recommended antimicrobials for surveillance and isolate characterization. AMR data from veterinary sector and fisheries can also be fed into WHONET, and could be consolidated at the state level.

Although samples from both healthy animals and sick animals are useful for surveillance, samples from healthy animals should be the primary focus for surveillance because such samples can provide an unbiased measure of antimicrobial resistance in source animals for the human food supply. The selection of foods for surveillance (beef, chicken, fish, milk, pork, etc.) should reflect consumption patterns in the state and the likely prevalence of antimicrobial resistance. Retail food is a priority specimen and must be included in a programme of integrated surveillance of antimicrobial resistance in foodborne bacteria. Four common retail foods; poultry, beef, fish, milk and one clinical sample (mastitis milk) along with four target organisms (*Salmonella*, *E. coli*, *Staph. aureus* and *Vibrio* spp.) constitute the 10 sample / bacterium combinations which are included in the survey to provide patterns of resistance.

Worldwide, Salmonella is usually the first priority for inclusion in the integrated surveillance programme (6). Since *E. coli* are also common and some strain variants may cause disease, it can be used as a sentinel organism for antimicrobial resistance. In addition to the major pathogens mentioned above, other bacteria (e.g. Staphylococcus) may be relevant, including those associated with aquaculture (e.g. Vibrio).

According to a study done by College of Veterinary and Animal Sciences (Mannuthy, Thrissur), a higher percentage of gram positive bacteria with resistance to quinolones, cephalosporins and tetracyclines was found in animal milk samples obtained in 2017 than in samples of 2008. More number of gram negative bacteria isolated from animal milk and pus samples in 2017 showed resistance to quinolones than gram negative isolated from same samples in the prior years.

A comprehensive residue control programme is missing, and because antibiotic residues cannot be destroyed once they enter food, suitable control plans are necessary. Also, control plans are usually difficult to implement due to inadequate traceability and lack of suitable laboratory support.

Although Kerala has a system of some traceability for milk samples, it lacks traceability with food of animal origin, thereby making it difficult to trace back the animal product to its farm of origin. Besides, a higher demand for fresh food in the State (by the time official sampling and analysis is completed, the food might have already been consumed) and high dependency on neighbouring states for beef and broiler, poses a major challenge to sample traceability.

Laboratory and surveillance based recommendations by Animal Husbandry Department, Government of Kerala to control AMR in livestock sector & food of animal origin are as follows:

- Antibiotic Sensitivity Testing facilities to be available at
    - Apex lab: Chief Disease Investigation Office (CDIO), Palode
    - Regional Disease Diagnostic Laboratories (RDDL)
        - Avian Disease Diagnostic Laboratory (ADDL), Thiruvalla
        - Rinder Pest Eradication (RP) Lab, Palakkad
        - Disease Investigation Officer (DIO) Lab, Kannur
    - State Laboratory for Livestock, Marine and Agriculture Products (SLMAP)
    - District Veterinary Centres (DVC) Laboratories
    - Strengthening of CDIO, ADDL, RP, SLMAP (foods) and district labs where necessary
- AST rapid kits for mastitis testing produced by Institute of Animal Health and Veterinary Biologicals to be distributed free of cost to field level hospitals; annual production of 5000 kits per year to be achieved
- The existing surveillance on antibiotics residues in broilers will be extended to cover other districts.

Department of Fisheries also collects samples of feed for culture and drug residue testing (at approved institutions). Besides, it checks all records for type of chemicals used, source, quantity and withdrawal period.

Environment sector

According to the first ever made report from any water body in Kerala, multiple antibiotic resistant *E. coli* expressing extended spectrum β-lactamase (ESBL) were found in Sasthamcotta lake. The study conducted by Post Graduate and Research Department of Chemistry and Polymer Chemistry, reported resistance to ampicillin, ceftazidime and gentamicin in 37%, 5% and 5% isolates of *E. coli* respectively. Although resistance pattern reported from environmental isolates has been variable, emergence of MDR in environmental strains has been a major concern.

RGCB has reported multidrug resistance phenotypes in majority of environmental isolates of *Vibrio cholera* (non-O1/non-O139) obtained from waters in South India, with some strains showing resistance to all major anti-cholera drugs. According to the drug resistance analysis, integrons, superintegrons and SXT (conjugative transposon) have a role in conferring drug resistance (7).

KSPCB also recommends antibiotic resistance (ABR) surveillance by CPCB and SPCBs.

INFECTION PREVENTION AND CONTROL

Health-care-associated infections (HAIs) are important patient safety issues in health care today. HAIs that are typically studied using standardized definitions include surgical site infections (SSI), central line-associated blood stream infections (CLABSI), ventilator-associated pneumonia (VAP) and catheter-associated urinary tract infections (CA-UTI). HAIs results in excessive use of antibiotics as well as chances of emerging drug resistance. Use of antibiotics in food producing animals also leads to emergence of antibiotic resistant bacteria. Application of good Infection Prevention Control (IPC) measures across human health, animal health and agriculture helps to prevent infections and limits use of antibiotics. It also helps to reduce antimicrobial residues in environment.

Human health

Steps are taken to tackle AMR at all government medical colleges in Kerala and include scaling up of infection control program to prevent spread of antibiotic resistant organisms, Hospital Infection Control Committee (HICC) meeting once in 2 months to ensure implementation of hand hygiene compliance and step up of hospital cleanliness at all government medical colleges.

A study was conducted to determine the impact of modular training and implementation of infection control practices on all health-care-associated infections (HAIs) in a cardiac surgery (CVTS) program of a tertiary care hospital in Kerala (8). Study outcomes showed that standardization of infection control training and practices is the most cost-effective way to reduce HCAIs and related adverse outcomes. The SSI rate had decreased in the post-intervention phase from 46 to 3.27% per 100 surgeries ($P < 0.0001$), CLABSI had decreased from 44 to 3.10% per 1000 catheter days ($P < 0.009$), VAP was reduced from 65 to 4.8% per 1000 ventilator days ($P < 0.0001$) and CA-UTI had reduced from 37 to 3.48% per 1000 urinary catheter days ($P < 1.0$). Investment of $1 results in $236 as a return of investment.

Amrita Institute Kochi recommends development and implementation of an appropriate antibiotic policy – based on institutional antibiogram, review (may be once in three months – but at least every year) and a surveillance program for multi drug resistant organisms. Amrita also recommends a need to validate NABH benchmarks for key performance indicators in India. In an attempt to control AMR, the Infection Control Team at Amrita, sends out personal emails to the prescribing physician responsible for committing multiple defaults. The global impact of Antimicrobial Stewardship Program has also helped in 84% and 78% decrease in use of linezolid and colistin respectively, at their hospital.

Animal/food sector

Resistant bacteria can be transmitted from food producing animals to humans through the food supply. Strategies recommended by Department of Animal Husbandry and the Veterinary Colleges in Kerala, for control of infection prevention and control in animals, are as follows:

- Compliance to strict biosecurity measures in farms
- Strict biosecurity measures in animal farms along with strengthening and monitoring
- Promote vaccination instead of chemoprophylaxis
- Sanitation
- Zero water exchange

Environment sector

Application of good IPC measures to animal husbandry is important to reduce antimicrobial residues in environment. KSPCB recommends adherence to good farm management practices for infection control among flock, issuance of improved biosecurity guidelines by Central Poultry Development Organisation for farm implementation and promotion of antibiotic alternatives (vaccination).

OPTIMIZATION OF ANTIMICROBIAL USE

Kerala is considered as a consumer state for pharmaceuticals with a total consumption of drugs in the state at around 20,000 crores per annum, and antibiotics making up 20% of the total drugs consumed annually in the state. Currently there is an extensive misuse of antibiotics in healthcare thereby contributing to the growing resistance in bacteria. According to the National Drug Survey, 10% drugs from government sources and 2% drugs from retail outlets are not of standard quality (NSQ). Poultry farmers in Kerala also use a variety of antibiotics either as growth promoters or for controlling infections. Many prescription medications used for human and animal health ultimately find their way into the environment and can affect the health and behaviour of wildlife.

Of the five recommended key components in the NAP-AMR, Drugs Control Department is entrusted with the responsibility of preventing 'over-the-counter' (OTC) accessibility of antibiotics.

Human health

Of the oral antibiotics consumed in human health, 40% are for pediatric use while rest are for non-pediatric use. Most antibiotics sold in Kerala belong to aminoglycoside class (33-35%), followed by beta lactams (20-25%), fluoroquinolones (16-18%), macrolides (8-10%), tetracyclines (4-7%) and polypeptides (3-5%).

OTC sale happens mainly in adult oral dosage forms of antibiotics and is commonly seen with amoxicillin, ampicillin and azithromycin. Chances of OTC sale are more in rural areas owing to poor access to hospitals and low economic status, thereby contributing to irrational antibiotic use. Overcrowding at government hospital pharmacies often leads to a sub therapeutic dispensing of antibiotics. Improperly stored medicines are often sold at rural clinics run by non-professionals, and without need for prescriptions. Patient non-compliance in adhering to treatment course due to poor economic status and unawareness, self-medication of antibiotics for minor diseased conditions like sore throat, common cold, dental problems and 'not of standard quality' drugs (NSQ), are other factors responsible for AMR. Kerala data for 2016-17 shows 92% beta lactams sold were of standard quality while 8% were NSQ (5% from government sector and 3% from retail sector).

According to a survey conducted by Amrita Institute of Medical Sciences and Research Centre in Kerala, various reasons for inappropriate antibiotic therapy include inappropriate duration (77.5%), inappropriate frequency (50%), inappropriate maintenance dose (36%), inappropriate loading dose (36%), inappropriate indication (12.8%) and inappropriate drug (11.5%). In addition, a physician level survey revealed that 79% physicians considered antimicrobial resistance a concern, 71% prescribes

antimicrobials on a daily basis, 65% believed that antibiotics were given more than necessary, 52% prescribed antibiotics under patient pressure and 35% did not know the mechanism of action for the antibiotics. Survey at a laboratory level revealed that 72% laboratories gave reports on unjustified combinations of antibiotics, 48% laboratories were run by microbiology technicians (and not microbiologists) and 37% laboratories did not adhere to CLSI guidelines. Survey at the pharmacist level revealed complete non adherence to Schedule H drug and 78% pharmacists prescribing OTCs.

GMC Thiruvananthapuram has initiated Antibiotic Stewardship Program (ASP) to ensure the right drug gets prescribed at the right time, in the right dose, for right duration and for the right patient, at all government medical colleges in Kerala. As part of the ASP, resource persons have been identified in core departments, to ensure formulary restriction is enforced with respect to WHO restricted drugs. Resource persons are members of ASP committee of the Colleges. GMC Thiruvananthapuram also conducts awareness classes for faculty and students regarding the need for rational antibiotic use & infection control practices, and importance of institutional antibiotic policy at all government medical colleges in Kerala. This includes issuance of directions improved antibiotic usage (correct prescription, timely cultures, initiation of antibiotics, reassessment after 24-48 hours, de-escalation of antibiotics and to know when to stop treatment.

Besides, antibiograms (including ICU specific antibiograms) have been formulated for all government medical colleges in Kerala. Based on updated antibiograms, existing Antibiotic Policy at all government medical colleges in Kerala have been revised and data shared with all department heads. Periodic changes in antibiograms are conveyed back to the department heads every 3 months (clinical audit & feedback) so as to modify the prescription practices. Monthly clinical audits are conducted in ICUs to assess usage of WHO restricted antibiotics & also to ensure compliance and effectiveness of de-escalation strategies. The global impact of Antimicrobial Stewardship Program has helped in 84% and 78% decrease in use of linezolid and colistin respectively, at Amrita Institute.

Measures taken by the State Drug Control Department for control of OTC sale of antibiotics in healthcare setups are as follows:

- Regular inspections of sale premises for identifying OTC sale of Antibiotics
- Verification of Schedule H & H1 registers for compliance of rules
- Strict disciplinary actions are taken by the Licensing Authorities, in case of violations

In addition, State Drug Control Department also suggests implementation of prescription audits in sale premises so that overuse of antibiotics can be identified and reported.

Action taken by State Drug Control Department

Year	Total suspensions	Suspensions due to unaccounted sales	Suspensions due to other reasons
2013	519	213	301
2014	579	263	315
2015	587	264	323
2016	340	278	62

Animal/food sector

Poultry farmers in Kerala use a variety of antibiotics either as growth promoters or for controlling infections. Sulphonamides, tetracyclines and fluoroquinolones are commonly used as feed additives or as therapeutics in broiler poultry production. Even though, infections in fish are mainly parasitic infestations and do not warrant application of antibiotics, the latter are commonly used as growth promoters. Drugs fed to fishes are metabolised in liver/hepato-pancreas, or excreted as it is, either through kidney or faecal matter. Use of antibiotics and chemotherapeutics has a negative impact in marine life including immunosuppression and drug resistance, as well as bioaccumulation in tissues and environment. As per advisory by Department of Animal Husbandry, Dairy and Fisheries (Government of India 2014):

- Antibiotics should not be used in feed as supplements or as growth promoters
- Prebiotics, probiotics and phototherapeutics for growth promotion in animals should be encouraged
- Use of antibiotics for prophylaxis, therapeutic and metaphylactic purpose should be under strict veterinary supervision
- That licensed antibiotic reaches the registered user through a registered stockist must be ensured
- Systems for identification of antibiotic from manufacturer to user must be in place

Animal Husbandry Department, Government of Kerala also suggests action in case of presence of residues. The affected consignment/flock can be withheld for a specific period so that residues fall below the MRLs, further targeted surveillance if frequent violations occur and withdrawal from market and penalties.

Other strategies proposed for optimization in use of antimicrobials in veterinary and animal health include:

- Good Pharmacovigilance Practices (GVP) at all steps of production/ processing of food of animal origin
- Formulation of standard treatment guidelines for treatment of animal diseases
- All drug stores to be instructed to dispense antibiotics including oral and parental on prescription of Registered Veterinary Doctor only
- Conduct surveys on antibiotic prescription practice by veterinary surgeons
- Veterinary stewardship program can be tried
- Periodic inspection of the fish farms and hatcheries to ascertain imprudent use of drugs/ chemicals are not carried out
- Inspection of records on chemicals used (source, quantity and withdrawal period) and licence cancellation of non-compliant fish farms
- Cancellation of license to fish farms which are noticed to abuse use of drugs/ chemicals

As per subsection 3 of section 8 of the Inland Fisheries and Aquaculture Act 2010, Government may by rules limit, regulate or prohibit permanently or temporarily medicines, antibiotics, pesticides for the use in aquaculture. As per sub rule 1 of rule 9 of Kerala Inland and Aquaculture rules, 2013 no person shall use, without prior permission of the Officer who has been authorized by the Government by notification for the purpose, pesticides, antibiotics or medicines in aquaculture farms in private water body, which is connected through drainage canal or directly to open water bodies. Penalty for non-compliance of the provisions of the act/rules attracts imprisonment for three months and a fine of INR 10000/- or both. The penalty for committing the same offence for the second time is imprisonment for six months or INR 10000/- or both. The state also enacted Kerala Fish Seed Act 2014 (Act 4 of 2015) for the quality certification of fish/shrimp seeds used in aquaculture. Aquaculture farmers who use these substances should follow product labels regarding dosage, withdrawal period, proper use, storage, disposal and other constraints including environmental and human safety precautions. The adoption of HACCP and GMP by aquaculturists is a practical way to tackle this hazard and to demonstrate safe and high-quality product to the international community.

Environment sector

In order to optimize the use of antimicrobials and prevent their incessant use, KSPCB recommends the following measures:

- Involvement of MoEFCC and CPCB in development of environmental regulations (antibiotic resistance centric) for farms and factories/industry
- Modification of CPCB guidelines for poultry farm for re-categorization of pollution causing potential
- Manure management causing lesser risk (i.e. biogas generation shall be preferred over land application of manure), use of in-house biogas generation plants by big/integrated poultry farm,

development and management of a common biogas generation plant for use by small poultry farmers operating in a cluster

- Prohibition of land application of untreated litter by way of laws
- Encouraging proper composting for treatment of manure with a very high level of supervision
- Prohibiting use of poultry litter as feed for fishes in aquaculture by Central and State fisheries
- Restricting antibiotic usage to prescription based cure of sick animals (and not for growth promotion)
- Prohibiting usage of antibiotics in feed and feed supplement
- Restricting use of antibiotics critical for humans for use in farm animals
- Encouraging use of antibiotic free growth promoters (herbal supplements)
- Ensuring access to licensed antibiotics through registered dealers
- Complete traceability of all antibiotics from manufacturing source to end-stage user
- Legal enforcement of guidelines on big companies
- Non-promotion of incentives for antibiotic prescription in animals
- Poultry labelling system to differentiate flock receiving antibiotics and development of a national level database with access to public

RESEARCH AND INNOVATIONS

The importance of research and innovations cannot be over emphasized. As the world is running out of effective antibiotics to fight even simple infections, alternate strategies and new molecules need to be discovered at the earliest.

Human health

According to new research, antibiotic resistance of bacteria can be reversed. An "adjustable cycling" protocol, in which antibiotics are changed based on the patient's condition, can be effective in reducing the evolution of resistance (9). If a pathogen is resistant to one drug, doctors can switch to another drug – one to which the pathogen is more vulnerable. When the new drug kills off the resistant bacteria, non-resistant versions will have a better chance of surviving. Alternating between antibiotics could lead to the evolution of strains that have lost their resistance to both drugs.

Animal/food sector

Department of Fisheries has introduced innovative farming techniques which require zero water exchange and adequate biosecurity measures which make farms less prone to disease attack for control of AMR. KPCB recommends involvement of Indian Council of Agricultural Research and State Colleges of Veterinary Sciences to develop an ABR agenda for reducing the spread of antibiotic resistance from farms. This should entail an understanding of impact of litter/manure treatment through composting/biogas generation on resistant bacteria and resistance transfer mechanism from farms to environment through waste.

Research findings reveal that there is a scope with probiotics, prebiotics, immune-stimulants, essential oils and bacteriophages to combat some infectious viral and bacterial diseases in fishes. Strengthening the defence mechanism of fish and shrimp through prophylactic administration of plant based immune-stimulants is considered as a promising alternative to antimicrobials.

Environment sector

Meta-genomic analyses of rigorously authenticated ancient DNA from 30,000-year-old permafrost sediments has identified a highly diverse collection of genes encoding resistance to β-lactam, tetracycline and glycopeptide antibiotics, and conclusively shows that antibiotic resistance is a natural phenomenon that predates the modern selective pressure of clinical antibiotic use (10).

Research is also underway to establish the role of phytochemicals as biofilm inhibitors as a means to fight antibacterial resistance. Resveratrol, a phytochemical commonly found in the skin of grapes and berries, was tested for its biofilm inhibitory activity against *Vibrio cholerae*. The results generated in this

study proved that resveratrol is a potent biofilm inhibitor of *V. cholerae* and can be used as a novel therapeutic agent against cholera (11).

In addition, research work is also being conducted on natural antimicrobial substances such as chitosan, *Moringa oleifera* seeds, cinnamaldehyde, eugenol, allicin and other plant extracts. Previous studies have shown that chitosan (0.03%-0.045%) is effective against Campylobacter spp., chitosan (0.1% & 1%) are effective against EHEC biofilm, chitosan (0.5%) effectively brings down the microbial load on duck egg quality, chitosan (1.5%) results in complete inhibition of *Listeria monocytogenes* biofilm formation on stainless steel and polypropylene surfaces. Studies have also shown complete inhibition of *Listeria monocytogenes* with 30µl of 1% nisin as well as effectiveness of 200 mg/ml of *Moringa oleifera* seeds on *L. monocytogenes* and *L. innocua*. Incorporation of cinnamaldehyde, eugenol and allicin controls growth of EHEC on beef. The aqueous and methanolic extract of leaf and flower of *Couroupita guanensis Aubl.* is effective against both planktonic and biofilm cells of *L. monocytogenes*. Other plant extracts shown to possess antimicrobial activity are *Annona squamosa* (Atha), *Cassia alata* (Anathakara), *Coleus amboiricus* (Panicoorka), *Myristiea fragnam* (Nutmeg) and *Tectora grandis* (Teak).

Multi-sectoral

Rajiv Gandhi Centre for Biotechnology (RGCB), Trivandrum, Kerala is a premier national research institute exclusive devoted to research in Molecular Biology and Biotechnology. It serves as a clinical and epidemiological research setting for sentinel sites and collaborators in Kerala (Department of Microbiology, Government Medical College Hospital, Trivandrum; Amala Institute, Thrissur), Karnataka (District Health Office, Belagavi), Tamil Nadu (Government Medical College, Trichy) and Andhra Pradesh (Sir Ronald Ross Institute of Tropical and Communicable Diseases, Nalakuntha, Hyderabad). The Centre has various laboratory capabilities for identification of bacterial pathogens. These comprise of biochemical testing, molecular identification, genotyping, virulence profiling, antibiotic resistance testing, antibiotic resistance gene profiling as well as testing for environmental persistence. Other facilities include Real Time PCR, NGS and proteomics. Kirby-Bauer disc diffusion method and E-strip method are used for calculation of Minimum Inhibitory Concentration (according to the Clinical Laboratory Standards Institute Guidelines). The antibiotic discs used are ampicillin (10 μg), chloramphenicol (30 μg), ciprofloxacin (5 μg), cotrimoxazole (25 μg), gentamycin (10 μg), streptomycin

(10 μg), trimethoprim (5 μg), tetracycline (30 μg), nalidixic acid (30 μg), norfloxacin (10 μg), erythromycin (10 μg), azithromycin (15 μg) and polymyxin B (50 μg). Escherichia coli ATCC 25922 and Staphylococcus aureus ATCC 25923 used for internal quality control. Resistance gene amplification is carried out for SXT element, strA, strB, sul2, dfr8.

ReAct, a civil society organization, is one of the first international independent networks to articulate the complex nature of antibiotic resistance and its drivers. ReAct started off its action in Kerala in early 2017 with an aim to engage all sectors and everyone from the public sector to civil society. ReAct is involved in various research activities including a WHO funded scoping study to determine current marketing and promotional activities for antibiotics that are adopted by pharmaceutical companies in low & middle income countries; as well as a self-funded study to determine cost of antibiotic resistant infections in intensive care settings of tertiary care hospitals.

COMMITMENT AND COLLABORATIONS

The resistance to antibiotics is a major public health issue, flagged by WHO and governments across the globe. It is critical to have an inter-sectoral collaboration, prioritise actions, build on existing activities/success stories, foster individual behaviour change and continually monitor progress towards a successful program implementation on AMR containment.

A systemic monitoring plan, vigilance and corrective action is very important to control this problem. A systemic surveillance programme such as the proposed “Integrated surveillance on AMR in Food & Food Animals” along with “Antibiotic Residue monitoring plan” is necessary to initiate suitable AMR interventions.

KPCB recommends involvement of Indian Council of Agricultural Research and State Colleges of Veterinary Sciences to develop an ABR agenda for reducing the spread of antibiotic resistance from farms. The Board also recommends involvement of MoEFCC and CPCB in development of environmental regulations in order to optimize the use of antimicrobials and prevent their incessant use.

The Government of Kerala is committed to take suitable action involving all stakeholders to implement the State Action Plan on AMR.

CHALLENGES AND WAY FORWARD

Successful implementation of a program towards containment of AMR is not devoid without its own problems. Various challenges on the way forward in Kerala are as follows:

- Shortage of staff/human resources in the departments especially in inland areas
- Over the counter sale of antibiotic is a common practice and complicates the process of regulating the medical use of antibiotics.
- Rate of antibiotic degradation depends almost entirely on photo period and environmental temperature; hence the degradation of antibiotics in environments of tropical countries
- Most urban sewerage does not pass through treatment plants leading to antibiotic residues and antibiotic resistant microbes contamination in the natural water
- Absence of antibiotic residue control programme

  As Antibiotic residues cannot be destroyed once they enter food, suitable control plans are necessary. However, control plans are usually difficult to implement due to inadequate traceability, lack of officials and lack of suitable laboratory support
- Traceability problems with food of animal origin. In Kerala, milk has some tractability but for the rest of food of animal origin, retracing the animal product to its farm of origin is very difficult
- Higher demand for fresh food in the State (by the time official sampling and analysis is completed, the food might have already been consumed) and high dependency on neighbouring states for beef and broiler, poses a major challenge to sample traceability

As a part of next steps, Microbiology Laboratory at Government Medical College Thiruvananthapuram proposes to expand AMR surveillance to the district to get more of community data, and expand 'One Health' approach to surveillance in animal, food and environment. The laboratory also plans to conduct a community based study that has been approved for health services institutions by State Public Health Laboratory in partnership with the Rajiv Gandhi Centre for Biotechnology. The need for a systemic surveillance programme such as the proposed "Integrated Surveillance on AMR in Food & Food Animals" along with "Antibiotic Residue Monitoring Plan" is necessary to initiate suitable AMR interventions.

CONCLUSION

The resistance to antibiotics is a major public health issue, and is flagged by WHO as well as governments across the globe. A systemic monitoring plan, vigilance and corrective action is needed to control this hazard.

Key strategies recommended to fight AMR in Kerala include (a) governance: Establishment of state level alliances against AMR and constitution of a multi-sectoral steering committee (b) regulatory:

Development and application of standard treatment guidelines in health and veterinary sectors; discouraging non-therapeutic use of drugs in animals; restricting OTC sale of antimicrobial agents (c) capacity building: surveillance of antimicrobial use and resistance; training prescribers for rational use of antimicrobials; reducing disease burden and infection control; undertaking operational research (d) community participation: educating for adherence to recommended regimens; discouraging self-prescription; AMR day concept (e) scientific community participation/research: development of alternative strategies to combat antimicrobial resistance; biofilm inhibition strategies; and research on probiotics.

Although there are challenges in way of implementation of AMR containment program in Kerala, the commitment of the Government of Kerala and strong collaborative networking among the stakeholders, holds promise to success as well as learning for the neighbouring states.

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