Tackling AMR starts with the environment

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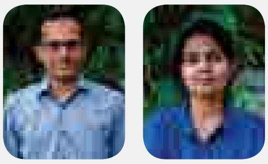

The environmental dimension of antimicrobial resistance (AMR) has largely been neglected. The human side of the AMR crisis has received maximum attention followed by the animal sector. The focus has been on "what is going in" and not on "what is coming out". We are missing the complete picture. It is time we re-think, re-prioritize and put the environment first. This can be achieved by adopting an AMR-centric approach to waste management and controlling the dissemination of AMR determinants into the larger environment, which sets resistance growing like a chain reaction.

The environment – a potential starting point

While environment is about all the living and non-living things around us, soil, water and waste from different sources are key elements of concern in the context of AMR. A common perception is that the "environment" is at the end of the spectrum. But this perception could be challenged. For the simple reason that environment is at the receiving end of what we do – sink as we know it – but it also acts as a source of what comes back to us. It can be a starting point of this two-way relationship. We should re-think and re-prioritize. Because so far, the focus has been on "what is going in" and not on "what is coming out". It is likely that the complete picture is missing. A picture, wherein one part – the environment – is potentially more relevant than the others. This is because the environment is big pool of AMR determinants (such as antibiotic-resistant bacteria, antibiotic-resistance genes and antibiotic residues), wherein continuous and perhaps the ever-lasting interplay among these determinants, potentially sets the ground for resistance growing like a chain reaction.

The environment – a missing link in global guidance and national action

AMR containment in the waste and environment sector has largely been neglected. The Global Action Plan on AMR (2015) provided limited guidance on environment despite recognizing the One Health nature of the problem and calling for a multi-stakeholder action *(1)*. While global deliberations now include environmental AMR issues, there is no environment-specific guidance such as WHO guidelines on use of medically important antimicrobials in food-producing animals or Guidance on Integrated surveillance of antimicrobial resistance in foodborne bacteria *(2, 3)*. This is disappointing but not surprising as managing the environment is not the key mandate of the three organizations, which came together a few years ago to guide countries in the global fight against AMR. These were the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). Consequently, both as a problem and as a solution, the human side of the crisis has received maximum attention, followed by the animal sector. In order to fill this gap, the United Nations Environment Programme (UNEP) has been a recent addition to the WHO-FAO-OIE tripartite. However, since it is a delayed entrant, a concrete set of guidance for national policy-makers and stakeholders – such as on discharge limits of AMR determinants in waste and on environmental AMR surveillance – appears to be a distant reality.

On the other hand, despite limited global guidance, countries – though at varying degrees – have outlined their approach to address the environmental side of AMR in their national action plans. While this is encouraging, and reflects willingness of a country to own up the problem, but without global guidance, it may result in inadequate on-the-ground response, which would also not be uniform across national boundaries. Our engagement with environmental policy-makers and regulators from different Asian and African countries points towards the need for a coordinated country-level advocacy exercise to make environmental stakeholders aware and secure their buy-in and commitment. Just as the way, the WHO country offices are doing with the AMR focal point of the health ministry. Until this happens, the One Health approach to contain AMR would not really be happening. But it is still unclear, who is going to do it and what is the plan for action, if any.

Structuring environmental AMR –waste from different sources

The point sources that are of concern regarding environmental AMR could be segregated into farms, factories, healthcare settings and household/community. AMR determinants in solid or liquid waste from these sources may directly, or after treatment, reach the external environment such as soil and water or into other point sources. Farms include those involved in rearing animals for food i.e. food-animal production farms such as of poultry, dairy, pig and fish. Intensive farms, which are characterized by high stocking densities, poor animal husbandry practices, higher use of chemical inputs such as antibiotics, are a big concern as 75–90% of antibiotics consumed by animals are excreted un-metabolized through fecal matter and urine. The excreta are also known to contain a high load of bacteria including resistance bacteria. Farm manure such as from poultry farms is found to harbour antibiotic resistant bacteria (ARBs) and antibiotic resistance genes (ARGs). The application of treated or untreated litter to agriculture fields is a common practice in different parts of the world and leads to a wider dissemination into the agriculture food chain *(4)*. Another example of such cross-sectoral dissemination of AMR determinants is use of poultry litter in fish ponds. In case of aquaculture, wherein antibiotics are dumped in a medium like water, the possibility of dissemination of AMR determinants into external water bodies is higher. Absence or inadequacies of primary effluent treatment plants at fish farms adds to the problem *(5)*. The other set of farms include those consisting of crops and plantations, wherein a big part of unspent sprayed antibiotics ends up in the agricultural soil and enters into water bodies through the run-off.

Factories are another important category of point source for waste. These include slaughter houses and units processing food such as meat, dairy and fish; pharmaceutical manufacturing plants and feed mills. Samples from drug manufacturing sites or from wastewater treatment plants receiving drug manufacturing sewage have been shown to contain high levels of pharmaceuticals, genes, mobile genetic elements as well as resistant bacteria *(6-8)*. A third set of point sources are healthcare settings and waste from these have high concentrations of AMR determinants *(9)*. These include primary, secondary, tertiary care hospitals and diagnostic laboratories as well as veterinary care clinics.

Sewage treatment plants (STPs), which receive waste from household and community area point sources, are a new concern. Conventional plants are not designed to address AMR. There are questions emerging on the potential role of STPs as breeding grounds for AMR *(10)*. Research also shows that STPs may not lead to the selection of resistance *(11)*. There is a need for new waste treatment technologies to achieve high efficiency of ARG or ARB removal.

Rivers, lakes, ponds, oceans, ground water and soil including agricultural soil act as sinks, which receive AMR determinants from different sources. These could be termed as non-point sources, since AMR determinants through these sinks enter back into humans, animals and the food chain. Studies have shown the prevalence of AMR determinants in groundwater, drinking water, surface water as well as in soil *(12, 13)*. A recent study indicated that air-borne transmission of ARGs is also posing a threat *(14)*. Other than AMR determinants, biocides and heavy-metals in the environment have been found to influence the emergence of AMR through co-selection and cross-resistance mechanisms. Water, sanitation and hygiene (WASH) aspects are also linked to the spread of AMR through environmental routes *(15)*. Limited hand washing behaviour, unsafe drinking water, lack of functional toilets and open defecation are known to drive up the rise of infections and thereby antibiotic use.

Tackling AMR from the environment – from policies to practice

AMR has no boundaries but countries manufacturing high quantities of antibiotics or food from animals and those which are big consumer of antibiotics (per capita or overall) or food from animals have ample reasons to prioritize waste management to contain AMR from the environment. A comprehensive approach is required to address this complex issue. The precautionary principle should be adopted and ongoing research should inform future policy and plans. To begin with, from the perspective of AMR containment, it is important to assess existing laws, policies and standards; scale and spread of key waste sources; prevalent waste management practices; type and extent of waste generated and discharged. Also, it is important to understand the resources, capacity and infrastructure for environmental AMR surveillance and the enforcement of policies.

Relevant laws, policies and standards include those which help the setting of discharge limits for residual antibiotics in industrial effluents such as the pharmaceutical sector and other industrial and healthcare settings. Until this happens, there is no yard-stick to check antibiotic discharge from these point sources of concern. This can be facilitated if antibiotics in effluents are considered as hazardous chemicals in view of their public health impact, similar to the way the issue of pesticide pollution is addressed. Countries need to adopt policies which favour an "AMR-centric" approach to waste management. Notably, the existing effluent standards typically cater to select parameters such as pH, biological oxygen demand, chemical oxygen demand and total suspended solids, which do not help monitor antibiotic residues. Scientists will also have to figure out how to keep a check on the discharge of ARBs and ARGs.

In case of farms, policies that help keeping a check on the land application of farm litter and reducing its impact on agriculture and grazing animals are important. Policies facilitating extended producer responsibility in the pharmaceutical sector and drug take-back programmes would help in the safe disposal of unused or expired antibiotics. Guidelines on siting, biosecurity, sanitation and hygiene for different point sources will further complement these policies.

AMR surveillance in the environment will be crucial from the point of view of a long-term AMR containment strategy (16). This should include surveillance of ARBs, ARGs and antibiotic residues. Such surveillance should be integrated with AMR surveillance in the human, animal, food and agricultural sectors. An integrated surveillance strategy or framework that provides guidance on key antibiotics, bacteria and genes, sample type, size, and locations, etc. is critical. Considering the resource intensive nature, environmental AMR surveillance should be prioritized well and implemented in a phased and progressive manner.

It is essential to recognize that AMR pollution (discharge of AMR determinants in the environment) is best avoided. If antibiotic misuse – such as in humans and animals – is eliminated in the first place, then this would mean that "what is going in" is controlled. If this does not happen, no matter how best we manage our waste, we would still continue to pollute more than we can clean up. It would not be sustainable. To conclude, it is time that an environment "first" approach was established to catch up on lost time not spent on this complex but critical public health issue of modern times. ■

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