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Combatting antimicrobial resistance in Nepal: the need for precision surveillance programmes and multi-sectoral partnership

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Sir,

There has been an increasing burden of antimicrobial resistance (AMR) in Nepal over the last two decades with a lot of published literature highlighting the widespread distribution of resistant superbugs.[1–6] Lack of compliance with prescribed doses and syndromic management approaches (where patients are diagnosed clinically and treated empirically) have been major causes behind the increased burden of AMR in the human health sector.[2,3,5]

The leading causes of premature mortality from infectious diseases in Nepal are lower respiratory infections, diarrhoeal diseases and tuberculosis.[7] Other serious diseases like bloodstream infections, urinary tract infections and sexually transmitted diseases are also rising. MDR organisms such as MRSA, ESBL and carbapenemase-producing Enterobacteriaceae, *Pseudomonas aeruginosa,* and *Acinetobacter* species are significant problems for public health stakeholders. In humans, self/over- and under-prescription, empirical antibiotic therapy and irrational prescription of powerful antibiotics are contributors to the development of antibiotic resistance. The use of antibiotics as growth promoters in feed and irrational prescriptions by veterinary professionals and non-qualified paraprofessionals have been the leading causes behind the increased burden of drug-resistant microbes in the animal health sector.[2,5,8] The Frontiers Report from the United Nations Environment Programme in 2017 identified AMR from environmental pollution as one of the biggest emerging health threats,[9] particularly in low- and middle-income countries (LMICs). A study presented at the Federation of European Microbiological Societies 2019 congress in Scotland showed a high rate (61.8%) of ESBL gene acquisition among gut flora of subsistence farming communities in remote rural Nepal.[10] Another study from the same rural region of Nepal highlights the high prevalence of MDR Enterobacteriaceae among gut flora of healthy organically raised backyard chickens, suggesting multiple pathways for the acquisition of AMR, i.e. via the contaminated environment, household contacts, etc. and not necessarily by the consumption of antibiotics.[10]

In Nepal, co-trimoxazole, amoxicillin, ciprofloxacin, chloramphenicol, nalidixic acid, gentamicin and cephalosporins are the major antibiotics used for the treatment of human infection,[3] whereas tetracyclines, sulphonamides, macrolides, polymyxin, bacitracin, nitrofurans, quinolones and aminoglycosides are the major antibiotics used for the treatment of animals;[2] resistance trends to these drugs are on the rise. The easy access to drugs over the counter, self-prescription, substandard and counterfeit drugs, lack of proper advice on scientific husbandry practices with poor hygiene and sanitation, overuse of antimicrobials and lack of awareness and observance of drug withdrawal periods are important factors in the growing AMR burden in Nepal.[2] Between 2000 and 2015, antibiotic consumption, expressed as DDDs, increased by 65% and was driven by LMICs, where rising consumption had significant correlation to gross domestic product per capita (GDPPC) growth. One Health genomic AMR surveillance programmes are essential for unravelling the complexities associated with the emergence, evolution and dissemination of AMR. The Ministry of Health and Population (MoHP) formulated the 2014 National Antibiotic Treatment Guidelines[11] and the National Antimicrobial Resistance Containment Action Plan Nepal 2016[12] to promote rational use of antibiotics, good surveillance systems and antibiotic stewardship. Similarly, the Department of Livestock Services (DLS) introduced a policy of zero tolerance to antibiotics[2,13] to stop the use of antibiotics in animal feed. In 2018, The Food and Agriculture Organization (FAO) of the United Nations, WHO and other government bodies jointly signed a memorandum of understanding (MOU) to coordinate and conduct an AMR national action plan among different sectors,[13] which is still in the process of being implemented. The antibiotic resistance problems in Nepal identified by the Alliance for the Prudent Use of Antibiotics (APUA) (https://apua.org/nepal/) included lack of regulation in human, animal and agricultural antibiotic use and the formulation of optimum treatment guidelines, along with strict enforcement of 'prescription-only' laws in the country.

Still, there exist no comprehensive data on the national burden of AMR. To address this gap in AMR surveillance in the country, a

Fleming Fund grant was awarded to Nepal.[14,15] This programme has focused on the surveillance system and laboratory capacity for AMR surveillance.[14] Under this programme, 12 participating laboratories, 8 from human health and 4 from animal health sectors, are working on active and passive surveillance of AMR through the One Health approach. All this work is handled by a multisectoral committee involving stakeholders from the animal and human health sectors. The protocol for active surveillance of AMR and standard operating procedures (SOPs) to conduct AMR surveillance in participating laboratories have been developed but need to be approved by the concerned ministries. Staff members from participating laboratories have been trained in active surveillance and culture and identification of bacteria. National-level workshops on AMR surveillance have been ongoing to train all the field-level practitioners and technicians in the rational and prudent use of antibiotics and through this the trends in antibiotic susceptibility patterns for each bacterium have been identified. Limited infection control practices and poor hospital waste management is a significant challenge in Nepal, with awareness being a major factor in understanding the problem of AMR. Improper waste segregation, disposal systems, handling, transport and treatment of medical waste not only leads to direct adverse effects on human health but also has a greater impact on the environment. A recent study demonstrated that basic healthcare workers in Nepal had poor knowledge of universal infection precautions and were unable to interpret the guidelines correctly. Lack of the appropriate number of healthcare personnel trained in infection control, healthcare infrastructure and political commitment are significant drivers of AMR in Nepal.

LMICs urgently need onsite cost-effective genomic technologies to identify region-specific AMR high-risk clones and AMR mobile genetic elements to restrict their dissemination nationally and internationally. A novel concept called 'precision surveillance' (genomic surveillance programmes customized specifically for each region and country) will enable LMICs to limit the regional spread of AMR and to use antimicrobials more effectively while extending their longevity. In our opinion, the introduction of cost-effective real-time genomic technologies (rapid onsite diagnostics in AMR) to track AMR genetic elements, and tailor-made specifically for the geographic region, will be beneficial in tackling AMR in LMICs. Research related to new vaccines/diagnostics/antimicrobial development/AMR genomic surveillance in all related sectors (a One Health approach) and its implementation is also important in combatting AMR. Activities for AMR containment and capacity building have been initiated in Nepal. To further minimize the risk of AMR, there is a need for multisectoral governmental partnership, which also involves non-government public sectors, to provide synergistic value in the promotion of health and the global tackling of AMR.[12]

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Transparency declarations

None to declare.

Supplementary data

The Reviewer report is available as Supplementary data at *JAC-AMR* Online.

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