

Antimicrobial Resistance from a One Health Perspective in Nepal



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The discovery and subsequent availability of antimicrobial drugs has revolutionized modern healthcare in humans and animals, but growing resistance to antimicrobials by bacterial pathogens threatens to undermine these important advances, particularly as the discovery of new antimicrobials has slowed while antibiotic use and subsequent resistance (AMR) is rising globally. Current human mortality rates due to AMR are already over half a million deaths annually worldwide, and recent reports have estimated that if AMR is not controlled, the mortality rate will exceed 10 million per year by 2050, with an economic burden of over \$100 trillion USD in lost output.

These impacts will be felt globally, with low- and middle-income countries being hardest hit, as AMR can spread easily in humans and agricultural settings in these countries, due to large variations in healthcare infection-control practices, high rates of infectious diseases, high population densities with inadequate water, sanitation, and hygiene regulations, and suboptimal agricultural regulations in place for biosecurity and use of veterinary antimicrobials.

PREDICT

Photo: A rhesus macaque chews on a swab designed to collect saliva samples for viral testing in Nepal (photo: Pranav Pandit)

Despite evidence indicating that many countries face particularly high-risk conditions for AMR, there remain substantial data gaps characterizing the prevalence and abundance of AMR in humans, animals, and the surrounding environment, especially for community-acquired illnesses.

This lack of One Health-focused research on AMR in low-income and underserved settings worldwide highlights the need for transdisciplinary work to identify drivers of antimicrobial resistance and to characterize AMR transmission across One Health domains (Fig. 1).

PREDICT has sought to address these gaps in evidence by developing a pilot study using a One Health framework to investigate where AMR genes are detected within and between species and to inform on reservoirs of resistance genes in an urban, informal settlement with intensifying livestock production in Kathmandu, Nepal. The community of Jadibuti in southeastern Kathmandu, Nepal, is an

ideal representation for studying how AMR might occur in informal settlements worldwide. This community exists at the intersection of urban and rural settings within Kathmandu, bordered by an international airport on one side and rice paddies on the other; people, live-stock, and wildlife share habitat; half of adults have no formal education, and sanitation infrastructure is limited to tube wells and pit latrines. However, regional and international travel by residents is common. This pilot study allowed for AMR characterization at several interfaces proposed for AMR transmission.

At the time of sampling, little information was available concerning AMR in Nepal in general and in urban, informal settlements such as Jadibuti in particular. Therefore, science to characterize resistance genes from a One Health perspective was needed to allow for more targeted discovery of specific resistance reservoirs in this community and in underserved settings similar to it.

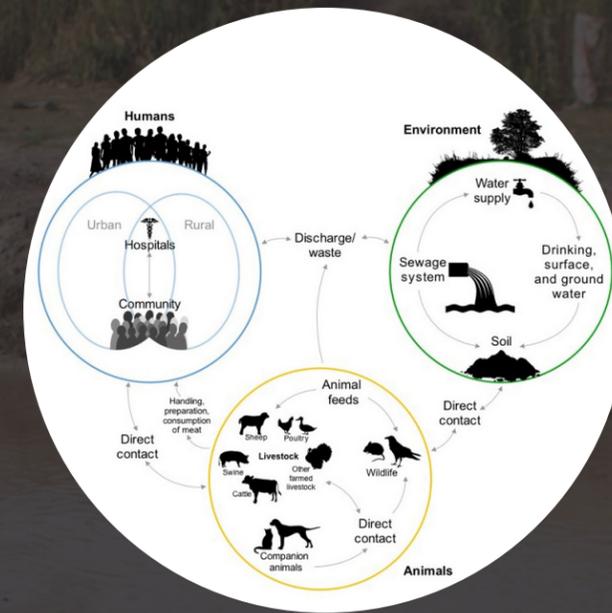


Figure 1. Schematic illustrating potential transmission routes (gray arrows) between humans, animals, and environmental reservoirs of antimicrobial resistance genes and pathogens.

Based on these findings, continuing public health efforts to provide improved sanitation and hygiene to residents in this community could protect against the spread of AMR.

Overall, a wide range of antimicrobial resistance genes from thirteen resistance classification groups were found to be broadly present and widely distributed across humans, animals, and water sources in this informal settlement in southeastern Kathmandu, Nepal. This work provides a community-based, One-Health framework that can be used to further the understanding of AMR gene detection in settings with animal-human interfaces.

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Photo: Ducks forage in a pen in Jadibuti settlement (credit: Pranav Pandit)

FINDINGS

- Test results indicated that AMR genes were widespread in this community among humans, domestic animals, water sources, and wild small mammals.
- In total, sixty-nine resistance genes were identified. Antibiotics associated with these resistance genes include doxycycline, azithromycin, and gentamicin, all of which are widely used in Nepal in both humans and animals, potentially resulting in high levels of resistance to these antibiotics circulating in the community.
- The highest prevalence of resistance genes were detected in domestic animals, including ducks, swine, and chickens, compared to humans, water sources, and wild small mammals such as rodents or shrews.
- AMR genes associated with antimicrobial drugs of global public health importance were predominately found in fecal samples and poultry, suggesting that intervention efforts for disrupting AMR transmission of critically important antibiotics for humans and animals in this community should focus on poultry and fecal transmission pathways.
- On average, households with animals had higher numbers of AMR genes in their water sources than households without animals.
- Resistance genes were detected in all people sampled (n=67), with an average of 7 genes from 10 antibiotic classification groups found per participant. Key findings include:
 - An increase in an individual's age was associated with higher gene burden (the total number of resistance genes found in a sample).
 - Having a dedicated location for human solid waste (e.g., a toilet) was highly protective against both resistance gene detection and burden in people.
 - Having and using a dedicated location for trash (including animal waste from slaughtering and butchering) was associated with a lower risk of finding AMR genes in people.
 - Having animals in or near the dwelling in the last year was associated with a higher risk of finding AMR genes in people.

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