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Narrative Review

Antimicrobial Resistance Through One Health Lens: Transmission Cycles, Epidemiology, and Stewardship Interventions

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ABSTRACT

Antimicrobial resistance (AMR) is a quintessential One Health challenge, where the health of people, animals, and ecosystems is inextricably linked and interdependent. This review evaluates the emergence and dissemination of multidrug-resistant (MDR) pathogens by mapping the dynamic transmission cycles that bridge the human-animal-environment interface. Rather than existing in sectoral silos, resistance determinants move fluidly through the global food chain, shared water systems, and the environmental resistome, driven by systemic selection pressures. We analyse how anthropogenic inputs, such as the discharge of unmetabolized drugs from intensive livestock production and pharmaceutical manufacturing, contaminate aquatic and terrestrial ecosystems, creating "evolutionary incubators" for novel resistance mechanisms. These mechanisms are rapidly disseminated via horizontal gene transfer (HGT) on mobile genetic elements, enabling the crossing of taxonomic boundaries and the eventual spillover into human populations through contaminated produce, recreational waters, and direct zoonotic contact.

The epidemiology of this crisis reveals an alarming narrowing of therapeutic options, with surveillance data from India (2017–2024) showing a steady decline in the efficacy of last-resort agents like carbapenems and colistin across all sectors. To interrupt these cycles, we advocate for integrated antimicrobial stewardship (AMS) that addresses the entire antimicrobial lifecycle, from production and community access to safe disposal. Successful national interventions, including restrictions on over-the-counter sales under India's Schedule H1 and the prohibition of colistin as a growth promoter, illustrate the necessity of unified policy frameworks. By leveraging advanced diagnostics, AI-driven predictive modelling, and intersectoral surveillance, this review provides a practice-oriented roadmap to preserve the global antimicrobial commons and safeguard health resilience for future generations.

KEYWORDS: Antimicrobial Resistance; One Health; Antimicrobial Stewardship; Resistome; Multidrug-Resistant Organis

INTRODUCTION

The discovery of penicillin, followed by the "Golden Age" of antibiotic discovery during the 1940s and 1960s,

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transformed the treatment of infectious diseases, allowing for sophisticated medical treatments such as major surgery, organ transplantation, and chemotherapy.[1] However, the unchecked and frequently careless application of these "magic bullets" in the fields of agriculture, veterinary medicine, and human health has led to an evolutionary reaction from the microbial community.[2] One of the top 10 challenges to global public health today is antimicrobial resistance (AMR), which threatens the efficacy of contemporary therapy and disrupts decades of advancements in infection control.[3] AMR-related consequences were linked to about five million fatalities in 2019, while resistant bacterial infections were directly responsible for about 1.27 million deaths.[4]

Because AMR involves the movement of bacteria, mobile genetic elements (MGEs), and drug residues across human, animal, and environmental domains, it is a quintessential One Health issue.[5] One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems by recognizing their close links and interdependence.[3] In this scenario, the human sector is both a source and a recipient of resistance, while the animal sector, particularly intensive livestock production, acts as a significant reservoir for emerging multidrug-resistant diseases.[6] The environment, which was often ignored in earlier management measures, is becoming more widely acknowledged as a potential channel and gene pool where resistance can emerge under the load of pharmaceutical waste and agricultural residue.[7] Effective treatment thus requires a multidisciplinary approach that incorporates environmental monitoring, veterinarian oversight, and clinical microbiology.[8]

The operational link between laboratory data, multisectoral stewardship, and national governance is frequently ignored in favor of sectoral narratives like clinical outcomes or veterinary consumption, despite the fact that the global burden and molecular drivers of AMR have been thoroughly documented.[8,9] This review stands out because it provides a cohesive synthesis of the AMR ecosystem, charting the dynamic transmission cycles that allow resistance determinants to travel freely between industrial hubs, wildlife vectors, and clinical settings.[10,11]

In contrast to conventional reviews, this work advocates for stewardship that starts at the level of demand-driven innovation and extends to the safe disposal of pharmaceutical waste by integrating the "One Health" paradigm into a "Antimicrobial Lifecycle" approach.[12] In order to convert raw data into useful bedside decisions and early-warning policy signals, we specifically position the clinical microbiology laboratory as the operational hub where whole-genome sequencing (WGS) and fast diagnostics (e.g., MALDI-TOF MS) are combined with artificial intelligence (AI).[8,13]

In addition, this assessment proposes a context-specific roadmap for low and middle-income countries (LMICs). By analysing the longitudinal susceptibility trends from India's AMRSN 2024 report and evaluating the success of national regulatory milestones such as the restriction of over-the-counter (OTC) sales via Schedule H1 and the ban on colistin as an animal growth promoter, this review offers a replicable framework for other nations battling the "world's AMR capital" status.[1,14,15] In summary, the insights gained from this review equip practitioners and policymakers with a multisectoral strategy to break the transmission loops across the One Health triad while preserving the global antimicrobial commons.[12,16]

MICROBIAL FOUNDATIONS AND EVOLUTIONARY DYNAMICS

AMR is fundamentally an evolutionary adaptation brought about by the selection pressure that antibiotics exert.[8] To mitigate the effects of drugs, bacteria use a variety of molecular methods that fall into four main categories. These include reduced membrane permeability, frequently due to the loss of porin proteins; enzymatic inactivation, such as the generation of β-lactamases that hydrolyse the structure of penicillin and cephalosporins; target site modification, where mutations in essential proteins prevent antibiotic binding; and the activation of efflux pumps that actively remove drugs from the bacterial cell.[4] These mechanisms are dynamic, moving between bacterial populations by vertical gene transfer during reproduction and horizontal gene transfer (HGT) via conjugation, transformation, and transduction.[17]

Mobilized resistance genes located on plasmids, transposons, and integrons pose the greatest threat to public health because they enable resistance to spread rapidly across various bacterial species.[8] For example, the plasmid-mediated colistin resistance gene mcr-1, which was originally discovered in animals and humans in China, has rapidly spread around the world, threatening the efficiency of one of our last-resort antibiotics.[1] Furthermore, the environmental microbiome contains a massive reservoir of resistance genes that have been there for ages, sometimes serving as survival mechanisms for soil bacteria fighting for resources.[7] Anthropogenic pollution, such as the release of large quantities of antibiotics from manufacturing facilities and untreated sewage,

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accelerates the recruitment of these ancient genes into human diseases.[8] Biofilm production adds an additional layer of complication because the protective matrix limits medication diffusion and promotes "persister" cells that survive treatment and regenerate infections.[8]

HUMAN DOMAIN

The human health sector remains the primary focus of the AMR challenge, serving as the most visible domain for the manifestation of treatment failure, morbidity, and mortality.[5] Despite being a naturally occurring evolutionary process, antimicrobial resistance is rapidly increasing due to antimicrobial-induced selection pressure, which causes resistant strains to multiply while vulnerable organisms are eradicated.[1] This is exacerbated by improper dosage, poor adherence, and inappropriate prescribing (e.g., usage for viral infections, inappropriate broad-spectrum therapy, absence of de-escalation). Irrational usage is further encouraged by societal variables like self-medication, access to over-the-counter antibiotics, and inadequate diagnostic capabilities. Furthermore, subtherapeutic exposure from substandard or counterfeit drugs may contribute to the emergence and spread of resistant bacteria.[1] Table 1 shows the chronology of the introduction and emergence of antibiotic resistance[1,5,15]

Table 1: Chronology of Antibiotic Introduction and Emergence of Resistance

Antibiotic Class	Year of Discovery / Introduction	First Reported Resistance	Primary Pathogen(s) Involved
Penicillin	1928 / 1940	1940	*Staphylococcus aureus*
Tetracyclines	1950	1959	*Shigella* species
Methicillin	1959	1960	*Staphylococcus aureus (MRSA)*
Vancomycin	1958	1989 (VRE) / 2002 (VRSA)	*Enterococcus* / *S. aureus*
Cephalosporins	1945 / 1964	1960s (Early) / 2000s (XDR)	*Gram-negative Enterobacterales*
Fluoroquinolones	1980s	1996	*Pneumococcus* / *Campylobacter*
Carbapenems	1980	2006	*Enterobacterales (CRE)*
Colistin	1940s / 1950s	2015 (mcr-1)	*E. coli, K. pneumoniae*

The use of broader-spectrum medications is required in the clinical sector due to high levels of resistance, which creates a "vicious cycle" that leads to the formation of even more resistant "superbugs," like those in the ESKAPE group.[4] In 2019, AMR was directly responsible for 1.27 million fatalities, a statistic that is expected to climb to 10 million annually by 2050 if existing trends in human consumption and infection management do not change dramatically.[1,18]

The spread of antimicrobial resistance in healthcare settings is driven by multiple human-related factors, summarized as follows:

1. Inappropriate antimicrobial prescribing (e.g., use for non-bacterial infections)
2. Excessive empirical broad-spectrum antibiotic use
3. Failure to de-escalate therapy based on microbiological results
4. Suboptimal dosing, incomplete treatment, and poor adherence
5. Poor infection prevention and control (IPC) practices
6. Inadequate hand hygiene compliance
7. Overuse of invasive devices (e.g., ventilators, catheters)
8. Inadequate diagnostic stewardship
9. Lack of antimicrobial stewardship program (AMS) implementation
10. Inadequate surveillance and feedback mechanisms
11. Overcrowding and high patient load

These factors work together to promote the emergence and spread of multidrug-resistant bacteria in hospitals. Cross-transmission between patients is facilitated by inadequate IPC and hand hygiene, and inappropriate antibiotic use increases selection pressure. Excessive reliance on empirical therapy, often due to a lack of diagnostic capacity, increases unnecessary antibiotic exposure. Particularly in critical care environments, invasive devices serve as reservoirs for organisms that develop biofilms. Furthermore, the cycle of AMR propagation in healthcare facilities is maintained by the lack of organized stewardship programs and reliable surveillance systems, which restricts the optimization of antimicrobial usage and monitoring of resistance patterns.[4,8,19,20]

Inadequate diagnostic, antimicrobial, and infection control stewardship are the main causes of the rise of antimicrobial resistance in hospital settings. While the lack of stewardship measures (such as antibiograms, policies, and PK-PD adherence) restricts treatment optimization, inadequate diagnoses encourage empirical and prolonged antibiotic use. Concurrently, ineffective infection control systems characterized by

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poor HAI surveillance, lack of monitoring, insufficient source management, and limited resources enable the persistence and propagation of resistant bacteria.

The absence of rapid point-of-care diagnostic tools is a significant systemic factor that drives doctors to rely on empirical broad-spectrum therapy.[8] In many regions, particularly in low- and middle-income countries (LMICs), laboratory infrastructure is so limited that less than 30% of facilities have access to routine culture and susceptibility testing, resulting in a "prescribing in the dark" scenario in which antibiotics are administered without knowledge of the causative agent.[8,20] Clinicians are forced to administer "Reserve" or "Watch" group antibiotics as a safety precaution due to this diagnostic delay, which frequently lasts 48 to 72 hours. This exposes the patient's commensal microbiota to high-potency drugs unnecessarily.[8,21] The effects are most serious in neonatal care, where MDR-associated sepsis causes an estimated 214,000 deaths each year, primarily in China, India, and Pakistan.[1,5]

In certain low- and middle-income countries (LMICs), it is estimated that up to 80% of all antibiotics designed for human use are consumed in community settings, frequently without a valid prescription.[11,22]

Specific regional studies have documented that the prevalence of low-quality or counterfeit medications can reach as high as 32% in parts of sub-Saharan Africa, such as Cameroon.[19,23] These falsified medications often provide sub-therapeutic doses that fail to eradicate pathogens while providing the ideal selective pressure for the development of genetic resistance.[1,19]

Sociocultural and behavioural elements, such as "prescribing etiquette," play an important role in maintaining inadequate use of drug practices.[9] Fear of undertreatment, perceived patient expectations, and institutional hierarchies where junior physicians may feel forced to follow senior consultants' practices despite evidence-based guidelines, all have an impact on clinician prescribing.[9,24] Gender disparities also exist in the human community; women, who are frequently the primary caregivers and handlers of food or small livestock, are more vulnerable to resistant diseases while also facing larger challenges to getting diagnostic services and high-quality care.[19] Traditional AMS methods, which concentrate solely on clinical guidelines without addressing the underlying power dynamics or socioeconomic realities, frequently ignore these social factors.[9]

The demographic change to an aging global population is emerging as a significant moderator of AMR trends.[4] Due to immunosenescence and chronic comorbidities, older persons are more vulnerable to serious infections and require regular medical care.[4] Because of their frequent contact with healthcare systems, long-term care institutions are more likely to become colonized by resistant strains, hence becoming reservoirs of resistance determinants.[4] The clinical management of infections in this population is further complicated by the use of non-antibiotic medications that are frequently used in geriatric care, such as beta-blockers and anti-inflammatories, which have been demonstrated in some studies to encourage the horizontal transfer of resistance genes through bacterial transformation.[4,25]

Worldwide travel and medical tourism play important roles in the spread of highly resistant organisms across borders.[4,26] After returning from endemic areas, foreign visitors may act as asymptomatic carriers, carrying MDR bacteria such as NDM-1 or the colistin-resistant gene mcr-1 in their gut microbiota for up to a year.[4,27] A resistance mechanism that appears in one location might spread to another continent in a matter of hours due to the globalization of trade and travel, exposing the vulnerability of national health security (Table 2).[5] Because of this "One World" reality, even nations with strong antimicrobial stewardship programs are susceptible to the importation of "superbugs" from areas with poor or non-existent regulations.[5]

Table 2: Clinical and Societal Drivers of AMR in the Human Domain[1,4,9,19]

Driver Category	Specific Factors	Impact on AMR
Clinical Practice	Empirical broad-spectrum use, lack of diagnostics	Selection of MDR strains (ESBL, CRE).
Hospital Environment	ICU density; invasive devices; poor Infection, Prevention and Control	Biofilm formation, hospital outbreaks.
Societal Behaviour	Self-medication, viral overuse, patient pressure	Community spread of resistance genes.
Socioeconomic	Poverty, substandard drugs, and gender inequality	Disproportionate burden on vulnerable groups.
Market/Innovation	R&D exit by pharma, low financial incentives	Dearth of novel antibiotics to treat superbugs.
Global Dynamics	Travel, migration, and medical tourism	Transboundary dissemination of ARGs.

AMR - Antimicrobial Resistance; ARG - Antimicrobial Resistance Gene; CRE - Carbapenem-Resistant Enterobacterales; ESBL - Extended-Spectrum Beta-Lactamase; ICU - Intensive Care Unit; MDR - Multidrug-Resistant

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The pharmaceutical industry's retreat from antibiotic research and development (R&D) has resulted in a crucial "innovation paradox".[8] Due to the high expenses of discovery, the length of time it takes for regulatory approval, and the low financial return on medications that are intended to be used for brief periods of time and maintained as "Reserve" agents, large pharmaceutical companies are beginning to view the development of new antibiotics as a financial liability.[1,8] Since the discovery of fluoroquinolones in the 1980s, the majority of "new" medications have been structural alterations of pre-existing classes rather than brand-new compounds.[1]

AMR TRENDS IN INDIA

Recent national surveillance statistics show the extent of antibiotic resistance in India. According to the ICMR-AMRSN (Indian Council of Medical Research - Antimicrobial Resistance Research and Surveillance Network) 2024 report, which examined 99,027 culture-positive isolates, 72.1% of bloodstream infections were caused by Gram-negative bacteria. Key infections such as Escherichia coli (imipenem susceptibility decreased to 57.6%) and Klebsiella pneumoniae (31.2%) have shown a notable decrease in carbapenem susceptibility, while Acinetobacter baumannii (~91% to meropenem) has shown very strong resistance. Vancomycin resistance in enterococci has reached 22%, while methicillin-resistant Staphylococcus aureus has risen to almost 53%.[15]

NAMS (National Academy of Medical Sciences) data show that E. coli produces >70% ESBLs (Extended Spectrum Beta-Lactamase), K. pneumoniae produces ≥80%, and carbapenem resistance is on the rise in important pathogens.[14] Furthermore, approximately 1,95,000 isolates are included in national surveillance by NARS-Net (National Antimicrobial Resistance Surveillance Network), highlighting India's extensive AMR prevalence across healthcare settings.[28]

ANIMAL DOMAIN

Antimicrobial Use and Selection Pressure

The livestock industry supports the livelihoods of about 1.3 billion people and accounts for 40% of the entire value of agricultural output, making it crucial to global food security and nutrition.[6] To feed the world's estimated 9.1 billion people by 2050, meat output must increase by more than 200 million tons to reach 470 million tonnes, placing a tremendous strain on animal agriculture systems.[6] Antimicrobial usage (AMU) is driven by this intensification; livestock account for more than 73% of the world's antimicrobial consumption, which is expected to rise by 67% between 2010 and 2030.[6] The animal domain is a significant reservoir where medication residues, microorganisms, and mobile genetic elements move and interact with human and environmental systems, according to the One Health concept.[10]

AMU in therapeutic, prophylactic, metaphylactic, and sub-therapeutic settings can result in AMR in animals. Metaphylaxis includes treating groups of animals in contact to prevent outbreak spread, whereas therapeutic use focuses on clinically ill animals.[6] Administration before the onset of clinical symptoms, such as intramammary infusions for the prevention of mastitis in dairy calves, is referred to as prophylaxis.[6] Low-dose antimicrobial supplementation in feed is known as sub-therapeutic dosage, and it is frequently employed to promote development. It is especially linked to prolonged selection pressure, which allows resistance genes like tetA and mcr-1 to become fixed in the animal gut.[5,6]

Microbiome and Resistance Amplification

The animal gut microbiome, which contains trillions of bacteria, contributes to the establishment of AMR by HGT.[6] When vulnerable commensals are eliminated by antibiotic exposure, resistant strains might spread and take over.[6] These organisms are then eliminated through faeces, creating a reservoir of antimicrobial resistance genes (ARGs) that contaminate water, soil, and the food chain.[6] Plasmid-mediated resistance, like mcr-1, shows effective transfer between strains of Escherichia coli and contributes to resistance in human infections like Pseudomonas aeruginosa and Enterobacteriaceae.[6]

Environmental and Transmission Pathways

Livestock-to-livestock and livestock-to-environment channels are examples of transmission dynamics in the animal domain.[6] Water systems are important because animal water supplies are contaminated by biofilms, sediments, and faeces.[6] Rainfall-induced agricultural runoff raises ARG levels in surface and groundwater, exposing animals through contact or ingestion.[6] Water bodies close to swine and poultry farms have been found to contain resistance genes such as tetW, tetO, tetQ, and tetM.[6] Resistance genes like blaTEM1 and ermB have been found in aerosols close to pig and chicken barns, indicating that airborne transmission from intensive farming also plays a role (Table 3).[6]

Table 3: Prevalence and AMR Patterns of Meat Products in Asia[6,10,38]

Meat Type	Pathogen Prevalence	Predominant Resistance (%)	Associated Genes

Poultry	*E. coli* (49.6%)	Ampicillin (79.7%), Oxytetracycline (72.8%)	*tetA, mcr-1, blaTEM*
Pork	*Salmonella* (31.7%)	Tetracycline (66.1%), Nalidixic acid (65.3%)	*sul1, blaCTX, tetB*
Beef	*S. aureus* (38.1%)	Penicillin (75.6%), Amoxicillin (69.2%)	*mecA, blaSHV*

SECTOR-SPECIFIC CONTRIBUTIONS

Poultry:

Due to the widespread use of tetracyclines, sulphonamides, and macrolides, the poultry industry significantly adds to the worldwide AMR burden.[8] Systematic investigations show pooled incidence rates of 49.6% for E. coli and 31.7% for Salmonella, with substantial resistance to ampicillin and oxytetracycline.[29] A recent meta-analysis of meat products across Asia revealed that approximately 24.7% of the total antimicrobial resistance (AMR) genes identified were specifically associated with the poultry production chain.[11] In situations when animals are kept indoors for up to 45 days in 12 months, antibiotics are often utilized to make up for inadequate biosecurity and overpopulation.[6] These circumstances encourage the accumulation of resistance cassettes in class 1 integrons and the quick clonal growth of resistant strains.[29]

Cattle and Dairy:

Dairy and cattle systems have a major role in the spread of AMR, especially when treating respiratory illnesses and mastitis.[30] Bacterial adaptability in the human gut is facilitated by antibiotic residues, particularly quinolones and sulphonamides, which are commonly found in raw and even pasteurized milk.[30] According to studies, MDR E. coli and Staphylococcus aureus carrying genes like blaTEM and blaCTX-M can be found in up to 70% of raw milk samples.[10,30] Due to a lack of knowledge about AMR and the possibility of the spread of resistant infections like Klebsiella pneumoniae and Clostridium perfringens, camel milk, which is frequently drunk unpasteurized in dry areas, presents extra dangers.[30,31]

Aquaculture:

Because antibiotics are directly administered into aquatic systems, aquaculture is a major hotspot for AMR selection.[8] Marine sediments serve as long-term ARG reservoirs due to the accumulation of antibiotic residues and resistant bacteria.[30] After being remobilized, they could re-enter the human food chain through seafood. Thai studies have linked untreated aquaculture effluents to the widespread prevalence of resistance genes like floR, sul1, and mcr-1 in water bodies, suggesting that they could spread globally.[11,30]

Companion Animals:

Through intimate human interaction, companion animals aid in the spread of AMR. Dogs and people may have strains of E. coli that are resistant to ceftazidime and enrofloxacin. Compared to adopted animals, animals from commercial breeding facilities are more likely to carry resistant strains.[16] On the other hand, better cleanliness habits or exposure to a variety of microbiota may provide protection. Puppies from retail chains have been directly connected to human outbreaks of MDR Campylobacter jejuni.[16]

Wildlife:

Wildlife species serve as both sentinels and reservoirs for anthropogenic AMR.[32] Pteropus medius is an example of a synanthropic species that interacts with shared water supplies and household animals.[32] These populations have been shown to contain ESBL-producing E. coli and resistance genes including blaTEM and blaCTX-M, which indicate environmental contamination. While faecal pollution brings resistance genes into agricultural systems, migration patterns encourage transboundary diffusion. The scope of environmental spread is highlighted when wildlife is found to be resistant to reserve antibiotics like imipenem.[32]

DRIVERS AND MITIGATION STRATEGIES

Economic incentives, such as veterinarians' reliance on medicine sales, lead to overuse of antibiotics, which frequently goes against stewardship objectives.[9,12] Farmers in low-income areas rely on over-the-counter antibiotics due to restricted access to veterinary treatment.[5] However, as demonstrated by programs like the Danish "Yellow Card" system, antibiotic consumption thresholds and regulatory monitoring can significantly reduce AMU without reducing productivity.[4] Preventive strategies including immunization, improved biosecurity, and alternatives like probiotics and bacteriophages are necessary to reduce antibiotic dependency and disrupt transmission channels.[6,30]

ENVIRONMENTAL DOMAIN

Reservoirs and Pathways

The environmental domain is becoming acknowledged as an important component of the AMR ecosystem, however its significance as a direct driver of clinical human infections is still being investigated.[33] According to the One Health framework, the environment is

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regarded as a dynamic interface where anthropogenic pollutants, such as heavy metals and pharmaceutical residues, may stimulate microbial evolution.[10] The environmental domain offers an unparalleled genetic resistome that pathogens may access through HGT, whereas the human and animal sectors are distinguished by direct treatment selection.[7] However, recent research reveals that, while ARGs are widely present in the environment, their relevance and total contribution to the worldwide clinical AMR burden have yet to be adequately assessed.[33]

Pharmaceutical Manufacturing: Industrial Hotspots of Selection

Pharmaceutical production effluents are regarded as substantial contributors to AMR environmental selection because they dump exceptionally large amounts of active pharmaceutical ingredients (APIs) directly into adjacent water bodies.[10] In some industrial centers, such as Patancheru, India, the fluoroquinolone ciprofloxacin has been detected in treatment plant effluents at amounts as high as 31 mg/L. This is hundreds of times higher than therapeutic doses.[10,30] According to Larsson and Elbehiry, these intense selection pressures help native aquatic microbial communities develop new resistance mechanisms that are then incorporated into human infections through horizontal gene transfer.[7,8] Localized resistomes are far more prevalent than those in unpolluted areas because these industrial waste streams are often released with inadequate treatment, particularly in places with inadequate regulatory enforcement.[10,14]

Wastewater Systems

Human-derived resistant bacteria interact with a variety of environmental microbes in municipal and hospital wastewater systems, which are considered important intersections.[10,34] High densities of MDR "ESKAPE" microorganisms, disinfectants, and drug residues that function as a powerful selection "soup" for carbapenemase and colistin resistance genes make hospital effluents especially dangerous.[8,30] Research conducted in India has shown that the isolation rate of Escherichia coli resistant to third-generation cephalosporins can approach 95% when treatment plant inlets receive hospital waste, but it is only 25% for domestic waste alone.[30] Treated effluents and sewage sludge (biosolids) act as chronic sources of AMR when released into rivers or utilized as agricultural fertilizer because conventional wastewater treatment plants (WWTPs) are not built to eliminate sub-inhibitory concentrations of antibiotics or ARGs.[10,14,35]

Terrestrial Systems: Soil, Manure, and Agricultural Runoff

Due to the frequent application of animal manure and biosolids containing drug residues and resistant microorganisms, agricultural soil acts as a major reservoir for antimicrobial resistance.[35] Manure is a major source of selective pressure that modifies the native soil microbiome. Soil microbial communities gradually produce stable populations of ARGs, such as tetA and sul1, which can be absorbed by crops or seep into groundwater following rains.[10,35] The use of untreated irrigation water exacerbates the soil-to-plant-to-human pathway by spreading resistant organisms such as Salmonella and ESBL-producing E. coli onto fresh vegetables, possibly endangering customers.[10,19]

Aquatic Ecosystems and Marine Sediments: Conduits and Sinks

Due to inputs from industrial waste, municipal sewage, and agricultural runoff, freshwater rivers, lakes, and groundwater are considered important channels that may facilitate the transboundary spread of AMR.[10,34] Due to sorption to particle matter, marine sediments in aquatic environments act as long-term sinks for ARGs, which may then be remobilized by benthic animals and re-enter the food chain through seafood.[10] The direct application of antibiotics to water causes localized "hotspots" in fish ponds, which then release untreated effluents containing genes like mcr-1 into natural water systems, making aquaculture a major contributor to this cycle.[8,10] Because of water's environmental connection, resistance in one localized watershed can swiftly spread to other watersheds and worldwide trade.[10,30]

Atmospheric Pathways: Bioaerosols and Dust Dissemination

Atmospheric routes and aerosols are emerging as a potentially important yet understudied vector for the spread of AMR.[10] Viable resistant bacteria like MRSA and Acinetobacter baumannii can be found in bioaerosols and dust particles from intensive animal farms and medical facilities. over considerable distances.[6,10] Farmworkers in agricultural contexts have a direct occupational danger when they breathe in contaminated dust, and the environmental resistome is further expanded when these particles settle into soil and water systems.[6,10] Environmental containment must take airborne spread into consideration, as evidenced by studies conducted in poultry operations that found high-risk factors like blaTEM and mcr-1 in the air surrounding the barns.[6,10]

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Ecological Drivers: Co-selection and Climate Change Amplification

Heavy metals and biocides, which co-select for resistance through common efflux mechanisms, frequently influence environmental selection in addition to antibiotics.[4,10] These processes are further accelerated by climate change; rising global temperatures are associated with both the acceleration of HGT and higher bacterial proliferation.[4,10] Additionally, resistant microorganisms and pharmaceutical residues from untreated sewage spread quickly into the surrounding ecosystem due to major weather events like flooding and cyclones.[10,11] Therefore, managing the ecological forces that worsen the current crisis requires incorporating climate resilience into AMR policy.[10,12]

ENVIRONMENTAL SURVEILLANCE AND REMEDIATION TECHNOLOGIES

Advanced treatment technologies must be implemented in conjunction with strong multisectoral surveillance in order to effectively mitigate environmental AMR.[8,10] Antibiotic residues can be broken down and ARGs removed from effluents before discharge by ozonation, UV irradiation, and membrane filtration.[10,14] Metagenomic sequencing is used by integrated monitoring systems such as the U.S. Surface Water Antimicrobial Resistance Monitoring System (SWAM) and the WHO "Tricycle" project to monitor sentinel gene mobility throughout the One Health triangle.[8,34] Enforceable industrial discharge rules and a global commitment to maintaining the ecological health of our shared planet are ultimately necessary to reduce the environmental load.[10,16]

ANTIMICROBIAL RESISTANCE THROUGH ONE HEALTH LENS

1. Transmission Cycles: The Fluidity of the Resistome

The transmission of AMR is a dynamic and multifaceted process characterized by the continuous movement of resistant bacteria and genetic determinants across humans, animals, and the environment.[36] To effectively implement stewardship interventions, it is necessary to move beyond simply identifying reservoirs and instead delineate the specific chains of transmission that allow resistance to disseminate.[37] By facilitating the bidirectional transmission of resistance, these channels guarantee that a selection event in one sector, like a hospital or a poultry farm, has systemic effects throughout the One Health triad.[8,10]

HGT, which permits the exchange of ARGs between various bacterial species and taxa, is the main molecular mechanism causing this dissemination.[8] This is accomplished through three major processes: conjugation (direct cell-to-cell plasmid transfer), transformation (free DNA uptake from the environment), and transduction (virus-mediated transfer).[1] Environmental commensals can act as a genetic "bridge" that transfers resistance into clinical pathogens because mobile genetic elements (MGEs), such as the mcr-1 gene for colistin resistance or blaNDM-1 for carbapenem resistance, frequently reside on promiscuous plasmids that can cross genus boundaries.[36,37]

The food chain is a significant channel for resistant bacteria from the animal sector to reach human populations through the consumption of contaminated items.[6] Under the pressure of mass prophylaxis or sub-therapeutic growth enhancement, pathogens such as Campylobacter jejuni and Salmonella Typhi often invade animals and subsequently infect humans through undercooked meat, unpasteurized milk, or contaminated eggs.[38,39] Strict agricultural laws, like India's 2019 ban on colistin as a growth stimulant, which was closely connected to a subsequent drop in the prevalence of the mcr-1 gene in food handlers, are necessary to break this chain in addition to clinical stewardship.[4,14]

Water systems and terrestrial runoff are regarded key conduits for the spread of ARGs and pharmaceutical residues into the environment.[34] High levels of unmetabolized medications and multidrug-resistant (MDR) microorganisms that are not entirely eliminated by standard treatment procedures are frequently found in hospital and pharmaceutical manufacturing facility effluents.[10,30] These factors pollute water used for crop irrigation when they enter rivers and lakes.[8] As a result, fresh produce and soil bacteria absorb ARGs, which eventually re-enter the human gut microbiota through consumption.[10,19]

Finally, anthropogenic migration and wildlife vectors promote the worldwide, transboundary spread of resistance.[11] International travel and trade enable humans to serve as asymptomatic carriers of highly resistant clones, such as NDM-1, which can spread across continents in hours.[1,4] Concurrently, migratory species and synanthropic wildlife acquire resistant bacteria from human-impacted ecosystems, such as sewage-polluted water, and transfer these genes across national boundaries through migration and the deposition of waste into soil and livestock feed systems.[10,11] An integrated One Health strategy that emphasizes enhanced wastewater cleanup,

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diagnostic-led stewardship to lessen selective pressure, and coordinated international surveillance is necessary to break these transmission loops.[8,16]

2. Epidemiology: Shifting Patterns and Global Burden

LMICs are disproportionately affected by the epidemiology of AMR, which is marked by an increase in MDR pathogen isolation rates and a reduction in treatment options.[19] According to surveillance in Northeast India, 75% of human diarrheagenic E. coli isolates are MDR/XDR, and new carbapenem resistance has been found in human, food, and animal sources.[40] Imipenem susceptibility in Klebsiella pneumoniae decreased from 70.8% in 2017 to only 42.8% in 2024, according to a longitudinal analysis from the ICMR-AMRSN report (2024).[15]

This epidemiological change is compounded by socioeconomic variables, such as a 32% prevalence of counterfeit or substandard medications in certain places, which deliver subtherapeutic doses that cause genetic modifications in surviving bacteria.[1] Furthermore, in the post-COVID-19 era, Minimum Inhibitory Concentrations (MICs) for medications like as ciprofloxacin in Salmonella Typhi have shifted to the right, indicating a growth of high-level resistance as a result of the pandemic's extensive empirical antibiotic use.[15]

3. Stewardship Interventions: Integrated and National Strategies

At the Indian policy level, Version 2.0 of the National Action Plan on AMR (NAP-AMR) promotes a "Whole of Government" strategy that combines human care with veterinary supervision and industrial environmental norms.[41] The 2019 prohibition on colistin as a growth promoter, which limited its usage to therapeutic human indications to maintain its status as a last-resort medication, was a significant action.[14]

Technological innovation is another vital pillar of modern stewardship. The application of AI and machine learning allows for real-time monitoring and the generation of personalized antibiograms, which can improve diagnostic speed by up to 50%.[13,19] In the clinical setting, interventions like the implementation of Schedule H1 (requiring valid prescriptions for high-end antibiotics) and the "Red Line Campaign" (empowering consumers to identify restricted drugs) have been crucial in curbing OTC sales.[14] Successful regional models, such as Thailand's "Antibiotics Smart Use" program, have demonstrated that community commitment devices can achieve a 30% reduction in inappropriate prescribing.[19]

TECHNOLOGICAL INNOVATIONS

By analyzing enormous volumes of genomic, clinical, and environmental data, AI systems are able to accurately forecast resistance patterns and the start of new epidemics.[8] For example, ML models evaluated millions of chemical compounds in a few days to discover new antibacterial drugs like halicin, a procedure that would have taken years using traditional techniques.[13] These technologies also support precision medicine by reducing trial-and-error prescribing by identifying the optimal treatment for a patient based on their unique disease profile.[6]

The identification of pathogens and resistance profiling have been changed by advanced diagnostic techniques including Whole-Genome Sequencing (WGS) and MALDI-TOF MS.[8] With the help of WGS, scientists can precisely track the clonal spread of resistant strains in humans, animals, and the environment, enabling targeted therapies in hotspots.[39]

SOCIOECONOMIC DISPARITIES AND LMIC REALITIES

The AMR epidemic disproportionately impacts low- and middle-income countries due to a combination of inadequate healthcare infrastructure, limited availability to novel antimicrobials, and unregulated drug access.[19] Poverty and poor sanitation exacerbate the growth of resistant pathogens in these settings, and because testing is expensive, physicians are often forced to utilize empirical broad-spectrum treatments.[35] Furthermore, a lack of comprehensive surveillance systems makes it difficult to identify many resistance patterns, which hinders the development of evidence-based policy.[42] Gender dynamics also play a role, since women are often the major caregivers and livestock handlers, increasing the risk to resistant infections while facing greater barriers to healthcare access.[19]

To address AMR in low- and middle-income countries, equity-focused solutions must go beyond modifying high-income models.[9] This includes making sure that foreign funding is allocated to local priorities and creating national action plans through the Global Antibiotic Resistance Partnership (GARP).[37] Community engagement, including commitment tools and public education campaigns, is essential to improving health and altering social drug-use behaviors.[8] To eliminate the selective pressure caused by inadequate dosages, policy improvements must focus on reducing over-the-counter sales and improving the antibiotic supply chain quality. Incorporating AMR management into more comprehensive sustainable development objectives could guarantee that mitigation

measures are both economically and culturally feasible.[42]

POLICY FRAMEWORKS AND GLOBAL GOVERNANCE

The Quadripartite Alliance, which includes the World Health Organization (WHO), Food and Agriculture Organization (FAO), World Organisation for Animal Health (WOAH), and United Nations Environment Programme (UNEP), coordinates the global response to AMR by supporting multisectoral coordination under the One Health concept.[8] This relationship has resulted in the establishment of international tracking systems such as GLASS, which standardizes AMR reporting across 130 countries, and global action plans.[8] National Action Plans (NAPs) are the primary vehicle for implementing these policies at the local level, but their effectiveness varies according to political backing and financial resources.[42] Although policy drafting is often sound, many countries lack the resources for implementation and oversight, particularly in the environmental and animal sectors, according to a 2023 thorough evaluation of 114 NAPs.[9]

In India, Schedule H1 (2014) restricts the sale of over-the-counter (OTC) antibiotics by requiring the prescription-only sale of 46 high-end antibiotics and maintaining sales records. The Red Line Campaign (2016) aims to raise awareness of this restriction.[8,14] By incorporating the WHO AWaRe classification into the National Essential Medicines List to direct sensible use and monitoring, antibiotic scheduling is further reinforced.[15,21,28] Policies limit the use of non-therapeutic antibiotics in the animal industry. One example is India's 2019 prohibition on colistin as a growth promoter, which forbids its production, distribution, and usage in animals raised for food.[41]

Financial incentives are an effective method for promoting change in the fight against AMR. Traditional market models often fail to promote antibiotic innovation because of the high costs of research and development and the poor returns from short treatment periods.[8] One solution is to create "pull" incentives, like subscription models that were first introduced in the UK and that pay pharmaceutical companies according to the therapeutic benefit of their drugs rather than sales volume.[8] To make sure that the production of antibiotics does not contribute to the spread of resistance in the environment, procurement standards should also address pollution management.[7] To ensure that surveillance signals from one sector stimulate timely action in others, sustainable governance requires the removal of bureaucratic obstacles between environmental, agricultural, and health authorities.[19]

RESEARCH GAPS AND PRIORITIES IN THE INDIAN AMR LANDSCAPE

The evidence for antimicrobial resistance (AMR) in India is primarily collected from tertiary care human data, with significant gaps in the community, livestock, and food animal sectors, restricting national-level inference.[14] A One Health understanding is limited by the insufficient correlation between AMU and resistance.[14,41] Infrastructure restrictions, such as inadequate laboratory capacity, a lack of skilled workers, and the absence of standardized genomic and bioinformatics frameworks, impede monitoring and pathogen tracking.[14,15]

According to NAP-AMR 2.0 (2025) and ICMR (2024), research goals include integrated One Health surveillance, mapping transmission paths, evaluating environmental AMR threats and residue standards, and bolstering decentralized diagnostics, digital integration, and genomic surveillance. Sustaining antimicrobial efficacy also requires measuring socioeconomic burden, assessing alternative treatments (phage, microbiome, AYUSH), and developing domestic antibiotics, point-of-care diagnostics, and innovation platforms.[14,15,41]

CONCLUSIONS

Antimicrobial resistance is a defining health problem of the twenty-first century, with its origins in the evolutionary and anthropogenic interactions between humans, animals, and the environment. This review has analysed the multidirectional transmission cycles that allow resistance determinants to disseminate through industrial waste, the food chain, and global mobility, underscoring that a siloed clinical response is insufficient to contain a borderless microbial threat. The epidemiology of this crisis, particularly in LMICs, reveals a critical loss of efficacy in last-resort antibiotics, requiring a shift from empirical therapy to diagnostic-led stewardship. Ultimately, this review provides practitioners and policymakers with a multisectoral roadmap that integrates rapid microbiology diagnostics (e.g., MALDI-TOF MS) and AI-driven surveillance with enforceable national policies such as India's Schedule H1 and the ban on colistin as a growth promoter to effectively break transmission loops across the One Health triad and preserve the long-term effectiveness of the global antimicrobial commons.[8,12,14,16]

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All authors (YR, MC, GR, AM, KS, BN) contributed substantially to the conception and design of the work, data acquisition and interpretation, manuscript drafting and critical revision, approved the final version, and agree to be accountable for all aspects of the work.

AI DECLARATION

Generative AI was used only for creating illustrative figures in this manuscript

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