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## Chapter

# Antimicrobial Resistance: A One Health Perspective in India

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## Abstract

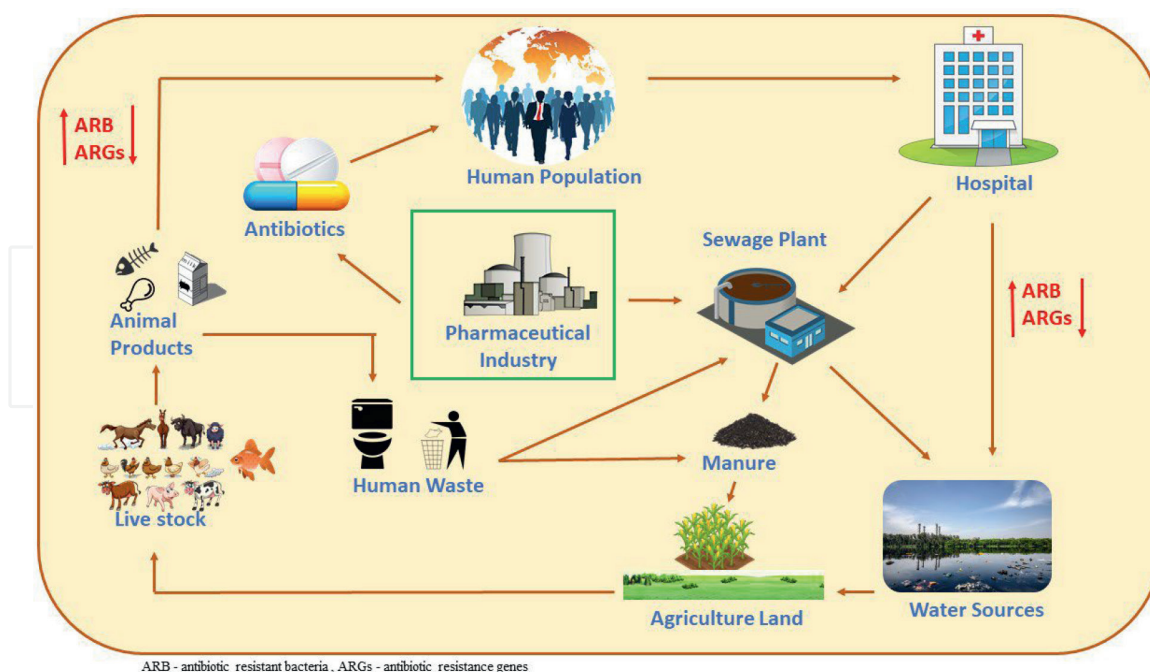
One health is a collaborative, multi-sectoral, trans-disciplinary approach used to achieve optimal health and well-being outcomes that recognize the interconnections among people, animals, plants, and their shared environment. This approach is crucial because animals and people are colonized by the same bacteria species and treated with the same antibiotic classes; the technique is instrumental in fighting antibiotic resistance. The microorganism developed antibiotic-resistant genes, which were transferred to the animal and human population via the environment. Human activities speed up the organism to acquire resistance rapidly. The primary sources of antimicrobial resistance from the environment were improper sewage and hospital waste sanitation, effluents from antibiotic production units, animal husbandry waste, agricultural manure use, livestock, and aquatic sources. This study analyzed the various routes by which antimicrobial-resistant gene is transferred into humans and their pathway in India. The study concludes that implementing strict regulation and monitoring regarding the irrational use of antibiotics in animals, sewage disposal, waste disposal, and hospital infection control practices, and providing awareness to the public regarding antibiotic resistance can reduce the rate of developing antibiotic resistance to some extent along with implementing antibiotic stewardship programmes for veterinary medicine.

**Keywords:** antimicrobial resistance (AMR), antimicrobial stewardship (AMS), one health, environment, sources

## 1. Introduction

One health is a collaborative, multi-sectoral, trans-disciplinary approach working at local, regional, national, and global levels to achieve optimal health and well-being outcomes that recognize the interconnections among people, animals, plants, and their shared environment [1]. This approach is crucial because animals and people are colonized by the same bacteria species and treated with the same antibiotic classes; the technique is instrumental in fighting antibiotic resistance [2].

Antimicrobial resistance is defined as a microorganism's acquired or inherited capability to resist the effect of a particular antimicrobial and then continue its proliferation



**Figure 1.**  
Schematic diagram of antibiotic-resistant gene transfer from various sources to human.

in the host. Superbugs are microorganisms that are capable of withstanding more than one antimicrobial. At the initial stage of antimicrobial discovery, primary sources were natural sources; therefore, the chances of developing antimicrobial resistance from natural sources are now at their peak. Every organism battles with antimicrobials for survival and existence, but human actions enhance this for an organism to acquire resistance. This has led to a global threat of antimicrobial resistance and treatment failures.

As per the World Health Organization (WHO), 07 lakh deaths are reported every year due to antimicrobial resistance resulting in treatment failure. Estimates show that 10 million deaths will be reported by 2050 due to antimicrobial-resistant infections. WHO further recognizes that antibiotic resistance bacteria (ARB) and resistant genes are the major contributors to environmental pollution, and they will be a significant threat to human and animal populations worldwide.

The prevalence and occurrence of antimicrobial resistance from environmental and natural sources is not studied extensively. The environmental factors also vary across locations based on the ethnicity, culture, belief, and practices of humans worldwide. As per the existing evidence, the primary sources of antimicrobial resistance from the environment were improper sewage and hospital waste disposal, effluents from antibiotic production units, animal husbandry waste, agricultural manure use, livestock, and aquatic sources (**Figure 1**). Due to globalization, these antibiotic-resistance genes spread rapidly from one region to another. Human migration and travel, importing and exporting goods primarily carry these resistant genes and organisms to different areas [3].

## 2. Antibiotics in humans

Various reports across the globe state that Asian countries are the most widespread consumers of antibiotics worldwide. More specifically, India (10.7 units per person)

stands first, followed by China (7.5 units per person) in antibiotic consumption. As per the latest study, the BRICS countries (Brazil, Russia, India, China, and South Africa) observed a 76% increase in the consumption of antibiotics [4]. As per the antimicrobial resistance (AMR) surveillance data from India, the most common pathogen isolated was *Escherichia coli* (*E. coli*), followed by *Klebsiella species* (22%), *Staphylococcus aureus* (*S. aureus*) (18%), *Pseudomonas species*. (10%), *Enterococcus species* (9%) and *Acinetobacter species* (8%), *Salmonella Typhi* and *Para typhi* (0.5%) [5]. The frequently consumed antibiotics in India were cephalosporins (32%), penicillin (28%) and macrolides (14%), followed by tetracyclines (6%) [6]. As per the study by ICMR, more resistance was found in cephalosporins (60%) and fluoroquinolones (41.5%) [7].

## 2.1 Antimicrobial resistance and human gut microbiome

The bacteria, their genomes and the environmental circumstances of the human digestive tract are referred to as the 'human gut microbiome'. The use of high-throughput, low-cost sequencing tools has fuelled research into the gut microbiome in the recent decade to determine its composition, function, and role in health and illness [8]. The gut includes hundreds of bacterial species, collectively known as the microbiota, where Bacteroidetes and Firmicutes bacteria account for 90% of all species in healthy individuals' guts [9]. Less common bacteria such as phyla Actinobacteria, Proteobacteria and Fusobacteria can protect against diseases [10, 11]. The human host has a symbiotic or commensal connection with most intestinal microorganisms. However, some organisms belonging to Enterobacteriaceae, including *Escherichia coli* and *Klebsiella pneumoniae*, and Enterococcaceae, particularly *Enterococcus faecalis* and *Enterococcus faecium*, are found in the gut microbiota. Intestinal carriage of these bacteria can predispose to urinary tract infections and more serious systemic infections in immunocompromised people [12–14]. Infections caused by antibiotic-resistant clones of *E. coli*, *Klebsiella pneumoniae* [15] and *E. faecium* [16] have increased globally in recent decades. Various studies have observed that multi-drug resistance diseases cause more morbidity and mortality in low- and middle-income countries in Asia, Africa and South America [17–19].

The essential methods by which bacteria might develop resistance to antibiotics are the prevention of antibiotics reaching toxic levels inside the cell, altering the antibiotic target, and modifying or degradation of the antibiotic itself [20]. These resistance mechanisms can occur due to chromosomal gene changes and the horizontal gene transfer (HGT) of antibiotic resistance genes (ARGs) from other strains of the same or different species. HGT aided significantly in the global distribution of ARGs. HGT can occur in any environment, especially when bacterial loads are high, such as in soil [21], wastewater treatment facilities [22, 23], and human and animal gut microbiomes [24–26]. Previous research has demonstrated that the gut has many antibiotic resistance determinants, known as 'gut resistome' [27, 28].

Oral ingestion of contaminated substances (food, trash, residual waste from occupational exposure or polluted surroundings) and inhalation of airborne ARB are two routes by which ARB and ARGs reach human gut ecosystems [29, 30]. The fate of ingested bacteria, including ARB, is determined by various factors such as pre-existing microbiome structure, medication, host age and dietary environment. Under normal nutritional and physiological conditions, the diversity and abundance of the gut microbiome operate as a significant barrier to the integration of ingested bacteria, and most ingested bacteria only colonize the human body transiently. Antibiotic

treatment or intake of antibiotic residues, on the other hand, may significantly modify gut microbiota structure, facilitate ARB integration by reducing competition, and enhance ARG proliferation by removing competition.

Due to a favorable environment (e.g. high concentrations of ARG, stable temperature, physiochemical conditions, and nutrient availability), long-term colonization by ARB may also accelerate HGT in the human gut and contribute to the emergence of multi-drug resistance genes by pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA).

## 2.2 Mechanism of horizontal gene transfer

The transfer of genetic information between bacterial species is a dynamic and continuous process resulting in the constant evolution of the bacteria. It is known to impact the host significantly with delayed or immediate effects. Most frequently recognized mechanisms of HGT occur by transduction, transformation or conjugation. Naked DNA from the extracellular environment is taken up by bacteria and integrated into their genomes during transformation. Bacteria that are naturally transformable or competent are required for the transformation process. The genes involved in DNA uptake in several other species show this trait is more prevalent [31]. Over 80 bacterial species have been experimentally demonstrated to be naturally competent. The factors that cause naturally transformable bacteria to enter a capable condition are unknown; however, nutritional deprivation and the presence of competence-inducing peptides have been identified as triggers [32]. Due to this process, competent natural pathogens such as *Neisseria gonorrhoeae*, *Vibrio cholera* and *Streptococcus pneumoniae* have acquired antibiotic resistance [33].

Membrane vesicles (MVs) are 20–250 nm spherical objects produced mainly by Gram-negative bacteria when the outer membrane bulges away from the cell and is released by constriction [34]. The cargo is delivered when MVs fuse with their target cells. MVs are generated *in vitro* by commensal bacteria in the gut. MVs formed by gut bacteria can also include cytoplasmic components, including DNA, which are significant in the context of HGT [35]. Protrusion of the outer and inner membranes is thought to create DNA-containing MVs, which leads to the incorporation of cytoplasmic components into the vesicles. Similarly, vesicle-mediated transfer of DNA has also been reported for *E. coli* [36]. While MVs are produced in the gut and can potentially influence host immune responses [37], it is unclear whether they can contribute to HGT in the gut microbiome.

Transduction is the transfer of chromosomal and extrachromosomal DNA between bacteria *via* a viral intermediary known as a bacteriophage. Generalized, specialized, and lateral transductions are the three basic transduction methods. Antibiotic-resistant genes can mobilize any portion of a bacterial genome if favorable factors exist. When bacteriophages in the lytic cycle incorporate parts of the bacterial host's DNA during capsid production, this is known as generalized transduction. Regions immediately flanking a lysogenic phage's integration site are excised and packed into the capsid in specialized transduction [38]. Prophages initiate DNA replication while still integrated into the host, known as lateral transduction.

Before excision from the host genome, this mechanism makes numerous copies of DNA. After being excised, the DNA—which can be hundreds of kilobases long and comprise both phage and neighboring genes—is packaged into new phage particles and distributed to other bacterial strains [39]. The human gut has a diverse community of bacteriophages [40, 41], and ARG-carrying phages can be found in large

numbers in the gut and other settings [42]. Antibiotic therapy enhances the number of these ARG-carrying phages in the human stomach [43]. The quantitative contribution of phages to the horizontal transfer of ARGs is still unknown.

Mobile genetic elements like plasmids and integrative and conjugative elements (ICEs) are transmitted from one bacteria to another in the conjugation process [44]. Due to their large size and the common occurrence of one or more toxin-antitoxin modules that ensure that plasmids are kept inside their microbial hosts, conjugative plasmids are likely the most relevant for transmitting ARGs among conjugative elements [45].

A pilus carries DNA between bacteria close to one other during conjugation, a complicated, multi-stage, and contact-dependent process [46]. With its rich mucous coating and high density of bacterial cells, the gut provides an ideal habitat for conjugation. While colonizing the human gut, commensals and opportunistic infections have been found to transfer antibiotic resistance plasmids and ICEs [47, 48]. Notably, conjugative plasmids can supply the machinery that allows non-self-transmissible DNA to be mobilized, considerably enhancing the potential for resistance determinant HGT [49].

### 3. Antibiotics use in animal husbandry

In 1940, studies observed that the addition of antibiotics in cattle feed led to an enhancement in the weight gain and feed conversion ratio, which led to the irrational use of antibiotics in animals to enhance cattle growth. Over several years, this irrational use of antibiotics in cattle feed led to an increased prevalence of infectious diseases in animals due to the development of antibiotic resistance [50].

The cross-sectional study conducted in Haryana, with high milk consumption in the Indian subcontinent, showed the irrational use of antibiotics as growth enhancers and animal feed supplements. About 81% of the total participants in the study agreed that they were about to add antibiotics to improve the production of animal products. The survey indicates that 46% of the participants accepted that animal products transmitted resistant bacteria to humans. In animal husbandry, the diagnosis is critical for prescribing antibiotics [51].

The prevalence of multi-drug resistant, extended-spectrum beta-lactamases producing *Escherichia coli* from pig farms in Mizoram was studied by analyzing the fecal samples collected from organized and unorganized farms. From the analysis, they inferred that the majority of the *E. coli* were resistant to amoxicillin (81.7%), cefalexin (85.42%), co-trimoxazole (50.78%), sulfafurazole (69.38%), tetracycline (65.89%) and trimethoprim (TR) (51.94%). The results indicated the misuse and overuse of antibiotics in pig farms in India [52].

There are many possible routes for transmitting antibiotic-resistant bacteria from farm animals and their products, directly or indirectly, of which horizontal gene transfer plays a significant role [53, 54]. **Table 1** depicts various antibiotic-resistant gene observed in livestock. Shotgun metagenomics was used to analyze the characterization of the resistome, showing the presence of plasmid metagenomes in AMR genes. The most common resistance in cattle and animal products was to tetracycline, quinolone, and beta-lactams.

The behavior and destiny of ARB and ARGs discharged from animal husbandry to soil (e.g. by land application of manure and wastewater irrigation) and aquatic ecosystems have been studied extensively (e.g. through wastewater discharge and runoff).

Class	Livestock animals	Antibiotic-resistant gene identified
Penicillin	Cattle, pigs, sheep, turkeys, horses. Dogs, cats, calves.	<i>ampC</i> , <i>blaTEM</i> , <i>qnrS</i> , <i>tetW</i> .
Sulfonamide	Rabbits, dogs, poultry dogs, turkeys, cats.	<i>sulI</i> , <i>sulII</i> .
Polypeptides	Food-producing animals. Beef cattle, dairy cattle, poultry, and swine, turkey.	<i>mprF</i> , <i>ycyG</i> , <i>rpoB</i> , <i>rpoC</i> , <i>cls2</i> , <i>pgsA</i> , <i>agrA</i> , <i>prs</i> , <i>pnpA</i> , <i>pmrHFIJKLM</i> , <i>pagP</i> , <i>phoP</i> .
Aminoglycosides	Cattle and sheep, chickens, goats, lambs, piglets, horses, turkey.	<i>rmtA</i> , <i>rmtB</i> , <i>armA</i> , <i>gar</i> .
Amphenicols	Poultry, birds.	<i>fexA</i> , <i>cat</i> , <i>cmlA</i> , <i>floR</i> , <i>cfr</i> , <i>fex</i>
Tetracycline	Calves, lambs, poultry, and swine.	<i>tet</i>
Cephalosporins	Chicks, turkey, cattle, goats, pigs, sheep.	<i>blaTEM-1</i> , <i>blaDHA-1</i> , and <i>cfxA</i> .
Polymyxins	Food-producing animals. Beef, cattle, dairy cattle, poultry, and swine.	<i>arnBCADTEFoperon</i> , <i>pmrE</i> , <i>pmrC</i> , <i>pmrA/pmrB</i> , <i>phoP/phoQ</i> , <i>mgrB</i> , <i>ptB</i> , <i>phoP/phoQ</i> and <i>mgrR</i> , <i>lpxM</i> , <i>acrAB</i> , <i>kpnEF</i> , <i>lpxA</i> , <i>lpxC</i> , <i>lpxD</i> , <i>colR/colS</i> , <i>cprR/cprS</i> , <i>parR/parS</i> , <i>oprH</i> .
Macrolides	Poultry, broilers, cattle, pigs, lambs.	<i>erm</i> , <i>carA</i> , <i>ole</i> , <i>smrB</i> , <i>tlrC</i> , <i>vgaA</i> , <i>vgaB</i> , <i>lmrA</i> , <i>mefA</i> , <i>msr</i> , <i>lsaA</i> , <i>lsaB</i> , <i>ereA</i> , <i>ereB</i> , <i>vgbA</i> , <i>vgbB</i> , <i>inuA</i> , <i>inuB</i> , <i>vat</i> , <i>mph</i> .
Streptogramins	Cattle, pigs swine, turkey, and broiler chickens.	<i>erm</i> , <i>carA</i> , <i>ole</i> , <i>smrB</i> , <i>tlrC</i> , <i>vgaA</i> , <i>vgaB</i> , <i>lmrA</i> , <i>mefA</i> , <i>msr</i> , <i>lsaA</i> , <i>lsaB</i> , <i>ereA</i> , <i>ereB</i> , <i>vgbA</i> , <i>vgbB</i> , <i>inuA</i> , <i>inuB</i> , <i>vat</i> , <i>mph</i> .
Glycopeptides	Poultry, broilers, turkeys, birds.	<i>Van A</i>
Lincosamides	Swine	<i>erm</i> , <i>carA</i> , <i>ole</i> , <i>smrB</i> , <i>tlrC</i> , <i>vgaA</i> , <i>vgaB</i> , <i>lmrA</i> , <i>mefA</i> , <i>msr</i> , <i>lsaA</i> , <i>lsaB</i> , <i>ereA</i> , <i>ereB</i> , <i>vgbA</i> , <i>vgbB</i> , <i>inuA</i> , <i>inuB</i> , <i>vat</i> , <i>mph</i> .
Fluoroquinolones	Dogs and cat Poultry.	<i>qnr</i>

**Table 1.**  
Antibiotic-resistant gene observed in livestock.

Horizontal gene transfer (HGT) can transmit intracellular and free ARGs in surface and groundwater, soil and air [55–58] to indigenous bacteria [59, 60] through several paths. These ARBs may finally reach and colonize humans [21, 61], producing acute infections or long-term quiet colonization that can eventually evolve into an infection.

Bacteria-carrying ARGs are discharged into diverse receiving habitats from livestock farms *via* drainage, treated wastewater and solid waste. ARB and indigenous bacteria may undergo HGT. Humans can potentially become infected with ARB if exposed to it (e.g. water ingestion, food ingestion and inhalation). ARB might then replicate in the human body (particularly the gut) and cause endogenous or external infections.

### 3.1 Antibiotic use in milk animals

Raw milk is a product that is sold unprocessed. Therefore, the presence or grade of heat-treatment stages is left to the consumer's discretion. Furthermore, the

consumption of non-heat-treated raw milk is now widely accepted as a trend in industrialized countries owing to its positive health effects.

The most identified antibiotics in milk animals, as per the National Dairy Research Institute (NDRI), were tetracycline, oxytetracycline, gentamicin, ampicillin, amoxicillin, cloxacillin, and penicillin due to their lower costs [62]. Studies show that farmers obtained antibiotics through various sources of consultancy. Only 50% of the small farmers consulted veterinary care for antibiotics, whereas 76.79% of medium and 87.50% of large farmers consulted the same. Other parakeet milk vendors have opted for over-the-counter medications [63]. A study conducted in 2021 at small-scale dairy farms in Assam and Haryana indicates that 53% of the small-scale farmers could not explain the term antibiotic, which stands out as an essential factor for the misuse of antibiotics in dairy farms. Residues of novobiocin, macrolides, and sulphonamides are found in the milk sample collected from the farmers [64].

The use of antibiotics and antibiotic residues in milk dates back to the 60s, indicating a swelling trend of antibiotic use in animal farms and animal products. The use of antibiotics in the milk industry may lead to antibiotic resistance and allergic reactions such as anaphylaxis and serum sickness. The antibiotic residues interact with DNA and RNA. Antibiotic residues may alter the chromosome, causing infertility due to mutation [65]. A study conducted by Modi et al. [66] studied the prevalence of *campylobacter* species in milk and milk products showing resistance against nalidixic acid, ciprofloxacin, and tetracycline. A study conducted in 2020 involved the detection of antibiotic-resistance genes in raw milk for human consumption. The traces of antibiotics in the milk clearly indicate giving antibiotics to the cattle, but there is no strict regulation to monitor and control the irrational use.

### 3.2 Antibiotic use in poultry

As per the reports, India was the fifth high consumer of antibiotics in animals as of 2010. However, this ratio will be doubled by 2030 [67]. Tetracycline, doxycycline, and ciprofloxacin were reported to be highly used in poultry and colistin as a growth promoter [68]. Several studies have shown traces of antibiotic residues in chicken meat intended for human consumption [69]. A survey conducted by Kaushik *et al.* in eastern India found that *E. coli* isolates showed high resistance to cefuroxime and penicillin in poultry [70].

Similarly, another study conducted in Mumbai reports a massive rise in tetracycline resistance among *Salmonella* species in poultry [71]. A recent study conducted in North India observed a high level of resistance genes against fluoroquinolones followed by tetracycline and beta-lactams [72]. Recent studies conducted in Kerala found that antibiotics were supplied along with feed, leading to antibiotic resistance [73]. Similarly, the study found *E. coli* resistance to beta-lactams and carbapenem in the poultry litter, and similar resistance has been observed and correlated with isolation from patients with UTI in that area.

Koirala *et al.* [74] conducted a cross-sectional study in 30 larger broiler poultry farms to understand the prevalence of antibiotic use and antibiotic resistance developed in poultry farms. The study found that 90% of the farms used antibiotics. Antibiotics were used for prophylaxis and therapeutic purposes. The standard categories of antibiotics used for prophylaxis are fluoroquinolone and aminoglycosides. For treatment, macrolides and polymyxin are used. In observation: 47% of them used tylosin and colistin. Neomycin and doxycycline were used in combination with antibiotic therapy. Gene mutation and enzyme production induced by chromosomes



Species	Poultry	Disease caused	Antibiotic resistance	Antibiotic-resistant gene
Staphylococcus species	Chicken, turkey.	Staphylococcus Pododermatitis Septicaemia	Beta-lactam Tetracycline Oxacillin	Altered DNA gyrase and reduced outer membrane <i>Mec A</i> resistant gene (MRSA).
Pseudomonas species	Chicken, turkey, ducks, geese, ostriches.	Sinusitis Keratitis Septicemia Endocarditis via wounds and needles for vaccines	Cephalosporins Penicillins Quinolones Monobactams	Class 1 integron to carry multiple drug-resistant genes.
Escherichia species	Chicken	Gastrointestinal illness	Tetracycline Penicillin Sulfonamides	<i>bla-TEM</i> , <i>sul2</i> , <i>sul3</i> , <i>aadA</i> , <i>strA</i> , <i>strB</i> , <i>tetA</i> , <i>tetB</i> <i>qnrS</i> resistance gene involved in transfer from farms to human population.
Salmonella species	Chicken, humans.	Gastrointestinal disease		Multi-drug resistant gene.
Streptococcus species	Cattle, pigeons, humans.	Mastitis-cattle Septicaemia-pigeons Meningitis-humans	Penicillin Tetracycline	Tetracycline resistant gene such as <i>tet(M)</i> , <i>tet(L)</i> , <i>tet(O)</i> .
Yersinia species	Poultry meat	Acute enteritis in human <i>via</i> poultry products.	Cephalothin Ampicillin	<i>ystB</i> virulence gene.

**Table 2.**  
*Antibiotic-resistant gene observed in poultry.*

within the bacteria chromosome exhibits intrinsic resistance. HGT is the reason for extrinsic or acquired resistance.

The use of antibiotics in the feed, exposure of the infected litter to the soil as manure, and consumption of meat by human can lead to the entry of resistant organisms into the human gut microbiota. **Table 2** depicts various antibiotic-resistant gene observed in poultry.

#### 4. Pollution from the antibiotic manufacturing industry

India is the third largest country in pharmaceutical production in terms of volume, and India has 3000 manufacturing companies and 10,500 manufacturing units over the country. As per the Indian economic survey 2021, the domestic market will triple in the upcoming decade [75]. Regarding antibiotics, 80% were produced and exported globally by giant pharmaceutical manufacturers from India and China.

The studies have observed that industrial waste from these antibiotic production units has significant traces of antibiotic residues [76–78]. The flow of this antibiotic

residue to the environment will be from the bulk Active Pharmaceutical Ingredients (API) manufacturing unit and the sub-manufacturing unit. The habitats impacted by pharmaceutical industrial pollution were rich in ARGs and had the highest relative abundance of ARGs of all the ecosystems studied. The relative abundances of ARGs in wastewater/sludge were also compared to the relative abundances of ARGs in most other environmental habitats (sediment, water, soil and mine), all of which are presumably less impacted by human fecal waste.

The existing Good Manufacturing Practices regulation in India mainly focuses on drug safety, raising concerns over the environmental impact. The Central Pollution Control Board (CPCB) and its constituent units scrutinize industrial waste disposal, where strict control over antibiotic residuals should also be exerted [79]. The runaway of antibiotic residue from the manufacturing companies will contaminate the soil and water sources, further enhancing antibiotic resistance development through the food chain.

## **5. Environmental sanitation**

Better sanitation facility is a basic need of human life. Over 2.0 billion people still need to catch up on common and basic sanitation facilities such as toilets or latrines. Of these, 673 million still defecate in the open, for example, in street gutters, behind bushes or into open bodies of water [80].

Even though India has improved drastically in providing better sanitation facilities, remote rural areas still need to be adequately equipped with sanitation facilities. The association between sanitation and the occurrence of antibiotic resistance is based on the two factors, such as the antibiotic resistance prevalence rate in the area and the concentration of resistant genes in the human gut.

Although on a lower scale, ARGs can also spread through receiving water and air habitats. ARG abundances in receiving surface water habitats are typically 100 times higher than those in upstream waters. When bacteria populate the intestinal mucosa of fishes, ARGs can be obtained by bacteria reaching receiving water bodies, where they can accumulate in sediments by sedimentation and adsorption. ARGs have been found in groundwater 250 meters downstream from treatment lagoons in swine farms [81]. ARGs are also identified in aerosols up to four orders of magnitude higher than at the source, downwind of animal husbandry operations [82].

The current practice of sewage waste treatment technologies like sludge will not extensively remove the wastewater's antibiotic residues and resistance genes. The sludge produced with antibiotic residues will freely flow to the soil and environment and, finally, can enter the food chain.

## **6. Hospital infection control practices**

Several studies have reported the resistant gene reservoir in clinical settings [83–87] occurring due to HGT, but the rate and extent of this transfer mechanism are not elaborately studied. Hospital infection control practices are pivotal in preventing antibiotic resistance in humans. Irrational use of antibiotics and poor compliance with infection control practices among healthcare providers contribute to antibiotic resistance. The lacunae in knowledge among healthcare providers regarding the growing trend of antibiotic resistance and infection control practice guidelines of the

hospitals lead to irrational or overuse of antibiotics in hospitals and more frequently among independent practitioners. These poor infection control practices contribute to the rapid transmission of superbugs like MRSA and vancomycin-resistant enterococci (VRE), and other multi-drug resistant Gram-negative bacterial infections among hospital patients [88–90].

The significant challenges in these areas were the gap between the implementation and practices of infection control guidelines. Lack of knowledge regarding hand hygiene to prevent the spread of hospital infections and lack of supervision, administration, and facilities lead to the decline in infection control practices.

## **7. Conclusion**

There is an alarming increase in antimicrobial resistance, and there is insufficient evidence regarding the prevalence and occurrence of developing antimicrobial resistance from environmental and natural sources. The environmental factors may vary across different geographical locations based on the ethnicity, culture, belief and practices of human populations. Therefore, location-based studies should be conducted to correlate the burden of ever-increasing antibiotic resistance and its impact on therapeutic outcomes. The lack of proper implementation of laws and regulations regarding the disposal of biological waste and the use of antimicrobials in the animal and agriculture field is significant contributors to the development of antibiotic resistance.

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## **Conflict of interest**

The authors declare no conflict of interest.

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## References

- [1] One health basics [Internet]. Cdc.gov.USA. 2022. [cited 2022 April 28]. Available from: <https://www.cdc.gov/onehealth/basics/index.html>
- [2] Smillie CS, Smith MB, Friedman J, et al. Ecology drives a global network of gene exchange connecting the human microbiome. *Nature*. 2011;**480**:241-244
- [3] O'Neill JIM. Tackling drug-resistant infections globally: final report and recommendations the review on antimicrobial resistance. 2016. Available from: [https://amr-review.org/sites/default/files/160518\\_Finalpaper\\_withcover.pdf](https://amr-review.org/sites/default/files/160518_Finalpaper_withcover.pdf)
- [4] van Boeckel TP, Gandra S, Ashok A, et al. Global antibiotic consumption 2000 to 2010: An analysis of national pharmaceutical sales data. *The Lancet Infectious Diseases*. 2014;**14**:742-750
- [5] NCDC, Containment NP on AMR, Containment NP on AMR. National Antimicrobial Resistance Surveillance Network (NARS-Net India). Delhi: National Centre for Disease Control. Available from: <https://ncdc.gov.in/WriteReadData/1892s/82438677601599818025.pdf>; 2020
- [6] Kotwani A, Holloway K. Trends in antibiotic use among outpatients in New Delhi, India. *BMC Infectious Diseases*. 2011;**11**:99
- [7] Ministry of Health & Family Welfare Government of India, New Delhi. Antimicrobial Resistance and its Containment in India. 2016. Available from: [https://cdn.who.int/media/docs/default-source/searo/india/antimicrobial-resistance/amrcontainment.pdf?sfvrsn=2d7c49a2\\_2](https://cdn.who.int/media/docs/default-source/searo/india/antimicrobial-resistance/amrcontainment.pdf?sfvrsn=2d7c49a2_2) [Accessed 12 June 2023]
- [8] Durack J, Lynch SV. The gut microbiome: Relationships with disease and opportunities for therapy. *Journal of Experimental Medicine*. 2019;**216**:20-40
- [9] Eckburg PB, Bik EM, Bernstein CN, et al. Diversity of the human intestinal microbial Flora. *Science*. 1979;**205**(308):1635-1638
- [10] Ducarmon QR, Zwittink RD, Hornung BVH, van Schaik W, Young VB, Kuijper EJ. Gut microbiota and colonization resistance against bacterial enteric infection. *Microbiology and Molecular Biology Reviews*. 2019;**83**(3):1-29. DOI: 10.1128/MMBR.00007-19
- [11] Yatsunencko T, Rey FE, Manary MJ, et al. Human gut microbiome viewed across age and geography. *Nature*. 2012;**486**:222-227
- [12] Gorrie CL, Mirceta M, Wick RR, et al. Gastrointestinal carriage is a major reservoir of *Klebsiella pneumoniae* infection in intensive care patients. *Clinical Infectious Diseases*. 2017;**65**:208-215
- [13] Price LB, Hungate BA, Koch BJ, et al. Colonizing opportunistic pathogens (COPs): The beasts in all of us. *PLoS Pathogens*. 2017;**13**:e1006369
- [14] Raven KE, Blane B, Leek D, Churcher C, Kokko-Gonzales P, Pugazhendhi D, et al. Methodology for whole-genome sequencing of methicillin-resistant *Staphylococcus aureus* isolates in a routine hospital microbiology laboratory. *Journal of Clinical Microbiology*. 2019;**57**(6):1-10. DOI: 10.1128/JCM.00180-19
- [15] Dunn SJ, Connor C, McNally A. The evolution and transmission of multi-drug

- resistant *Escherichia coli* and *Klebsiella pneumoniae*: The complexity of clones and plasmids. *Current Opinion in Microbiology*. 2019;**51**:51-56
- [16] Guzman Prieto AM, van Schaik W, Rogers MRC, Coque TM, Baquero F, Corander J, et al. Global emergence and dissemination of enterococci as nosocomial pathogens: Attack of the clones? *Frontiers in Microbiology*. 2016;**7**:788. DOI: 10.3389/fmicb.2016.00788
- [17] Stewardson AJ, Marimuthu K, Sengupta S, et al. Effect of carbapenem resistance on outcomes of bloodstream infection caused by Enterobacteriaceae in low-income and middle-income countries (PANORAMA): A multinational prospective cohort study. *The Lancet Infectious Diseases*. 2019;**19**:601-610
- [18] Lim C, Takahashi E, Hongsuwan M, Wuthiekanun V, Thamlikitkul V, Hinjoy S, et al. Epidemiology and burden of multidrug-resistant bacterial infection in a developing country. *eLife*. 2016;**5**:1-18. DOI: 10.7554/eLife.18082
- [19] Gandra S, Tseng KK, Arora A, et al. The mortality burden of multidrug-resistant pathogens in India: A retrospective, observational study. *Clinical Infectious Diseases*. 2019;**69**:563-570
- [20] Blair JMA, Webber MA, Baylay AJ, et al. Molecular mechanisms of antibiotic resistance. *Nature Reviews Microbiology*. 2015;**13**:42-51
- [21] Forsberg KJ, Reyes A, Wang B, et al. The shared antibiotic Resistome of soil Bacteria and human pathogens. *Science*. 1979;**2012**(337):1107-1111
- [22] Karkman A, Do TT, Walsh F, et al. Antibiotic-resistance genes in waste water. *Trends in Microbiology*. 2018;**26**:220-228
- [23] Che Y, Xia Y, Liu L, et al. Mobile antibiotic resistome in wastewater treatment plants revealed by Nanopore metagenomic sequencing. *Microbiome*. 2019;**7**:44
- [24] Thanner S, Drissner D, Walsh F. Antimicrobial Resistance in Agriculture. *MBio*. 2016;**7**:2. DOI: 10.1128/mBio.02227-15
- [25] San Millan A. Evolution of plasmid-mediated antibiotic resistance in the clinical context. *Trends in Microbiology*. 2018;**26**:978-985
- [26] Huddleston JR. Horizontal gene transfer in the human gastrointestinal tract: Potential spread of antibiotic resistance genes. *Infection and Drug Resistance*. 2014;**7**:167-176
- [27] Ruppé E, Ghoulane A, Tap J, et al. Prediction of the intestinal resistome by a three-dimensional structure-based method. *Nature Microbiology*. 2019;**4**:112-123
- [28] van Schaik W. The human gut resistome. *Philosophical Transactions of the Royal Society B: Biological Sciences*. 2015;**370**:20140087
- [29] Pérez-Cruz C, Delgado L, López-Iglesias C, et al. Outer-inner membrane vesicles naturally secreted by gram-negative pathogenic Bacteria. *PLoS One*. 2015;**10**:e0116896
- [30] Lester CH, Frimodt-Møller N, Sørensen TL, et al. In vivo transfer of the *vanA* resistance gene from an *Enterococcus faecium* isolate of animal origin to an *E. faecium* isolate of human origin in the intestines of human volunteers. *Antimicrobial Agents and Chemotherapy*. 2006;**50**:596-599

- [31] Johnston C, Martin B, Fichant G, et al. Bacterial transformation: Distribution, shared mechanisms and divergent control. *Nature Reviews. Microbiology*. 2014;**12**:181-196
- [32] Chen I, Dubnau D. DNA uptake during bacterial transformation. *Nature Reviews. Microbiology*. 2004;**2**:241-249
- [33] Blokesch M. Natural competence for transformation. *Current Biology*. 2016;**26**:R1126-R1130
- [34] Gill S, Catchpole R, Forterre P. Extracellular membrane vesicles in the three domains of life and beyond. *FEMS Microbiology Reviews*. 2019;**43**:273-303
- [35] Klieve AV, Yokoyama MT, Forster RJ, et al. Naturally occurring DNA transfer system associated with membrane vesicles in cellulolytic *Ruminococcus* spp. of ruminal origin. *Applied and Environmental Microbiology*. 2005;**71**:4248-4253
- [36] Yaron S, Kolling GL, Simon L, et al. Vesicle-mediated transfer of virulence genes from *Escherichia coli* O157:H7 to other enteric Bacteria. *Applied and Environmental Microbiology*. 2000;**66**:4414-4420
- [37] Shen Y, Torchia MLG, Lawson GW, et al. Outer membrane vesicles of a human commensal mediate immune regulation and disease protection. *Cell Host & Microbe*. 2012;**12**:509-520
- [38] Chiang YN, Penadés JR, Chen J. Genetic transduction by phages and chromosomal islands: The new and noncanonical. *PLoS Pathogens*. 2019;**15**:e1007878
- [39] Chen J, Quiles-Puchalt N, Chiang YN, et al. Genome hypermobility by lateral transduction. *Science*. 1979;**2018**(362):207-212
- [40] Aggarwala V, Liang G, Bushman FD. Viral communities of the human gut: Metagenomic analysis of composition and dynamics. *Mobile DNA*. 2017;**8**:12
- [41] Shkoporov AN, Hill C. Bacteriophages of the human gut: The “known unknown” of the microbiome. *Cell Host & Microbe*. 2019;**25**:195-209
- [42] Debroas D, Siguret C. Viruses as key reservoirs of antibiotic resistance genes in the environment. *The ISME Journal*. 2019;**13**:2856-2867
- [43] Fernández-Orth D, Miró E, Brown-Jaque M, et al. Faecal phageome of healthy individuals: Presence of antibiotic resistance genes and variations caused by ciprofloxacin treatment. *Journal of Antimicrobial Chemotherapy*. 2019;**74**:854-864
- [44] Ilangovan A, Connery S, Waksman G. Structural biology of the gram-negative bacterial conjugation systems. *Trends in Microbiology*. 2015;**23**:301-310
- [45] Pal C, Bengtsson-Palme J, Kristiansson E, et al. Co-occurrence of resistance genes to antibiotics, biocides and metals reveals novel insights into their co-selection potential. *BMC Genomics*. 2015;**16**:964
- [46] Cabezón E, Ripoll-Rozada J, Peña A, de la Cruz F, Arechaga I. Towards an integrated model of bacterial conjugation. *FEMS Microbiology Reviews*. 2015;**39**(1):81-95. DOI: 10.1111/1574-6976.12085
- [47] Porse A, Gumpert H, Kubicek-Sutherland JZ, Karami N, Adlerberth I, Wold AE, et al. Genome dynamics of *Escherichia coli* during antibiotic treatment: Transfer, loss, and persistence of genetic elements In situ of the infant gut. *Frontiers in Cellular*

- and Infection Microbiology. 2017;7:1-12. DOI: 10.3389/fcimb.2017.00126
- [48] Shoemaker NB, Vlamakis H, Hayes K, et al. Evidence for extensive resistance gene transfer among *Bacteroides* spp. and among *Bacteroides* and other genera in the human Colon. Applied and Environmental Microbiology. 2001;67:561-568
- [49] Ramsay JP, Firth N. Diverse mobilization strategies facilitate transfer of non-conjugative mobile genetic elements. Current Opinion in Microbiology. 2017;38:1-9
- [50] von Wintersdorff CJH, Penders J, van Niekerk JM, Mills ND, Majumder S, van Alphen LB, et al. Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer. Frontiers in Microbiology. 2016;7:173. DOI: 10.3389/fmicb.2016.00173
- [51] Parkunan T, Ashutosh M, Sukumar B, et al. Antibiotic resistance: A cross-sectional study on knowledge, attitude, and practices among veterinarians of Haryana state in India. Veterinary World. 2019;12:258-265
- [52] Mandakini R, Roychoudhury P, Subudhi PK, et al. Higher prevalence of multidrug-resistant extended-spectrum  $\beta$ -lactamases producing *Escherichia coli* in unorganized pig farms compared to organized pig farms in Mizoram, India. Veterinary World. 2020;13:2752-2758
- [53] Economou V, Gousia P. Agriculture and food animals as a source of antimicrobial-resistant bacteria. Infection and Drug Resistance. 2015:49-61
- [54] Rossi F, Rizzotti L, Felis GE, et al. Horizontal gene transfer among microorganisms in food: Current knowledge and future perspectives. Food Microbiology. 2014;42:232-243
- [55] Han X-M, Hu H-W, Chen Q-L, et al. Antibiotic resistance genes and associated bacterial communities in agricultural soils amended with different sources of animal manures. Soil Biology & Biochemistry. 2018;126:91-102
- [56] Koike S, Krapac IG, Oliver HD, et al. Monitoring and source tracking of tetracycline resistance genes in lagoons and groundwater adjacent to swine production facilities over a 3-year period. Applied and Environmental Microbiology. 2007;73:4813-4823
- [57] Fang H, Han L, Zhang H, et al. Dissemination of antibiotic resistance genes and human pathogenic bacteria from a pig feedlot to the surrounding stream and agricultural soils. Journal of Hazardous Materials. 2018;357:53-62
- [58] Sancheza HM, Echeverria C, Thulsiraj V, et al. Antibiotic resistance in airborne Bacteria near conventional and organic beef cattle farms in California, USA. Water, Air, and Soil Pollution. 2016;227:280
- [59] Zhang Y, Snow DD, Parker D, et al. Intracellular and extracellular antimicrobial resistance genes in the sludge of livestock waste management structures. Environmental Science & Technology. 2013;47:10206-10213
- [60] Fang H, Wang H, Cai L, et al. Prevalence of antibiotic resistance genes and bacterial pathogens in long-term manured greenhouse soils As revealed by metagenomic survey. Environmental Science & Technology. 2015;49:1095-1104
- [61] Zeng J, Pan Y, Yang J, et al. Metagenomic insights into the distribution of antibiotic resistome between the gut-associated environments and the pristine environments. Environment International. 2019;126:346-354



- [62] Grover CR, Bhavadasan MK. Antibiotic Residues in Milk: A Public Health Concern. Haryana: National Dairy Research Institute; 2020. Available from: [https://cdn.cseindia.org/userfiles/antibiotic\\_milk\\_chand%20ram.pdf](https://cdn.cseindia.org/userfiles/antibiotic_milk_chand%20ram.pdf) [Accessed 12 June 2023]
- [63] Kumar V, Gupta J. Prevailing practices in the use of antibiotics by dairy farmers in eastern Haryana region of India. *Veterinary World*. 2018;**11**:274-280
- [64] Kumar N, Sharma G, Leahy E, et al. Understanding antibiotic usage on small-scale dairy farms in the Indian states of Assam and Haryana using a mixed-methods approach—Outcomes and challenges. *Antibiotics (Basel)*. 2021;**10**:1-13
- [65] Sachi S, Ferdous J, Sikder MH, et al. Antibiotic residues in milk: Past, present, and future. *Journal of Advanced Veterinary and Animal Research*. 2019;**6**:315-332
- [66] Modi S, Brahmabhatt MN, Chatur YA, et al. Prevalence of *Campylobacter* species in milk and milk products, their virulence gene profile and anti-bio gram. *Veterinary World*. 2015;**8**:1-8
- [67] Tóth AG, Csabai I, Krikó E, et al. Antimicrobial resistance genes in raw milk for human consumption. *Scientific Reports*. 2020;**10**:7464
- [68] van Boeckel TP, Brower C, Gilbert M, et al. Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences of the United States of America*. 2015;**112**:5649-5654
- [69] Brower CH, Mandal S, Hayer S, et al. The prevalence of extended-Spectrum Beta-lactamase-producing multidrug-resistant *Escherichia Coli* in poultry chickens and variation according to farming practices in Punjab, India. *Environmental Health Perspectives*. 2017;**125**:77015
- [70] Gandra S, Joshi J, Trett A, Lamkang AS, Laxminarayan R. Scoping Report on Antimicrobial Resistance in India. Washington, DC: Center for Disease Dynamics, Economics & Policy; 2017. Available from: <https://onehealthtrust.org/wp-content/uploads/2017/11/scoping-report-onantimicrobial-resistance-in-india.pdf> [Accessed 12 June 2023]
- [71] Ramakant Sahu, Poornima Saxena. Antibiotics in Chicken Meat. New Delhi: Centre for Science and Environment; 2014. Available from: [https://cdn.cseindia.org/userfiles/Antibiotics%20in%20Chicken\\_Lab%20Report\\_Final%2029%20July.pdf](https://cdn.cseindia.org/userfiles/Antibiotics%20in%20Chicken_Lab%20Report_Final%2029%20July.pdf) [Accessed 12 June 2023]
- [72] Kaushik P, Anjay A, Kumari S, et al. Antimicrobial resistance and molecular characterization of *E. coli* from poultry in eastern India. *Veterinaria Italiana*. 2018;**54**:197-204
- [73] Sebastian S, Tom AA, Babu JA, et al. Antibiotic resistance in *Escherichia coli* isolates from poultry environment and UTI patients in Kerala, India: A comparison study. *Comparative Immunology, Microbiology and Infectious Diseases*. 2021;**75**:101614
- [74] Koirala A, Bhandari P, Shewade HD, et al. Antibiotic use in broiler poultry farms in Kathmandu Valley of Nepal: Which antibiotics and why? *Tropical Medicine and Infectious Disease*. 2021;**6**:47
- [75] Pharmaceuticals Export Promotion Council IQVIA A-A, (PIB) PIB, Pharmaceuticals Export Promotion Council IQVIA A-A. Indian Pharmaceuticals Industry Report.

New Delhi: Department for Promotion of Industry and Internal Trade (DPIIT); 2021

[76] Gothwal R, Shashidhar. Occurrence of high levels of fluoroquinolones in aquatic environment due to effluent discharges from bulk drug manufacturers. *Journal of Hazardous, Toxic, and Radioactive Waste*. 2017;**21**:5016003

[77] Larsson DG, de Pedro C, Paxeus N. Effluent from drug manufactures contains extremely high levels of pharmaceuticals. *Journal of Hazardous Materials*. 2007;**148**:751-755

[78] Lübbert C, Baars C, Dayakar A, et al. Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended-spectrum beta-lactamase and carbapenemase-producing pathogens. *Infection*. 2017;**45**:479-491

[79] Ministry of Environment & Forests. *Bio-medical Waste Management Rules 2016*. New Delhi: Government of India; 2016

[80] Kizny Gordon AE, Mathers AJ, Cheong EYL, et al. The hospital water environment as a reservoir for Carbapenem-resistant organisms causing hospital-acquired infections—A systematic review of the literature. *Clinical Infectious Diseases*. 2017;**64**:1435-1444

[81] Breathnach AS, Cubbon MD, Karunaharan RN, et al. Multidrug-resistant *Pseudomonas aeruginosa* outbreaks in two hospitals: Association with contaminated hospital wastewater systems. *Journal of Hospital Infection*. 2012;**82**:19-24

[82] Hota S, Hirji Z, Stockton K, et al. Outbreak of multidrug-resistant

*Pseudomonas aeruginosa* colonization and infection secondary to imperfect intensive care unit room design. *Infection Control and Hospital Epidemiology*. 2009;**30**:25-33

[83] Paterson DL, Bonomo RA. Extended-Spectrum  $\beta$ -lactamases: A clinical update. *Clinical Microbiology Reviews*. 2005;**18**:657-686

[84] Weingarten RA, Johnson RC, Conlan S, Ramsburg AM, Dekker JP, Lau AF, et al. Genomic analysis of hospital plumbing reveals diverse reservoir of bacterial plasmids conferring Carbapenem resistance. *MBio*. 2018;**9**(1):1-16. DOI: 10.1128/mBio.02011-17

[85] Rowe WPM, Baker-Austin C, Verner-Jeffreys DW, et al. Overexpression of antibiotic resistance genes in hospital effluents over time. *The Journal of Antimicrobial Chemotherapy*. 2017;**72**:1617-1623

[86] Acharya AS, Khandekar J, Sharma A, et al. Awareness and practices of standard precautions for infection control among nurses in a tertiary care hospital. *The Nursing Journal of India*. 2013;**104**:275-279

[87] Goyal A, Narula H, Gupta PK, et al. Evaluation of existing knowledge, attitude, perception and compliance of hand hygiene among health care workers in a tertiary care Centre in Uttarakhand. *Journal of Family Medicine and Primary Care*. 2020;**9**:1620-1627

[88] Sodhi K, Shrivastava A, Arya M, et al. Knowledge of infection control practices among intensive care nurses in a tertiary care hospital. *Journal of Infection and Public Health*. 2013;**6**:269-275

[89] Taneja J, BibhaBati M, Aradhana B, et al. Evaluation of

knowledge and practice amongst nursing staff toward infection control measures in a tertiary care hospital in India. *The Canadian Journal of Infection Control*. 2009;**24**:104-107

[90] Tenna A, Stenehjem EA, Margoles L, et al. Infection control knowledge, attitudes, and practices among healthcare workers in Addis Ababa, Ethiopia. *Infection Control and Hospital Epidemiology*. 2013;**34**:1289-1296

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