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Review Article

Escherichia coli, as the Indicator Microorganism of Antibiotic Resistance Across Human-animal-Environmental Interfaces

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Abstract

Antibiotic resistance (ABR) is a major global public health problem. However, emerging hospital and community-based data indicated a rise in the prevalence of antibiotic resistance in developing low and middle-income countries (LMIC) like India. Determining antibiotic use, the causes and evolution of antibiotic resistance, regional variations, and interventional techniques tailored to each nation is challenging. ABR in *Escherichia coli* (*E. coli*) is a common problem in the twenty-first century, mostly seen in humans, animals, poultry, and the environment. The majority of antibiotic-resistant genes that *E. coli* obtains are through horizontal gene transfer. The most problematic mechanisms observed in *E. coli* are associated with the acquisition of genes encoding for carbapenemases, plasmid-mediated quinolone resistance, 16S rRNA methylases, Extended spectrum β-lactamases (ESBL), and *mcr* genes. *E. coli* is primarily isolated from clinical isolates that are resistant to antimicrobial drugs such as carbapenems, fluoroquinolones, co-trimoxazole, aminoglycosides, and nitrofurantoin, but *E. coli* of animal origin often resists these drugs. However, resistance to tetracyclines, phenicols, sulfonamides, trimethoprim, and fosfomycinis mostly noted in animal isolates. The resistance to trimethoprim-sulfamethoxazole, amoxicillin, penicillins, ampicillin, tetracycline, aminoglycosides, etc. is higher in the environmental samples. *E. coli* serves as a sensor for integrated antibiotic resistance screening. The purpose of this study was to investigate the role of *E. coli* as an ABR marker in the public health concern. The findings of the study could shed the spotlight on the wide range of *E. coli* strains and strengthen infection prevention and control protocols.

Keywords: *Escherichia coli*; Antibiotic Resistance (ABR); Indicator; β-lactam Antimicrobials; Surveillance

Abbreviations

ABR: Antibiotic Resistance; ESBL: Extended-Spectrum ß-lactamase; GNB: Gram-negative Bacteria; GLASS: the Global Antimicrobial Resistance and Use Surveillance System; MDR: Multidrug-Resistant; PMQR: Plasmid-Mediated Quinolone Resistance; UTI: Urinary Tract Infection; *E. coli*: Escherichia coli; WASH: Water: Sanitation, and Hygiene; WHO: the World Health Organization

Introduction

Antibiotic resistance (ABR) is a serious global health issue [1]. Drug resistance raises the risk of disease transmission, severe illness, disability, and death by taking antibiotics and other antimicrobial treatments ineffective and making infections difficult or impossible to treat. The emergence of antimicrobial resistance poses a severe threat to public health, impeding progress in the management of cancer, organ transplantation, infectious disorders,

and critical care. Furthermore, drug-resistant illnesses harm the health of both livestock and crops, impair farm productivity, and affect food security [2]. Drug-resistant illnesses resulting from antibiotic resistance cause approximately 7 lakh fatalities globally each year, and if effective action is not taken, it is estimated that these diseases will cause 10 million deaths by the period 2050 [3]. A more effective and well-coordinated worldwide response to reduce ABR has been demanded by the World Health Organisation (WHO). The WHO global strategy for containment of ABR was developed in 2001 and provides a framework of measures to stop the development and propagation of antimicrobial-resistant bacteria [4]. The rising threat of ABR was first released by the WHO in 2012 [5]. The discovery and development of new, appropriate medications and vaccines, the prevention and control of infections, the enhancement of the use of appropriate antibiotics in hospitals and local communities, improvement of surveillance and health systems are only a few suggestions that can reduce ABR trends to some extent [6]. In April 2014, WHO published the first worldwide report on ABR surveillance, which supported the theory that surveillance should be a key component to resist infectious disease and was based on data from national and international monitoring systems [7]. Regardless of the state of their economy, every nation is concerned about ABR. A few contributing factors are the absence of safe water, sanitation, and hygiene (WASH) for people and animals, the poor prevention and control of infections and diseases in homes, hospitals, and farms, the scarcity of reasonably high-quality vaccines, diagnostics, and medications, the lack of awareness, knowledge, and the lack of enforcement of relevant legislation. The causes and consequences of ABR adversely affect those living in underprivileged environments and communities [8].

The facultative anaerobic bacteria *Escherichia coli (E. coli)* is found in both human and animal gastrointestinal tracts. Contamination with *E. coli* was transmitted by unsanitary conditions, uncooked meat, vegetables, and water sources. The use of biocides during cultivation, as well as inadequately cleaned water and fertilizers, can contaminate vegetables. Workers who handle human waste can pollute food or water supplies, thereby exposing animals to disease. Bacteria can penetrate the food chain through improper handling and processing of meat and animal products [8]. Although *E. coli* has been shown to exchange genetic material with other species of bacteria, these bacteria may spread antibiotic-resistant genes to human pathogenic bacteria that are migratory. Resistance genes are becoming more prevalent these days and have been identified in isolates of *E. coli*, many of which were acquired through horizontal gene transfer. Therefore, antibiotic resistance has so emerged as a significant global health concern [9].

Epidemiology of antibiotic resistance

Antibiotics are the "magic bullets" for combating bacteria, and they are regarded as the most significant medical discovery of the twentieth century. Millions of lives remain protected by antibiotics annually from bacterial illnesses. These have been considered a blessing to humanity for decades, many developing and underdeveloped nations have utilized them for preventive measures in animal husbandry and production [10,11]. ABR prevalence (>50%) against ampicillin, cefuroxime, cefotaxime, ceftazidime, ciprofloxacin, and Trimethoprim/sulfamethoxazole (SXT) was shown to be significantly higher in GNB overall in retrospective research. For amikacin, ertapenem, meropenem, and piperacillin/tazobactam, low resistance prevalence (<10%) was found. Compared to other locations, the incidence of ABR was significantly higher in *E. coli* isolates from ICU, medical, and surgical wards. Multidrug resistance (MDR) was seen in 38.7% of cases overall. *E. coli* isolates from respiratory specimens (48%), wounds, bones, or other tissues (47.7%), and body fluids (47.1%) had the highest MDR prevalence [12].

The drugs that were most effective against *E. coli* were found to be meropenem, imipenem, ciprofloxacin, and norfloxacin. An Indian study revealed that 29.54% of the *E. coli* isolates showed carbapenem resistance. However, other studies conducted in Nepal and India discovered a substantially higher (60-75%) meropenem resistance [13,14]. The World Health Organisation reported that every three minutes, a child dies from sepsis caused by multi-drug resistant (MDR) pathogens. 1.27 million deaths every year due to bacterial ABR; by 2050, livestock will have decreased by 7.5% [15].

Pathogenic *E. coli*

In 1884, German microbiologist and physician Theodor Escherich started investigating the function of infected newborn gut microbes in infection and digestion. *E. coli*, the biological rock star, is the current designation for the rapidly evolving microorganisms he discovered during this study, which he initially named *Bacterium coli commune* [16]. *E. coli* is currently the most widely used model organism in genetic, molecular, and microbiological research. It is also regarded as "the most intensively studied and best-understood organism on the planet. "Gram-negative *E. coli* is a rod-shaped member of the Enterobacteriaceae family and Gammaproteobacteria class. Under the proper growth conditions, this can

grow very quickly. It is the host bacterium in numerous distinct genetic modifications, allowing it to produce many commercial goods and enzymes. The *E. coli* genome sequence study was originally published in 1997. More than 4800 *E. coli* genomes have been sequenced since then. On the other hand, *E. coli* is frequently used as a faecal indicator bacterium (FIB) to assess environmental development and water quality. Different *E. coli* strains and serotypes can cause illnesses in humans, it is crucial to comprehend the natural habitat of this bacteria to prevent infection and the spread of the pathogen to food, soil, and water [17].

Hemolytic-uremic syndrome, meningitis, peritonitis, UTIs, intra-amniotic and puerperal infections in pregnant women, endocarditis in humans, and gram-negative bacterial hospital-acquired pneumonia are all caused by *E. coli* [18]. Based on their virulence traits, enteric *E. coli* is classified as enterotoxigenic, enteropathogenic, enteroinvasive, verotoxigenic, enterohemorrhagic, and enteroaggregative. Food animals such as pigs, cattle, and poultry, have commensal bacteria called *E. coli* in their intestines. More recently, it has been shown that extra-intestinal diseases, like urinary tract infections, are also associated with *E. coli* originating from animals. In the past, enteropathogenic, enterotoxigenic, and verotoxigenic *E. coli* were the only associated with meat [19]. Currently, MDR *E. coli* is predominantly found in human bodies and is steadily spreading throughout the world. Despite being practically susceptible to all clinically significant antibiotics by nature, it is capable of acquiring resistance genes, mostly through horizontal gene transfer. The methods are responsible for the majority of issues in *E. coli* are linked to the acquisition of genes encoding carbapenemases, plasmid-mediated resistance to quinolone (PMQR), ESBLs, and *mcr* genes [20].

Pathotypes of *E. coli*

At present, there are five types of foodborne diarrheagenic *E. coli* pathotypes: enteropathogenic *E. coli* (EPEC), Shiga toxin-producing *E. coli*/enterohemorrhagic *E. coli* (STEC/EHEC), Shigella/enteroinvasive *E. coli* (EIEC), enteroaggregative *E. coli* (EAEC), and enterotoxigenic *E. coli* (ETEC). These pathotypes are differentiated by virulence factors, patterns of bacterial adherence to host cells, effects of relationships on host cells, production of toxins, and invasion. *E. coli* exhibits a wide range of clinical traits, affects a variety of organs, uses unique pathogenesis mechanisms, and differs noticeably in patterns of transmission [21].

Phylogroups of *E. coli*

Eight phylogroups, or the five cryptic clades, are assigned to this organism: A, B1, B2, C, D, E, F, and G. Based on specific genetic markers (chuA, yjaA, and tspE4.C2), *E. coli* strains are divided into these groups. Groups B2 and D are thought to contain the most virulent extraintestinal *E. coli*, while groups A and B1 are considered to mainly exhibit commensal traits [22,23].

Virulence of *E. coli*

Extraintestinal pathogenic *E. coli* (ExPEC) and avian pathogenic *E. coli* (APEC), the strains that cause human infections, are closely related phylogenetically and share multiple virulence genes, according to different relevant studies [24]. APEC strains may have human-pathogenic ExPEC virulence genes, according to a genomic study conducted by Rodriguez-Siek and associates. This could lead to the pathogenic strains of *E. coli* having more genetic diversity and gene exchange. Certain strains of human extraintestinal pathogenic *E. coli* carry the gene that boosts the survival of bacteria in serum. The gene is present in plasmid ColV, a significant virulence plasmid shared by avian pathogenic *E. coli* strains. This means that virulence genes can be transferred between human and avian pathogenic *E. coli* strains by exchanging plasmids [25].

The advancements in molecular biology techniques have enabled the whole genome sequencing of typical *E. coli* strains, such as commensal *E. coli* K-12, as well as pathogenic strain O157:H7, which causes intestinal infections, and uropathogenic *E. coli* J96. Additionally, full genomic sequences for a minimum of twenty strains of *E. coli* exist. MutliLocus Sequence Typing (MLST), an analysis of housekeeping gene sequences, made it possible to examine the evolutionary structure of *E. coli* species with greater accuracy. This approach is predicated on identifying the allele types of particular strains and housekeeping genes, which are subsequently categorized [26]. Though *E. coli* was previously classified into four major phylogenetic categories, analysis using the MLST method revealed errors and omissions. Having 80 to 85 percent of *E. coli* strains mistakenly assigned to phylogenetic categories, sequencing analysis indicated hybrid groupings among *E. coli* species [27]. Sequence Type 131 (ST131) is the most prevalent multidrug-resistant extraintestinal pathogenic strain of *E. coli*, this ST131 is a global *E. coli* clone that is resistant to a wide range of antibiotics

[28].

One health aspect of antibiotic resistance

ABR is a worldwide public health concern that causes illnesses that are incurable and raises expenses associated with medical care, hospital stays, and mortality. It is believed that the primary cause of ABR is the use of antibiotics in both people and animals. Because antibiotic exposure in healthcare (humans), agriculture (animals, plants, or food-processing technology), and the environment (sea, soil, drinking water, and wastewater) drives the development of antibiotic resistance, studies on the interactions between humans, animals, and the environment as well as between the various sectors involved are crucial [29]. Decreasing resistance in the food, water waste, and pharmaceutical industries requires the implementation of a one-health approach. In the gut microbiota of both humans and animals, *E. coli* is a common commensal. The growing ABR and mortality associated with resistance have drawn substantial attention in this literature [29].

E. coli in animals

Several studies defined *E. coli* as indicator organism of ABR across human-animal-environmental interfaces (Table 1). Since 2000, the percentage of *E. coli* that is resistant to antibiotics has remained constant, with streptomycin resistance falling from 78% to 46% by 2015. The resistance rates to streptomycin, tetracycDuring 2001-2004, the ABR surveillance reflected colonization and contamination of *E. coli* resistant to extended-generation cephalosporins, fluoroquinolones, and SXT in poultry and retail foods, respectively [30,31]. Brazil has low ABR surveillance statistics and high antibiotic resistance rates to ampicillin, erythromycin, lincomycin, and oxolinic acid [32]. A surveillance-based study in China done on Swine, Chicken & cattle samples indicated higher resistance to penicillin, tetracyclines, sulphonamide, aminoglycoside, chloramphenicol, and also the presence of cmlA1-aadB-cmlA6, aacA4-

Country	Duration	Study type	Sample	Rate of Isolation	Resistance	Gene	*Resistance genes*	Ref
US	2002-2004	Surveillance	Poultry (n = 931)	35%	TMP-SMZ, quinolones/fluoroquinolones, extended-spectrum cephalosporins	-	*papA and/or papC,sfa/focDE, afa/draBC,iutA, and kpsM II*	[30]
Minneapolis, USA	2001-2003	Surveillance	Retail food (n = 1648)	24%	ciprofloxacin and nalidixic acid	ESBL	*PapAand/orpapC,afa/dra,sfa/foc*	[31]
Brazil	July2014-March2015	Surveillance	Broiler Chicken (n = 100)	95.9%	tetracycline (95.4%), ciprofloxacin (91.4%), ampicillin (87.3%), chloramphenicol (51.1%), azithromycin (48.8%) ceftiofur (42.5%), fosfomycin (33.3%), gentamycin (27.6%) andpolymyxin B (1.1%)	-	-	[32]
China	1970-2000	Surveillance	Food animal (Swine, Chicken and cattle) (n = 326)	-	penicillin, tetracyclines, sulphonamide, aminoglycoside, chloramphenicol	-	*cmlA1-aadB-cmlA6, aacA4-catB3-dfrA1,blaP1a-aadA2-ereA. CmlA and catB, blaP1a and ere*A	[33]
China	1993-2013	Symptomatic	Sick chicken (n = 540)	87.2%	tetracycline (90.6%), nalidixic acid (80.6%), ampicillin (77.2%), trimethoprim-sulfamethoxazole (76.9%), and streptomycin (72.8%)	ESBL, PMQR	-	[34]
South Korea	2010-2011	Surveillance	Korean street food (n = 4330)	17.7 %	tetracycline (15.6%), streptomycin (12.5%), ampicillin (10.4%), ticarcillin (9.4%), Nalidixic acid (9.4%)	ESBL	*tetA, tetB, $bla_{TEM,}$ aphA1, strA/B,aac(3)-IV*	[35]
South Korea	2013-2015	Surveillance	fecal and carcass samples of animals (n = 10576)	154 (1.46%)	Ceftazidime	ESBL	$bla_{CTX-M-1}$	[36]

Nepal	1 February-31 July 2019	Surveillance	Poultry (n = 227 broilers, and 43 layers)	53.3% (144/270)	tetracyclin, ciprofloxacin, cefoxitin, and imipenem	-	-	[37]
Bangladesh		Surveillance	Poultry and poultry environment (n = 250)	145 (58%)	penicillin, ciprofloxacin, rifampicin, kanamycin, streptomycin, cefixime, erythromycin, ampicillin, tetracycline, and chloramphenicol and neomycin.			[38]
Chattogram, Bangladesh	January-February 2016	Surveillance	Broiler chicken (n = 60)	37 (61.67%)	ampicillin, tetracycline, sulfur		bla_{TEM}, *Sul2,tet*A	[39]
Bangladesh	2016	Surveillance	Milk samples from cattle and buffalo (n = 34)	12 (35.29%)	gatifloxacin, ciprofloxacin and levofloxacin	-	-	[40]
Bangladesh	April- December 2019	Surveillance	Frozen chicken (n = 113)	74 (65.49%)	oxytetracycline, amoxicillin, ampicillin,trimethoprim–sulfamethoxazole, and pefloxacin, and tetracycline, carbapenems.	ESBL	$bla_{TEM,}$ $bla_{SHV,}$ $bla_{CTX-M-1,}$ *and* $bl_{aCTX-M-}$2	[41]
Bangladesh	April 2021-January 2022	Surveillance	raw milk samples from healthy cows (n = 100)	70%	gentamicin, streptomycin, quinolone,fluoroquinolone, macrolide,tetracycline, sulfonamides/dihydrofolate reductase,phenicol, cefoxitin	ESBL	$bla_{CTX-M,}$ $bla_{TEM,}$ *and* $bla_{SHV,}$	[42]
West Bengal, India	April – June 2018	Surveillance	Bovine milk samplesfrom unorganized dairy farms (n = 182)	22 (12.1%)	colistin (100%), levofloxacin (83.33%), imipenem (66.67%), cefotaxime (100%), ceftazidime (91.67%), amoxicillin/clavulanic acid (83.33%), tetracycline (75.00%), gentamicin (58.33%)	ESBL	bla_{CTX-M}	[43]
West Bengal, India	2020	Surveillance	Cattle milk samples (n = 450)	205 (45.6%)	penicillin-G (100%), cefoxitin (100%), ampicillin (42%), trimoxazole (13.5%), levofloxacin (5.2%)	ESBL, *AmpC*	$bla_{CMY-2,}$*sul1, sul2*	[44]
Kolkata, India	September 2011- February 2012	Surveillance	Meat and meat products (n = 80)	26.25%	ceftazidime, ciprofloxacin and imipenem(100%)	ESBL	-	[45]
Southern Karnataka, India	January-June 2018	Surveillance	Healthy broiler chicken (n = 256)	187 (73.05%)	ciprofloxacin and levofloxacin (94%)	ESBL	*qnrA,* $bla_{TEM,}$ $bla_{SHV,}$ $bla_{CTX-M-15}$	[46]
Maharashtra, India	December 2019 – December 2020	Symptomatic	Diarrheic piglet-fecal sample(n = 30)	12 (40%)	sulpha/trimethoprim (100%),amoxicillin (50%), ciprofloxacin (16.6%), amikacin (100%)	-	-	[47]
Mangalore, India	2017	Surveillance	Fish, livestock waste, piggery, and fish farm (n = 67)	67 (100%)	nitrofurantoin (26.86%), tetracycline (22.38%), ampicillin(20.89%), cotrimoxazole (13.43%), ciprofloxacin (11.94%), gentamicin (10.44%),piperacillin/tazobactam (7.46%), chloramphenicol (7.46%), and cefotaxime (4.47%)	-	*tetA,tetB,tetD, tetG, and tetM, Sul1,sul2,sul3.* *qnrA, qnrB,cat1 and cat2, cmlA, cat3, cmlB, and floR.*	[48]
Karnataka, Telangana, Andhra Pradesh, and Maharashtra, India	February, 2015-September, 2015	Surveillance	Commercial broiler, retail chicken (n = 168)	100%	tetracycline (84%) ciprofloxacin (70%), co-trimoxazole (45%), and gentamicin (32%), chloramphenicol (8%) and fosfomycin (4%)		$bla_{CTX-M-1}$5	[49]

Table 1: Antibiotic resistance in *Escherichia coli* recovered from animal sources.

catB3-dfrA1, blaP1a-aadA2-ereA. CmlA and catB, blaP1a, and ereA [33]. Another study was also done in China on diseased chickens that showed resistance rates ranging from 50% for aminoglycosides, cephalosporins, quinolones, and penicillins to 80% for tetracyclines and sulfonamides [34]. A surveillance was conducted in South Korea, between 2010 and 2011, 4330 South Korean food samples were collected from restaurants, retail stores, and street sellers in Seoul, Korea. The Korea Food & Drug Administration (KFDA) required every sample to test negative for *E. coli*. The most prevalent resistance genes were streptomycin-resistant strA and strB, tetracycline resistance genestet A, and tetB. β-lactams resistance gene bla_{TEM} [35]. The $bla_{\text{CTX-M-1}}$ gene was found in 2015 in another investigation done in South Korea that used animal feces and carcass samples [36]. The greatest resistance to imipenem, ciprofloxacin, tetracycline, and cefoxitin was found in broiler and layer birds in Nepal, based on a surveillance study [37]. bla_{TEM}, Sul2, tetA, bla_{SHV}, $bla_{\text{CTX-M-1}}$, and $bla_{\text{CTX-M-2}}$ were found in samples of chicken, cattle, and buffalo collected throughout different time frames across Bangladesh between 2016 and 2022 [38-42].

In India, two studies focusing on ESBL and *AmpC* production with $bla_{\text{CMY-2}}$, *sul1, and sul2* genes were carried out in several dairy farms in the West Bengal region [44]. Furthermore, another investigation conducted in Kolkata, West Bengal, detected ESBL in meat and meat products [45]. The region of southern Karnataka produced a total of 256 healthy broiler chicken samples. ESBL-producing, fluoroquinolone- or tetracycline-resistant *E. coli* was found in 94% of the samples, according to PCR analysis. This result was observed across all age groups. There were numerous ESBLs such as bla_{TEM}, bla_{SHV}, and $bla_{\text{CTX-M-1}}$, as well as the tetracycline efflux genes tetA and tetB [46]. Additional studies from various Indian states, such as Karnataka, Telangana, Andhra Pradesh, Maharashtra, and Mangalore, also examined the presence *oftetA, tetB, tetD, tetG, tetM, Sul1, sul2, sul3, qnrA, qnrB, cat1, cat2, cmlA, cat3, cmlB*, and *floR* and $bla_{\text{CTX–M–15}}$ from fecal samples of diarrheal piglets, fish farms, livestock waste, and retail chicken [47-49].

E. coli in human

A comprehensive investigation on UTI outpatients was carried out in the US from 1995 to 2001, during which 286,187 samples were collected. About 20% of these samples in the US were confirmed SXT resistance. 6938 isolates from 58,065 samples in 2001 had co-resistance to ampicillin and SXT [50]. Another study conducted in the US between 2002 and 2004 found that human fecal samples contained *papA* and/or *papC, sfa/focDE, afa/draBC, iutA*, and *kpsM* II in addition to TMP-SMZ, quinolones/fluoroquinolones, and extended-spectrum cephalosporin resistance [30]. Research conducted in the UK, Ireland, and North America revealed the presence of $bla_{CTX\text{-}M}$ and multi-drug resistance (MDR) ESBL in clinical blood and urine cultures [51,52]. Several investigations conducted in Europe, notably in Germany and Spain, demonstrated the presence of *tetA, tetB, tetD*, and ESBL from clinical blood and fecal samples, including bla_{TEM}, bla_{SHV}, bla_{OXA}, $bla_{\text{CTX-M}}$. In contrast, other research was conducted in Asian continents, including Bangladesh, China, and South Korea [57-59]. A study involving 249 hospitalized patients in South Korea identified the presence of $bla_{\text{CTX-M-55}}$, $bla_{\text{NDM-1,}}$ bla_{TEM}, *qepA1*, and *rmtB* in addition to carbapenemase production [57]. More than fifty percent of all patient UTI infections are caused by *E. coli*. Extended-range β-lactamases were produced by 56.9% of the 7580 clinical *E. coli* strains that were isolated from different sources in China between 2014 and 2022. The eastern coastal regions of China, major cities, densely populated neighborhoods, and healthcare facilities are all highly susceptible to the transmission of ESBL-producing infections [58]. In Dhaka, Bangladesh, an investigation on 100 *E. coli* isolates from clinical specimens revealed that 98% of the patients had resistance to cefuroxime, cotrimoxazole, and amoxicillin. The efficacy of β-lactam and β-lactamase inhibitors combined was not sufficient to combat 60% of the isolates. Patients with resistance to ciprofloxacin, norfloxacin, azithromycin, gentamicin, and chloramphenicol ranged from 34% to 49%. High levels of MDR were present in the isolates, and metallo-β-lactamase bla_{NDM} was the most common ABR gene identified [59].

In India, different studies were found. A study done in Assam, collected from 241 symptomatic UTI patients, including 188 *E. coli* isolates that were resistant to nalidixic acid (81.91%), ampicillin (82.44%), cefexime (71.27%), cefoperazone (61.17%), cefepime (49.46%), and aztreonam (54.25%). These isolates were identified as ESBL and carbapenemase along with the presence of $bla_{\text{C-TX-M}}$, bla_{TEM} and bla_{SHV} [60]. In Chandigarh 307 urine samples from UTI patients were collected which were resistant to amoxicillin/clavulanic acid (53%), amoxicillin (44%), norfloxacin (49%), nalidixic acid (46%), and ciprofloxacin (41%) [61] (Table 2). In the Eastern India case study, 1006 samples were collected from elderly UTI patients during 2013-2014. These samples contained 69.9% *E. coli* isolates and were 73% resistant to quinolones [62]. Two more investigations, carried out in India in 2005-2006 and 2013 determined the presence of bla_{SHV} (5%), bla_{TEM} (52%), bla_{CTXM} (100%), bla_{OXA}-1 (81%) from fecal samples of primary school students and neonates. [63,64].

Country	Duration	Study type	Sample collection from	Rate of Isolation	Resistance	Gene	Resistance gene	Ref
United States	2002-2004	Surveillance	Human faces (n = 931)	35%	TMP-SMZ, quinolones/fluoroquinolones, extended-spectrum cephalosporins	-	papA and/or papC, sfa/focDE, afa/draBC,iutA, and kpsM II	[30]
United States	2001	Symptomatic	Urine samples collection from UTI patients (n = 58,065)	14,793 (25%)	ampicillin, SXT, ciprofloxacin, nitrofurantoin	_	_	[50]
UK and Ireland	2001- 2002	Surveillance	Blood cultures isolates(n = 495)	101	amoxicillin, ciprofloxacin:	ESBL	bl_{aCTX-}M	[51]
North America	April 2003 – June 2004	Symptomatic	Urine sample (n = 1142)	862 (75.5%)	Ampicillin (37.7%), SMX/TMP (21.3%), nitrofurantoin (1.1%), ciprofloxacin (5.5%) and levofloxacin (5.1%)	-	-	[52]
European country	1997 -1998	Symptomatic	Blood (n = 1918)	0.36%	ampicillin (46.7%), ciprofloxacin (8.1%)	ESBL	-	[53]
Germany	1999 - 2000	Surveillance	Fecal sample (n = 750)	406	Ampicillin (16.7%), ciprofloxacin (0.7%), cotrimoxazole: 8.6%	-	-	[54]
Spain	November 2000- January 2001	Surveillance	Stool of healthy children (n = 41)	82%	ampicillin, gentamicin, tobramycin, ciprofloxacin, tetracyclines, nalidixic acid, tetracycline	-	bla_{TEM}, bla_{SHV}, and bla_{OXA},tetA, tetB (5), and tetD	[55]
Spain	2001- 2003	Surveillance	Blood (n = 7098)	50%	ampicillin, cotrimoxazole, ciprofloxacin, gentamicin, and tobramycin	ESBL	bl_{aCTX-}M	[56]
South Korea	2018	Symptomatic	Hospital's Patient (n = 249)	100%	colistin	carbapenem	$bla_{CTX-M-55}$ gene, and the $bla_{NDM-1,}$ bla_{TEM}, qepA1, and rmtB	[57]
China	2014-2022	Symptomatic	Hospital from human blood, sputum wounds, urine specimen (n = 7580)	56.9%	penicillins (75– 85%), tetracycline (64%), quinolones (64–67%), sulfamethoxazole (59.3%), cephalosporins (22–72%), aztreonam (34%), chloramphenicol (21%), amikacin (2.8%), colistin (1.4%), meropenem (1.1%), and imipenem (1%)	ESBL, CRE, NESBL	-	[58]
Dhaka, Bangladesh	January 2019- April 2019	Symptomatic	Urine and sputum collection from different diagnostic centre (n = 100)	98%	amoxicillin (98%), cefuroxime (75%) and cotrimoxazole (62%).	ESBL, Carbapenem (34%), AmpC (68%)	bla_{NDM} (80%), bla_{OXA} (48%),$bla_{CTX-M-15}$ (32%), tetC gene	[59]

Assam, India	November 2012- August 2014	Symptomatic	Urinary Infection (n = 241)	188 (78%)	nalidixic acid (81.91%), ampicillin (82.44%), cefexime (71.27%), cefoperazone (61.17%), Cefepime (49.46%) aztreonam (54.25%)	ESBL, carbapenem	bla_{CTX-M}, bla_{TEM} and $bl_{aSH}V$	[60]
Chandigar, India	January 2010 – December 2011	Symptomatic	Urine samples from UTI patients (n = 307)	75 (24.4%)	augmentin (53%), amoxicillin (44%), norfloxacin (49%), nalidixic acid (46%) and ciprofloxacin (41%)	-	-	[61]
Mumbai, India	September 2013- July 2014	Symptomatic	Urine samples from geriatric UTI patients (n = 1006)	69.6%	quinolone (73%)	_	_	[62]
Tamilnadu, India	2005-2006	Surveillance	Facal samplefrom primary school students (n = 119)	75 (63%)	amoxicillin, cotrimoxazole, and ampicillin, cephalosporins, ciprofloxacin, tetracyclines, nalidixic acid	-	-	[63]
India	2013	Symptomatic	Faecal samples from neonates (n = 210)	123 (59%)		ESBL	bla_{SHV} (5%), bla_{TEM} (52%), bla_{CTXM} (100%),bla_{OXA}-1 (81%)	[64]

Table 2: Antibiotic resistance in *Escherichia coli* recovered from human samples.

E. coli in environments

From October 2008 to May 2009, 118 potable water,well water, and sewage water samples were collected for a surveillance program in Leo'n, Nicaragua, North America. This research focused on ESBLS such as bla_{SHV}, bla_{TEM}, $bla_{OXA,}$ and bla_{CTX-M}. A different study collected 201 *E. coli* isolates from urban wastewater in Wisconsin, North America. Additionally, due to the presence of $bla_{CTX-M-1}$ (50%) and bla_{TEM} (100%) in these samples, the most prevalent isolates are tetracycline- and trimethoprim-sulfamethoxazole-resistant [66]. Wastewater from hospitals in Bulawayo, Zimbabwe, contained 94 different types of *E. coli*. A combination of biotyping and PCR for targeting the uidA housekeeping gene, 48 (53.3%) isolates of *E. coli* were obtained; of them, 48 (53.3%) were enterotoxigenic, 1 (1.06%) enterohaemorrhagic, and 2.13% enteroaggregative. Apart from ampicillin (92.6%) and sulphamethoxazole-trimethoprim (90.4%), *E. coli* was highly susceptible to azithromycin (75.5%) and trimethoprim (98.9%). *E. coli* isolates exhibited MDR in 79 (84%) of the instances [67]. Seventy-seven *E. coli* isolates from municipal and hospital sewage from three sewage treatment facilities in Austria were studied [68]. The isolates showed the highest resistance rates to cephalosporin, ampicillin, cefuroxime, quinolones, trimethoprim/sulfamethoxazole, and tetracycline [68] (Table 3).

Interestingly, one study identified ampicillin-resistant *E. coli* in the Baltic Sea in Poland. Additionally, 32% of these isolates showed resistance to amoxicillin/clavulanate, 20% to trimethoprim/sulfamethoxazole, and 15% to fluoroquinolones. Additionally, these had been identified to contain several genes, including dfrA1-aadA1, dfrA17, aadA5, and aadA1 [69]. Higher resistance rates were found in comparison to inflow whenever both pure and impure wastewater from different sources, including agricultural areas, were present. 168 microorganisms resistant to aminoglycosides were found in wastewater and river water during a study performed in Barcelona, Spain. In wastewater and rivers, *E. coli* was the most common Enterobacteriaceae species. The rmtB 16S-RMTase gene was present in most wastewater isolates, while armA was present in every river isolate. *E. coli* isolates from wastewater treatment plants were more resistant to cefotaxime, whereas those from rivers were more vulnerable [70]. 624 samples were collected throughout the summer and winter in the Wenyu River Basin, situated near Beijing, China. The isolates exhibited resistance to ampicillin (97%), tetracycline (90%), and sulfonamide (97%). Additionally, bla_{TEM}, $bla_{SHV,}$ and carbapenemases were noted [71]. Another study assessed the production of AmpC and ESBL in Tai'an, China. Wastewater plant samples were obtained to detect the presence of bla_{TEM} and bla_{CTX-M}

[72]. Six distinct hospital-derived wastewater sources in Noakhali, Bangladesh, were used for the collection of *E. coli* isolates. These 10 isolates were resistant to azithromycin, gentamycin, ciprofloxacin, tetracycline, ceftazidime, cefotaxime, and ampicillin [73].

Country	Duration	Study type	Sample collection from	Rate of Isolation	Resistance	Gene	Resistance gene	Ref
Leo´n, Nicaragua, North America	October 2008-May 2009	Surveillance	Drinking water, well water, sewage water (n = 118)	18	aminoglycosides, β-lactams and tetracyclines methicillin-resistant	ESBL	bla_{SHV}, bla_{TEM}, bla_{OXA} and bla_{CTX-M}	[65]
Medical College of Wisconsin, North America	October 2018	Surveillance	Hospital Wastewater (n = 201)	144	tetracycline, trimethoprim-sulfamethoxazol	ESBL	tetA and tetB, blaCTX-M-	[66]
Bulawayo, Zimbabwe, Africa	February-march 2020	Surveillance	Hospital Wastewater (n = 94)	51	ertapenem (98.9%), azithromycin (75.5%), ampicillin (92.6%) and sulphamethoxazole—trimethoprim (90.4%)	ESBL	-	[67]
Austria, Europe	April- September 2000	Surveillance	Sewage and sludge (n = 767)	9.8%	cefalothin (35%), cefuroxime-axetil (11%), nalidixic acid (15%), trimethoprim/sulfamethoxazole (13%), tetracycline(57%).	ESBL	-	[68]
Baltic sea, Poland, Europe	February- December 2011	Surveillance	Wastewater treatment plant (n = 774)	92	amoxicillin/clavulanate, trimethoprim/sulfamethoxazole and fluoroquinolone	ESBL	dfrA1-aadA1, dfrA17-aadA5, and aadA1	[69]
Barcelona, Spain, Europe	July- November 2023	Surveillance	Wastewater and River water (n = 168)	Wastewater (75.76%) and river water (19.61%)	aminoglycoside, cefotaxime	ESBL	16S-RMTase, $bla_{CTX-M-55}$ and $bla_{CMY-2,}$	[70]
Beijing, China	2007	Surveillance	River water (n = 624)	109	ampicillin, cefazolin, cefamandole, cefoperazone, and imipenem, tetracycline, sulfamethoxazole-trimethoprim, levofloxacinand gentamicin		bla_{TEM}, bla_{SHV} and carbapenemases	[71]
Tai'an, China	September 2016	Surveillance	Wastewater treatment plant (n = 80)	50	cephamycin, carbapenem, fluoroquinolones	ESBLs and AmpC,		[72]
Bangladesh	2018 (6 months)	Surveillance	Hospital wastewater (n = 10)	10	ampicillin, ceftazidime, cefotaxime,tetracycline, chloramphenicol, gentamycin, ciprofloxacin and azithromycin	_	_	[73]
Lake Nainital, India	2021	Surveillance	Sample from lake site (n = 20)	20	penicillin G = 100%, erythromycin (80%), ampicillin (60%), cefotaxime (55%), cefuroxime (45%); cefixime, norfloxacin &tetracycline(40% each), amikacin, cotrimoxazole, nalidixic Acid (15% each), chloramphenicol (10%), kanamycin and streptomycin (5% each)	-	-	[74]

New Delhi, India	2018	Surveillance	Sewage water	-	Colistin	Colistin	mcr	75
Himachal pradesh, India	2019	Surveillance	River water	-	Colistin	Colistin	mcr	75

Table 3: Antibiotic resistance in Escherichia coli recovered from environmental sources.

Twenty samples are taken, seen from an Indian perspective, from the site and surrounding area of Lake Nainital, India. Penicillin-G (100%), erythromycin (80%), and chloramphenicol (90%) antibiotic resistance were seen in these samples [74]. The presence of the *mcr* gene was confirmed in additional investigations carried out in 2018 and 2019 using river water from Himachal Pradesh and sewage water from New Delhi [75].

Conclusion

E. coli can colonize the gut of animals and humans, thus entering through the fecal-oral pathway. *E. coli* have a capacity to antibiotic resistance genes through horizontal gene transmission and virulence properties which can also develop many diseases in human health. *E. coli* could be used as an antibiotic resistance indicator in the environment and livestock. *E. coli* comprises resistant genes including papA or papC, sfa/focDE, afa/draBC, iutA, kpsM II, tetA, tetB, bla_{TEM}, sul (I), sul (II), bla_{SHV}, bla_{TEM}, bla_{OXA}, and bla_{CTX-M} that provide development to antibiotic resistance. The greatest number of *E. coli* samples exhibit resistance to ampicillin, tetracycline, penicillins, erythromycin, cefotaxime, cefuroxime, cefixime, amikacin, cotrimoxazole, nalidixic acid, chloramphenicol, trimethoprim, levofloxacin, fluoroquinolone, trimoxazole, and gentamicin etc. This study shows *E. coli* as an indicator of antibiotic resistance. Furthermore, although *E. coli* can be used as a general indicator of selection pressures for resistance to widely used, clinically important medications, it does not directly resist the majority of antibiotics used to treat foodborne enteric illnesses. Incorporating ABR in *E. coli* into an ABR monitoring system is a very simple approach, and it can provide an overview of potential environmental stressors, including antibiotic use, even when specific target bacteria might not be present.

Conflict of Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This review article is based on earlier studies and does not involve any experiments with humans or animals by any of the authors.

Consent to Participants

Not applicable.

Consent for Publication

Not applicable.

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