Review

Antimicrobial Resistance in Diverse Escherichia coli Pathotypes from Nigeria

Kenneth Nnamdi Anueyiagu , Chibuzor Gerald Agu , Uzal Umar , Bruno Silvester Lopes *

Posted Date: 20 August 2024

doi: 10.20944/preprints202408.1429.v1

Keywords: Escherichia coli; E. coli O157:H7; Shiga-toxins; antimicrobial resistance; STEC; Diarrheagenic E. Coli; blaCTX-M; ESBL

Review

Antimicrobial Resistance in Diverse *Escherichia coli* Pathotypes from Nigeria

Kenneth Nnamdi Anueyiagu [1], Chibuzor Gerald Agu [2], Uzal Umar [3] and Bruno Silvester Lopes [4,5,*]

[1] Department of Public Health Technology, Federal College of Animal Health and Production Technology, Vom
[2] National Veterinary Research Institute, Vom
[3] Department of Medical Microbiology, University of Jos, Nigeria
[4] School of Health and Life Sciences, Teesside University, Middlesbrough, United Kingdom.
[5] National Horizons Centre, Teesside University, Darlington, United Kingdom.
* Correspondence: brunoldlopez@yahoo.co.in or b.lopes@tees.ac.uk

Abstract: *Escherichia coli* is a gram-negative commensal bacterium living in human and animal intestines. Its pathogenic strains are cause of high morbidity which can adversely affect people by causing urinary tract infections, food poisoning, septic shock, or meningitis. Humans can contract *E. coli* by eating contaminated food—such as raw or undercooked raw milk, meat products, and fresh produce sold in open markets—as well as by coming into contact with contaminated settings like wastewater, municipal water, soil, and faeces. Some pathogenic strains of *E. coli* have been identified in Nigeria such as enterohemorrhagic (EHEC), as well as enterotoxigenic (ETEC), enteropathogenic (EPEC), enteroinvasive (EIEC), enteroaggregative (EAEC), and verotoxigenic (VTEC). This causes acute watery or bloody diarrhoea, stomach cramps, and vomiting. Apart from the virulence profile of *E. coli*, antibiotic resistance mechanisms such as the presence of *bla*$_{CTX-M}$ found in humans, animals and environmental isolates which are of great importance and require surveillance and monitoring for emerging threats in resource-limited countries. This review is aimed at understanding the underlying mechanisms of evolution and antibiotic resistance in *E. coli* in Nigeria and highlighting the use of improving One Health approaches to combat the problem of emerging infectious diseases.

Keywords: *Escherichia coli*; *E. coli* O157:H7; Shiga-toxins; antimicrobial resistance; STEC; Diarrheagenic *E. coli*; *bla*$_{CTX-M}$; ESBL

1. Introduction

Theodor von Escherich, a German-Austrian paediatrician was the first to isolate intestinal bacteria in neonates and infant faecal matter in 1857, which he termed '*Bacterium coli commune*'[1]. This bacterium was originally called Bacillus coli in 1895 and renamed *Escherichia coli* in 1919 in honour of Escherich. The nomenclature was then formally acknowledged in 1958, forming *Escherichia* as a genus, with *E. coli* as its first species [2]. *E. coli* is a Gram-negative, non-spore-forming, facultative anaerobic, rod-shaped bacteria belonging to the Family Enterobacteriaceae, Class Gammaproteobacteria, and Phylum Pseudomonadota. These are normal intestinal commensals of humans and warm-blooded animals and to date, thirteen species have been described of which *E. adecarboxylata*, *E. albertii*, *E. blattae*, *E. coli*, *E. fergusonii*, *E. hermannii*, *E. marmotae*, *E. ruysiae*, *E. vulneris* and *E. whittamii* are validly published under the International Code of Nomenclature of Prokaryotes (ICNP) whereas *E. faecium*, *E. hominis* and *E. pseudocoscoroba* are not validly published.

Escherichia coli is the most widely studied organism, a lactose fermenter with colonies on MacConkey agar, appearing bright pink with a typical diameter of 0.5 to 1 mm after overnight incubation at 37°C/24 h. The colony appearance on blood agar plates can vary from grey to white, transparent to opaque, and raised convex to flat. On Eosin Methylene Blue (EMB) agar, *E. coli* produces a characteristic green metallic sheen. This bacterium can survive in water for 4 – 12 weeks

 doi:10.20944/preprints202408.1429.v1

and as a result, it is used as a faecal indicator organism for determining bacterial contamination in water, because of the availability of simple, and affordable techniques [3]. Some pathotypes of *E. coli* such as the O157: H7 strain are sorbitol non-fermenters, which is a feature that can help it to be distinguished from other strains of *E. coli* [4].

Most *E. coli* strains are harmless and essential to the human digestive system. *E. coli* can synthesise some essential vitamins for human health, such as vitamin K and some B vitamins, and aids in the breakdown of food and the absorption of nutrients. Additionally, they guard the gut by preventing the colonisation of harmful bacteria through colonisation resistance and resource limitation [5].

Most *E. coli* strains are harmless, but pathogenic types can adversely affect people and cause food poisoning, urinary tract infections, septic shock, or meningitis. *E. coli* can be divided into two broad categories: commensal and pathogenic [6]. Commensal *E. coli* is crucial for maintaining normal intestinal bacteria, supports innate and adaptive immunity, and is also important for the gastrointestinal tract because it produces vitamin K and vitamin B12 required by man [7]. Extra-intestinal pathogenic *E. coli* (ExPEC) can be divided into many main genetic subgroups such as A, B1, B2, C, D, E and I. Group A often includes isolates from the colon, ileum, and duodenum [8]. Phylogroup B1 contains both commensal and some strains belonging to the Enterohemorrhagic *E. coli* (EHEC) pathotype. B2, C, D1, D2, and E represent Intestinal Pathogenic *E. coli* (InPEC) which relates mainly to diarrheal diseases. Many ExPEC belong to group B2 and are primarily associated with adult urinary tract infections (UPEC) and neonatal meningitis (NMEC) [9].

The main source of pathogenic *E. coli* variations' capacity to cause intestinal or extraintestinal disease is their development of several specific virulence factors, including toxins, lipopolysaccharides, iron acquisition factors, adhesins, polysaccharide capsules, and invasins. These elements aid the organism's ability to get past the host's defences and infiltrate or colonize the organs.

E. coli is transmitted to humans primarily through the consumption of contaminated foods, such as raw or undercooked ground meat products and raw milk. An increasing number of outbreaks are associated with the consumption of fruits and vegetables (including sprouts, spinach, lettuce, coleslaw, and salad) whereby contamination may be due to contact with faeces from domestic or wild animals at some stage during cultivation or handling [10]. The reservoir of this pathogen includes cattle, sheep, goats, deer, pigs, horses, rabbits, dogs, cats, and birds including chicken and turkeys. Faecal contamination of water and other foods, as well as cross-contamination during food preparation (with beef and other meat products, contaminated surfaces and kitchen utensils), can also lead to infection [11].

Apart from the virulence profile of *E. coli*, antibiotic resistance mechanisms of this bacterium are one of the most significant issues in recent research. Antibiotic resistance happens when bacteria evade the effect of antibiotics either by mutations in functional genes or by acquiring genes that can hydrolyse antibiotics and can also be transferred via plasmids between different strains [12]. One of the most clinically and epidemiologically significant mechanisms of antibiotic resistance in Enterobacteriaceae is the synthesis of carbapenemases, AmpC-type β-lactamases, and extended-spectrum β-lactamases (ESBLs) [13]. In this study, we review the prevalence of different *E. coli* pathotypes and their underlying mechanisms of antibiotic resistance in Nigeria.

1.1. Diarrheagenic E. coli Pathotypes

According to the WHO Global Burden of Foodborne Diseases report, diarrheagenic *E. coli* (DEC) causes around 200,000 deaths and over 300 million illnesses worldwide each year [10]. Approximately 40% of bouts of acute diarrhoea in children in underdeveloped countries are caused by diarrheagenic *E. coli* [14]. Additionally, they significantly contribute to both adult and paediatric diarrhoea in Nigeria [14]. Enterotoxigenic (ETEC), enterohaemorrhagic (EHEC), enteroinvasive (EIEC), enteropathogenic (EPEC), enteroaggregative (EAEC), diffusely adherent (DAEC), cytolethal distending toxin-producing (CDTPEC), and cell-detaching *E. coli* (CDEC) are the eight pathotypes of DEC strains that are currently known [14,15]. Each pathotype of DEC has a unique set of virulence factors encoded either on the plasmids or on the chromosomes. *E. coli* pathotypes cause substantial

 doi:10.20944/preprints202408.1429.v1

diarrheal illnesses in Nigeria. These infections are especially serious for children under five, as they increase morbidity and mortality and exacerbate public health issues in an environment where access to clean water and quality healthcare is frequently restricted.

1.2. Enterohaemorrhagic E. coli (EHEC)

One of the major foodborne infections, enterohaemorrhagic *E. coli* O157:H7, frequently results in a high death rate among humans [16]. Common infections brought on by this bacterium have the potential to be fatal. Haemorrhagic colitis and other problems including hemolytic uremic syndrome and thrombotic thrombocytopenic purpura are among the symptoms that susceptible people may experience [17,18]. Toxin tests and stool cultures are used for diagnosis. *E. coli* O157 was found to be one of the main causes of foodborne disability-adjusted life years, placing Nigeria in a sub-region with the greatest prevalence of foodborne disease worldwide. According to Gambushe et al [19], this infection is also common in South Africa and Ethiopia. Wells, water troughs, and bodies of water (such as ponds and streams) have all been shown to contain EHEC which could be due to the contamination of water with ruminant faeces which are common carriers of this pathogen. Nigeria is among the nations where 90 million people lack access to potable water, and 130,000 children under the age of five pass away every year from preventable waterborne illnesses as a result of government agencies' disorganised efforts, lack of funding, and basic public education about hygienic practices, public health policies, and engaging with various stakeholders. The majority of people, especially those living in rural and suburban areas, use untreated water from wells and streams for domestic use, which puts them at risk of *E. coli* infection through the faecal-oral route [20,21]. Waterborne transmission where 88.9% of *E. coli* isolates were of EHEC pathotype has been reported in Nigeria, both from contaminated drinking water and recreational waters [22].

Although it has also been found to survive for months in manure, beef and mutton used in steaks; however, in Nigeria, meats are cooked thoroughly and therefore STEC outbreaks linked with undercooked meat are rare. Interpersonal contact is a crucial means of transmission via the faecal-oral pathway. There have been reports of an asymptomatic carrier condition, in which a person can infect others yet exhibit no clinical symptoms of the illness. Another known risk factor for STEC infection is going to farms and other places where the general public may have direct contact with farm animals. Ruminants such as cattle, sheep and goats are largely reared by pastoralists & agro-pastoralists and common practice in the Fulani tribe can also be exposed to strains such as *E. coli* O157 [23].

Antibiotic therapy is generally not recommended for EHEC infections [24] because it is of no benefit [25], or even harm, in particular, but an increased risk of hemolytic uremic syndrome (HUS) development in patients treated with antibiotics during the initial period of diarrhoea [26]. Shiga toxin (*Stx*), the primary virulence component of EHEC implicated in the pathogenesis of HUS, is produced and/or released more frequently when antibiotics are used, which is one conceivable mechanism by which they raise the chance of developing HUS [27]. The goal of treating STEC is to remove the bacteria from the intestine without causing it to start producing toxins. Recently, STEC has been treated with different methods such as antisera or monoclonal antibodies [28].

1.3. Enterotoxigenic E. coli (ETEC)

ETEC is a primary enteric pathogen that is responsible for annual millions of diarrheal diseases, globally [29]. In the laboratory, ETEC is diagnosed when the microbe is cultured from faecal samples and tested for the presence of toxins *(LT, STh, and STp)* using phenotypic assays like dot blotting or through the use of conventional PCR [30]. Children less than 5 years old are vulnerable to ETEC, especially in developing countries like Nigeria where the disease is endemic. ETEC accounts for about 100 million diarrhoea episodes and 60,000 mortalities in 2015 [29]. ETEC is also the major cause of traveller's diarrhoea affecting travellers visiting developing countries of the world [31]. In underdeveloped nations, where there is no infrastructure for the collection of human waste and the supply of clean drinking water, ETEC infections are caused by consuming contaminated food and

 doi:10.20944/preprints202408.1429.v1

water. Previous research has shown that ETEC may live in faeces for up to six months and that it often grows in water as biofilms, which gives it a better chance of surviving [32].

1.4. Enteroinvasive E. coli (EIEC)

EIEC appear to be a less frequent cause of diarrheal sickness than other *E. coli* infections, however, this may be due to the methods employed to identify these organisms [33]. It is diagnosed in the laboratory by culturing stool samples and by the detection of EIEC pathogenicity genes by DNA hybridization or PCR. EIEC produce a diarrheal illness that is indistinguishable from shigellosis. The majority of diarrheal illness cases that are caused by EIEC seem to be sporadic. *Shigella* spp. are closely linked to the EIEC which uses Shigella-like genetic material to encode virulence components including the type III secretion system (TTSS). The EIEC enters the intestinal cell, multiplies intracellularly, and extends into neighbouring intestinal cells via virulence proteins known as "invasins." Cell death and occasionally bloody diarrhoea result from this process [33]. The majority of EIEC illness manifests clinically as watery diarrhoea and is difficult to recognize at the bedside from the many other causes of diarrhoea [33].

1.5. Enteropathogenic E. coli (EPEC)

According to Lanata and Walter [34], enteropathogenic *Escherichia coli* (EPEC) is a common strain of *E. coli* that causes persistent diarrhoea and is one of the main causes of pediatric *E. coli* infections worldwide [35]. Over the past few decades, the importance of EPEC as a pathogen has generally decreased in the published [36,37]. In contrast to more recent studies that relied on molecular techniques and/or adherence assays to identify EPEC, it is unclear whether the decrease in EPEC infections is the result of interventions, particularly breastfeeding promotion, or if earlier studies that overestimated the relative contribution of these organisms in diagnosis based on O- or O: H-typing [38].

1.6. Enteroaggregative E. coli (EAEC)

Enteroaggregative *E. coli* (EAEC) has gained increased attention in the last ten years as a potential cause of persistent, watery diarrhoea. According to Kaur et al. [39], EAEC is a rather diverse category of an emerging enteric pathogen connected to episodes of acute or chronic diarrhoea in children and adults worldwide. In both developing and wealthy nations, EAEC infection is a significant contributor to diarrhoea in both outbreak and non-outbreak situations. Irritable bowel syndrome has recently been linked to EAEC, albeit this has not yet been proven [39].

1.7. Diffusely Adherent E. coli (DAEC)

DAEC strains are a varied group of isolates that all exhibit diffuse adherence (DA) to epithelial cells in the conventional laboratory assay of adherence to HEp-2 or HeLa cells [40]. The production of adhesins encoded by a family of operons connected to afa/dra/daa is often the cause of the DA pattern of DAEC isolates.

1.8. Cytolethal-Distending Toxin-Producing E. coli (CDTEC)

Escherichia coli strains obtained from patients with diarrhoea were shown to have the cytolethal distending toxin (CDT) in 1987 [41]. Since then, several pathogenic Gram-negative bacteria have been found to express CDT, including *Aggregatibacter* (formerly *Actinobacillus*) *actinomycetemcomitans*, *Campylobacter* spp., *Escherichia* spp., *Haemophilus ducreyi*, *Helicobacter* spp., *Providencia alcalifaciens*, and *Shigella* sp. In vitro studies, it has been shown to stop the proliferation of various cell lines [42].

1.9. Cell-Detaching E. coli (CDEC)

When CDEC was initially identified, it was discovered to relate to diarrhoea in Australian aboriginal children [43]. Although no conclusive evidence links it to diarrhoea, it has also been

 doi:10.20944/preprints202408.1429.v1

discovered in Brazil [44]. Notably, the majority of the CDEC isolates found in this investigation (87.0%) did not ferment lactose and were like a group of non-lactose-fermenting haemolytic strains that had been previously isolated from stool specimens in Somalia [45]. Lactose-negative CDEC strains may be significant pathogens in Africa [46]. Unfortunately, as is the case with most *E. coli* strains, their slow rate of lactose fermentation means that they are likely to be disregarded (or mistaken for Shigella or other non-lactose fermenters) in a lot of investigations. Additionally, diarrhoea may potentially be linked to diffusely adherent *E. coli* (DAEC). However, rates of infection vary by region in Africa [47].

The clonal classification of pathogenic strains of *E. coli* is listed in Table 1 highlighting the symptom, pathogenic mechanism, reservoirs and epidemiological aspects for each of those groups.

Table 1. Properties of clonal strains of *E. coli* .

Clonal group	Symptoms	Pathogenic mechanism	Reservoirs	Epidemiological aspects
Enterohaemorrhagic (EHEC)	Mild to severe diarrhoea frequently containing blood, Haemorrhagic colitis, (Haemolytic Uremic Syndrome)	Attaching effacing and production of potent verocytotoxins (Stx) that target renal structures (Kidney Failure).	Zoonotic (ruminants, water)	In developed countries, most infections are in children or the elderly. Treated by intravenous fluids, corticosteroids, Plasma filtration/exchange, dialysis (no antibiotics)
Enterotoxigenic (ETEC)	Mild to severe watery self-limiting diarrhoea	Possess either or both heat liable (LT) and heat-stable toxins (ST) like those produced by *Vibrio cholera*	Zoonotic (contaminated food and water)	Associated with childhood/traveller's diarrhoea in developing countries treated by ORS
Enteroinvasive (EIEC)	Watery to dysentery-like diarrhoea - with blood & mucus in faeces, fever, abdominal cramps, inflammatory colitis	Ability to invade and replicate in intestinal epithelial cells Related to *Shigella* spp.	Poor sanitary practices, food/waterborne	more important in developing countries with high morbidity and mortality of children.
Enteropathogenic (EPEC)	Watery diarrhoea, Vomiting	Attaching-effacing lesions. Localised clusters adhere to the surface of cells	Zoonotic (water, ruminants, chicken, faeces)	Associated with infantile diarrhoea (nurseries), especially in developing countries
Enteroaggregative (EAEC)	Acute watery diarrhoea	Adherence by an	Largely unknown,	Implicated with persistent diarrhoea

 doi:10.20944/preprints202408.1429.v1

	sometimes containing blood & mucous, mild fever, abdominal cramps, nausea, vomiting	aggregative adherence fimbria (AAF). Release of enterotoxin homologous to *Shigella flexneri*	new-class foodborne outbreaks	(>14days) in developing and developed countries
Diffusely adherent (DAEC)	Acute diarrhoea, vomiting, and sometimes fever	Fimbrial uniform adhesion - host cell elongates and wraps around the adherent bacteria	Largely unknown –new class	DAEC associated with infantile diarrhoea
Cytolethal-distending toxin-producing *E. coli* (CDTEC)	Watery diarrhea; could progress to bloody diarrhea, abdominal pain, and fever.	Produces a toxin called cytolethal distending toxin (CDT) which has DNase activity, meaning it can damage DNA within the host cells.	Humans and animals (livestock and wild)	Affects individuals of all ages but young children, the elderly, and immunocompromised individuals are at higher risk of developing severe disease.
Cell-detaching *E. coli* (CDEC)	Watery diarrhoea, which can sometimes progress to more severe forms such as bloody diarrhoea. Abdominal pain, nausea, and vomiting may also be present.	CDEC strains produce a toxin or factors that cause the detachment of epithelial cells from the intestinal lining.	The primary reservoir for CDEC is believed to be humans, although it may also be present in animals.	CDEC can affect individuals across all age groups, but children, especially those under five years old, are more susceptible to infections. The elderly and immunocompromised individuals are also at higher risk.

2. Molecular Mechanisms of Antibiotic-Resistant *E. coli*

Globally, there is a growing issue with resistance to broad-spectrum β-lactams, which is caused by enzymes such as AmpC β-lactamases (AmpC), Metallo β-lactamases (MBL), and extended-spectrum β-lactamases (ESBL) [48]. The most common mechanism for β-lactam resistance in clinical isolates from the *Enterobacteriaceae* family is the synthesis of β-lactamases [49]. These groups of resistant *E. coli* have more diarrheagenic pathotypes than uropathogenic *E. coli* but could increase the risk for the latter [50].

2.1. Community-Acquired Antibiotic-Resistant E. coli

 doi:10.20944/preprints202408.1429.v1

The rise of community-acquired antibiotic-resistant *E. coli* is primarily attributed to several factors. One key factor is the overuse and misuse of antibiotics in both human medicine and livestock production. It is noteworthy to mention that there are either no or little regulations of the use of antibiotics in Africa [51]. Widespread and irrational use of antibiotics creates an environment where bacteria can develop resistance mechanisms, rendering antibiotics ineffective at killing them. The implications of community-acquired antibiotic-resistant *E. coli* infections are significant. These infections are often more difficult to treat, as the bacteria are resistant to commonly used antibiotics which can result in prolonged illness, increased healthcare costs, and in some severe cases, life-threatening complications. Furthermore, treating these infections requires the use of more potent and costly antibiotics, which can further contribute to the emergence of antibiotic resistance. Globally, there is currently significant concern over the advent of strains of *E. coli* that produce extended-spectrum beta-lactamases (ESBLs) and community-acquired resistance to fluoroquinolones. A higher frequency of *E. coli* with elevated resistance to antibiotics is identified in patients suffering from complex UTIs [52]. This is a result of the organisms acquired after being exposed to hospital settings, as well as the fact that many individuals with persistent abnormalities who suffer from recurring infections have taken numerous courses of antibiotics in the past [53].

2.2. Hospital-Acquired Antibiotic-Resistant E. coli

Worldwide, urinary tract infections (UTIs), are the most prevalent type of hospital-acquired illnesses. *E. coli* is the most frequent bacterium associated with UTIs. Different *E. coli* strains obtained from community and hospital sources may have different levels of antibiotic resistance and can often display multi-drug resistant phenotypes. Studies show that ESBL-producing *E. coli* is becoming increasingly prevalent in hospitals [54,55].

2.3. Extraintestinal Pathogenic E. coli (ExPEC)

According to Nicolas-Chanoine et al.[56], ST131 is currently the most prevalent *E. coli* lineage discovered in extraintestinal pathogenic *E. coli* (ExPEC) isolates worldwide. Based on population genetics, ST131 is composed of several clades, including A, B, and C. Of these, clade C is the most widely distributed worldwide [57]. Compared to other traditional group B2 ExPEC isolates, almost all of the ST131 isolates are fluoroquinolone-resistant and are often reported to produce extended-spectrum β-lactamases, like CTX-M-15 [56]. Furthermore, ST131 *E. coli* isolates are thought to be extremely dangerous due to the range of infections they can cause in both community and hospital settings, as well as the quantity of virulence-associated genes they carry [56].

2.4. Antibiotic-Resistant E. coli of Origins in Animals and the Environment

E. coli of animal origin exhibits resistance against a range of antibiotics due to overuse and abuse, including tetracyclines, aminoglycosides, β-lactams, fluoroquinolones, and third-generation cephalosporins [58]. A recent report revealed that the extended-spectrum beta-lactamase *Escherichia coli* (ESBL-EC) strains from the human, chicken, and chicken market environments had the same sequence type (ST-155), indicating that there may have been a transmission between these hosts and the environment [59]. This finding also shows that co-colonization of antimicrobial-resistant *E. coli* from a shared source is a possibility. The ESBL-positive *E. coli* ST-155 represents a significant zoonotic strain that is responsible for the transmission to humans [60,61].

It is also important to note that ST-155 has been detected in *E. coli* isolates from water samples [61] and was detected in isolates from environmental samples [62]. Antibiotic-resistant *E. coli* concentrations in some wastewater treatment facilities and aquatic ecosystems reached 10^4-10^5 CFU/mL, which is more than what is needed for irrigation water usage presenting a severe risk to public health [62].

3. Distribution of *E. coli* with Sources in Nigeria

3.1. Prevalence of Urinary Tract Infections Caused by E. coli

 doi:10.20944/preprints202408.1429.v1

Among other studies, Olorunshola et al., [63] reported a 6% prevalence of *E. coli* in Nigeria (Table 2). This study which was in a city of more than 13.4 million in 2000 was the least while Mofolorunsho et al showed a higher prevalence of 70.3% in Anyigba town in Kogi State which has less than 500,000 people in 2021.

Table 2. *E. coli* isolated from humans in Nigeria.

S/No	Source	Prevalence (n)	Author
1.	Human stool sample (DEC)	6% (100)	Olorunshola et al., [63]
2.	Hospital-acquired	19.55% (22,941)	Ige et al., [64]
3.	UTI in Abuja	37% (6,763)	Iregbu and Nwajiobi, [65]
4.	UTI in South West	39.69% (514)	Oladeinde et al., [66]
5.	UTI in South East	18.8% (266)	Okafor and Nweze, [67]
6.	UTI in North Central	70.3% (200)	Mofolorunsho et al [68]
7.	UTI in North West	68.7% (128)	Muhammed et al [69]
8.	UTI in North East	41% (1,590)	Ohieku and Magaji, [70]
9.	UTI in South South	40% (300)	Ojezele, [70]

3.2. E. coli in Food and Environment

Table 3 describes the prevalence of *E. coli* in food and environment. Besides human samples, *E. coli* can also be found in animals, animal products, plants, and environmental samples including water and soil. Adesiji et al., [72]showed a very high prevalence of the organism in fresh meat on sale which could be due to faecal contamination. The prevalence of the organism from other animals and animal products has public health implications. Wastewater and dumpsite have a high prevalence which is expected. Ruminant milk samples were seen to be contaminated by *E. coli* with prevalence rates of 44.8%, 43.1% and 39.2% in cows, goats and ewes respectively [73,74]. Anueyiagu et al., [75] also isolated 22.73% of *E. coli* from domestic birds and 6.67% of *E. coli* from wild birds found in the same vicinity.

Fresh fruits and vegetables sold in Nigerian flea markets have been reported to be laden with microorganisms such as *E. coli*. Maikai and Akubo [76] recorded a 21.3% prevalence while Reuben and Makut [77] recorded a 17.5% prevalence.

Environmental sources of *E coli* were reported by Edward et al., (2020) [78], Garba et al (2009) and Ijabani et al. (2022) [80] among many other authors.

Table 3. *E. coli* isolated from humans in Nigeria.

S/No	Source	Prevalence (n)	Author
1.	Raw milk from cows	44.8% (640)	Anueyiagu et al., [74]
2.	Raw milk from does	43.1% (206)	Anueyiagu et al., [74]
3.	Raw milk from ewes	39.2% (206)	Anueyiagu et al., [74]
4.	Fresh meat on sale	26% (300)	Adesiji et al [72]
5.	Fresh/Roasted beef	52.5% (300)/ 25.3% (150)	Dahiru et al., [81]
6.	Poultry	31.8% (111)	Aworh et al., [59]
7.	Wild birds	48.1% (160)	Oludairo et al., [82]
8.	Vegetables	17.5% (40)	Reuben and Makut, [77]
9.	Fresh fruits	21.3% (108)	Maikai and Akubo, [76]
10.	Wastewater	62.4% (700)	Edward et al., [78]
11.	Municipal water	45.5% (300)	Garba et al., [79]
12.	Soil	20% (75)	Ijabani et al., [80]

4. Genotypes of *E. coli* in Nigeria and Other African Countries

 doi:10.20944/preprints202408.1429.v1

The prevalence of Shiga toxigenic *E. coli* (STEC) differs by country. Most regions of the world, including several African nations, have reported cases of Shiga toxigenic *E. coli* infections [83]. One or more Shiga-toxin (stx) strains are produced by human pathogenic STEC. These strains are classified into two groups: stx1 (which includes the three variants stx1a, stx1c, and stx1d) and stx2 (which includes seven unique variants stx2a, stx2b, Stx2c, Stx2d, Stx2e, Stx2f, and Stx2g). Among these variations, stx2b and stx2e are connected to minor clinical symptoms or asymptomatic faecal carriage, while stx2a, stx2c, and stx2d are linked to severe disease [84–86]. The main STEC serogroups include *E. coli* O26, O45, O91, O103, O111, O113, O121, O128, O145, and O157, and they are all capable of producing Shiga toxins. In addition to stx1 and stx2, certain isolates also have eaeA and/or hlyA [87]. The *hlyA* genes encode for cytolysin while *eae* gene encodes for intimin which plays a vital role in the attaching and effacing (A/E) lesions on epithelial surfaces [88].

In 1990, in the South African city of Johannesburg, the first *E. coli* O157:H7 infection in humans was identified and recorded [89,90]. Nonetheless, in the Central African Republic in 1996, deadly pathogenic bacteria were discovered in patients suffering from hemorrhagic colitis. Following the emergence of bloody diarrhoea in Cameroon in 1998, STEC O157:H7 isolation in humans was reported [91]. There have been reports of pathogen isolation in Tanzania, Kenya, and Ethiopia in East Africa. In terms of the zoonotic disease epidemic on the African continent, Ethiopia is ranked second only to Nigeria [89]. In Nigeria, pathogenic STEC such as *stx1*, *stx2*, *eaeA* and *hylA* are common according to the literature. *Stx1, stx2*, *eaeA* and *hylA* were isolated from beef & beef products, faeces and meat of food-animal and beef abattoirs according to Fayemi et al., [92], Ojo et al., [93], and Ayoade et al., [94] respectively. The same *E. coli* variants were isolated from diarrheic patients from southwestern Nigeria [95]. In general, the evidence of STEC O157:H7 infection among the environment, animals, and humans, is obvious in Africa. In the laboratory, Sorbitol MacConkey agar is used to isolate STEC in Nigeria.

5. Antibiotic Resistance

The O157:H7 strain's high resistance is recognized as one of the key elements that contributes to the possibility of the bacterium becoming more harmful. *E. coli* O157:H7 is found in food samples obtained from animals, particularly meat. It is extremely resistant to a class of widely used antibiotics, including quinolones, aminoglycosides, macrolides, cephalosporins, sulfonamides, fluoroquinolones, and tetracyclines. Antimicrobial resistance genes, such as those that confer resistance to cephalosporins (*bla*$_{CTX-M}$), broad-spectrum penicillins/beta-lactams (*bla*$_{SHV}$), gentamicin (*aac(3)-IV*), sulphonamide (*sul1*), tetracycline (*tet*A and *tet*B), and trimethoprim (*dfrA1*), are among those that enable resistance. However, it has been shown that the antimicrobial resistance of STEC strains is caused by aminoglycoside resistance genes (aadA1) [96–98]. Investigating the distribution and prevalence of antimicrobial-resistance variables and antimicrobial resistance patterns of *E. coli* O157:H7 strains acquired from raw beef, goat, chicken, and turkey meats is crucial given the ambiguity surrounding the dissemination of *E. coli* O157:H7 in raw meat samples.

Numerous studies conducted across the African continent have identified and documented resistance of *E. coli* O157:H7 to a range of antimicrobial drugs. For instance, multidrug-resistant *E. coli* O157:H7 was isolated from humans, animals, and the environment in Egypt and its detection and documentation have been reported [91]. A multidrug-resistant *E. coli* O157:H7 was found and claimed to have been isolated from a cow in South Africa. In Nigeria, similar outcomes have been documented. Antimicrobial drugs' severe overuse in treating *E. coli* O157:H7 infections is one of the main causes of concern. This leads to multidrug resistance, which is not only concerning because it doesn't seem to be given much attention, but it also aids in the selection of resistance genes [91].

Given the advent of CTX-M-type extended-spectrum β-lactamases (ESBLs), recent reports in the literature indicated that *E. coli* is emerging as the Enterobacteriaceae species most impacted by ESBLs. It has been discovered that *bla*$_{CTX-M}$ bacteria can have virulence genes in addition to resistance genes. Out of 9 UTI samples collected from patients in Southwest Nigeria, 6 were positive for *bla*$_{CTX-M}$ [95], and in Minna Metropolis of Nigeria, 60% of 10% *E. coli* isolated from urine harboured *bla*$_{CTX-M}$ [99]. In

 doi:10.20944/preprints202408.1429.v1

ruminant mastitis, the genetic characterization revealed a higher prevalence of *bla*$_{CTX-M}$ (24.39 %) than *bla*$_{TEM}$ (12.19 .0%) in the bovine milk samples analysed [75].

Additionally, it has been noted that the majority of blaCTX-M from *E. coli* strains implicated in outbreaks across various nations also demonstrated the presence of additional antibiotic resistance genes, including *bla*$_{OXA-1}$, *bla*$_{TEM-1}$, *tet*A, *aac(6)-Ib*, and *aac(3)-II*, as well as occasionally a class 1 integron [100].

6. Conclusions

Nigeria and Africa face serious public health issues because of the spread of *E. coli-resistant* strains. Due to a lack of access to good healthcare, overused and misused of antibiotics, and use of antibiotics without a prescription, AMR can spread quickly throughout Nigerian communities. In addition to its enhanced virulence, highly pathogenic and antibiotic-resistant *E. coli* poses a severe hazard to food systems. These infections have been linked to one or more genetic factors of pathogenicity and pose a risk to human health. As a result of this research, policymakers should create a more proactive strategy to reduce the rise in *E. coli* infections in Nigeria. Therefore, to reduce the spread of potentially harmful or resistant *E. coli* strains, surveillance, low-cost diagnosis, and stringent hygiene practices of food (of animal and plant origin) should be continuously monitored. In general, individuals should prepare and consume food with greater hygiene standards. This assessment encourages Nigeria and other African nations to write and adopt new legislative measures for infectious diseases.

Author Contributions: Anueyiagu Kenneth Nnamdi: Conceptualization, Project management, Supervision, Writing – original draft, Writing – review & editing. Agu Chibuzor Gerald: Writing – original draft, Writing – review & editing. Umar Uzal: Writing – original draft, Writing – review & editing. Bruno Silvester Lopes: Conceptualization, Visualization, Writing – original draft, Writing – review & editing.

Funding information: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability: No new data were created or analyzed in this study.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Escherich, T. Die Darmbakterien des Neugeboren und Sauglings Fortschr. Med 1885, 3, 515–522 and 547–554.
2. Henry, R. Etymologia: Escherichia coli. Emerg. Infect. Dis 2015, 21(8), 1310.
3. Curutiu, C.; Iordache, F.; Gurban, P.; Lazar, V.; Chifiriuc, M.C. Main Microbiological Pollutants of Bottled Waters and Beverages. Bottled and Packaged Water 2019, 403–422. doi: 10.1016/B978-0-12-815272-0.00014-3. Epub 2019 Feb 22. PMCID: PMC7204880.
4. King, L.A.; Loukiadis, E.; Mariani-Kurkdjian, P.; Haeghebaert, S.; Weill, F-X.; Baliere, C.; et al. Foodborne transmission of sorbitol-fermenting Escherichia coli O157:[H7] via ground beef: an outbreak in northern France, 2011. Clinical Microbiology and Infection 2014, 20 (12), 01136-01144.
5. Kaper, J. B.; Nataro, J. P.; Mobley, H. L. T. Pathogenic Escherichia coli. Nature Reviews Microbiology 2004, 2(2), 123-140.
6. Eckburg, P.B.; Bik, E.M.; Bernstein, C.N.; et al. Diversity of the human intestinal microbial flora. Science 2005, 308(5728),1635–1638.
7. Lim, J.Y; Yoon, J.W.; Hovide, C.J. A BRIEF overview of Escherichia coli O157:H7 and Its Plasmid O157. J Microbiol Biotechnol 2010, 20 (1), 5–14. doi:10.4014/jmb.0908.080072.
8. Clermont, O.; Christenson, J.K.; Denamur, E.; Gordon, D.M. The Clermont Escherichia coli phylo-typing method revisited: improvement of specificity and detection of new phylo-groups. Environ Microbiol Rep 2013, 5(1), 58–65. doi:10.1111/1758-2229.12019
9. Pokharel, P.; Sabin, D.; Charles, M.D. The Diversity of Escherichia coli Pathotypes and Vaccination Strategies against This Versatile Bacterial Pathogen. Microorganisms 2023, 11(2), 344. https://doi.org/10.3390/microorganisms11020344

10. Balali, G.I.; Yar, D.D.; Afua Dela, V.G.; Adjei-Kusi, P. Microbial Contamination, an Increasing Threat to the Consumption of Fresh Fruits and Vegetables in Today's World. Int J Microbiol 2020, 22. doi: 10.1155/2020/3029295. PMID: 32565813; PMCID: PMC7269610.
11. Bintsis, T. Foodborne pathogens. AIMS Microbiol 2017, 3(3), 529-563. doi: 10.3934/microbiol.2017.3.529. PMID: 31294175; PMCID: PMC6604998.
12. Rybak, B.; Krawczyk. B.; Furmanek-Blaszk, B.; Wysocka, M.; Fordon, M.; Ziolkowski, P.; et al. Antibiotic resistance, virulence, and phylogenetic analysis of Escherichia coli strains isolated from free-living birds in human habitats. PLoS ONE 2022, 17(1), e0262236. https://doi.org/10.1371/journal.pone.0262236
13. Martı´nez-Martı´nez, L.; Gonza´lez-Lo´pez, J.J. Carbapenemases in Enterobacteriaceae: types and molecular epidemiology. Enferm Infecc Microbiol Clin 2014, 32, 4–9. https://doi.org/10.1016/S0213-005X(14)70168-5 PMID: 25542046
14. Odetoyin, B.; Ogundipe, O.; Onanuga, A. Prevalence, diversity of diarrhoeagenic Escherichia coli and associated risk factors in well water in Ile-Ife, Southwestern Nigeria. One Health Outlook 2022, 4, 3. https://doi.org/10.1186/s42522-021-00057-4
15. Collins, J.; Tack, D.; Pindyck, T.; Griffin, P. Escherichia coli, Diarrheagenic. Centre for Disease Control and Prevention. Assessed on 2023 from: https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/escherichia-coli-diarrheagenic
16. Mir, R.A.; Kudva, I.T. Antibiotic-resistant Shiga toxin-producing Escherichia coli: An overview of prevalence and intervention strategies. Zoonoses Public Health 2018, 66,1–13. doi: 10.1111/zph.12533
17. Lyimo, B.; Buza, J.; Subbiah, M.; Smith., W. Comparison of antibiotic resistant Escherichia coli obtained from drinking water sources in northern Tanzania: a cross-sectional study. BMC Microbiol 2016, 16, 254. doi: 10.1186/s12866-016-0870-9.
18. Wang, J.; Stanford, K.; McAllister, T.A.; et al. Biofilm formation, virulence gene profiles, and antimicrobial resistance of nine serogroups of non-O157 Shiga toxin-producing Escherichia coli. Foodborne Pathog Dis 2016, 13(6), 316–324. doi:10.1089/fpd.2015.2099138.
19. Gambushe, S.M.; Zishirim O.T.; El Zowalaty, M.E. Review of Escherichia coli O157:H7 Prevalence, Pathogenicity, Heavy Metal and Antimicrobial Resistance, African Perspective. Infect Drug Resist 2022, 23, 15:4645-4673. doi: 10.2147/IDR.S365269. PMID: 36039321; PMCID: PMC9420067.
20. Peter, A.K.; Uzal, U. Combating diarrhoea in Nigeria: the way forward. J Micro Experiment 2018, 6(4).
21. Oyedeji, O.; Olutiola, P.O.; Owolabi, K.D.; Adeojo, K.A. Multiresistant faecal indicator bacteria in stream and well waters of Ile-Ife City, southwestern Nigeria: public health implications. J Public Health Epidemiol 2011, 3, 371–81.
22. Tula, M. Y.; Enabulele, O. I.; Ophori, E. A. Occurrence and antibiotic resistance profile of shiga toxin-producing Escherichia coli (STEC) and enteropathogenic Escherichia coli (EPEC) from sources of water in Mubi Region, Adamawa State, Nigeria. Public Health and Toxicology 2023, 3(3), 15. https://doi.org/10.18332/pht/172303.
23. Kolodziejek, A.M.; Minnich, S.A.; Hovde, C.J. Escherichia coli 0157:H7 virulence factors and the ruminant reservoir. Curr Opin Infect Dis 2022, 35(3), 205-214. doi: 10.1097/QCO.0000000000000834. PMID: 35665714; PMCID: PMC9302714.
24. Holtz, L.R.; Neill, M.A.; Tarr, P.I. Acute bloody diarrhoea: a medical emergency for patients of all ages. Gastroenterology 2009, 136,1887–1898.
25. Tarr, P.I.; Gordon, C.A.; Chandler, W.L. Shiga-toxin-producing Escherichia coli and haemolytic uraemic syndrome. Lancet 2005, 365, 1073–1086
26. Smith, K. E.; Wilker, P. R.; Reiter, P. L.; Hedican, E. B.; Bender, J. B.; Hedberg, C. W. Antibiotic treatment of Escherichia coli O157 infection and the risk of hemolytic uremic syndrome, Minnesota. The Pediatric infectious disease journal 2012, 31(1), 37–41. https://doi.org/10.1097/INF.0b013e31823096a8.
27. Karch, H.; Tarr, P.I.; Bielaszewska, M. Enterohaemorrhagic Escherichia coli in human medicine. Int. J. Med. Microbiol 2005, 295, 405–418.
28. Mühlen, S.; Dersch, P. Treatment Strategies for Infections With Shiga Toxin-Producing Escherichia coli. Front Cell Infect Microbiol 2020, 6, 10, 169. doi: 10.3389/fcimb.2020.00169. PMID: 32435624; PMCID: PMC7218068.
29. Anderson, J.D.; Bagamian, K.H.; Muhib, F.; Amaya, M.P.; Laytner, L.A.; Wierzba, T.; Rheingans, R. Burden of enterotoxigenic Escherichia coli and shigella non-fatal diarrhoeal infections in 79 low-income and lower-middle-income countries: a modelling analysis. Lancet Glob Health 2019, 7(3), 321–322. doi: 10.1016/s2214-109x(18)30483-2.
30. Silwamba, S.; Chilyabanyama, O.N.; Liswaniso, F.; Chisenga, C.C.; Chilengi, R.; Dougan, G.; Kwenda, G.; Chakraborty, S.; Simuyandi, M. Field evaluation of a novel, rapid diagnostic assay, and molecular epidemiology of enterotoxigenic E. coli among Zambian children presenting with diarrhoea. PLoS Negl Trop Dis 2022,16(8), e0010207. doi: 10.1371/journal.pntd.0010207. PMID: 35930612; PMCID: PMC9385031.
31. Steffen, R.; Hill, D.R.; DuPont, H.L. Traveller's diarrhoea: a clinical review. JAMA 2015, 313(1), 71–80. doi: 10.1001/jama.2014.17006.

32. Ahmed, D.; Islam, M.S.; Begum, Y.A.; Janzon, A.; Qadri, F.; Sjoling, A. The presence of enterotoxigenic Escherichia coli in biofilms formed in water containers in poor households coincides with epidemic seasons in Dhaka. J Appl Microbiol 2013, 114(4), 1223–1229. doi: 10.1111/jam.12109.
33. Poolman, J. T. Escherichia coli. International Encyclopaedia of Public Health (Second Edition) 2017. Academic Press, Pages 585-593. https://www.sciencedirect.com/science/article/pii/B978012803678500504X.
34. Lanata, C.F.; Fischer-Walker, C.L.; Olascoaga, A.C.; Torres, C.X.; Aryee, M.J.; Black, R.E.; et al. Global Causes of Diarrheal Disease Mortality in Children <5 Years of Age: A Systematic Review. PLoS ONE 2013, 8(9), e72788. https://doi.org/10.1371/journal.pone.0072788.
35. Abba, K.; Sinfield, R.; Hart, C.A.; Garner, P. Pathogens associated with persistent diarrhoea in children in low and middle-income countries: systematic review. BMC Infect Dis 2009, 9, 88.
36. Ochoa, T.J.; Barletta, F.; Contreras, C.; Mercado, E. New insights into the epidemiology of enteropathogenic Escherichia coli infection. Trans R Soc Trop Med Hyg 2008, 102, 852–856.
37. Okeke, I.N. Diarrheagenic Escherichia coli in sub-Saharan Africa: status, uncertainties and necessities. J Infect Dev Ctries 2009, 3, 817–842.
38. Ochoa, T.J.; Contreras, C.A. Enteropathogenic Escherichia coli infection in children. Curr Opin Infect Dis 2011, 24(5), 478-83. doi: 10.1097/QCO.0b013e32834a8b8b. PMID: 21857511; PMCID: PMC3277943.
39. Kaur, P.; Chakraborti, A.; Asea, A. Enteroaggregative Escherichia coli: An Emerging Enteric Food Borne Pathogen. Interdiscip Perspect Infect Dis 2010, 254159. doi: 10.1155/2010/254159.
40. Cravioto, A.; Tello, A.; Navarro, A.; Ruiz, J.; Villafan, H.; Uribe, F.; Eslava, C. Association of Escherichia coli HEp-2 adherence patterns with type and duration of diarrhoea. Lancet 1991, 337, 262–264.
41. Johnson, W.M.; Lior, H. A new heat-labile cytolethal distending toxin (CLDT) produced by Escherichia coli isolates from clinical material. Microb Pathog 1988, 4, 103-113. 10.1016/0882-4010(88)90052-6.
42. Ceelen, L.M.; Decostere, A.; Ducatelle, R.; Haesebrouck, F. Cytolethal-distending toxin generates cell death by inducing a bottleneck in the cell cycle. Microbiological Research 2006, 161(2), 109-120, ISSN 0944-5013, https://doi.org/10.1016/j.micres.2005.04.002.
43. Gunzburg, S.T.; Chang, B.J.; Elliott, S.J.; Burke, V.; Gracey M. Diffuse and enteroaggregative patterns of adherence of enteric Escherichia coli isolated from aboriginal children from the Kimberley region of Western Australia. J Infect Dis 1993, 167, 755–758.
44. Okeke, I.N.; Lamikanra, A.; Steinrück, H.; Kaper, J.B. Characterization of Escherichia coli strains from cases of childhood diarrhoea in provincial southwestern Nigeria. J Clin Microbiol 2000, 38(1), 7-12. doi: 10.1128/JCM.38.1.7-12.2000. PMID: 10618054; PMCID: PMC86005.
45. Nicoletti, M.; Superti, F.; Conti, C.; Calconi, A.; Zagaglia, C. Virulence factors of lactose-negative Escherichia coli strains isolated from children with diarrhoea in Somalia. J Clin Microbiol 1988, 26, 524–529.
46. Okeke, I.N.; Steinrück, H.; Kanack, K.J.; Elliott, S.J.; Sundström, L.; Kaper, J.B.; Lamikanra, A. Antibiotic-resistant cell-detaching Escherichia coli strains from Nigerian children. J Clin Microbiol 2002, 40(1), 301-305. doi: 10.1128/JCM.40.1.301-305.2002. PMID: 11773139; PMCID: PMC120082.
47. Winstead, A.; Hunter, J.C.; Griffin, P.M. Escherichia coli, Diarrheagenic. In: Chapter 4—2020 Yellow Book | Travelers' Health | CDC. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/escherichia-coli-diarrheagenic, 2002, Accessed: 16 August 2021].
48. Singhal, S.; Mathur, T.; Khan, S.; Upadhyay, D.J.; Chugh, S.; Gaind, R.; et al. Evaluation of methods for AmpC beta-lactamase in gram-negative clinical isolates from tertiary care hospitals. Indian J Med Microbiol 2005, 23, 120–124.
49. Conceição, T.; Brízio, A.; Duarte, A.; Barros, R. First isolation of bla (VIM-2) in Klebsiella oxytoca clinical isolates from Portugal. Antimicrob Agents Chemother 2005, 49(1), 476.
50. Ruppe, E.; Lixandru, B.; Cojocaru, R.; Buke, C.; Paramythiotou, E.; Angebault, C.; et al.; Relative Faecal Abundance of Extended-Spectrum-β-Lactamase-Producing Escherichia coli Strains and Their Occurrence in Urinary Tract Infections in Women. Antimicrobial Agents and Chemotherapy 2013, 57 (9), 4512–4517.
51. Gulumbe, B.H.; Haruna, U.A.; Almazan, J.; et al.; Combating the menace of antimicrobial resistance in Africa: a review on stewardship, surveillance and diagnostic strategies. Biol Proced Online 2022, 19, https://doi.org/10.1186/s12575-022-00182-y.
52. Johnson, J.R.; Menard, M.E.; Lauderdale, T.L.; et al.; Global distribution and epidemiology associations of Escherichia coli clonal group A, 1998 – 2007. Emerg Infect Dis 2011, 17, 2001–2009.
53. Nicolle, L.E. Antimicrobial resistance in community-acquired Escherichia coli isolated from urinary infection: Good news or bad? Can J Infect Dis Med Microbiol 2013, 24(3), 123-124. doi: 10.1155/2013/182615.
54. Deng, Q.; Li, Q.; Lin, X.M.; Li, Y.M. Epidemiology and antimicrobial resistance of clinical isolates about hospital infection from patients with haematological diseases. [Article in Chinese] Zhonghua Xue Ye Xue Za Zhi2012, 33(12), 994–999.
55. Wang.; M, Wei, H.; Zhao, Y.; Shang, L.; Di, L.; Lyu, C.; Liu, J. Analysis of multidrug-resistant bacteria in 3223 patients with hospital-acquired infections (HAI) from a tertiary general hospital in China. Bosn J Basic Med Sci 2019, 12, 19(1), 86-93. doi: 10.17305/bjbms.2018.3826.

56. Pitout, J.D.; DeVinney, R. Escherichia coli ST131: a multidrug-resistant clone primed for global domination. F1000Res 2017, 28, 6. F1000 Faculty Rev-195. doi: 10.12688/f1000research.10609.1. PMID: 28344773; PMCID: PMC5333602.
57. Nicolas-Chanoine, M.H.; Bertrand, X.; Madec, J.Y. Escherichia coli ST131, an intriguing clonal group. Clin Microbiol Rev 2014, 27(3), 543-574. doi: 10.1128/CMR.00125-13. PMID: 24982321; PMCID: PMC4135899.
58. Manishimwe, R.; Moncada, P.M.; Musanayire, V.; Shyaka, A.; Scott, H.M.; Loneragan, G.H. Antibiotic-resistant Escherichia coli and Salmonella from the faeces of food animals in the east province of Rwanda. Animals 2021, 11, 1013. doi: 10.3390/ani11041013.
59. Aworh, M.K.; Kwaga, J.; Okolocha, E.; Harden, L.; Hull, D.; Hendriksen, R.S.; Thakur, S. Extended-spectrum ß-lactamase-producing Escherichia coli among humans, chickens and poultry environments in Abuja, Nigeria. One Health Outlook 2020, 2, 8 https://doi.org/10.1186/s42522-020-00014-7.
60. Salim, A.; Babu, P.; Mohan, K.; Moorthy, M.; Raj, D.; Kallampillil, T. S.; et al.; Draft genome sequence of an Escherichia coli sequence type 155 strain isolated from sewage in Kerala, India. Microbiol Resour Announc 2019, 8, 1707–1718. https://doi.org/10.1128/ MRA.01707-18.
61. Gomi, R.; Matsuda, T.; Matsumura, Y.; et al.; Whole-genome analysis of antimicrobial-resistant and Extraintestinal pathogenic Escherichia coli in river water. Appl Environ Microbiol 2017, 83(5), 2703–2716. https://doi.org/10.1128/AEM.02703-16.
62. Van Hamelsveld, S.; Adewale, M.E.; Kurenbach, B.; Godsoe, W.; Harding, J.S.; Remus-Emsermann, M.N.P.; Heinemann, J.A. Prevalence of antibiotic-resistant Escherichia coli isolated from urban and agricultural streams in Canterbury, New Zealand. FEMS Microbiol. Lett 2019, 366, fnz104.
63. Olorunshola, I. D.; Smith, S. I.; Coker, A. O. Prevalence of EHEC O157:H7 in patients with diarrhoea in Lagos, Nigeria. APMIS: acta pathologica, microbiologica, et immunologica Scandinavica 2000, 108(11), 761–763. https://doi.org/10.1034/j.1600-0463.2000.d01-26.x
64. Ige, O.K.; Adesanmi, A.A. Asuzu, M.C. Hospital-acquired infections in a Nigerian tertiary health facility: An audit of surveillance reports. Niger Med J 2011, 52(4), 239-243. doi: 10.4103/0300-1652.93796.
65. Iregbu, K.C.; Nwajiobi-Princewill, P.I. Urinary Tract Infections in a Tertiary Hospital in Abuja, Nigeria. African Journal of Clinical And Experimental Microbiology 2013, 14(3), 169-173. http://dx.doi.org/10.4314/ajcem.v14i3.9
66. Oladeinde, B.H.; Omoregie, R.; Olley, M.; Anunibe, J.A. Urinary tract infection in a rural community of Nigeria. N Am J Med Sci 2011, 3(2), 75-77. doi: 10.4297/najms.2011.375. PMID: 22540069; PMCID: PMC3336890.
67. Okafor, J.; Nweze, E. I. Antibiotic susceptibility of Escherichia coli isolated in cases of urinary tract infection in Nsukka, Nigeria. J Pre Clin Clin Res 2020, 14(1), 1-7. https://doi.org/10.26444/jpccr/118949.
68. Mofolorunsho, K.C.; Ocheni, H.O.; Aminu, R.F.; Omatola, C.A.; Olowonibi, O.O. Prevalence and antimicrobial susceptibility of extended-spectrum beta lactamases-producing Escherichia coli and Klebsiella pneumoniae isolated in selected hospitals of Anyigba, Nigeria. *Afr Health Sci* 2021, 21(2), 505-512. doi: 10.4314/ahs.v21i2.4. PMID: 34795702; PMCID: PMC8568240.
69. [1]. Muhammed, M.S.; Bello, H.Y.; Shehu, A.; Pal, S.K. Incidence and Antibiotic Susceptibility Pattern of Urinary Tract Infection in Aminu Kano Teaching Hospital (AKTH) Kano, Nigeria. Biosc. Biotech.Res. Comm 2022, 15(2).
70. [1]. Ohieku, J.D.; Magaji, R.A. Urinary Tract Infections Associated with Escherichia Coli: A 2005 to 2009 Clinical Assessment of Trends in Fluoroquinolones Activities in Maiduguri-City, Nigeria. J App Pharm Sci 2013, 3 (08), 084-091.
71. Ojezele, M.O. Urinary tract infection: prevalence, isolated organisms and antimicrobial susceptibility pattern, South-south Nigeria. Central African Journal of Medicine 2020, 65, 7-12.
72. Adesiji, Y.O.; Alli, O.T.; Adekanle, M.A.; Jolayemi, J.B. Prevalence of Arcobacter, Escherichia coli, Staphylococcus aureus and Salmonella species in Retail Raw Chicken, Pork, Beef and Goat meat in Osogbo, Nigeria. Sierra Leone Journal of Biomedical Research 2011, 3(1), 8-12.
73. Anueyiagu, K.N.; Ayanbimpe, G.; Ikeh, E. Bovine mastitis due to coliform bacteria and susceptibility to antibiotics, Nigeria. International Journal of Veterinary and Animal Husbandry 2020, 6(1), 054-061.
74. Anueyiagu K.N.; Audu, S.K.; Joshua, B.D.; Pelumi, O.E.; Haji, S.A. Prevalence and antibiogram of coliform bacteria, occurrence of fungi in subclinical mastitis in small ruminants in Plateau State, Nigeria. Journal of Animal Science and Veterinary Medicine 2020, 5(3), 83-91. https://doi.org/10.31248/JASVM2020.206
75. Anueyiagu, K. N.; Agusi, E. R.; Audu, B. J.; Achi, L. Ch.; Ayanbimpe, G. M.; Ikeh, E. I.; Kamani, J. Prevalence and Phylodiversity of ESBL-producing coliforms Isolated from ruminant mastitis. Folia Veterinaria 2022, 66, 1, 1-14.
76. Maikai, B.V.; Akubo, D.O. Coliform Count and Isolation of Escherichia coli in Fresh Fruits and Vegetables sold at Retail Outlets in Samaru, Kaduna State, Nigeria. Nig. Vet. J. 2018, 39 (4), 327 -337.
77. Reuben, C.R.; Makut, M.D. Occurrence of Escherichia coli O157:H7 in vegetables grown and sold in Lafia metropolis, Nigeria. World Journal of Microbiology 2014, 1(3), 17-21.

78. Edward, K.C.; Ibekwe, V.I.; Amadi, E.S.; Umeh, S.I. Prevalence and antibiotic susceptibility pattern of Escherichia coli isolated from abattoir wastewaters in Abia State, Nigeria. International Research Journal of Public and Environmental Health 2020, 7 (5), 140-148.
79. Garba, I.; Tijjani, M.B.; Aliyu M.S.; Yakubu, S.E.; Wada-Kura, A.; Olonitola, O.S. Prevalence of Escherichia coli in some public water sources in Gusau Municipal, North -Western Nigeria. Bayero Journal of Pure and Applied Sciences 2009, 2(2), 134 – 137.
80. Ijabani, E.; Salihu, A.; Pola, B.J. Antibiotic Resistance Pattern and Plasmid Curing of Escherichia coli Isolated from Soil Samples in Girei, Nigeria. Asian Soil Research Journal 2022, 6(2), 1-8.
81. Dahiru, M.; Uraih, N.; Enabulele, S. A.; Shamsudeen, U. Prevalence of Escherichia coli O157:H7 in fresh and roasted beef in Kano City Nigeria. Bayero Journal of Pure and Applied Sciences 2008, 1(1), 39-42.
82. Oludairo, O.O.; Kwaga, J.K.P.; Dzikwi, A.A.; Kabir, J. Isolation and Prevalence of Escherichia coli In wild animals at the National Zoological Garden Jos, Nigeria. Bangl. J. Vet. Med. 2016, 14 (2), 233-236.
83. Valilis, E.; Ramsey, A.; Sidiq, S.; DuPont, H. L. Non-O157 Shiga toxin-producing Escherichia coli—A poorly appreciated enteric pathogen: Systematic review. Int. J. Infect. Dis. 2018, 76, 82–87. https://doi.org/10.1016/j.ijid.2018.09.00
84. Stephan, R.; Hoelzle, L. E. Characterization of Shiga toxin type 2 variant B-subunit in Escherichia coli strains from asymptomatic human carriers by PCR-RFLP. Lett. Appl. Microbiol 2000, 31, 139–142. doi: 10.1046/j.1365-2672.2000.00778.
85. Friedrich, A. W.; Bielaszewska, M.; Zhang, W. L.; Pulz, M.; Kuczius, T.; Ammon, A.; et al. Escherichia coli harbouring Shiga toxin 2 gene variants: frequency and association with clinical symptoms. J. Infect. Dis 2002, 185, 74–84. doi: 10.1086/33811.
86. Fuller, C. A.; Pellino, C. A.; Flagler, M. J.; Strasser, J. E.; Weiss, A. A. Shiga toxin subtypes display dramatic differences in potency. Infect. Immun 2011, 79, 1329–1337. doi: 10.1128/IAI.01182-1.
87. Babolhavaeji, K.; Shokoohizadeh, L.; Yavari, M.; Moradi, A.; Alikhani, M. Y. Prevalence of Shiga Toxin-Producing Escherichia coli O157 and Non-O157 Serogroups Isolated from Fresh Raw Beef Meat Samples in an Industrial Slaughterhouse. International journal of microbiology 2021, 1978952. https://doi.org/10.1155/2021/1978952.
88. Makhado, U.G.; Foka, F.E.T; Tchatchouang, C.K.; Ateba, C.N.; Manganyi, M.C. Detection of virulence gene of Shiga toxin-producing Escherichia coli (STEC) strains from animals with diarrhoea and water samples in the North-West Province, South Africa. Gene Reports 2022, 27, 101617, ISSN 2452-0144, https://doi.org/10.1016/j.genrep.2022.101617. https://www.sciencedirect.com/science/article/pii/S245201442200125X
89. Carattol, A.; Zankari, E.; García-Fernández, A.; et al. In silico detection and typing of plasmids using 92 Plasmid Finder and plasmid multilocus sequence typing. Antimicrob Agents Chemother 2014, 58(3), 895–903.
90. Beyi, A.F.; Fite, A.T.; Tora, E.; et al. Prevalence, and antimicrobial susceptibility of Escherichia coli O157 in beef at butcher shops and restaurants in central Ethiopia. BMC Microbiol. 2017, 17(49), 1–6. doi:10.1186/s12866-017-0964-z123.
91. Havelaar, A.H.; Kirk, M.D.; Torgerson, P.R.; Gibb, H.J.; Hald, T.; Lake, R.J. World Health Organization Global Estimates and regional comparisons of the burden of foodborne disease in 2010. PLoS Med 2010, 12(12), e1001923.124.
92. Fayemi, O.E.; Akanni, G.B.; Elegbeleye, J.A.; Aboaba, O.O.; Njage, P.M. Prevalence, characterization and antibiotic resistance of Shiga toxigenic Escherichia coli serogroups isolated from fresh beef and locally processed ready-to-eat meat products in Lagos, Nigeria. Int J Food Microbiol. 2021, 2, 347: 109191. doi: 10.1016/j.ijfoodmicro.2021.109191. Epub 2021 Mar 31. PMID: 33838477.
93. Ojo, O.E.; Ajuwape, A.T.; Otesile, E.B.; Owoade, A.A.; Oyekunle, M.A.; Adetosoye, A.I. Potentially zoonotic Shiga toxin-producing Escherichia coli serogroups in the faeces and meat of food-producing animals in Ibadan, Nigeria. Int J Food Microbiol. 2010, 15, 142(1-2), 214-221. doi: 10.1016/j.ijfoodmicro.2010.06.030.
94. Ayoade, F.; Oguzie, J.; Eromon, P.; et al. Molecular surveillance of shiga toxigenic Escherichia coli in selected beef abattoirs in Osun State Nigeria. Sci Rep 11, 13966 (2021). https://doi.org/10.1038/s41598-021-93347.
95. Olowe, O.A.; Choudhary, S.; Schierack, P.; Wieler, L.H.; Makanjuola, O.B.; Olayemi, A.B.; Anjum, M. Pathotyping bla CTX-M Escherichia coli from Nigeria. Eur J Microbiol Immunol (Bp) 2013, 3(2),120-125. doi: 10.1556/EuJMI.3.2013.2.5.
96. Ming, P.X.; Ti, Y.L.X.; Bulmer, G.S. Outbreak of Trichophyton verrucosum in China transmitted from cows to humans. Mycopathologia 2006, 161 (4), 225–228. doi:10.1007/s11046-005-0223-y137.
97. Wang, L.; Qu, K.; Li, X.; Cao, Z.; Wang, X.; et al. Use of bacteriophages to control Escherichia coli O157:H7 in domestic ruminants, meat products, and fruits and vegetables. Foodborne Pathog Dis 2017, 14, 483–493. doi: 10.1089/fpd.2016.2266.
98. Amézquita-López, B.A.; Quiñones, B.; Soto-Beltrán, M.; et al. Antimicrobial resistance profiles of Shiga toxin-producing Escherichia coli O157 and non-O157 recovered from domestic farm animals in rural

 doi:10.20944/preprints202408.1429.v1

communities in Northwestern Mexico. Antimicrob Resist Infect Control 2016, 5(1), 1. doi:10.1186/s13756-015-0100-5139.

99. Iseghohi, F.; Igwe, J. C.; Galadima, M.; Kuta, A.F.; Abdullahi, A.M.; Chukwunwejim. C.R. Prevalence of Extended Spectrum Beta-Lactamases (ESBLs)-Producing Escherichia Coli Isolated from UTI Patients Attending some Selected Hospitals In Minna, Nigeria. Nigerian Journal of Biotechnology 2020, 37(2), 56-73.
100. Lavollay, M.; Mamlouk K.T. A.; Burghoffer, B.; Ben Redjeb, S.; Bercion, R.; Gautier, V.; Arlet, G. Clonal Dissemination of a CTX-M-15 β-Lactamase-Producing Escherichia coli Strain in the Paris Area, Tunis, and Bangui. Antimicrob Agents Chemother 2006, 50, https://doi.org/10.1128/aac.00150-06.