EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 12
Issue: 7
Year: 2025

PREVALENCE OF EXTENDED SPECTRUM BETA LACTAMASE PRODUCING *ESCHERICHIA COLI* ISOLATED FROM PATIENTS ATTENDING FAITH MEDIPLEX HOSPITAL, BENIN CITY, NIGERIA

[1]*Ehiaghe J.I. and [1]Bulus A.A.

[1]Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Benson Idahosa University, Benin City, Nigeria.

***Corresponding Author: Ehiaghe J.I.**
Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Benson Idahosa University, Benin City, Nigeria. **Email id:**

Article Received on 09/05/2025 **Article Revised on 29/05/2025** **Article Published on 19/06/2025**

ABSTRACT
Extended-spectrum beta-lactamases (ESBLs) poses a significant threat to healthcare due to their ability to confer resistance to multiple classes of antibiotics, limiting treatment options for infections caused by Gram-negative bacteria. This aim of this study was to determine the prevalence of extended spectrum beta lactamase producing *Escherichia coli* isolated from patients attending Faith Mediplex, Benin city, Nigeria. A total of one hundred isolates of *Escherichia coli* were confirmed using gram staining and biochemical tests from clinical samples which included urine, pus, endocervical swab and wound swab. ESBL screening was done using the double disc method while antimicrobial susceptibility test was done using the Kirby Bauer disc diffusion method according to the Clinical Laboratory Standards Institute (CLSI) guidelines. The results showed that the overall prevalence of ESBL producing *E. coli* was 24%. Females exhibited a higher prevalence (66.7%) compared to males (33.3%), though no significant age-related differences were observed. Among clinical specimens, urine samples had the highest ESBL positivity (66.7%), followed by wound and endocervical swabs (16.7%), with no positive cases in pus samples. Inpatient prevalence (54.2%) was higher than outpatient prevalence (45.8%), but this difference was not statistically significant. Antibiotic susceptibility testing revealed Imipenem as the most effective antibiotic (70.0% sensitivity), while most other antibiotics, including Augmentin and Ceftriaxone, showed high resistance (71.0% to 89.0%). In conclusion, result from this study shows the need for enhanced antibiotic stewardship and targeted infection control strategies to manage the high prevalence and significant resistance patterns of ESBL-producing *E. coli* in this Benin City.

KEYWORDS: Beta lactamases, Extended spectrum, Antibiotics, Clinical specimens, Gram negative, Susceptibility.

INTRODUCTION
Beta-lactamases are a diverse group of enzymes produced by bacteria to resist beta-lactam antibiotics. These enzymes are categorized into classes A, B, C, and D, each with unique substrate preferences and mechanisms of action, making them a significant hurdle in antibiotic treatment.[1] Class A beta-lactamases, such as penicillinases, break down narrow-spectrum penicillins and cephalosporins. In contrast, Class B metallo-beta-lactamases, commonly found in Gram-negative bacteria, need metal ions for their catalytic activity.[2] Class C enzymes, known as cephalosporinases, primarily target cephalosporins and are typically encoded on the chromosome, while Class D oxacillinases are frequently found in Acinetobacter baumannii and are more resistant to inhibition.[3]

Extended-spectrum beta-lactamases (ESBLs) are a subset of Class A beta-lactamases that can hydrolyze extended-spectrum cephalosporins like cefotaxime, ceftriaxone, and ceftazidime, as well as monobactams such as aztreonam.[4] These enzymes pose a major healthcare threat due to their ability to confer resistance to multiple antibiotic classes, thus reducing treatment options for Gram-negative bacterial infections. ESBLs are often linked to hospital-acquired infections, making patient management more challenging and increasing morbidity and mortality rates.[5] Their spread is driven by factors like the overuse of broad-spectrum antibiotics, poor infection control, and international travel.[6] Detecting ESBLs is crucial for directing antibiotic therapy, as they can render many beta-lactam antibiotics ineffective.[7] Treating infections caused by ESBL-producing bacteria typically requires alternative antibiotics, such as

carbapenems, though even these are increasingly threatened by the rise of carbapenem-resistant strains.[8] Common producers of ESBLs include bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*.[9]

Escherichia coli, a bacterium in the Enterobacteriaceae family, is typically found in the intestines of humans and animals. While many *E. coli* strains are harmless and part of the normal gut flora, some pathogenic strains can cause a variety of illnesses, from mild gastrointestinal distress to serious conditions like urinary tract infections (UTIs), bloodstream infections, and foodborne diseases.[10] *E. coli* is a major cause of diarrheal disease worldwide, particularly in developing regions with poor sanitation.[11] Certain strains produce toxins, such as Shiga toxins, which can result in severe complications like haemolytic uremic syndrome (HUS).[12] The global spread of ESBL-producing *E. coli* (ESBL-EC) is driven by highly transmissible clones like *E. coli* ST131, especially prevalent in long-term care facilities (LTCFs).[13] For instance, French LTCFs observed an increase in ESBL-EC, with an 18.1% prevalence of ST131 clones from 1996 to 2014, indicating clonal spread.[14] Similarly, in Swiss nursing homes, the proportion of ESBL-EC rose from 5% to 22% between 2007 and 2017.[15] The rise of *E. coli* ST131 in LTCFs is mainly due to the expansion of multi-resistant ESBL-EC clones[16], leading to undetected clusters among residents.[17] This clone's success is believed to stem from enhanced anaerobic metabolism and other factors that boost human colonization and virulence, helping it outcompete normal gut bacteria.[18-19]

The emergence and spread of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* pose a significant public health concern globally. These bacteria are increasingly implicated in various infections, including urinary tract infections (UTIs), bloodstream infections, and gastrointestinal illnesses. The prevalence of ESBL-producing *E. coli* strains among patients has been on the rise, leading to challenges in clinical management and treatment outcomes. This study aimed to determine the prevalence of extended spectrum beta lactamase producing *Escherichia coli* isolated from patients in Faith Mediplex, Benin City, Nigeria.

MATERIALS AND METHODS

Study Design

A cross-sectional design was used for this study.

Study Area

The study was carried out at Faith Mediplex Hospital in Benin City, Edo State, Nigeria. Edo State is located at latitude 6.6342°N and longitude 5.9304°E of the equator and prime meridian, respectively. The state covers an area of 19,794 km² and had a provisional population of 2,159,484, with Benin City estimated at 1,147,188 (National Population Census, 2006). Faith Mediplex Hospital is a private medical facility in Benin City, Edo State, Nigeria. Renowned for its commitment to quality healthcare services.

Study Population

The study was carried out on both male and female individuals who had requested a culture of a body sample and provided informed consent at Faith Mediplex Hospital in Benin City.

Sample Size

Sample size was determined using single population proportion estimate considering the level of significances at 5% and the prevalence of extended-spectrum beta-lactamase (ESBL) production in gram negative bacteria from HVS sample from a previous study conducted in Ile Ife, Nigeria which was 6%.[20]

$$Sample\ size = \frac{Z^2 P\ (1-P)}{d^2}$$

N = required sample size
Z = confidence level at 95% (standard value of 1.96)
P = prevalence of extended-spectrum beta-lactamase (ESBL) production in gram negative bacteria (6% = 0.06)
D = margin of error at 5% (standard value = 0.05)

$$N = \frac{1.96^2 \times 0.06\ (1-0.06)}{0.05^2} = 87.$$

Minimum sample size calculated is 87. In order to account for non-response, 10% of the sample size (i.e., 8.7) will be added to the calculated sample size; this gives a sample size of 95.7, which is approximated to 100 study subjects. A total number of 100 *Escherichia coli* isolates will be used for this study.

Inclusion Criteria

Escherichia coli isolates of patients attending and receiving treatment at Faith Mediplex Hospital in Benin City, Edo state, Nigeria who gave their consent for inclusion in the study.

Exclusion Criteria

Non-*Escherichia coli* isolates of patients attending and receiving treatment at Faith Mediplex Hospital in Benin City, Edo state, Nigeria who did not give their consent for inclusion in the study.

Ethical Approval

Approval for this research was sought from the research and ethics committee, Faith Mediplex Hospital, Benin City, Edo State, Nigeria. Informed consent was also sought and obtained from all participants.

Isolation and Identification of *Escherichia coli*

Isolation of *Escherichia coli* was done using standard microbiological techniques. Initially, samples were streaked onto MacConkey agar. Following incubation at appropriate temperatures, characteristic colonies showing lactose fermentation (pink to red colonies) were selected

for further analysis. Gram staining was performed on isolated colonies to confirm their Gram-negative morphology. Additionally, biochemical tests such as motility, Indole, Urea, and Citrate utilization tests were performed to validate the identity of *E. coli*. Outcomes in these tests, along with observations of colony morphology and Gram staining characteristics, collectively confirmed the presence of *Escherichia coli* in the culture.

Determination of ESBL Producing *Escherichia coli*

The presence of ESBL was detected using the double disc method test. Briefly, the test organism was emulsified in sterile water and the turbidity matched with 0.5 McFarland standard. Once matched, a sterile cotton wool swab was placed in the organism suspension and excess liquid was removed by turning the swab on the side of the test tubes. The entire surface of a Mueller Hinton agar plate was seeded by swabbing in three directions with the swab. A disc containing 30 µg of amoxicillin-clavulanate was placed at the center of the agar plate. A 30-µg ceftazidime disc was placed 25 mm from the amoxicillin-clavulanate disc and another disc containing 30 µg of cefotaxime was placed on the opposite side of the amoxicillin-clavulanate disc (25 mm apart). The plates were incubated at 37ºC overnight and ESBL production was inferred as positive if there was an expansion of the zone of inhibition between the ceftazidime and amoxicillin-clavulanate disc, cefotaxime and amoxicillin-clavulanate disc, or both.

Determination of Antimicrobial Susceptibility using Disc Diffusion Method

Prior to conducting the test, microbial strains were sub-cultured on MacConkey agar plates to obtain a pure culture. Colonies from the culture were then transferred to sterile water and adjusted to match the turbidity of a 0.5 McFarland standard, ensuring standardized inoculum density. The agar plates were evenly inoculated with the standardized microbial suspension using a sterile swab, ensuring uniform distribution across the agar surface on Mueller-Hinton agar plates. Antibiotic discs impregnated with specific concentrations of antibiotics, including augmentin, ceftriaxone, ciprofloxacin, cefepime, cefuroxime, imipenem, gentamycin, and oxacillin were placed onto the agar surface. The agar plates were allowed to stand at room temperature for a brief period to allow diffusion of the antimicrobial agents into the agar. Subsequently, the plates were incubated at 37°C for 24 hours.

Measurement of Zones of Inhibition

After incubation, the plates were examined for the presence of clear zones of inhibition around the wells, and the diameter of each zone was measured using a calibrated ruler or automated zone reader. Larger zones indicated greater susceptibility of the microorganism to the test substance. The diameter of the zones of inhibition was then compared to established interpretive criteria provided by the Clinical and Laboratory Standards Institute (CLSI), and results were reported as susceptible, intermediate, or resistant based on these criteria.

Statistical Analysis

Data obtained from this research were presented and analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Inc., USA). Results were expressed in tables and charts as appropriate. The Chi-square test was used to determine if there were significant associations between categorical variables. Differences were considered statistically significant when the p-value obtained was <0.05.

RESULTS

Sociodemographic Characteristics of Participants

Table 1 shows the sociodemographic characteristics of the participants in the study. The age distribution shows that the majority of participants were between 35-50 years old, accounting for 56.0% of the sample, followed by age 20-34 (32.0%), 51-64 (10.0%), and the smallest group was aged 65-80, representing only 2.0%. The mean age of the participants was 38.94 years with a standard deviation of 10.47 years, ranging from a minimum age of 24 years to a maximum of 74 years. Regarding sex distribution, 58.0% of the participants were female, and 42.0% were male. When considering occupation, a larger proportion of the participants were civil servants (59.0%), compared to 41.0% who were engaged in business or trading activities. In terms of religion, the majority of participants identified as Christians (73.0%), followed by Muslims (24.0%), and a small percentage (3.0%) practiced other religions. The patient type distribution indicated that 46.3% of the participants were inpatients, while 30.7% were outpatients. The percentages of patient types do not sum to 100% due to rounding or potential categorization issues in the original data collection.

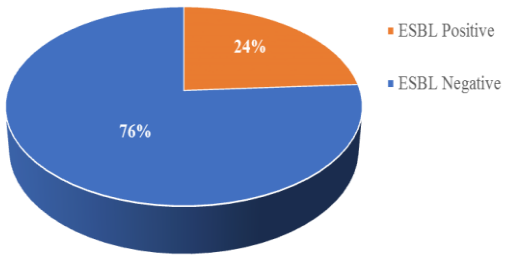

Figure 1: Prevalence of ESBL Producing *Escherichia coli* among Participants.

Prevalence of ESBL Producing *Escherichia coli*

The prevalence of Extended spectrum beta lactamase (ESBL) producing *Escherichia coli* among participants was found to be 24% (24/100) as shown in figure 1. Table 2 shows the frequency of ESBL-producing *Escherichia coli* in relation to the age and sex of

participants. Among the males, 42 were examined (42.0%) and 8 (33.3%) were ESBL positive while 58 females were examined (58.0%) and 16 (66.7%) were ESBL positive. There was no significant difference in relation to age (OR=0.618, 95% CI: 0.236-1.616, p = 0.324). In terms of age, 32 participants were in the 20-34 years age group (32.0%), with 6 (25.0%) testing positive. The 35-50 years age group had 56 participants (56.0%), with 18 (75.0%) testing positive. For ages 51-64 years, 10 participants (10.0%) were examined, with none testing positive. Similarly, in the 65-80 years age group, 2 participants (2.0%) were examined, with no positive cases. The differences in ESBL positivity among age groups were not statistically significant (p = 0.098).

Table 3 shows the frequency of ESBL-producing *Escherichia coli* in relation to clinical specimens. Out of the 68 urine samples examined (68.0%), 16 (66.7%) were ESBL positive. Among the pus samples, 6 were examined (6.0%), with none testing positive. For wound swabs, 18 samples were examined (18.0%), with 4 (16.7%) testing positive. Similarly, out of 8 endocervical swabs examined (8.0%), 4 (16.7%) were ESBL positive. The differences in ESBL positivity among the various clinical specimens were not statistically significant (p = 0.179).

Table 4 shows the frequency of ESBL-producing *Escherichia coli* in relation to patient type. Among the 39 inpatients examined (39.0%), 13 (54.2%) were ESBL positive. Out of the 61 outpatients examined (61.0%), 11 (45.8%) were ESBL positive. The differences in ESBL positivity between inpatients and outpatients were not statistically significant (OR=0.618, 95%CI=0.236-1.616, p = 0.324).

Table 5 shows the susceptibility profile of ESBL-producing *Escherichia coli* to various antibiotics. Imipenem showed the highest sensitivity, with 70 (70.0%) of the isolates being sensitive and 30 (30.0%) being resistant. Gentamycin showed moderate sensitivity with 34 (34.0%) sensitive and 66 (66.0%) resistant. Most of the antibiotics, including Augmentin, Ceftriaxone, Ciprofloxacin, Cefepime, Cefuroxime, and Oxacillin, had low sensitivity, ranging from 11.0% to 29.0%, and high resistance, ranging from 71.0% to 89.0%.

Table 1: Sociodemographic Characteristics of Participants.

Variable	Number (n=100)	Percentage (%)
Age		
20-34	32	32.0
35-50	56	56.0
51-64	10	10.0
65-80	2	2.0
Sex		
Male	42	42.0
Female	58	58.0
Occupation		
Business/Trading	41	41.0
Civil Servant	59	59.0
Religion		
Christianity	73	73.0
Islam	24	24.0
Others	3	3.0
Patient Type		
Inpatients	185	46.3
Outpatients	123	30.7

Mean age=38.94±10.47 years, Minimum age = 24 years, Maximum age = 74 years.

Table 2: Frequency of ESBL Producing *Escherichia coli* in Relation to Age and Sex of Participants.

Variable	No. Examined (%)	ESBL Positive (%)	OR	95%CI	p value
Sex					
Male	42 (42.0)	8 (33.3)	0.618	0.236-1.616	0.324
Female	58 (58.0)	16 (66.7)			
Age (years)					
20-34	32 (32.0)	6 (25.0)			0.098
35-50	56 (56.0)	18 (75.0)			
51-64	10 (10.0)	0 (0.0)			
65-80	2 (2.0)	0 (0.0)			

ESBL=Extended spectrum beta lactamase, OR=odds ratio, CI=Confidence Interval, p<0.05 is considered significant

Table 3: Frequency of ESBL Producing *Escherichia coli* in Relation to Clinical Specimen.

Clinical Specimens	No. Examined (%)	ESBL Positive (%)	p value
Urine	68 (68.0)	16 (66.7)	0.179
Pus	6 (6.0)	0 (0.0)	
Wound Swab	18 (18.0)	4 (16.7)	
Endocervical Swab	8 (8.0)	4 16.7)	

ESBL=Extended spectrum beta lactamase, p<0.05 is considered significant

Table 4: Frequency of ESBL Producing *Escherichia coli* in Relation to Patient Type.

Patient Type	No. Examined (%)	ESBL Positive (%)	OR	95%CI	p value
Inpatients	39 (39.0)	13 (54.2)	0.618	0.236-1.616	0.324
Outpatients	61 (61.0)	11 (45.8)			

ESBL=Extended spectrum beta lactamase, OR=odds ratio, CI=Confidence Interval, p<0.05 is considered significant

Table 5: Susceptibility Profile of ESBL Producing *Escherichia coli.*

Antibiotics	Sensitive (%)	Resistant (%)
Augmentin	25 (25.0)	75 (75.0)
Ceftriaxone	11 (11.0)	89 (89.0)
Ciprofloxacin	20 (20.0)	80 (80.0)
Cefepime	14 (14.0)	86 (86.0)
Cefuroxime	25 (25.0)	75 (75.0)
Imipenem	70 (70.0)	30 (30.0)
Gentamycin	34 (34.0)	66 (66.0)
Oxacillin	29 (29.0)	71 (71.0)

DISCUSSION

The prevalence of extended spectrum beta lactamase (ESBL) among participants in this study was 24%. This prevalence is low when compared to that of a study by Hertz *et al*. carried out in northeastern part of Nigeria which was 53%.[21] Another study carried out by Igbinosa *et al*. in Edo state also reported a high prevalence of ESBL producing *E coli* (68%)[22] while Mofolorunsho *et al*. reported a prevalence of 69% in Anyigba, Nigeria.[23] However, in contrast to these findings, other studies have reported similar and even lower prevalence of ESBL producing *Escherichia coli*. Ajuga *et al*. in their study in Aba reported the prevalence of ESBL producing *E coli* to be 1.2%.[24] Iseghohi *et al*. reported a prevalence of 25% which was similar to that observed in this present study.[25] These disparities in the prevalence of Extended-Spectrum Beta-Lactamase (ESBL) producing *E. coli* across different regions can be attributed to a variety of factors. These include differences in antibiotic usage practices, with some regions experiencing higher rates of antibiotic consumption, which can drive the selection of resistant strains.[26] Variations in healthcare infrastructure and infection control measures can also play a significant role; regions with inadequate sanitation, limited access to healthcare, and poor infection control protocols may see higher prevalence rates. Additionally, differences in agricultural practices, such as the use of antibiotics in livestock, can contribute to regional variations. Socioeconomic factors, including population density, education levels, and healthcare accessibility, further influence these disparities.[27]

This study showed that females exhibited a higher prevalence of ESBL-producing *E. coli* compared to males, which could be attributed to several factors. Anatomically, females are more susceptible to urinary tract infections (UTIs) due to a shorter urethra, facilitating easier bacterial ascension. Hormonal fluctuations might also play a role in altering the vaginal microbiota, predisposing women to colonization by resistant strains.[28] Additionally, females often have more frequent interactions with healthcare services, including for reproductive health, increasing their exposure to antibiotics and the risk of acquiring resistant bacteria.[29] The study also showed that the prevalence of ESBL-producing *E. coli* was not significantly associated with age. Typically, older age groups exhibit higher rates of ESBL colonization due to factors such as more frequent hospitalizations, increased use of invasive devices, and prolonged antibiotic treatments, which are less common in younger populations.[30] The absence of ESBL-positive cases in the older age groups within this study might be explained by the relatively small sample size, particularly in the 51-64 and 65-80 age brackets, limiting the statistical power to detect differences. In contrast to findings from this study, sex and age has been cited as factors associated with prevalence of ESBL in previous studies.[31-32]

In this study, the highest clinical specimen with ESBL producing *E. coli* was using urine samples. This aligns with the study of Singh *et al*. the highest prevalence of ESBL *E. coli* in urine samples.[33] The high prevalence of ESBL-positive *E. coli* in urine samples can be attributed to the urinary tract being a common site for *E. coli* infections, often leading to recurrent and prolonged antibiotic use, which causes resistance.[34] The absence of ESBL-positive results in pus samples could be due to the lower overall number of samples tested, or possibly different bacterial pathogens predominating in such infections. The moderate prevalence in wound and endocervical swabs suggests that these sites, while not as commonly associated with *E. coli* infections as the urinary tract, still harbor resistant strains, likely due to similar pressures from antibiotic use in treating skin and soft tissue infections as well as gynecological conditions. Comparing these results with other studies, it is often found that urinary specimens tend to show the highest rates of ESBL-producing *E. coli* due to the reasons

mentioned above. For example, studies in other regions also report high ESBL rates in urinary samples[25,33,35], reinforcing the need for stringent antibiotic stewardship in managing urinary tract infections.

This study revealed a higher prevalence of ESBL-producing *Escherichia coli* among inpatients compared to outpatients, although the difference is not statistically significant. Several factors could contribute to this observation. Inpatients are typically more exposed to hospital environments, where the use of broad-spectrum antibiotics is more common, potentially promoting the selection of resistant strains.[36] Additionally, inpatients often have more severe or chronic conditions, necessitating longer hospital stays and increased interactions with healthcare workers and medical devices, further increasing the risk of acquiring resistant infections. In comparison, outpatients, who generally have milder conditions and shorter durations of antibiotic exposure, are less likely to encounter resistant strains.[37] Comparing these results with other studies, similar trends are often reported. For instance, research has consistently shown higher rates of ESBL-producing bacteria in hospital settings due to the intensive antibiotic pressure and the concentration of vulnerable patients.[27,38-39]

The susceptibility profile of ESBL-producing *Escherichia coli* to various antibiotics, as shown in this study shows the critical challenge of antibiotic resistance. Imipenem's high sensitivity rate suggests that carbapenems remain a robust treatment option for infections caused by ESBL-producing strains, likely due to their broad spectrum and stability against beta-lactamase enzymes.[40] The moderate sensitivity to Gentamycin could be attributed to its aminoglycoside class mechanism, which remains effective against some resistant strains but is still susceptible to resistance mechanisms like enzymatic inactivation.[41] The low sensitivity rates observed for antibiotics such as Augmentin, Ceftriaxone, and Ciprofloxacin highlight the widespread resistance, possibly due to the extensive and often inappropriate use of these antibiotics in clinical settings, leading to selective pressure favoring resistant strains.[42] This finding is also consistent with that of Singh *et al.* who reported a high resistance of ESBL producing *E. coli* to cefuroxime, cefotaxime, ciprofloxacin, cefixime and ceftriaxone.[33] Other studies globally report similar trends similar to that of this study, with carbapenems generally maintaining higher efficacy against ESBL-producing *E. coli*.[43-44]

CONCLUSION

The study revealed a 24% prevalence of ESBL-producing *Escherichia coli* among participants. Females exhibited a higher prevalence compared to males, though age did not significantly affect ESBL positivity. The highest prevalence was in the 35-50 years age group, with no cases found in participants over 50 years old. Among clinical specimens, urine samples had the highest positivity rate, while pus samples showed no ESBL presence. The prevalence between inpatients and outpatients was not significantly different. Antibiotic susceptibility testing highlighted Imipenem as the most effective, while most other antibiotics, including commonly used ones like Augmentin and Ceftriaxone, exhibited low sensitivity and high resistance.

REFERENCES

1. Nagshetty K, Shilpa BM, Patil SA, Shivannavar CT, Manjula NG. An overview of extended spectrum beta lactamases and metallo beta lactamases. *Advances in Microbiology*, 2021; 11(01): 37.
2. Cantón R. Epidemiology and Evolution of Beta-Lactamases. *Evolutionary Biology of Bacterial and Fungal Pathogens*, 2007; 2(1): 249-270.
3. Bush K. Past and present perspectives on β-lactamases. *Antimicrobial Agents and Chemotherapy*, 2018; 62(10): 10-1128.
4. Ali T, Ali I, Khan NA, Han B, Gao J. The growing genetic and functional diversity of extended spectrum beta-lactamases. *BioMed Research International*, 2018; 2(1): 1-4.
5. Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MA. Antibiotic resistance and extended spectrum beta-lactamases: Types, epidemiology and treatment. *Saudi Journal of Biological Sciences*, 2015; 22(1): 90-101.
6. Aldrazi FA, Rabaan AA, Alsuliman SA, Aldrazi HA, Alabdalslam MJ, Alsadiq SA, Bueid AS. ESBL expression and antibiotic resistance patterns in a hospital in Saudi Arabia: do healthcare staff have the whole picture? *Journal of Infection and Public Health*, 2020; 13(5): 759-766.
7. Silago V. Beta-lactam antibiotics and extended spectrum beta-lactamases. *GSC Advanced Research and Reviews*, 2021; 9(2): 015-024.
8. Peri AM, Doi Y, Potoski BA, Harris PN, Paterson DL, Righi E. Antimicrobial treatment challenges in the era of carbapenem resistance. *Diagnostic Microbiology and Infectious Disease*, 2019; 94(4): 413-425.
9. Chong Y, Shimoda S, Yakushiji H, Ito Y, Miyamoto T, Kamimura T, Akashi K. Community spread of extended-spectrum β-lactamase-producing *Escherichia coli, Klebsiella pneumoniae* and *Proteus mirabilis*: a long-term study in Japan. *Journal of Medical Microbiology*, 2013; 62(7): 1038-1043.
10. Galindo-Méndez M. Antimicrobial resistance in *Escherichia coli*. *E. Coli Infections-Importance of Early Diagnosis and Efficient Treatment*, 2020; 2(1): 1-20.
11. Qadri F, Svennerholm AM, Faruque ASG, Sack RB. Enterotoxigenic *Escherichia coli* in developing countries: epidemiology, microbiology, clinical features, treatment, and prevention. *Clinical Microbiology Reviews*, 2005; 18(3): 465-483.

12. Tarr PI, Gordon CA, Chandler WL. Shiga-toxin-producing *Escherichia coli* and haemolytic uraemic syndrome. *The Lancet*, 2005; 365(9464): 1073-1086.
13. Brodrick HJ, Raven KE, Kallonen T, Jamrozy D, Blane B, Brown NM, Peacock SJ. Longitudinal genomic surveillance of multidrug-resistant *Escherichia coli* carriage in a long-term care facility in the United Kingdom. *Genome Medicine*, 2017; 9(1): 1-11.
14. Sauget M, Cholley P, Vannier A, Thouverez M, Nicolas-Chanoine MH, Hocquet D, Bertrand X. Trends of extended-spectrum β-lactamase-producing *Escherichia coli* sequence type 131 and its H30 subclone in a French hospital over a 15-year period. *International Journal of Antimicrobial Agents*, 2016; 48(6): 744-747.
15. Kohler P, Fulchini R, Albrich WC, Egli A, Balmelli C, Harbarth S, Kronenberg A. Antibiotic resistance in Swiss nursing homes: analysis of National Surveillance Data over an 11-year period between 2007 and 2017. *Antimicrobial Resistance and Infection Control*, 2018; 7(1): 1-9.
16. Ludden C, Decano AG, Jamrozy D, Pickard D, Morris D, Parkhill J, Downing T. Genomic surveillance of *Escherichia coli* ST131 identifies local expansion and serial replacement of subclones. *Microbial Genomics*, 2020; 6(4): e000352.
17. Willemsen I, Nelson J, Hendriks Y, Mulders A, Verhoeff S, Mulder P, Kluytmans J. Extensive dissemination of extended spectrum β-lactamase–producing Enterobacteriaceae in a Dutch nursing home. *Infection Control and Hospital Epidemiology*, 2015; 36(4): 394-400.
18. McNally A, Kallonen T, Connor C, Abudahab K, Aanensen DM, Horner C, Corander J. Diversification of colonization factors in a multidrug-resistant *Escherichia coli* lineage evolving under negative frequency-dependent selection. *Microbiology*, 2019; 10(2): 10-1128.
19. Kallonen T, Brodrick HJ, Harris SR, Corander J, Brown NM, Martin V, Parkhill J. Systematic longitudinal survey of invasive *Escherichia coli* in England demonstrates a stable population structure only transiently disturbed by the emergence of ST131. *Genome Research*, 2017; 27(8): 1437-1449.
20. Daniel W. Biostatistics: A Foundation for Analysis in the Health Sciences, 7th Edition. Wiley. New York, 1999; 141(2).
21. Hertz FB, Jansåker F, Okon KO, Abdulmumin IS, Onah JO, Ladan J, Knudsen JD. ESBL-production in *Escherichia coli* and *Klebsiella pneumoniae* isolates from Nigeria. *Microbiology Open*, 2019; 8(9): e00816.
22. Igbinosa EO, Beshiru A, Igbinosa IH, Cho GS, Franz CM. Multidrug-resistant extended spectrum β-lactamase (ESBL)-producing *Escherichia coli* from farm produce and agricultural environments in Edo State, Nigeria. *PloS One*, 2023; 18(3): e0282835.
23. Mofolorunsho KC, Ocheni HO, Aminu RF, Omatola CA, Olowonibi OO. Prevalence and antimicrobial susceptibility of extended-spectrum beta lactamases-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated in selected hospitals of Anyigba, Nigeria. *African Health Sciences*, 2021; 21(2): 505-512.
24. Ajuga MU, Otokunefor K, Agbagwa OE. Antibiotic resistance and ESBL production in *Escherichia coli* from various sources in Aba metropolis, Nigeria. *Bulletin of the National Research Centre*, 2021; 45(1): 1-9.
25. Iseghohi F, Igwe JC, Galadima M, Kuta AF, Abdullahi AM, Chukwunwejim CR. 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.
26. Schmiege D, Zacharias N, Sib E, Falkenberg T, Moebus S, Evers M, Kistemann T. Prevalence of multidrug-resistant and extended-spectrum beta-lactamase-producing *Escherichia coli* in urban community wastewater. *Science of The Total Environment*, 2021; 785(1): 147-149.
27. Onduru OG, Mkakosya RS, Aboud S, Rumisha SF. Genetic determinants of resistance among ESBL-producing enterobacteriaceae in community and hospital settings in east, central, and Southern Africa: A systematic review and meta-analysis of prevalence. *Canadian Journal of Infectious Diseases and Medical Microbiology*, 2021; 2(1): 515-518.
28. Hickling DR, Sun TT, Wu XR. Anatomy and physiology of the urinary tract: relation to host defense and microbial infection. *Urinary tract infections: Molecular Pathogenesis and Clinical Management*, 2017; 2(1): 1-25.
29. Jones N, Mitchell J, Cooke P, Baral S, Arjyal A, Shrestha A, King R. Gender and antimicrobial resistance: what can we learn from applying a gendered lens to data analysis using a participatory arts case study? *Frontiers in Global Women's Health*, 2022; 3(1): 745862.
30. Zaha DC, Bungau S, Aleya S, Tit DM, Vesa CM, Popa AR, Aleya L. What antibiotics for what pathogens? The sensitivity spectrum of isolated strains in an intensive care unit. *Science of the Total Environment*, 2019; 687(1): 118-127.
31. Flammang A, Morello R, Vergnaud M, Brouard J, Eckart P. Study of bacterial resistance profiles in pediatric pyelonephritis in 2014. *Archives of Pediatrics*, 2017; 24(3): 215-224.
32. Ahmed I, Sajed M, Sultan A, Murtaza I, Yousaf S, Maqsood B, Anees M. The erratic antibiotic susceptibility patterns of bacterial pathogens causing urinary tract infections. *EXCLI Journal*, 2015; 14(1): 916-917.
33. Singh N, Pattnaik D, Neogi DK, Jena J, Mallick B. Prevalence of ESBL in *Escherichia coli* isolates among ICU patients in a tertiary care

hospital. *Journal of Clinical and Diagnostic Research: JCDR*, 2016; 10(9): 19-23.
34. Nicolle LE. Urinary tract infection. *Critical Care Clinics*, 2013; 29(3): 699-715.
35. Hassan SA, Jamal SA, Kamal M. Occurrence of multidrug resistant and ESBL producing E. coli causing urinary tract infections. *Journal of Basic and Applied Sciences*, 2011; 7(1): 1-5.
36. Zaha DC, Kiss R, Hegedűs C, Gesztelyi R, Bombicz M, Muresan M, Micle O. Recent Advances in Investigation, Prevention, and Management of Healthcare-Associated Infections (HAIs): Resistant Multidrug Strain Colonization and Its Risk Factors in an Intensive Care Unit of a University Hospital. *BioMed Research International*, 2019; 2(1): 2510875.
37. Bodenheimer T, Berry-Millett R. Care management of patients with complex health care needs. *Policy*, 2009; 1(6): 1-16.
38. Bezabih YM, Bezabih A, Dion M, Batard E, Teka S, Obole A, Bezabhe WM. Comparison of the global prevalence and trend of human intestinal carriage of ESBL-producing *Escherichia coli* between healthcare and community settings: a systematic review and meta-analysis. *JAC-Antimicrobial Resistance*, 2022; 4(3): 48-51.
39. Vink J, Edgeworth J, Bailey SL. Acquisition of MDR-GNB in hospital settings: a systematic review and meta-analysis focusing on ESBL-E. *Journal of Hospital Infection*, 2020; 106(3): 419-428.
40. Karaiskos I, Giamarellou H. Carbapenem-sparing strategies for ESBL producers: when and how. *Antibiotics*, 2020; 9(2): 61-63.
41. Jana S, Deb JK. Molecular understanding of aminoglycoside action and resistance. *Applied Microbiology and Biotechnology*, 2006; 70(2): 140-150.
42. Ballal M. Trends in antimicrobial resistance among enteric pathogens: a global concern. *Antibiotic Resistance*, 2016; 63: 1-5.
43. Kumar D, Singh AK, Ali MR, Chander Y. Antimicrobial susceptibility profile of extended spectrum β-lactamase (ESBL) producing *Escherichia coli* from various clinical samples. *Infectious Diseases: Research and Treatment*, 2014; 7(1): 2-7.
44. Al-Attar ZI. The prevalence and antimicrobial sensitivity of ESBL *Escherichia coli*. in clinical isolates. *Al-Kindy College Medical Journal*, 2014; 10(2): 96-99.