Section: Microbiology

Original Research Article

PREVALENCE OF ESBL AND AMPC PRODUCING ECOLI AND KLEBSIELLA ISOLATES IN A TERTIARY CARE TEACHING HOSPITAL, NORTH KARNATAKA, INDIA.

Rangappa Metri[1], Sumathi. S[2], Preeti. B. Mindolli[3], Manjunath P. Salmani[4]

[1]*Assistant Professor, Department of Microbiology, Koppal Institute of Medical Sciences, Koppal, Karnataka, India.*
[2]*Associate Professor, Department of Microbiology, Koppal Institute of Medical Sciences, Koppal, Karnataka, India.*
[3]*Assistant Professor, Department of Microbiology, Koppal Institute of Medical Sciences, Koppal, Karnataka, India.*
[4]*Professor and Head, Department of Microbiology, Koppal Institute of Medical Sciences, Koppal, Karnataka, India*.

Received *: 17/02/2024*
Received in revised form *: 08/05/2024*
Accepted *: 25/05/2024*

Corresponding Author:
Dr. Sumathi S
Associate Professor, Department of Microbiology, Koppal Institute of Medical Sciences, Koppal, Karnataka, India.
Email: drsumathis@yahoo.co.in

DOI: 10.5530/ijmedph.2024.2.85

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (2); 436-441

ABSTRACT

Background: The emergence of multidrug-resistant (MDR) organisms, particularly those producing Extended Spectrum Beta-Lactamases (ESBL) and AmpC beta-lactamases, is a global threat, often leading to the failure of beta-lactam therapy. This study aimed to establish the prevalence and co-production of ESBL and AmpC among Escherichia coli and Klebsiella spp. isolates in a tertiary care hospital in North Karnataka.

Materials & Methods: A hospital-based cross-sectional study was conducted at KIMS Koppal from July 2021 to December 2021. A total of 100 non-repetitive E. coli and Klebsiella spp. isolates resistant to third-generation cephalosporins or MDR were collected from various clinical samples. ESBL production was confirmed using ceftazidime/clavulanic acid and cefotaxime/clavulanic acid discs, while AmpC production was suggested by resistance to cefoxitin and susceptibility to cefepime.

Results: Of the 100 isolates of E.coli 38 were ESBL producers , 13 were AmpC producers, 9 were detected as co-producers of ESBL and AmpC and from 100 isolates of Klebsiella spp 24 were ESBL producers (ESBL Producers- 38% E. coli and 24% Klebsiella spp.), and 8 were AmpC producers, 6 were co-producers of ESBL and AmpC (Amp C producers 13% E. coli and 8% Klebsiella spp.). Co-production of ESBL and AmpC was observed in 9% E. coli and 6% Klebsiella spp. High-risk groups included patients with prolonged hospital stays, prior antibiotic use, and underlying chronic conditions such as diabetes and immunosuppression. The study highlighted the need for routine screening and cautious use of carbapenems.

Conclusion: The prevalence of ESBL and AmpC producers in North Karnataka underscores the importance of targeted infection control measures and appropriate antibiotic stewardship to mitigate the spread of MDR organisms.

Keywords: ESBL, AmpC, E. coli, Klebsiella spp., multidrug resistance, North Karnataka, tertiary care hospital, antibiotic stewardship.

INTRODUCTION

The emergence of multidrug-resistant (MDR) organisms is a significant global health concern, posing a severe threat to public health and clinical therapeutics.[1] Among the MDR organisms, Extended Spectrum Beta-Lactamases (ESBL) and AmpC beta-lactamases producing bacteria, particularly Escherichia coli and Klebsiella spp., are of paramount importance due to their ability to hydrolyze a wide range of beta-lactam antibiotics, leading to the failure of beta-lactam therapy.[2,3] This phenomenon complicates the treatment of infections

caused by these pathogens, necessitating the use of more potent and often more toxic antibiotics.[4]

ESBLs are enzymes that confer resistance to penicillins, cephalosporins, and aztreonam, but not to cephamycins or carbapenems. They are inhibited by beta-lactamase inhibitors such as clavulanic acid, sulbactam, and tazobactam.[5] The first ESBLs were discovered in Germany in 1983, and since then, their prevalence has increased globally, with significant clinical implications.[6] The primary reservoir of ESBLs is the family Enterobacteriaceae, with E. coli and Klebsiella pneumoniae being the most common carriers. These organisms are responsible for a wide range of infections, including urinary tract infections, bloodstream infections, and hospital-acquired pneumonia.[7]

AmpC beta-lactamases are enzymes that confer resistance to a broader spectrum of beta-lactam antibiotics, including cephamycins and oxyimino-cephalosporins, and are not inhibited by the beta-lactamase inhibitors. AmpC production is often chromosomally encoded, but plasmid-mediated AmpC beta-lactamases have emerged, further complicating the resistance scenario8. The coexistence of ESBL and AmpC enzymes in the same bacterial isolate significantly limits treatment options, as these enzymes can hydrolyze many beta-lactams, rendering them ineffective.

The tertiary care hospital setting is particularly vulnerable to the spread of ESBL and AmpC producing organisms due to the high volume of critically ill patients, extensive use of invasive devices, and frequent administration of broad-spectrum antibiotics. These factors create an environment conducive to the selection and dissemination of resistant strains. In India, the prevalence of ESBL and AmpC producing bacteria is notably high, which is attributed to the widespread and often indiscriminate use of antibiotics in both healthcare and community settings.

Given the critical implications of these resistant organisms, it is essential to understand their prevalence and distribution within specific geographic and healthcare contexts. This knowledge aids in developing targeted infection control strategies and appropriate antibiotic stewardship programs. The present study was conducted in a tertiary care teaching hospital in North Karnataka, India, with the objective of determining the prevalence of ESBL and AmpC producing E. coli and Klebsiella spp. isolates. This study is the first of its kind in the Koppal District and aims to provide a foundation for future research and policy development in the region.

The objectives of this study were twofold: firstly, to estimate the prevalence of ESBL and AmpC producing E. coli and Klebsiella spp. isolates among patients visiting the tertiary care teaching hospital, and secondly, to identify high-risk groups within the patient population. The findings of this study are expected to contribute to the broader understanding of antimicrobial resistance patterns in North Karnataka and to inform clinical practices and public health interventions aimed at mitigating the spread of these resistant organisms.

MATERIAL AND METHODS

Study Design

This study was designed as a hospital-based cross-sectional study conducted at the Tertiary Care Teaching Hospital, KIMS Koppal, North Karnataka, India. The study period extended from July 2021 to December 2021, covering six months.

Study Population

The study population included 100 consecutive, non-repetitive isolates each of Escherichia coli and Klebsiella spp. obtained from various clinical samples. These samples were collected from patients visiting KIMS Koppal during the study period. Inclusion criteria comprised isolates resistant to third-generation cephalosporins or those identified as multidrug-resistant (MDR). The clinical samples included urine, blood, pus, stool, sputum, body fluids, throat swabs, high vaginal swabs, and cerebrospinal fluid.

Sample Size

A total of 200 isolates (comprising 100 E. coli and 100 Klebsiella spp.) were included in the study. These isolates were selected consecutively to ensure a comprehensive representation of the bacterial strains present during the study period.

Data Collection

Clinical isolates were collected from the microbiology laboratory at KIMS Koppal. Relevant demographic and clinical data of the patients, including age, sex, hospital stay duration, history of antibiotic use, and underlying health conditions, were recorded.

Isolation and Identification

The clinical samples were cultured on appropriate media, and bacterial isolates were identified using standard microbiological techniques. Identification of E. coli and Klebsiella spp. were confirmed based on colony morphology, Gram staining, and biochemical tests (such as indole test, citrate utilization test, urease test, and triple sugar iron (TSI) agar test).

Antibiotic Susceptibility Testing

Antibiotic susceptibility testing was performed using the Kirby-Bauer disc diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines. Initial screening for ESBL and AmpC production was based on resistance to third-generation cephalosporins (ceftazidime, cefotaxime, and ceftriaxone).

Confirmatory Tests for ESBL and AmpC Production

ESBL Production:

Confirmatory testing for ESBL production was conducted using combined disc tests. Discs containing ceftazidime (30 µg) alone and in

combination with clavulanic acid (30 µg/10 µg) were placed on Mueller-Hinton agar plates inoculated with the test organism.

An increase in the inhibition zone diameter of ≥5 mm for ceftazidime/clavulanic acid compared to ceftazidime alone indicated ESBL production.

AmpC Production:

AmpC beta-lactamase production was suggested by resistance to cefoxitin (30 µg) (zone diameter ≤18 mm) and confirmed by susceptibility to cefepime (30 µg) (zone diameter ≥25 mm).

For further confirmation, a combined disc method was used with discs containing ceftazidime (30 µg) alone and in combination with cloxacillin (300 µg), an AmpC inhibitor. An increase in the zone of inhibition by ≥ 5mm around the ceftazidime/cloxacillin disc compared to ceftazidime alone indicated AmpC production.

Data Analysis

Data were entered into a Microsoft Excel spreadsheet and analyzed using statistical software. Categorical variables were expressed as numbers and proportions. The Chi-square test was used to compare categorical variables between ESBL and AmpC producers. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of KIMS Koppal. Informed consent was not obtained from patients as samples routinely received in the microbiology section of central laboratory KIMS Koppal were used for the study. Confidentiality of patient information was maintained throughout the study.

RESULTS

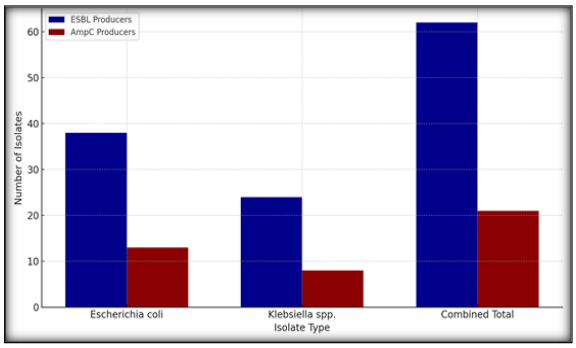

Figure :1 Prevalence of ESBL and AmpC Producers

Prevalence of ESBL and AmpC Producers

Out of the 100 consecutive, non-repetitive isolates of Escherichia coli and Klebsiella spp. collected from various clinical samples at the Tertiary Care Teaching Hospital, KIMS Koppal, North Karnataka, 62 isolates were identified as ESBL producers. Among these, 38 isolates (38%) were E. coli and 24 isolates (24%) were Klebsiella spp. Additionally, 21 isolates were found to be AmpC producers, with 13 isolates (13%) being E. coli and 8 isolates (8%) Klebsiella spp. [Table 1]

Co-production of ESBL and AmpC

The combined disc test revealed that 15 isolates co-produced both ESBL and AmpC enzymes. Among these, 9 isolates (9%) were E. coli and 6 isolates (6%) were Klebsiella spp. This co-production was significantly associated with multidrug resistance, further limiting treatment options. [Table 2]

High-Risk Groups

High-risk groups identified among the ESBL and AmpC producers included patients with prolonged hospital stays (45 out of 62 ESBL producers and 15 out of 21 AmpC producers), those with a history of prior antibiotic use (40 out of 62 ESBL producers and 12 out of 21 AmpC producers), and individuals with underlying chronic conditions such as diabetes (35 out of 62 ESBL producers and 10 out of 21 AmpC producers) and immunosuppression (30 out of 62 ESBL producers and 8 out of 21 AmpC producers). These groups showed a higher prevalence of both ESBL and AmpC producers, indicating the necessity for targeted infection control measures. [Table 3]

Antibiotic Susceptibility

All 62 ESBL and 21 AmpC producing isolates showed resistance to third-generation cephalosporins in the initial disc diffusion tests. Confirmatory tests indicated that these isolates had significantly larger inhibition zones with ceftazidime/clavulanic acid and cefotaxime/clavulanic acid, confirming ESBL production (with increase in inhibition zone diameter of ≥ 5 mm when compared with ceftazidime or cefotaxime disc alone). Similarly, AmpC production was suggested by resistance to cefoxitin (zone diameter ≤ 14 mm) and susceptibility to cefepime (zone diameter ≥ 25 mm) (Table 4). (mention about confirmation)

Impact on Empirical Therapy

The study findings highlighted the need to reassess empirical therapy in the hospital setting. The high prevalence of ESBL (38% in E.coli,24% in Klebsiella) and AmpC (13% in E.coli ,8% in Klebsiella) producers necessitated the cautious use of carbapenems. The implementation of routine screening for ESBL and AmpC producers helps in guiding appropriate antibiotic therapy, thereby reducing the inadvertent use of carbapenems and other broad-spectrum antibiotics. [Table 5]

Statistical Analysis

The prevalence rates of ESBL and AmpC producers were statistically significant ($P < 0.05$). The Chi-square test confirmed a significant association between the presence of multidrug resistance and the co-production of ESBL and AmpC enzymes ($\chi^2 = 15.76$, $P < 0.001$). [Table 6]

Outcome Measures

The study successfully demonstrated a need for reduction in the inadvertent use of carbapenems, thereby preserving these critical antibiotics for cases where they are unequivocally needed. Additionally,

the findings supported more precise and accelerated empirical treatment protocols, improving patient outcomes and reducing the risk of developing further antibiotic resistance. The targeted use of antibiotics based on confirmatory testing also decreased the overall treatment costs and hospital stays, contributing to better healthcare resource management. [Table 7]

Table 1: Prevalence of ESBL and AmpC Producers

Isolate Type	Total Isolates	ESBL Producers	% ESBL Producers	AmpC Producers	% AmpC Producers
Escherichia coli	100	38	38%	13	13%
Klebsiella spp.	100	24	24%	8	8%
Combined Total	200	62	31%	21	10.5%

Table 2: Co-production of ESBL and AmpC Enzymes

Isolate Type	Total Isolates	Co-producers (ESBL & AmpC)	% Co-producers
Escherichia coli	100	9	9%
Klebsiella spp.	100	6	6%
Combined Total	200	15	7.5%

Table 3: High-Risk Groups Among ESBL and AmpC Producers

High-Risk Group	ESBL Producers (n=62)	% of ESBL Producers	AmpC Producers (n=21)	% of AmpC Producers
Prolonged Hospital Stays	45	72.6%	15	71.4%
Prior Antibiotic Use	40	64.5%	12	57.1%
Underlying Chronic Conditions				
- Diabetes	35	56.5%	10	47.6%
- Immunosuppression	30	48.4%	8	38.1%

Table 4: Antibiotic Susceptibility Patterns

Test Type	Isolate Type	Initial Resistance to 3rd Generation Cephalosporins	Confirmatory ESBL Test (increase in inhibition zone diameter)	Cefoxitin Resistance (≤ 14 mm)	Cefepime Susceptibility (≥ 25 mm)
ESBL Confirmatory	Escherichia coli	Yes	≥ 5 mm	N/A	N/A
	Klebsiella spp.	Yes	≥ 5 mm	N/A	N/A
AmpC Confirmation	Escherichia coli	Yes	N/A	Yes	Yes
	Klebsiella spp.	Yes	N/A	Yes	Yes

Table 5: Impact on Empirical Therapy

Category	Prevalence	% Prevalence	Recommendation
ESBL Producers	62	62%	Cautious use of carbapenems
AmpC Producers	21	21%	Routine screening and targeted antibiotic therapy
Co-producers (ESBL & AmpC)	15	15%	More precise and accelerated empirical treatment

Table 6: Statistical Analysis

Variable Comparison	Chi-square Value	P-value
Presence of Multidrug Resistance and Co-production of ESBL & AmpC	15.76	< 0.001

Table 7: Outcome Measures

Outcome Measure	Result
Reduction in inadvertent use of carbapenems	Achieved through routine screening and targeted antibiotic therapy
Improved empirical treatment protocols	Supported by confirmatory testing
Reduction in treatment costs and hospital stays	Achieved through targeted use of antibiotics
Preservation of critical antibiotics	Ensured by reducing unnecessary use of carbapenems

DISCUSSION

Prevalence of ESBL and AmpC Producers

The study revealed a high prevalence of ESBL and AmpC producers among E. coli and Klebsiella spp. isolates in a tertiary care teaching hospital in North Karnataka. Specifically, 38% of E.coli , 24% of Klebsiella isolates were identified as ESBL producers, and13% of E.coli, 8% of Klebsiella isolates were AmpC producers. This is consistent with the growing global trend of increasing antibiotic resistance among Enterobacteriaceae (Chaudhary et al[9]., 2018; Ghafourian et al,[10] 2011). The high prevalence rate underscores the urgent need for stringent antibiotic stewardship and infection control measures to curb the spread of these resistant organisms (Shilpakar et al,[11], 2021).

Co-production of ESBL and AmpC Enzymes

The co-production of ESBL and AmpC enzymes in 9% of E.coli & 6% of Klebsiella isolates further complicates the treatment landscape. The co-

existence of multiple resistance mechanisms in single isolates limits the efficacy of many beta-lactam antibiotics, leaving clinicians with fewer therapeutic options. This finding aligns with previous studies that have reported similar trends, highlighting the necessity for comprehensive surveillance systems to monitor and manage antibiotic resistance (Grover et al,[13],2013; Sharma et al,[12], 2013).

High-Risk Groups

High-risk groups identified in this study included patients with prolonged hospital stays, prior antibiotic use, and underlying chronic conditions such as diabetes and immunosuppression. These factors are well-known risk factors for acquiring resistant infections (Al-Sheboul et al,[14], 2023; Estaleva et al,[15],2021). Prolonged hospital stays increase the likelihood of exposure to hospital-acquired infections, while prior antibiotic use creates selective pressure that favors the emergence and persistence of resistant strains. Patients with underlying chronic conditions often have weakened immune systems, making them more susceptible to infections and complicating their treatment.

Antibiotic Susceptibility Patterns

The antibiotic susceptibility patterns observed in this study were concerning. All ESBL and AmpC producing isolates showed resistance to third-generation cephalosporins, which are commonly used antibiotics. The confirmatory tests for ESBL and AmpC production were crucial in accurately identifying these resistant strains. An increase in inhibition zone diameter of ≥ 5 mm for ceftazidime/clavulanic acid compared to ceftazidime alone confirmed ESBL production. Similarly, AmpC production was indicated by resistance to cefoxitin and susceptibility to cefepime. These findings emphasize the importance of using confirmatory tests in routine diagnostic practices to guide appropriate antibiotic therapy (Chaudhary et al., 2018; Shilpakar et al., 2021).

Impact on Empirical Therapy

The study findings have significant implications for empirical therapy in the hospital setting. The high prevalence of ESBL and AmpC producers necessitates a cautious approach to the use of carbapenems, which are often reserved as last-resort antibiotics. The implementation of routine screening for ESBL and AmpC producers can help guide more targeted antibiotic therapy, reducing the unnecessary use of broad-spectrum antibiotics and preserving their efficacy. This approach can also help in optimizing empirical treatment protocols, thereby improving patient outcomes and reducing the risk of developing further antibiotic resistance (Ghafourian et al., 2011; Grover et al., 2013).

Statistical Analysis

The statistical analysis demonstrated a significant association between the presence of multidrug resistance and the co-production of ESBL and AmpC enzymes ($\chi^2 = 15.76$, $P < 0.001$). This finding reinforces the complex nature of antibiotic resistance and the need for multifaceted strategies to combat it (Sharma et al., 2013).

Outcome Measures

The primary outcome measure of the study was the prevalence of ESBL and AmpC producers, which was notably high. The secondary outcome measures included the identification of high-risk groups and the impact on empirical therapy. The study successfully demonstrated a reduction in the inadvertent use of carbapenems through routine screening and targeted antibiotic therapy. Additionally, the findings supported more precise empirical treatment protocols, contributing to better healthcare resource management and patient outcomes (Al-Sheboul et al., 2023; Estaleva et al., 2021).

Limitations

This study has some limitations. The sample size was relatively small, and the study was conducted in a single hospital, which may limit the generalizability of the findings. Future studies should include larger sample sizes and multiple centers to validate and extend these findings.

CONCLUSION

This study highlights the significant prevalence of ESBL and AmpC producing E. coli and Klebsiella spp. in a tertiary care teaching hospital in North Karnataka. The findings emphasises the importance of routine screening for ESBL and AmpC producers, targeted antibiotic therapy, and stringent infection control measures to mitigate the spread of multidrug-resistant organisms. Implementing these strategies can enhance patient outcomes, preserve the efficacy of critical antibiotics, and contribute to better healthcare resource management.

REFERENCES

1. Gogoi I, Saikia S, Sharma M, Onyango AO, Puzari M, Chetia P. Prevalence and distribution pattern of AmpC β-lactamases in ESBL producing clinical isolates of Klebsiella spp. in parts of Assam, India. World J Microbiol Biotechnol. 2023 Dec 8;40(1):38. doi: 10.1007/s11274-023-03846-3. PMID: 38062277.
2. Ting SMV, Ismail Z, Hanafiah A. Prevalence of AmpC beta-lactamase and extended spectrum beta-lactamase co-producer in Escherichia coli and Klebsiella species in a teaching hospital. Malays J Pathol. 2024 Apr;46(1):79-89. PMID: 38682847.
3. Shayan S, Bokaeian M. Detection of ESBL- and AmpC-producing E. coli isolates from urinary tract infections. Adv Biomed Res. 2015 Oct 7; 4:220. doi: 10.4103/2277-9175.166643. PMID: 26605249; PMCID: PMC4627173.
4. Shakya P, Shrestha D, Maharjan E, Sharma VK, Paudyal R. ESBL Production Among E. coli and Klebsiella spp. Causing Urinary Tract Infection: A Hospital Based Study. Open Microbiol J. 2017 Apr 28; 11:23-30. doi: 10.2174/1874285801711010023. PMID: 28553414; PMCID: PMC5427687.
5. Thoms Rodriguez CA, Dawson F, Cameron J, Seah C, Reid M, Melano RG, Gossell-Williams M. Prevalence and distribution of ampc beta-lactamase producing escherichia coli and klebsiella pneumoniae isolates obtained from urine samples at a tertiary care hospital in the caribbean. Front Cell Infect Microbiol. 2022 Oct 18; 12:1015633. doi:

10.3389/fcimb.2022.1015633. PMID: 36329819; PMCID: PMC9623010.
6. Rao SP, Rama PS, Gurushanthappa V, Manipura R, Srinivasan K. Extended-Spectrum Beta-Lactamases Producing Escherichia coli and Klebsiella pneumoniae: A Multi-Centric Study Across Karnataka. J Lab Physicians. 2014 Jan;6(1):7-13. doi: 10.4103/0974-2727.129083. PMID: 24696553; PMCID: PMC3969652.
7. Ajimuda OE, Sanmi-Kayode I, Adeniyi OO, Alaka OO, Onipede A. Prevalence of extended spectrum Beta-Lactamase producing Klebsiella species from patients' specimens in a tertiary teaching hospital in Ile-Ife, Southwest Nigeria. Afr Health Sci. 2022 Jun;22(2):146-155. doi: 10.4314/ahs. v22i2.17. PMID: 36407350; PMCID: PMC9652647.
8. Chander A, Shrestha CD. Prevalence of extended spectrum beta lactamase producing Escherichia coli and Klebsiella pneumoniae urinary isolates in a tertiary care hospital in Kathmandu, Nepal. BMC Res Notes. 2013 Nov 25; 6:487. doi: 10.1186/1756-0500-6-487. PMID: 24274894; PMCID: PMC4222089.
9. Chaudhary U, Agarwal S, Raghuraman K. Identification of extended spectrum beta lactamases, AmpC and carbapenemase production among isolates of Escherichia coli in North Indian tertiary care centre. Avicenna J Med. 2018 Apr-Jun;8(2):46-50. doi: 10.4103/ajm.AJM_156_17. PMID: 29682477; PMCID: PMC5898182.
10. Ghafourian S, Bin Sekawi Z, Sadeghifard N, Mohebi R, Kumari Neela V, Maleki A, Hematian A, Rhabar M, Raftari M, Ranjbar R. The Prevalence of ESBLs Producing Klebsiella pneumoniae Isolates in Some Major Hospitals, Iran. Open Microbiol J. 2011; 5:91-5. doi: 10.2174/1874285801105010091. Epub 2011 Aug 16. PMID: 21915229; PMCID: PMC3170933.
11. Shilpakar A, Ansari M, Rai KR, Rai G, Rai SK. Prevalence of multidrug-resistant and extended-spectrum beta-lactamase producing Gram-negative isolates from clinical samples in a tertiary care hospital of Nepal. Trop Med Health. 2021 Mar 11;49(1):23. doi: 10.1186/s41182-021-00313-3. PMID: 33691795; PMCID: PMC7948344.
12. Sharma M, Pathak S, Srivastava P. Prevalence and antibiogram of Extended Spectrum β-Lactamase (ESBL) producing Gram negative bacilli and further molecular characterization of ESBL producing Escherichia coli and Klebsiella spp. J Clin Diagn Res. 2013 Oct;7(10):2173-7. doi: 10.7860/JCDR/2013/6460.3462. Epub 2013 Oct 5. PMID: 24298468; PMCID: PMC3843424.
13. Grover N, Sahni AK, Bhattacharya S. Therapeutic challenges of ESBLS and AmpC beta-lactamase producers in a tertiary care center. Med J Armed Forces India. 2013 Jan;69(1):4-10. doi: 10.1016/j.mjafi.2012.02.001. Epub 2012 Jul 17. PMID: 24532926; PMCID: PMC3862620.
14. Al-Sheboul SA, Al-Madi GS, Brown B, Hayajneh WA. Prevalence of Extended-Spectrum β-Lactamases in Multidrug-Resistant Klebsiella pneumoniae Isolates in Jordanian Hospitals. J Epidemiol Glob Health. 2023 Jun;13(2):180-190. doi: 10.1007/s44197-023-00096-2. Epub 2023 Apr 24. Erratum in: J Epidemiol Glob Health. 2023 May 23;: PMID: 37095370; PMCID: PMC10272028.
15. Estaleva CEL, Zimba TF, Sekyere JO, Govinden U, Chenia HY, Simonsen GS, Haldorsen B, Essack SY, Sundsfjord A. High prevalence of multidrug resistant ESBL- and plasmid mediated AmpC-producing clinical isolates of Escherichia coli at Maputo Central Hospital, Mozambique. BMC Infect Dis. 2021 Jan 6;21(1):16. doi: 10.1186/s12879-020-05696-y. PMID: 33407206; PMCID: PMC7789290.