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Estimation of effectiveness of Ceftazidime-Avibactam on multi drug resistant gram-negative bacilli isolated from samples of patients attending a tertiary care hospital at Lucknow

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Abstract

INTRODUCTION: The utilization of Ceftazidime –avibactam (CAZ-AVI) presents as a viable treatment option for infections resulting from multidrug-resistant gram-negative bacteria (MDR-GNB). This study aims to evaluate the effectiveness of Ceftazidime-avibactam, a novel antibiotic combination, against MDR GNB isolated from various clinical samples of patients attending a tertiary care hospital of Lucknow during 2023-2024.

AIM: The aim of this study was to estimate the effectiveness of Ceftazidime-Avibactam on multi drug resistant gram-negative bacilli isolated from various clinical samples

MATERIALS AND METHODS: Samples of urine sputum & pus were collected from various patients admitted in ward. The objectives include assessing the antimicrobial susceptibility patterns of MDR isolates using the disk diffusion method and determining the minimum inhibitory concentrations (MIC) of ceftazidime-avibactam using the Epsilometer test (E-test). Additionally, the study compares the MIC results obtained via E-test with those from the broth microdilution method to establish consistency and reliability in susceptibility testing.

RESULTS: A total 1472 samples were collected from January to August 2023. Among these, 222 (15.07%) samples were identified GNB. Out of these 100 (45.04%) ESBL isolates were meticulously selected to encompass a spectrum of bacterial species commonly associated with ESBL-mediated resistance mechanismsto isolate MDR GNB, followed by testing for susceptibility to ceftazidime-avibactam. Resistance to ceftazidime- avibactam was observed in 22% of isolates by the BMD method and 23% by E-test, with higher resistance in MBL-producing strains.

CONCLUSION: These results highlight the potential of ceftazidime-avibactam as an effective therapeutic option for treating MDR infections, underscoring the critical role of robust antimicrobial stewardship and precise susceptibility testing in clinical management.

KEY WORDS: Antibiotic Resistance; ESBL producing Enterobacterales; Urinary tract infection; Nosocomial Pneumonia

INTRODUCTION

Antimicrobial resistance (AMR) is a multifaceted and evolving challenge driven by a combination of factors. Direct contributors include the overuse and misuse of antibiotics in human healthcare and agriculture. Indirect influences, like environmental contamination and inadequate sanitation, further exacerbate the issue. Additionally, the inherent adaptive abilities of bacteria play a significant role. AMR has been likened to a "silent tsunami" threatening contemporary medical practices.[1,2]

Despite ongoing efforts by the scientific community, mass media, and policy initiatives to raise awareness about antibiotic resistance, it continues to rise globally.[3] Gram-negative bacterial (GNB) infections, particularly in the bloodstream, urinary tract, wounds, and surgical sites, remain prevalent. These infections are significant contributors to morbidity, mortality, and increased healthcare costs, especially among patients in intensive care units (ICUs).[4-6]

Patients in intensive care units (ICUs) are highly vulnerable to multidrug-resistant (MDR) gram-negative bacterial infections due to invasive procedures, weakened immune systems, and overuse of broad-spectrum antibiotics

These infections are often fueled by horizontal gene transfer of resistance traits and poor adherence to infection prevention protocols. Common MDR pathogens include Enterobacterales, Pseudomonas aeruginosa, and Acinetobacter baumannii, which produce enzymes like carbapenemases and ESBLs, limiting treatment options. This results in worse clinical outcomes, increased mortality, and higher healthcare costs, especially when proper antibiotic guidelines are not followed. Resource-limited settings face additional challenges due to inadequate lab capabilities and insufficient infection control measures.[7-12]

According to a study by Van Boeckel et al., India leads in global antibiotic consumption with approximately 13 billion units, followed by China and the United States. Despite increased awareness of antibiotic resistance through scientific, media, and policy efforts, resistance rates continue to rise globally. Ceftazidime-avibactam, currently in Phase III clinical trials, shows promise for treating complex urinary and intra-abdominal infections, as well as carbapenem-resistant Enterobacteriaceae (CRE) infections. However, gram-negative bacterial infections, particularly in the respiratory tract, urinary tract, wounds, and bloodstream, continue to cause significant illness, death, and increased healthcare costs, especially in ICU patients.[4-6]

MATERIAL AND METHODS

The investigation was undertaken at the Department of Microbiology, Integral Institute of Medical Science & Research, Lucknow, India from December 2022 to May 2024.The test group comprised patients from various departments of the hospital. A total of 100 ESBL isolates were collected without regard to age, gender, occupation, religion, or ethnicity.

Sample Collection:

Over the course of one year, 100 positive samples were collected from various hospital wards. These samples varied and could include urine, sputum, pus. Each sample was collected carefully to maintain cleanliness and prevent contamination, then promptly transported to the laboratory under ideal conditions for analysis.

In this study, various methods were employed to assess the antimicrobial susceptibility and minimum inhibitory concentration (MIC) of multidrug-resistant gram-negative bacterial isolates. For antimicrobial testing, materials like Mueller-Hinton agar plates, antibiotic discs, and swab sticks were used for disk diffusion assays following the Kirby-Bauer method.

Additionally, the Epsilometer test (E-test) was used to determine MIC, where E-test strips were applied to inoculated agar plates, and results were interpreted as susceptible (S), intermediate (I), or resistant (R) based on the zone of inhibition. For more precise MIC determination, the broth microdilution method (BMD) was employed using a standardized inoculum prepared from isolated colonies and incubated in a 96-well microtiter plate, where the lowest concentration of the antimicrobial agent inhibiting bacterial growth was recorded as the MIC.

Ceftazidime-avibactam, a broad-spectrum antibiotic, was one of the key agents tested against these isolates, with interpretations based on CLSI standards, where an MIC of ≤8/4 μg/ml was considered susceptible, and ≥16/4 μg/ml resistant. This comprehensive approach allowed for accurate testing of antibiotic resistance patterns, critical for guiding

Treatment decisions in cases of multidrug-resistantinfection

RESULTS

Total 1472 samples were collected from January to August 2023. Among these, 222 (15.07%) samples were identified GNB. The study focused on investigating extended-spectrum beta-lactamase (ESBL) producing isolates, which represent a significant challenge in the management of antimicrobial resistance. A total of 100 (45.04%) ESBL isolates were meticulously selected to encompass a spectrum of bacterial species commonly associated with ESBL-mediated resistance mechanisms. The distribution of these isolates are shown in **(Figure-1)**

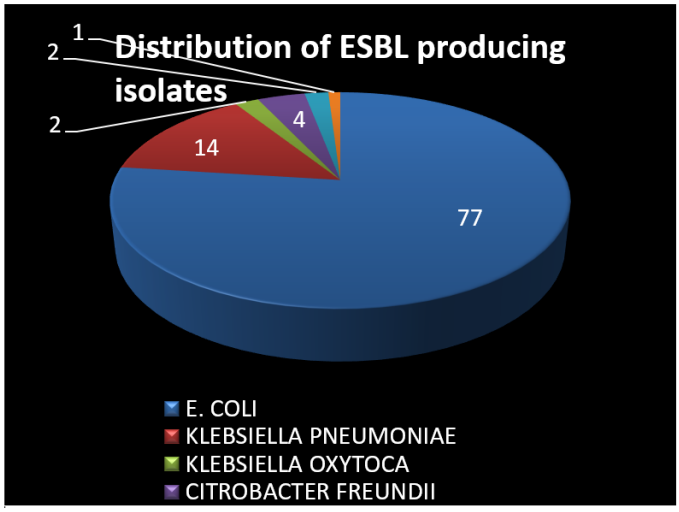

FIGURE 1: Distribution of ESBL producing isolates

These ESBL producing isolates represent a subset of clinical specimens chosen based on their potential impact on antimicrobial resistance dynamics and patient outcomes. **(Figure-2)**

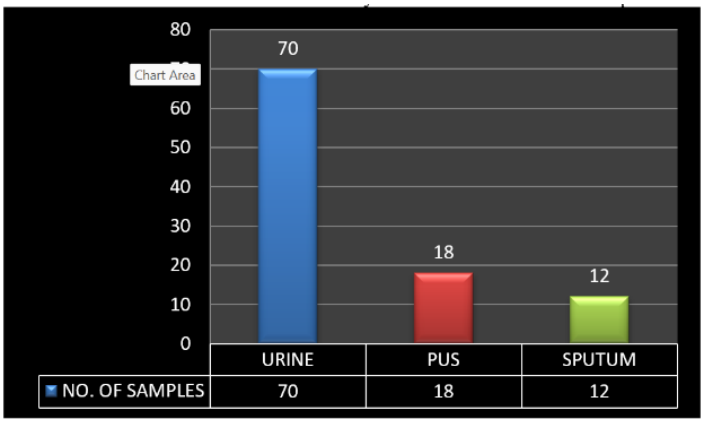

FIGURE 2: Distribution of samples

To ensure a diverse representation of the patient population, the study included patient samples from both outpatient (OPD) and inpatient (IPD) settings, in addition to clinical specimens. **(Figure-3)**

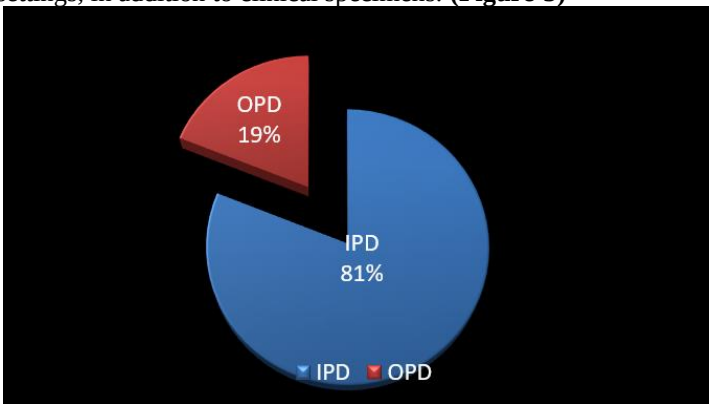

FIGURE 3: Distribution of Inpatients &Outpatients

Understanding antibiotic resistance patterns in bacterial pathogens is crucial for optimizing treatment regimens and infection control measures. In this study, we examine the resistance profiles of several key bacterial isolates obtained from clinical specimens, focusing on Escherichia coli (E. coli), Klebsiella pneumoniae, Citrobacter freundii, Klebsiella oxytoca, and Proteus spp. The comparative analysis of resistance rates across these species provides valuable insights into the distribution of antibiotic resistance in clinical settings.

Escherichia coli (E. coli) – Figure 4

Among the bacterial species analyzed, E. coli demonstrated the highest antibiotic resistance, with over 70% resistance to several commonly used antibiotics. The highest resistance was observed against ceftriaxone (98.7%), followed by 100% resistance to ceftazidime, and 92% resistance to both aztreonam and ciprofloxacin. Additionally, resistance to

tetracycline and cefepime was found in 70.1% and 84.4% of E. coli isolates, respectively. Moderate resistance was noted for piperacillin/tazobactam, gentamicin, tobramycin, and trimethoprim/sulfamethoxazole. However, a single E. coli isolate was sensitive to trimethoprim/sulfamethoxazole, suggesting it could be a treatment option for certain strains. Carbapenems like meropenem, doripenem, and imipenem showed high sensitivity, indicating their potential effectiveness against ESBL-producing E. coli. Among the 61 urine-derived E. coli isolates, 96.7% were resistant to norfloxacin, and 18% were resistant to nitrofurantoin, highlighting the challenge of treating urinary tract infections caused by this pathogen.

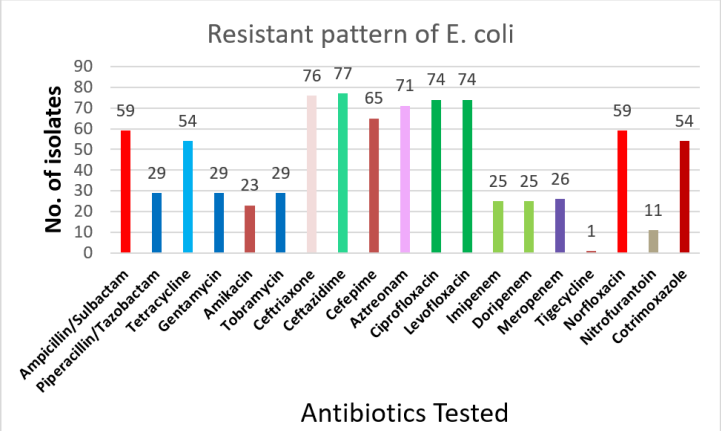

FIGURE 4: The antibiotic resistance pattern of ESBL-producing Escherichia coli (E. coli)

Klebsiella pneumonia – Figure 5

Klebsiella pneumonia isolates exhibited significant resistance to several antibiotics, highlighting the need for careful selection of treatment options. The highest resistance was observed in 71.4% of isolates against ampicillin/sulbactam, ceftriaxone, and aztreonam, indicating widespread resistance to these commonly used antibiotics. Moderate resistance was found in 21.4% of isolates for piperacillin/tazobactam, amikacin, tetracycline, imipenem, and meropenem. Among the 14 urine-derived isolates, 1 isolate was resistant to norfloxacin, and 2 isolates showed resistance to nitrofurantoin, further underscoring the complexity of treating urinary tract infections caused by Klebsiella pneumoniae.

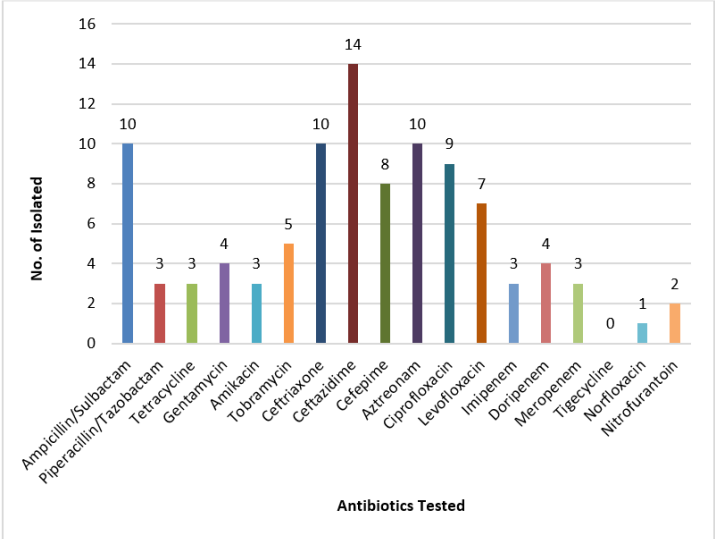

FIGURE 5: The antibiotic resistance pattern of ESBL-producing Klebsiella pneumoniae

Citrobacter freundii – Figure 6

Citrobacter freundii isolates demonstrated concerning antibiotic resistance patterns, with complete resistance (100%) observed to both ceftazidime and ceftriaxone. Moderate resistance was seen in 75% of isolates against ampicillin/sulbactam, tetracycline, cefepime, ciprofloxacin, levofloxacin, norfloxacin, and cotrimoxazole. Additionally, 50% of isolates showed resistance to piperacillin/tazobactam, aztreonam, imipenem, meropenem, and doripenem. Resistance to gentamicin, amikacin, tobramycin, and nitrofurantoin was lower, with only 25% of isolates resistant to these antibiotics. These findings highlight the challenge of treating infections caused by Citrobacter freundii, particularly with limited options for effective therapy.

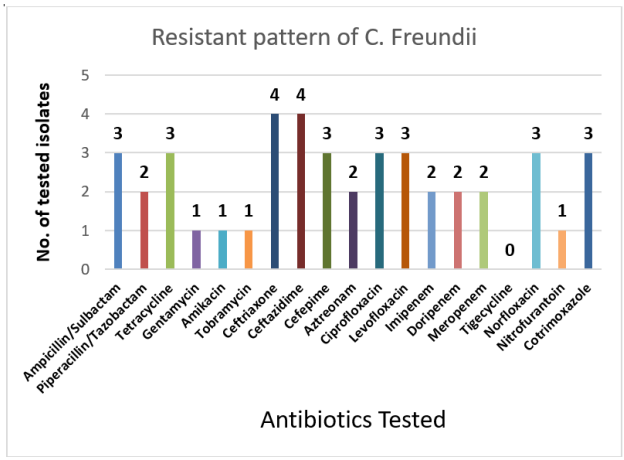

FIGURE 6: Antibiotic Resistance Pattern in ESBL producing Citrobacter freundii Isolates

Klebsiella oxytoca – Figure 7

Klebsiella oxytoca isolates exhibited high resistance to several commonly used antibiotics, with complete resistance (100%) to ceftazidime, ceftriaxone, cefepime, aztreonam, ciprofloxacin, and norfloxacin. Moderate resistance was observed in 50% of isolates to ampicillin/sulbactam, gentamicin, levofloxacin, and meropenem. However, Klebsiella oxytoca showed sensitivity to several other antibiotics, including piperacillin/tazobactam, tetracycline, amikacin, tobramycin, imipenem, doripenem, tigecycline, nitrofurantoin, and cotrimoxazole, with no resistance detected. This profile suggests that while Klebsiella oxytoca poses treatment challenges, certain antibiotics remain effective.

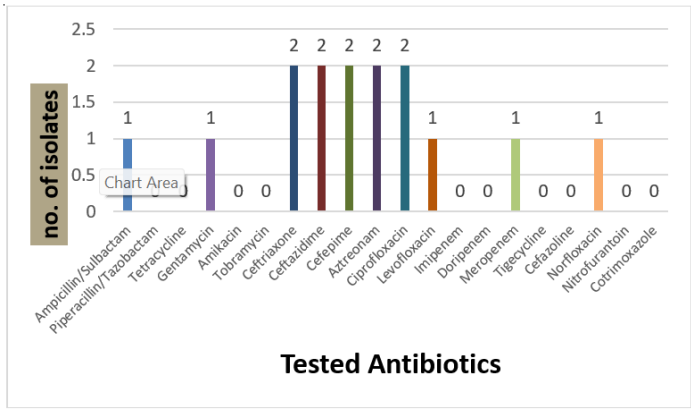

FIGURE 7: The Antibiotic Resistance Pattern in ESBL producing Klebsiella oxytoca Isolates

Proteus spp. – Figure 8

The resistance profiles of Proteus spp. showed significant variability, with 75% of isolates demonstrating high resistance to commonly used antibiotics such as ampicillin/sulbactam, tetracycline, ceftriaxone, ciprofloxacin, and levofloxacin. Moderate resistance was observed in 25% of isolates to gentamicin, amikacin, tobramycin, cefepime, aztreonam, and imipenem. Among the Proteus isolates, one strain (33.3%) was collected from a urine sample. However, the isolates remained fully sensitive to several antibiotics, including piperacillin/tazobactam, doripenem, meropenem, tigecycline, cefazolin, norfloxacin, nitrofurantoin, and cotrimoxazole, indicating that these agents may still be effective treatment options.

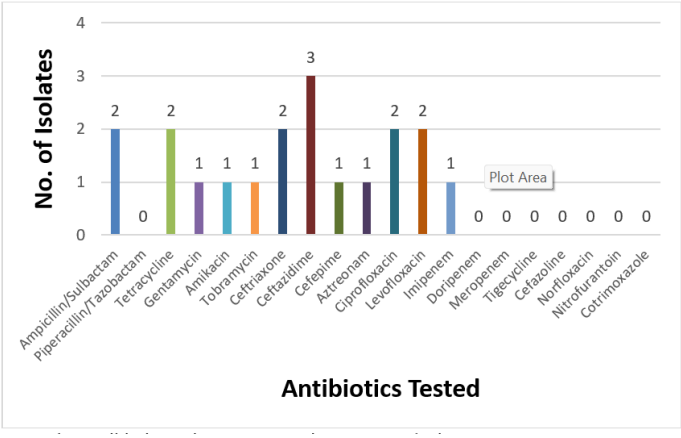

Figure 8: The Antibiotic Resistance Pattern in ESBL Producing Proteus spp.

In the BMD method, 22% of ESBL isolates were resistant to ceftazidime-avibactam. The E-test showed no major errors (ME), but one isolate was resistant by E-test and susceptible by BMD. The very major error (VME) rate was 1%, with an overall categorical agreement (CA) of 99% and essential agreement (EA) of 22%.**(Table 1)**

Table 1: Comparison of Ceftazidime-avibactam resistance of ESBL isolates by BMD method and E-test.

Organism	**No.of isolates tested (n)**	**No. of resistant isolates by BMD (n)**	**No. of resistant isolates by E-test (n)**	**No. (%) of CA**	**No. (%) of EA**	**No. (%) of VME**	**No. (%) of ME**
Gram-Negative Bacilli	100	22	23	99%	22%	1%	0%

In this study, a total of 100 ESBL isolates were collected, of which 35 were identified as carbapenemase-producing isolates. Among these carbapenemase-producing isolates, 22 were determined to be metallo-beta-lactamase (MBL) producers**(Figure 9)**.

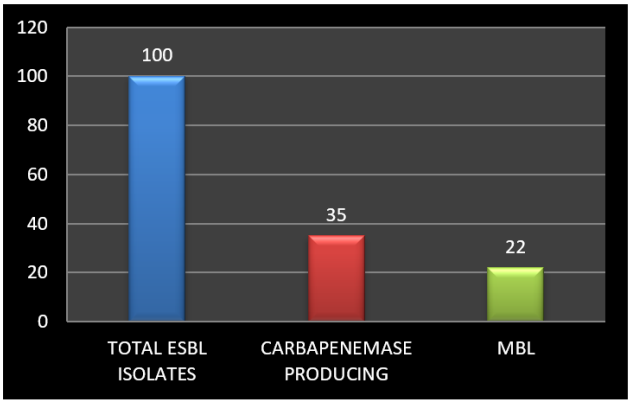

FIGURE 9: Distribution of MBL among ESBL isolates

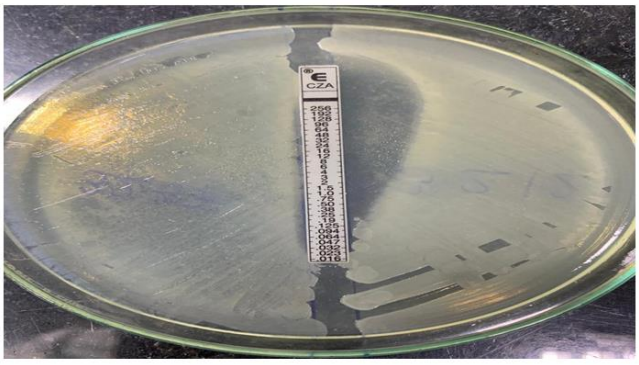

FIGURE 10: Ceftazidime-avibactam E-test for MBL (resistant) & ESBL (MIC=0.19mg/L) isolates

Of the 100 isolates tested, 22 were found to be resistant by the BMD method, while 23 isolates exhibited resistance using the E-strip method**(Figure:11)**.

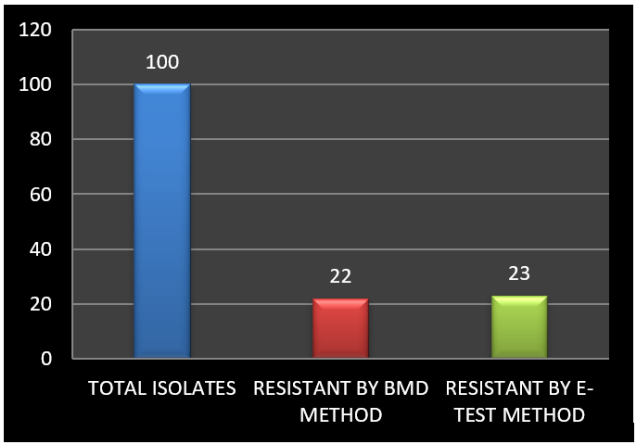

FIGURE 11: Prevalence of ceftazidime avibactam by both methods

Analysis of MBL-producing isolates showed that 19 out of 22 were resistant by BMD, while 20 out of 22 were resistant by the E-strip method. One K. pneumoniae strain was resistant to ceftazidime-avibactam by E-test but susceptible by BMD.**(Figure 12)**

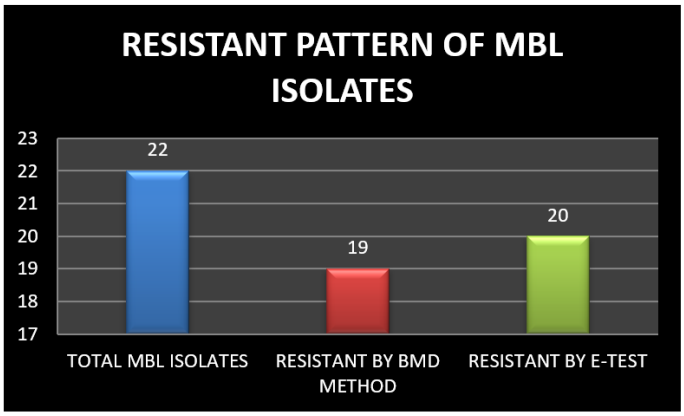

FIGURE 12: Distribution of resistance among MBL isolates

Additionally, it was observed that 2 out of the 65 ESBL isolates**(Figure:13)** that were not carbapenemase producers exhibited resistance to ceftazidime avibactam by both methodologies.

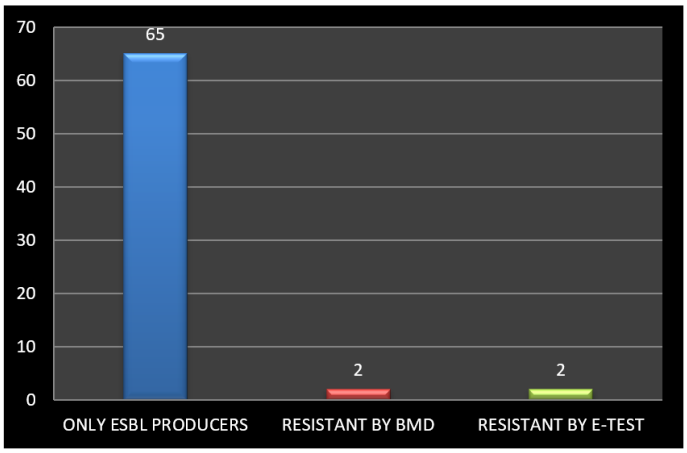

FIGURE 13: Distribution among only ESBL producing isolates

The study reveals significant variability in resistance patterns among ESBL, carbapenemase, and MBL-producing isolates, with MBL producers showing the highest resistance to ceftazidime-avibactam. This suggests that MBL production leads to stronger resistance compared to ESBL or carbapenemase production. While resistance rates were generally lower in ESBL and carbapenemase isolates, there was still considerable variation within each group. The comparison of E-test and BMD results showed that 52% of isolates had consistent MICs, while 36% had MICs one dilution higher by E-test, and only 6% showed discrepancies exceeding a two-fold dilution.

DISCUSSION

The study found an ESBL production rate of 45.04%, which is similar to the 45.5% reported by Suhaila A. Al-Sheboul et al. However, this rate is higher than the 14.9% observed by Al Muharrmi Z et al. and 13.9% by Chandramohan et al.In contrast, it is lower than the rates found by Suwantarat and Carroll et al. (55.1%) and Nabil Abdullah El Aila et al. (51.6%).[7-11]

The study found significant variation in ESBL production based on the type of sample and microorganism, with the highest ESBL production seen in E. coli (77%) followed by K. pneumoniae (14%). These rates are much higher compared to the 1.4% for E. coli and 4.4% for K. pneumonia reported in the USA in 2004, and the 10.8% for E. coli and 13.6% for K. pneumoniae in Europe (Goossens H et al.).[12]

The study showed that E. coli had the highest rate of ESBL production (77%), followed by K. pneumoniae at 14%. These rates were notably higher than those reported in the USA (1.4% for E. coli and 4.4% for K. pneumoniae) and Europe (10.8% for E. coli and 13.6% for K. pneumoniae). This highlights a significant regional difference in ESBL prevalence.[13-14]

The study found that E. coli (72.16%) and K. pneumoniae (10.3%) were the most common bacterial strains causing UTIs, with the highest ESBL production (70%) observed in urine samples. This is consistent with findings by Al Muharrmi et al., who reported 70.8% of ESBLs came from urine samples. Other studies, such as by Babypadmini et al. (40%) and Mekki et al. (53%), also found significant ESBL prevalence in urinary isolates of E. coli and K. pneumoniae.[14-19]

In this study, tigecycline, amikacin, and carbapenems showed the highest susceptibility rates against ESBL-producing bacteria, with 99%, 72%, and 68% sensitivity, respectively. On the other hand, ciprofloxacin, ceftriaxone, and ceftazidime exhibited high resistance rates of 90%, 94%, and 100%. Gentamicin and tobramycin resistance was observed in 36%, while 18.57% resistance was seen to nitrofurantoin. The study found all ESBL-producing isolates were resistant to ceftazidime, with 46% resistance to gentamicin, similar to findings from other studies. Additionally, ciprofloxacin had very low activity (3.89% susceptibility) against ESBL-producing E. coli, aligning with global reports of low ciprofloxacin effectiveness. Amikacin showed a moderate susceptibility rate of 70.12%, while ceftazidime-avibactam resistance was observed in 22% of isolates by the BMD method and 23% by E-test, with higher resistance in MBL-producing strains. These findings highlight the growing resistance patterns in ESBL-producing pathogens and emphasize the importance of monitoring antibiotic susceptibility trends for better treatment strategies.[20-23]

In this study, 22% of ESBL isolates were resistant to ceftazidime-avibactam, as determined by the BMD method. The E-test showed no major errors (ME) and a very major error (VME) rate of 1%. The overall categorical agreement (CA) was 99%, while the essential agreement (EA) rate was 22%.

Rehnru et al. found that the E-test, compared to the broth microdilution method, had a categorical agreement (CA) of 99.6%, essential agreement (EA) of 94.8%, with major and very major errors both at 0.2%.[22]

CONCLUSION

Among 100 isolates of ESBL producers, Escherichia coli was the most prevalent (77 isolates), followed by Klebsiella pneumoniae, Citrobacter freundii, Klebsiella oxytoca, and Proteus species. The findings highlight the significant presence of antibiotic resistance within these bacterial groups. Additionally, the study assessed the minimum inhibitory concentrations (MICs) of ceftazidime -avibactam for ESBL isolates using the broth microdilution (BMD) method and the E-test, which showed slight discrepancies between the two methods. Specifically, 22 isolates were resistant according to BMD, while 23 showed resistance with the E-test, underscoring the need for multiple testing methodologies to ensure accurate resistance profiling. The results emphasize the importance of robust surveillance, improved laboratory protocols, and standardization in susceptibility testing to enhance clinical decision-making and curb the growing threat of antibiotic resistance.

REFERENCES

1. Knight GM, Costelloe C, Murray KA et al. Addressing the unknowns of antimicrobial resistance: quantifying and mapping the drivers of burden. Clin Infect Dis 2018; 66: 612–6.
2. Cox D. Antibiotic resistance: the race to stop the silent tsunami facing modern medicine. The Guardian. 2015 Access date: 17 March 2018. Available from:https://www.theguardian.com/society/blog/2015/aug/21/antibiotic-resistance-the-race-to-stop-the-silent-tsunami-facing-modern-medicine.
3. Exner M, Bhattacharya S, Christiansen B, Gebel J, Goroncy-Bermes P, Hartemann P, et al. Antibiotic resistance: what is so special about multidrug-resistant Gram-negative bacteria? GMS Hyg Infect Control 2017;12:1–24.
4. Saha M, Sarkar A. Review on multiple facets of drug resistance: a rising challenge in the 21st century. J Xenobiot. 2021;11(4):197–214.
5. Abraham EP. The antibiotics. ComprBiochem. 1963;11(4):181–224.
6. Breijyeh Z, Jubeh B, Karaman R. Resistance of gram-negative bacteria to current antibacterial agents and approaches to resolve it. Molecules. 2020;25(6):1340.
7. Prevalence of Extended-Spectrum β-Lactamases in Multidrug-Resistant Klebsiella pneumoniae Isolates in Jordanian Hospitals (researchgate.net)
8. Al Muharrmi Z, Rafay AM, Balkhair A, Al-Tamemi S, Al Mawali A, Al Sadiri H. Extended-spectrum β-lactamase (ESBL) in Omani Children: study of prevalence, risk factors and clinical outcomes at Sultan Qaboos University Hospital, Sultanate of Oman. Sultan Qaboos Univ Med J. 2008;8(2):171–7.
9. Chandramohan L, Revell PA. Prevalence and molecular characterization of extended-spectrum-β-lactamase-producing Enterobacteriaceae in a pediatric patient population. Antimicrob Agents Chemother.
10. Suwantarat, N., Carroll, K. C. (2016). Epidemiology and molecular characterization of multidrug-resistant gram-negative bacteria in southeast Asia. *Antimicrob. Resist. Infect. Control* 5, 15. doi: 10.1186/s13756-016-0115-6
11. Prevalence of extended spectrum beta lactamase and molecular detection of blaTEM, blaSHV and blaCTX-M genotypes among Gram negative bacilli isolates from pediatric patient population in Gaza strip (researchgate.net)
12. Goossens H, Grabein B. Prevalence and antimicrobial susceptibility data for extended-spectrum beta-lactamase- and AmpC-producing Entero - bacteriaceae from the MYSTIC Program in Europe and the United States (1997–2004). DiagnMicrobiol Infect Dis. 2005;53(4):257–64.
13. Aminzadeh Z, Sadat Kashi M, Sha'bani M. Bacteriuria by extended-spec - trum beta-lactamase-producing Escherichia coli and Klebsiellapneumo - niae: isolates in a governmental hospital in South of Tehran, Iran. Iran J Kidney Dis. 2008;2(4):197–200.
14. Ullah F, Malik S, Ahmed J. Antibiotic susceptibility pattern and ESBL prevalence in nosocomial Escherichia coli from urinary tract infections in Pakistan. Afr J Biotechnol. 2009;8(16):3921–6.
15. Epidemiology-and-outcome-of-bacteremia-caused-by-extended-spectrum-beta-lactamase-ESBL-producing-Escherichia-Coli-and-Klebsiella-Spp-in-a-tertiary-care-teaching-hospital-in-South-India.pdf (researchgate.net).

16. Comprehensive study of antimicrobial susceptibility pattern and extended spectrum beta-lactamase (ESBL) prevalence in bacteria isolated from urine samples | Scientific Reports (nature.com)Gharavietal
17. Babypadmini S, Appalaraju B. Extended spectrum ß-lactamases in urinary isolates of Escherichia coli and Klebsiella pneumoniae—prevalence and susceptibility pattern in a tertiary care hospital. Indian J Med Microbiol. 2004;22(3):172–4.
18. Mekki AH, Hassan AN, Elsayed DEM. Extended spectrum beta lactamases among multi drug resistant Escherichia coli and Klebsiella species causing urinary tract infections in Khartoum. Afr J Microbiol Res. 2010;2(3):18–21.
19. Koshesh, M., Mansouri, S., Hashemizadeh, Z. &Kalantar-Neyestanaki, D. Identification of extended-spectrum β-lactamase genes and AmpC-β-lactamase in clinical isolates of *Escherichia coli*recovered from patients with urinary tract infections in Kerman, Iran. *Arch. Pediatr. Infect. Dis.* 5, e37968.
20. Khan, I. U. *et al.* Antimicrobial susceptibility pattern of bacteria isolated from patients with urinary tract infection. *J. Coll. Physicians Surg. Pak.* 24, 840–844.
21. Ejaz H, Zafa A, Mahmood S, Javed MM. Urinary tract infections caused by extended spectrum β-lactamase (ESBL) producing Escherichia coli and Klebsiella pneumoniae. Afr J Biotechnol. 2011;10(73):16661–6.
22. In-vitro Susceptibility Testing Methods for Ceftazidime-avibactam against Carbapenem-resistant Enterobacterales: Comparison with Reference Broth Microdilution Method - PubMed (nih.gov)
23. Assessment of Ceftazidime-Avibactam 30/20-µg Disk, Etest versus Broth Microdilution Results When Tested against Enterobacterales Clinical Isolates - PMC (nih.gov).