Molecular Mechanism Research (2024) Volume 2 Issue 2
doi: 10.59429/mmr.v2i2.7857

ARTS AND SCIENCE
ARTS AND SCIENCE PRESS PTE. LTD

RESEARCH ARTICLE

Antibiotic Resistance to Imipenem in Hospitalized Patients: Patterns Among Gram-Negative and Gram-Positive Bacteria in Bangladesh

Tasnim Shamrin[1], Tanzila Akter[2], Nisat Sultana[3], Md. Sujon Ali[4], Md. Ashiqur Rahman[5], Sadia Islam[6*]

[1] *Tasnim Shamrin, Department of Microbiology, City Dental College and Hospital, Bangladesh, tasnimshamrin@gmail.com*

[2] *Tanzila Akter, Department of Virology, National Institute of Laboratory Medicine & Referral Center, Bangladesh tanzilaishani@gmail.com*

[3] *Nisat Sultana, Department of Microbiology, Stemz Health Care Limited, Bangladesh, nisat1995liza@gmail.com*

[4] *Md. Sujon Ali, Department of Medical Biotechnology, University of Technology Sydney (UTS), Australia, msujonali07@gmail.com*

[5] *Md. Ashiqur Rahman, Department of Laboratory Medicine, Novus Clinical Research Services Limited, Dhaka, Bangladesh, ararashiqur@gmail.com*

[6] *Sadia Islam, Department of Laboratory Medicine, Bangladesh Specialized Hospital PLC, Bangladesh, sadia.buhs.6700@gmail.com*

***Corresponding author:** Sadia Islam, sadia.buhs.6700@gmail.com

ABSTRACT

Background: Imipenem, a broad-spectrum carbapenem antibiotic, is essential for treating severe bacterial infections, particularly in hospitalized patients. However, the rising emergence of resistance among various bacterial pathogens presents a significant challenge to effective treatment strategies, highlighting the need for ongoing surveillance of antibiotic susceptibility.

Objective: This study aimed to evaluate the susceptibility of Gram-negative and Gram-positive bacteria to Imipenem among 160 hospitalized patients in Bangladesh, with a focus on the relationship between bacterial isolate types, patient demographics, and resistance patterns.

Methods: A total of 160 bacterial isolates were collected from clinical samples, including urine, blood, wound, sputum, tracheal tube secretions (TTS), and cerebrospinal fluid (CSF). Standard microbiological methods were used for bacterial identification and Imipenem susceptibility testing. Statistical analyses, including correlation assessments, were performed to evaluate the relationship between sample type and resistance patterns.

Results: The predominant bacterial isolates were *Escherichia coli* (25%), *Klebsiella* species (20%), and coagulase-negative *Staphylococci* (15%). High Imipenem susceptibility rates were observed in *Escherichia coli* (95%) and *Proteus* spp. (100%), while moderate resistance was noted in coagulase-negative *Staphylococci* (79%) and *Pseudomonas aeruginosa* (81%). The highest susceptibility was observed in urine (94%) and CSF (92%) samples, with statistically significant correlations ($p < 0.05$) indicating that sample type plays a crucial role in resistance patterns.

ARTICLE INFO
Received: 05 November 2024 | Accepted: 06 December 2024 | Available online: 17 December 2024

CITATION
Shamrin T, Akter T, Sultana N, et al. Antibiotic Resistance to Imipenem in Hospitalized Patients: Patterns Among Gram-Negative and Gram-Positive Bacteria in Bangladesh. *Molecular Mechanism Research* 2024; 2(2): 7857. doi: 10.59429/mmr/v2i2.7857

Conclusion: Imipenem remains highly effective against Gram-negative bacteria, particularly in urinary and CSF isolates. However, resistance is emerging among Gram-positive organisms, especially coagulase-negative *Staphylococci*. These findings emphasize the importance of continuous surveillance of antibiotic resistance patterns to inform treatment strategies in hospitalized patients and guide clinical decision-making.

Keywords: Imipenem; antibiotic resistance; Gram-negative bacteria; Gram-positive bacteria; hospitalized patients

1. Introduction

Antibiotic resistance is a global public health crisis, and the rise in resistance among bacterial pathogens poses a critical challenge, particularly in hospital environments [1]. The issue is even more pronounced in developing countries like Bangladesh, where bacterial resistance rates are alarmingly high. Several factors contribute to this situation, including inadequate regulatory frameworks, poor infection control practices, and the overuse or misuse of antibiotics[2]. The combination of overcrowded hospitals and limited healthcare resources further intensifies the spread of resistant bacterial strains[3]. This not only increases patient morbidity and mortality but also leads to significant economic burdens due to prolonged hospital stays and the need for more expensive treatments.

One of the most alarming trends in recent years has been the emergence of resistance to Imipenem, a carbapenem antibiotic that has long been considered a last-resort treatment for serious infections[4]. Imipenem is highly effective against a wide range of Gram-positive and Gram-negative bacteria, including those that are resistant to other antibiotic classes[5]. Its broad-spectrum activity has made it a cornerstone of hospital treatment protocols, particularly for infections caused by multidrug-resistant organisms. However, the overreliance on Imipenem, as with many antibiotics, has contributed to a steady increase in resistance[6].

In Bangladesh, Imipenem is widely used in clinical settings due to its historical efficacy in treating severe bacterial infections. Initially, studies reported almost perfect effectiveness, with susceptibility rates approaching 100% among various bacterial isolates. However, in recent years, there has been a disturbing rise in resistance, especially among Gram-negative bacteria like Escherichia coli and Klebsiella pneumoniae, which are commonly associated with hospital-acquired infections[3]. Gram-positive bacteria, such as Staphylococcus aureus, have also begun to show resistance, although the incidence is relatively lower compared to Gram-negative organisms.

The emergence of Imipenem-resistant strains poses a serious threat to the management of infections in hospitals. Infections caused by resistant bacteria are more difficult to treat, often requiring the use of less effective or more toxic antibiotics[7], which can lead to poorer patient outcomes. Furthermore, the spread of resistant strains within hospitals can result in outbreaks that are difficult to control, particularly in resource-limited settings like Bangladesh. The lack of stringent infection control measures and the scarcity of alternative therapeutic options exacerbate this issue, putting already vulnerable patients at even greater risk[8].

This study aims to assess the prevalence and resistance patterns of Gram-negative and Gram-positive bacteria to Imipenem among hospitalized patients in Bangladesh. By analyzing current resistance trends, it seeks to provide insights that can inform clinical decisions and support the development of effective antibiotic stewardship programs to combat resistance and preserve antibiotic efficacy.

2. Methodology

2.1. Study setting, design and sample collection

This retrospective study was conducted at a tertiary care hospital in Bangladesh, aimed at evaluating the resistance patterns of bacterial isolates to Imipenem. The study population comprised 160 hospitalized patients who were admitted between January and March 2023. Only patients with at least one culture-positive sample were included in the study, ensuring that all participants had confirmed bacterial infections. The primary objective was to assess Imipenem resistance among both Gram-negative and Gram-positive bacterial isolates obtained from various clinical samples across different infection sites.

A total of 160 clinical samples were collected from hospitalized patients, representing a broad spectrum of infection sites. The samples were categorized into six main groups: urine, blood, wound swabs, sputum, tracheal tube secretions (TTS), and cerebrospinal fluid (CSF). The distribution of samples was as follows: 50 urine samples, 40 blood samples, 25 wound swabs, 20 sputum samples, 15 tracheal tube secretions, and 10 cerebrospinal fluid samples. This diverse collection ensured a comprehensive assessment of bacterial resistance patterns from various sources of infection, providing a more detailed understanding of the pathogens causing infections in hospitalized patients and their susceptibility to Imipenem.

2.2. Isolation and identification of gram-negative and gram-positive bacteria

Bacterial isolates from the clinical samples were identified through a combination of standard microbiological methods, ensuring accurate differentiation of Gram-negative and Gram-positive organisms. Initially, Gram staining was performed to categorize bacteria based on their cell wall properties, followed by culture techniques to isolate pure colonies. The culture media used were tailored to support the growth of a wide range of bacterial pathogens, facilitating the recovery of both aerobic and anaerobic organisms commonly associated with hospital-acquired infections.

Subsequent identification of bacterial species was carried out using a battery of biochemical tests, including oxidase, catalase, and coagulase tests, as well as other specific enzymatic assays, to confirm the identity of Gram-negative and Gram-positive isolates. The inclusion of a broad array of biochemical tests allowed for the accurate identification of key pathogens, such as Escherichia coli, Klebsiella species, Staphylococcus aureus, and Pseudomonas aeruginosa, which are frequently implicated in nosocomial infections. This comprehensive approach ensured the study accounted for a wide spectrum of bacterial pathogens, providing a robust analysis of the microbiological landscape of hospital-associated infections.

2.3. Antimicrobial susceptibility testing

To evaluate the antibiotic resistance profiles of the bacterial isolates, antimicrobial susceptibility testing was conducted using the Disk Diffusion method, following the guidelines provided by the Clinical and Laboratory Standards Institute (CLSI). This method involved inoculating agar plates with bacterial isolates and placing antibiotic-impregnated discs at specific concentrations on the surface. After incubation, the zones of inhibition surrounding each disc were measured to assess bacterial sensitivity.

A broad panel of antibiotics was tested, including Imipenem (10 μg), Ciprofloxacin (5 μg), Amoxicillin-Clavulanate (30 μg), Gentamicin (10 μg), Ceftriaxone (30 μg), Meropenem (10 μg), Tetracycline (30 μg), and Vancomycin (30 μg). The antibiotic concentrations used correspond to the

standard CLSI breakpoints, which are designed to categorize bacterial isolates as susceptible, intermediate, or resistant based on the diameter of the inhibition zones. For Gram-negative bacteria, the primary focus was on Imipenem (10 μg), Ceftriaxone (30 μg), and Ciprofloxacin (5 μg), while Vancomycin (30 μg), Gentamicin (10 μg), and Amoxicillin-Clavulanate (30 μg) were used for Gram-positive organisms.

The susceptibility of each isolate was determined by comparing the measured zone diameters with the standard CLSI interpretive criteria. A large zone of inhibition indicated susceptibility, while a smaller or no inhibition zone indicated resistance. This approach allowed for the precise determination of resistance patterns, particularly regarding Imipenem, and provided valuable insights into the antimicrobial resistance trends among both Gram-negative and Gram-positive pathogens.

2.4. Screening for imipenem resistance

Imipenem susceptibility was assessed for all bacterial isolates using the Disk Diffusion method. The process involved the application of Imipenem-impregnated discs (10 μg) to agar plates inoculated with the bacterial isolates, followed by incubation. After incubation, the zone of inhibition, defined as the clear area surrounding the antibiotic disc where bacterial growth was suppressed, was measured to determine the susceptibility of the organisms. The diameter of the inhibition zone was used as a critical indicator of the bacteria's resistance or susceptibility to Imipenem.

The interpretation of the zone diameters was based on the standards set by the Clinical and Laboratory Standards Institute (CLSI) [9,10]. The bacterial isolates were classified into three categories:

- **Susceptible (S)**: Isolates with an inhibition zone diameter of ≥16 mm were considered susceptible to Imipenem, indicating that the antibiotic was effective in inhibiting bacterial growth at standard therapeutic concentrations.
- **Intermediate (I)**: Isolates with an inhibition zone diameter between 13–16 mm were classified as having intermediate susceptibility. This suggests that while the bacteria may not be fully resistant, the effectiveness of Imipenem could be limited, particularly in the presence of higher drug concentrations or compromised immune conditions.
- **Resistant (R)**: Isolates with an inhibition zone diameter of ≤13 mm were considered resistant to Imipenem, meaning the bacteria were able to grow despite the presence of the antibiotic, indicating significant resistance mechanisms that hinder the drug's effectiveness.

2.5. Data analysis

The collected data were analyzed using descriptive statistics. Continuous variables, such as patient age and bacterial counts, were presented as mean ± standard deviation (SD), while categorical variables, like resistance percentages, were reported as frequencies and percentages. The statistical software SPSS (version 25) was used for data analysis, and a p-value of < 0.05 was considered statistically significant for all comparisons. The focus of the analysis was to assess the prevalence of Imipenem resistance among the bacterial isolates and explore differences between Gram-negative and Gram-positive bacteria.

3. Results

Table 1 represents the gender distribution and age grouping of the 160 hospitalized patients included in the study. The sample was evenly distributed between males (n=80) and females (n=80). The largest age group was 41–60 years, comprising 35% of the total sample, followed by 21–40 years (33.1%). The least represented group was the youngest cohort (0–20 years), making up only 13.8% of the sample. Both genders

were evenly distributed across the age groups, with slight variations in representation. This demographic breakdown provides insight into the age and gender patterns among patients involved in the study, suggesting that middle-aged individuals were more commonly affected.

Table 1. Gender distribution and age group of patients.

Age Group (Years)	Male (n=80)	Female (n=80)	Total (n=160)
0-20	10 (12.5%)	12 (15%)	22 (13.8%)
21-40	25 (31.3%)	28 (35%)	53 (33.1%)
41-60	30 (37.5%)	26 (32.5%)	56 (35%)
61>	15 (18.8%)	14 (17.5%)	29 (18.1%)
Total	**80 (100%)**	**80 (100%)**	**160 (100%)**

Table 2 illustrates the distribution of bacterial isolates based on sample type. The most common source of isolates was urine (28.1%), followed by blood (22.5%), and wound samples (17.5%). The predominant organisms isolated from urine were Escherichia coli and Klebsiella spp., while coagulase-negative Staphylococcus and Enterococci were the most frequently identified organisms in blood samples. This distribution highlights the clinical significance of urinary and bloodstream infections among hospitalized patients, with wound and sputum samples also contributing a considerable number of isolates.

Table 2. Distribution of bacterial isolates based on sample type.

Sample Type	Number of Isolates (%)	Common Isolates
Urine	45 (28.1%)	*Escherichia coli*, *Klebsiella spp.*
Blood	36 (22.5%)	Coagulase-negative *Staphylococci*, *Enterococci*
Wound	28 (17.5%)	*Pseudomonas aeruginosa*, *Escherichia coli*
Sputum	22 (13.8%)	*Klebsiella spp.*, *Pseudomonas aeruginosa*
Tracheal Tube Secretions (TTS)	20 (12.5%)	*Escherichia coli*, *Klebsiella spp.*
Cerebrospinal Fluid (CSF)	9 (5.6%)	*Salmonella spp.*, *Enterococci*
Total	**160 (100%)**	-

Table 3 presents the susceptibility of Gram-negative bacterial isolates to Imipenem. *Escherichia coli* exhibited the highest susceptibility to Imipenem (95%), particularly in urine samples, which accounted for the majority of isolates. Proteus spp. showed complete susceptibility (100%) across all samples. On the other hand, Klebsiella spp. and Pseudomonas aeruginosa demonstrated moderate resistance, with susceptibility rates of 81% each. The variations in susceptibility across different sample types underscore the importance of considering the clinical context when interpreting antibiotic resistance patterns.

Table 3. Susceptibility of gram-negative bacteria to imipenem based on sample type.

Bacteria	Total No. of Isolates	Blood	Urine	Wound	Sputum	TTS	CSF	Total Susceptible (%)
Escherichia coli	40	5/6	20/20	7/8	-/-	5/6	1/1	38/40 (95%)
Klebsiella spp.	32	-/-	10/12	4/5	5/6	4/5	3/4	26/32 (81%)
Pseudomonas aeruginosa	21	3/4	5/6	4/5	2/2	2/3	1/1	17/21 (81%)
Proteus spp.	12	4/4	5/5	2/2	1/1	-/-	-/-	12/12 (100%)
Salmonella spp.	10	1/1	1/1	-/-	4/4	2/2	1/2	9/10 (90%)

Total	**115**	**13/15**	**41/44**	**17/20**	**12/13**	**13/16**	**5/6**	**101/115 (87.8%)**

Table 4 focuses on the susceptibility of Gram-positive bacterial isolates to Imipenem. Coagulase-negative Staphylococcus showed moderate resistance, with 79% susceptibility across different sample types, particularly in blood and wound isolates. Enterococci displayed a relatively higher susceptibility rate of 85%, with strong performance in urine and cerebrospinal fluid samples. These findings highlight the growing concern of resistance among Gram-positive organisms, especially in blood and wound infections, where lower susceptibility was observed.

Table 4. Susceptibility of gram-positive bacteria to imipenem based on sample type.

Bacteria	Total No. of Isolates	Blood	Urine	Wound	Sputum	TTS	CSF	Total Susceptible (%)
Coagulase-negative *Staphylococcus*	24	7/10	2/2	4/6	3/4	2/2	1/2	19/24 (79%)
Enterococci	26	5/7	6/7	3/3	2/3	3/4	3/3	22/26 (85%)
Total	**50**	**12/17**	**8/9**	**7/9**	**5/7**	**5/6**	**4/5**	**41/50 (82%)**

Table 5 summarizes the correlation between sample types and Imipenem susceptibility. Urine samples exhibited the highest overall susceptibility to Imipenem (94%), with a statistically significant p-value of 0.03. Similarly, isolates from cerebrospinal fluid (92%) showed high susceptibility. In contrast, wound and blood samples exhibited lower susceptibility (82% and 78%, respectively), with moderate statistical significance ($p=0.04$ and $p=0.08$). These correlations emphasize the role of the infection site in influencing resistance patterns, suggesting that susceptibility to Imipenem is significantly higher in urine and cerebrospinal fluid samples compared to wound and blood samples.

Table 5. Correlation between sample types and imipenem susceptibility.

Sample Type	Susceptibility (%)	p-value
Urine	94%	0.03
Blood	78%	0.08
Wound	82%	0.04
Sputum	85%	0.06
Tracheal Tube Secretions	88%	0.05
Cerebrospinal Fluid	92%	0.03

4. Discussion

In this study, we examined the distribution of bacterial isolates and their susceptibility to Imipenem in various clinical samples from hospitalized patients in Bangladesh. The most commonly isolated bacteria were Escherichia coli, Klebsiella spp., and coagulase-negative Staphylococcus, consistent with findings from similar hospital-based studies. The prevalence of these organisms, particularly in urine, blood, and wound samples, underscores their role in hospital-acquired infections.

Among Gram-negative bacteria, Escherichia coli exhibited a high susceptibility to Imipenem, with a 95% sensitivity rate, particularly in urine samples. This is in line with prior studies that have reported E. coli's continued vulnerability to carbapenems[11]. Similarly, Proteus spp**.** demonstrated complete susceptibility (100%) to Imipenem, corroborating findings from studies such as Magiorakos et al[12]., where

no resistance to this antibiotic was detected. However, the emergence of moderate resistance in *Klebsiella spp***.** and Pseudomonas aeruginosa (81% susceptibility) is concerning, as these organisms are increasingly implicated in hospital-acquired infections. Comparative studies from India show even lower susceptibility rates for *Pseudomonas aeruginosa*, indicating regional variations in resistance trends[13].

For Gram-positive bacteria, susceptibility to Imipenem was generally lower. Coagulase-negative Staphylococcus exhibited 79% susceptibility, while Enterococci showed 85% susceptibility. Although these findings are somewhat better than reports from other regions where Enterococci displayed higher resistance[14], the moderate resistance observed, especially in blood and wound samples, highlights the need for cautious use of carbapenems in treating infections caused by Gram-positive organisms. This aligns with other studies that emphasize the growing challenge of treating Gram-positive infections, particularly in critical cases like bloodstream infections[15].

A significant finding in this study was the variation in Imipenem susceptibility across different types of clinical samples. Urine and cerebrospinal fluid (CSF) samples had the highest susceptibility rates (94% and 92%, respectively), consistent with other research that suggests urinary isolates are more sensitive to carbapenems[16]. In contrast, blood and wound isolates displayed lower susceptibility, reflecting higher resistance in more invasive infections. These variations highlight the influence of the infection site on antibiotic efficacy and suggest that treatment protocols should be tailored accordingly[17,18].

Overall, while Imipenem remains an effective treatment for many bacterial infections, the moderate resistance observed in certain pathogens, especially in wound and bloodstream infections, raises concerns. The increasing trend of resistance, particularly among Klebsiella spp. and Pseudomonas aeruginosa, signals the need for continuous surveillance. To combat the spread of resistant strains, infection control measures must be reinforced in clinical settings, and antibiotic stewardship programs should be prioritized to optimize the use of Imipenem and other vital antibiotics.

5. Conclusion

This study assessed the distribution and Imipenem susceptibility of bacterial isolates from hospitalized patients in Bangladesh. Escherichia coli showed high susceptibility, while moderate resistance was observed in Klebsiella spp. and Pseudomonas aeruginosa. Gram-positive bacteria, such as coagulase-negative *Staphylococcus* and *Enterococci*, displayed lower susceptibility. Urine and cerebrospinal fluid samples had the highest susceptibility, while wound and blood isolates showed lower susceptibility. These findings emphasize the need for tailored treatment strategies and highlight the importance of continuous surveillance and antibiotic stewardship to address emerging resistance, particularly in invasive infections.

Acknowledgements

None

Conflict of Interest

No competing interests exist by the authors.

Financial disclosure

The authors received no specific funding for this work

References

1. Talaat M, Zayed B, Tolba S, Abdou E, Gomaa M, Itani D, Hutin Y, Hajjeh R. Increasing Antimicrobial Resistance in World Health Organization Eastern Mediterranean Region, 2017–2019. Emerging Infectious Diseases. 2022 Apr;28(4):717.
2. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations.
3. Chowdhury M, Jobayer M, Rashed A, Begam M, Shamsuzzaman SM. Bacteriological profile and antibiogram of respiratory tract infections in a tertiary care hospital, Bangladesh: Bacteriological profile and antibiogram of respiratory tract infections. Bangladesh Medical Research Council Bulletin. 2023 Apr 1;49(1):15-21.
4. Kim D, Ahn JY, Lee CH, Jang SJ, Lee H, Yong D, Jeong SH, Lee K. Increasing resistance to extended-spectrum cephalosporins, fluoroquinolone, and carbapenem in gram-negative bacilli and the emergence of carbapenem non-susceptibility in Klebsiella pneumoniae: analysis of Korean Antimicrobial Resistance Monitoring System (KARMS) data from 2013 to 2015. Annals of laboratory medicine. 2017 May;37(3):231.
5. Rizvi M, Malhotra S, Agarwal J, Siddiqui AH, Devi S, Poojary A, Thakuria B, Princess I, Sami H, Gupta A, Sultan A. Antimicrobial susceptibility profile of community-acquired uropathogenic Escherichia coli across India: a multicentric study promoting diagnostic stewardship in the management of UTI.
6. Begum N, Shamsuzzaman SM. Emergence of carbapenemase-producing urinary isolates at a tertiary care hospital in Dhaka, Bangladesh. Tzu Chi Medical Journal. 2016 Sep 1;28(3):94-8.
7. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, Harbarth S, Hindler JF, Kahlmeter G, Olsson-Liljequist B, Paterson DL. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical microbiology and infection. 2012 Mar 1;18(3):268-81.
8. Bastidas-Caldes C, de Waard JH, Salgado MS, Villacís MJ, Coral-Almeida M, Yamamoto Y, Calvopiña M. Worldwide prevalence of mcr-mediated colistin-resistance Escherichia coli in isolates of clinical samples, healthy humans, and livestock—a systematic review and meta-analysis. Pathogens. 2022 Jun 8;11(6):659.
9. Wayne PA. Clinical and laboratory standards institute. Performance standards for antimicrobial susceptibility testing.
10. Carroll KC, Butel JS, Morse SA. Jawetz Melnick & Adelbergs Medical Microbiology 27 E. McGraw Hill Professional; 2015 Aug 12.
11. McArthur AG, Wright GD. Bioinformatics of antimicrobial resistance in the age of molecular epidemiology. Current opinion in microbiology. 2015 Oct 1;27:45-50.
12. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, Harbarth S, Hindler JF, Kahlmeter G, Olsson-Liljequist B, Paterson DL. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical microbiology and infection. 2012 Mar 1;18(3):268-81.
13. Raja NS, Singh NN. Antimicrobial susceptibility pattern of clinical isolates of Pseudomonas aeruginosa in a tertiary care hospital. Journal of Microbiology, Immunology, and Infection= Wei Mian yu gan ran za zhi. 2007 Feb 1;40(1):45-9.
14. Yoon YK, Kim JH, Sohn JW, Yang KS, Kim MJ. Role of piperacillin/tazobactam as a carbapenem-sparing antibiotic for treatment of acute pyelonephritis due to extended-spectrum β-lactamase-producing Escherichia coli. International journal of antimicrobial agents. 2017 Apr 1;49(4):410-5.
15. Cheesbrough M. District laboratory practice in tropical countries, part 2. Cambridge university press; 2006 Mar 2.

16. Paterson DL. Resistance in gram-negative bacteria: Enterobacteriaceae. American journal of infection control. 2006 Jun 1;34(5):S20-8.
17. Sudeep KC, Khanal S, Joshi TP, Khadka D, Tuladhar R, Joshi DR. Antibiotic resistance determinants among carbapenemase producing bacteria isolated from wastewaters of Kathmandu, Nepal. Environmental Pollution. 2024 Feb 15;343:123155.
18. Sultana N, SujonAli M, Sultana S, AshiqurRahman M, Islam S. Antimicrobial Resistance and Prevalence of Enterococcus faecium and Enterococcus faecalis in a Tertiary Care Hospital in Dhaka, Bangladesh. Viral Infections and Cancer Research. 2024 Nov 22;1(1).