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Survey on Opinions about Carbapenem Antibiotics Usage in Secondary and Tertiary Care Hospitals among Health Care Professionals in Coimbatore

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ABSTRACT

Background: Carbapenem antibiotics are vital in treating multidrug-resistant bacterial infections, especially in secondary and tertiary care hospitals. The overuse and misuse of these antibiotics lead to resistance, posing a global healthcare challenge. Assessing the awareness and practices of healthcare professionals regarding carbapenem usage is crucial.**Objective:** This study aims to evaluate the current usage patterns and perceptions of healthcare professionals regarding carbapenem antibiotics. Additionally, it aims to identify barriers, gather recommendations for improvement, and analyze attitudes toward antibiotic stewardship. **Materials and Methods:** A cross-sectional questionnaire-based survey was conducted among healthcare professionals, including physicians and clinical pharmacists from June to October 2024. A validated questionnaire was used to collect data on their knowledge, attitudes, and practices related to carbapenem antibiotics. 50 responses were collected from healthcare professionals. Descriptive and inferential statistics were applied to analyze the collected responses. **Results:** The survey revealed significant variations in awareness and prescription practices among healthcare professionals. While most respondents acknowledged the importance of carbapenem in treating severe infections, gaps in adherence to antibiotic stewardship programs were observed. Concerns about rising resistance patterns and the need for stricter protocols were emphasized by 70% of participants. **Conclusion:** The study highlights the need for continuous education and awareness programs among healthcare professionals to promote the rational use of carbapenem antibiotics. Strengthening stewardship practices can mitigate resistance and ensure the efficacy of these critical antibiotics in the future.

Keywords: Carbapenem antibiotics, antibiotic stewardship, imipenem, meropenem, doripenem, ertapenem.

INTRODUCTION:

The term “antibiotics” refers to substances naturally produced by microorganisms, such as bacteria or fungi that can inhibit the growth of other microorganisms and destroy their cells [1].

Carbapenems are a class of beta-lactam antibiotics with a broad-spectrum of activity, targeting both Gram-positive and Gram-negative organisms, including anaerobic bacteria [8]. These antibiotics are typically reserved for severe, life-threatening infections that do not respond to standard therapies[8]. Of the many β-lactams, carbapenems are the most potent, often serving as “last-line agents” or “antibiotics of last resort” for severe infections, particularly when resistant pathogens are involved[8][9].

Carbapenems inhibit bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs), resulting in bacterial cell wall death[8]. Their unique fused beta-lactam ring structure makes them resistant to many beta-lactamase enzymes produced by bacteria, enhancing their effectiveness compared to other beta-lactam antibiotics such as cephalosporins and penicillins [8][9].

Carbapenems show efficacy against a wide range of bacteria, including ***Streptococci, Enterococci, Staphylococci, Enterobacteriaceae,*** and ***Pseudomonas*** species. However, they are ineffective against **Methicillin-resistant *Staphylococcus aureus* (MRSA)**[8]**.** Carbapenems also remain useful against **Extended-spectrum Beta-Lactamase (ESBL)** producing bacteria, which are resistant to cephalosporins [8]. The patients with the history of anaphylactic reactions to penicillins and cephalosporins should not be treated with carbapenem antibiotics[5].

Classification:

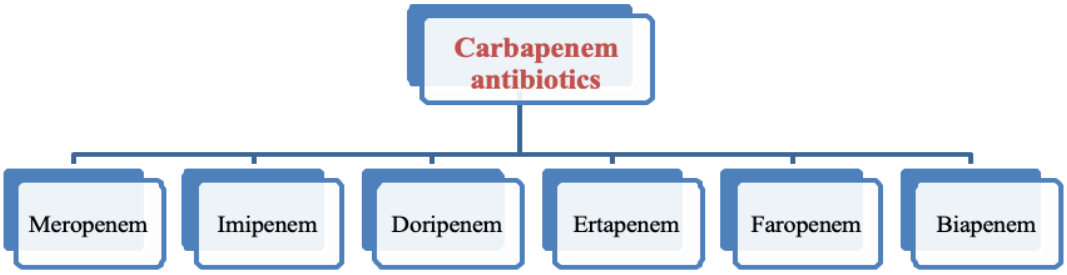


Figure 1: Classification of Carbapenem Antibiotics

Combinations of Carbapenem Antibiotics:

The combinations of carbapenem antibiotics available in India are in the following,

1. Meropenem + vaborbactam
2. Meropenem + colistin
3. Meropenem + tazobactam
4. Meropenem + ciprofloxacin
5. Meropenem + vancomycin
6. Meropenem + clindamycin
7. Meropenem + tigecycline
8. Meropenem + doxycycline
9. Meropenem + gentamicin
10. Panipenem + betamipron[9]

Mechanism of Resistance:

The emergence of **Carbapenem-resistant *Enterobacteriaceae* (CRE)** poses significant global challenge. CRE bacteria, including *Klebsiella* species and *Escherichia coli*, produce carbapenemase enzymes that degrade the β-lactam ring, rendering carbapenems ineffective. Some major carbapenemase enzymes include:

- ***Klebsiella pneumoniae* carbapenemase (KPC)**
- **New Delhi Metallo-beta-lactamase (NDM)**
- **Verona integron-mediated Metallo-beta-lactamase (VIM)**[8][9].

CRE infections primarily occur in hospitals and healthcare settings, especially among patients undergoing long- term antibiotic treatments. These infections are often life-threatening due to limited options. ***Stenotrophomonas maltophilia***, an inherently resistant pathogen, further complicates treatment due to its production of **Metallo-β-lactamase** enzymes.

The importance of our study is to review the carbapenem usage and check how often they are prescribed, the conditions treated, and adherence to guidelines, and to analyse the healthcare professionals' awareness of carbapenems, antimicrobial resistance, to improve antibiotic stewardship ,to enhances the challenges like limited resources, lack of training, and follow-up along with institutional barriers, and suggestions from healthcare professionals can improve protocols, encourage stewardship, and prevent resistance.

Table 1: DIFFERENCIATION BETWEEN CARBAPENEM ANTIBIOTICS

ERTAPENEM	Broad-spectrum antibiotic for treating moderate to severe infections caused by susceptible (community-acquired pneumonia, CIAI, complicated UTI, CSASSI and pelvic infections)	ADULTS: 1g once daily Adjustment may be required for renal impairment	Injectable powder for reconstitution.	Approximately 4 hours
DORIPENEM	Broad-spectrum antibiotic for treating complicated intra-abdominal infections and complicated UTIs, including pyelonephritis.	ADULTS: 500mg every 8 hours. Adjustment may be required for renal impairment	Injectable powder for reconstitution.	Approximately 1 hour
MEROPENEM	Broad-spectrum antibiotic for treating severe bacterial infections (bacterial meningitis, skin and skin structure infections, intra-abdominal infections.	ADULTS: 500mg-2g every 8 hours depending on the severity of the infections. Adjustment may be required for renal impairment	Injectable powder for reconstitution.	Approximately 1 hour
IMIPENEM/ CILASTATIN	Broad-spectrum antibiotic for treating severe infections caused by susceptible bacteria (UTI, IAI, lower UTI, gynecological infections, septicemia, bone and joint infections and skin infections.	ADULTS: 250-500 mg every 6 hours (max. 4g/day) Adjustment may be required for renal impairment	Injectable powder for reconstitution.	Approximately 1 hour
PROPERTIES	USES/ INDICATIONS	DOSE	AVAILABLE DOSAGE	HALF-LIFE

ERTAPENEM	Often used as monotherapy; may be combined with other antibiotics if needed.	Store at 20-25° C; protected from sunlight	Nausea, vomiting, diarrhea, rash, local reactions at the injection site, seizures, headache	Seizures (less common), hypersensitivity reactions, pseudo-membranous colitis, anaphylaxis.
DORIPENEM	Often used as monotherapy; may be combined with other antibiotics if necessary.	Store at 20-25° C; protected from sunlight	Nausea, vomiting, diarrhea, rash, local reactions at the injection site, seizures, headache, phlebitis	Seizures, hypersensitivity reactions, pseudo-membranous colitis, anaphylaxis.

MEROPENEM	Sometimes used in combination with other antibiotics for synergistic effects.	Store at 20-25° C; protected from sunlight	Nausea, vomiting, diarrhea, rash, local reactions at the injection site, seizures, headache	Seizures, hypersensitivity reactions, pseudo-membranous colitis, anaphylaxis.
IMIPENEM/ CILASTATIN	Combined with cilastatin to prevent renal metabolism of imipenem by dehydropeptidase-I.	Store at 20-25° C; protected from sunlight	Nausea, vomiting, diarrhea, rash, local reactions at the injection site, seizures (particularly in patients with CNS disorders of compromised renal function.	CNS toxicity (seizures), hypersensitivity reactions, pseudo-membranous colitis, anaphylaxis.
PROPERTIES	COMBINATIONS	STORAGE	SIDE EFFECTS	ADVERSE EFFECTS

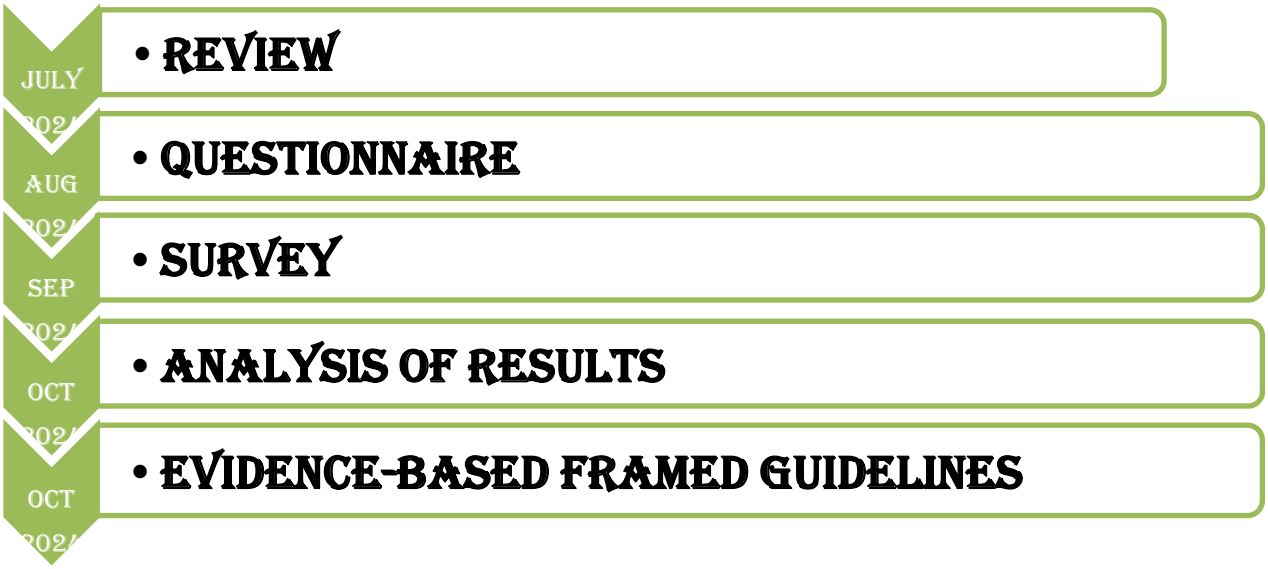
ERTAPENEM	Supportive care and symptomatic treatment; hemodialysis may help in case of overdose.	Rapid distribution; excreted primarily via urine.	Bactericidal; inhibits bacterial cell wall synthesis	Generally well-tolerated; less CNS toxicity compared to other carbapenems.	Use caution in patients with renal impairment, CNS disorders, or a history of seizures.
DORIPENEM	Supportive care and symptomatic treatment; hemodialysis may help in case of overdose.	Rapid distribution; excreted primarily via urine.	Bactericidal; inhibits bacterial cell wall synthesis	Generally well-tolerated; high dose can cause CNS toxicity.	Use caution in patients with renal impairment, CNS disorders, or a history of seizures.
MEROPENEM	Supportive care and symptomatic treatment; hemodialysis may help in case of overdose.	Rapid distribution; excreted primarily via urine.	Bactericidal; inhibits bacterial cell wall synthesis	Generally well-tolerated; high dose can cause CNS toxicity.	Use caution in patients with renal impairment, CNS disorders, or a history of seizures.
IMIPENEM/ CILASTATIN	Supportive care and symptomatic treatment; hemodialysis may be useful.	Rapid distribution; excreted primarily via urine.	Bactericidal; inhibits bacterial cell wall synthesis	Generally well-tolerated; high dose can cause CNS toxicity.	Use caution in patients with renal impairment, CNS disorders, or a history of seizures.
PROPERTIES	OVER DOSAGE TREATMENT	PHARMACOKINETICS	PHARMACO-DYNAMICS	TOXICITY	PRECAUTIONS

ERTAPENEM	Risk of anaphylactic reactions, super-infection, *Clostridium difficile*-associated diarrhea (CDAD).	1g IV or IM once daily	**Valproic acid:** Can significantly reduce valproic acid levels, increasing the risk of seizures **Probenecid:** Can increase ertapenem levels by decreasing renal excretion.	ERTACRIT FORSTAL
DORIPENEM	Risk of anaphylactic reactions, super-infection, *Clostridium difficile*-associated diarrhea (CDAD).	500mg IV every 8 hours	**Valproic acid:** Can significantly reduce valproic acid levels, increasing the risk of seizures **Probenecid:** Can increase doripenem levels by decreasing renal excretion.	ICUPEN, SUDOPEN
MEROPENEM	Risk of anaphylactic reactions, super-infection, *Clostridium difficile*-associated diarrhea (CDAD).	500mg-2g IV every 8 hours	**Valproic acid:** Can significantly reduce valproic acid levels, increasing the risk of seizures **Probenecid:** Can increase meropenem levels by decreasing renal excretion.	MEROPRIME, MEROWAK, MERONEM, MEROCRIT, ALTIPENEM, MEROSTER
IMIPENEM/ CILASTATIN	Risk of anaphylactic reactions, super-infection, *Clostridium difficile*-associated diarrhea (CDAD).	250mg-1g IV/IM every 6-8 hours, depending on the infection severity	**Valproic acid:** Can significantly reduce valproic acid levels, increasing the risk of seizures **Gancyclovir:** May increase the risk of seizures	PROCILA, VOCEF, CILANEM, CARBINEM, IMICELUM, IMICANN, IMIUM, IMPLATIN
PROPERTIES	WARNING	PREGNANCY DOSE	DRUG INTERACTIONS	BRAND NAME

ERTAPENEM	▪ CrCl greater than 30mL/min/1.73 m2: No adjustment recommended. ▪ Severe renal dysfunction (CrCl up to 30 mL/min/1.73 m^2) & ESRD (CrCl up to 10 mL/min/1.73 m^2): 500 mg IV or IM once a day	*CrCl – Creatinine Clearance, IV – Intravenous, IM – Intramuscular.
DORIPENEM	▪ CrCl greater than 50 mL/min: No adjustment recommended. ▪ CrCl 30 to 50mL/min: 250 mg via IV infusion every 8 hours ▪ CrCl greater than 10 to less than 30 mL/min: 250 mg via IV infusion every 12 hours	
MEROPENEM	▪ Greater than 50 mL/min: Recommended dose every 8 hours ▪ CrCl greater than 25 to 50mL/min: Recommended dose every 12 hours ▪ CrCl 10 to 25 mL/min: One-half recommended dose every 12 hours ▪ CrCl less than 10 mL/min: One-half recommended dose every 24 hours	
IMIPENEM/ CILASTATIN	▪ CrCl at least 90 mL/min: 500 mg (imipenem component) IV every 6 hours or 1 g (imipenem component) IV every 8 hours ▪ CrCl 60 to less than 90 mL/min: 400 mg (imipenem component) IV every 6 hours or 500 mg (imipenem component) IV every 6 hours	

	▪ CrCl 30 to less than 60 mL/min: 300 mg (imipenem component) IV every 6 hours or 500 mg (imipenem component) IV every 8 hours ▪ CrCl 15 to less than 30 mL/min: 200 mg (imipenem component) IV every 6 hours or 500 mg (imipenem component) IV every 12 hours ▪ CrCl less than 15 mL/min (not undergoing hemodialysis): Not recommended.	
PROPERTIES	RENAL DOSE ADJUSTMENTS (ADULTS)	

MATERIALS AND METHODOLOGY:



This study employed a cross-sectional survey using a questionnaire issued to physicians and clinical pharmacists at secondary and tertiary care hospitals in Coimbatore. The survey was conducted from August to October of 2024.

Prior to designing the questionnaire, we reviewed several monographs and research articles focused on carbapenems to gain a deeper understanding of their clinical applications and limitations. The literature review covered various aspects, including individual carbapenems like imipenem, meropenem, ertapenem, and doripenem, exploring their efficacy, pharmacokinetics, and use in sepsis management. Furthermore, we examined studies that highlighted prescribing practices, antimicrobial resistance trends, and the role of carbapenems in treating multidrug-resistant infections. This review informed the structure and focus areas of the questionnaire to ensure it aligned with the current challenges and practices reported in both local and global healthcare settings.

The questionnaire was distributed to physicians and clinical pharmacists, by visiting hospitals in Coimbatore directly and online using the SurveyHeart application. The objective of this study is to capture real-time experiences of healthcare professionals regarding the use of carbapenems in sepsis management.

This survey was structured to gather insights into the clinicians' and clinical pharmacist perceptions of carbapenem use, common indications and duration of treatment, cure rates of infected patients, usage in special categories and challenges encountered during administration. Clinicians were requested to complete the questionnaire at their convenience with their consent.

The questionnaire, which was in English, comprised 21 questions and was developed to assess the perceptions of physicians and clinical pharmacists in Coimbatore regarding prescribing practices. The questionnaire was validated by the head of the department and a few physicians. It was divided into 5 main sections:

- Section 1: Demographic data (6 questions)
- Section 2: Carbapenem usage and prescribing patterns (9 questions)

- Section 3: Challenges and concerns regarding carbapenem use (2 questions)
- Section 4: Clinicians' perceptions of carbapenem use (2 questions)
- Section 5: Additional comments and suggestions (2 questions)

The finalized list of questions was aligned with the study objectives and reviewed by the study team before the questionnaire was administered. A total of **50** responses were received, which were analyzed and compared with findings from the existing literature. Descriptive analysis of results has been done and we framed evidence-based guidelines for carbapenem antibiotics.

QUESTIONNAIRE AND RESULTS:

Q.No: 1- Frequency of prescribing/administering carbapenems in a day

a) 1

b) 2

c) 3

d) 4

e) 5

f) More than 5

Received answer: 1

The data reveals the frequency of prescribing or administering carbapenems in a day. It shows that **40%** of healthcare professionals prescribe or administer carbapenems once a day. A notable portion**, 22%,** does so twice a day, while **28%** opts for three times a day. A smaller group, **2%**, administers carbapenems exactly five times a day, and **8%** do so more than five times a day. None of the respondents prescribe or administer carbapenems four times a day. This highlights the varying practices among healthcare professionals in the usage of carbapenems.

Expected answer: 3 (TID)

According to ***"Drugs.com" and "the monographs of carbapenems",*** these antibiotics are typically prescribed ***ter in die,*** with each dose administered every 8 hours. This regimen ensures steady therapeutic levels in the bloodstream, maximizing their efficacy against severe bacterial infections.

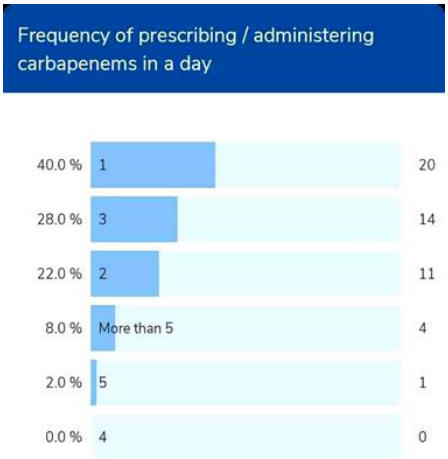


Figure: 2

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Q.No:2 Common indication for carbapenem use: (select all that apply)

a) Severe bacterial infections

b) Multi-drug resistance

c) Nosocomial infections

d) Intra-abdominal infection

e) Bacteremia/Sepsis

f) CNS infection

g) Complicated skin & soft tissue infections

h) Complicated urinary tract infections

Received answer: Carbapenem antibiotics are often prescribed to manage a variety of severe infections due to their broad-spectrum efficacy. As indicated in the data, the most common use is for **severe bacterial infections,** accounting for **21.7%** of cases. **Bacteremia or sepsis**, a life-threatening bloodstream infection, follows closely at **16.3%.** These antibiotics are also frequently utilized for **complicated urinary tract infections (15.8%)** and infections caused by **multi-drug resistant organisms (13.8%). Intra-abdominal infections** represent **11.3%** of carbapenem use, emphasizing their role in addressing complex infections within the abdominal cavity. Additionally, **9.9%** of prescriptions target **nosocomial (hospital-acquired) infections,** which are often difficult to treat with standard antibiotics**. Central nervous system (CNS) infections** account for **6.4%** of use, showcasing the ability of carbapenems to cross the blood-brain barrier. Lastly, **4.9%** of the usage is for **complicated skin and soft tissue infections.** These diverse applications highlight the importance of carbapenems in treating critical infections, especially in settings where other antibiotics may fail due to resistance.

Expected answer: According to the article, ***"Doripenem for Injection", by Dennis J.Cada et al.,*** the **intra-abdominal infection** is the most common indication of the carbapenem antibiotics. But carbapenem antibiotics are widely used for the treatment of severe bacterial infections, particularly those caused by drug-resistant pathogens.

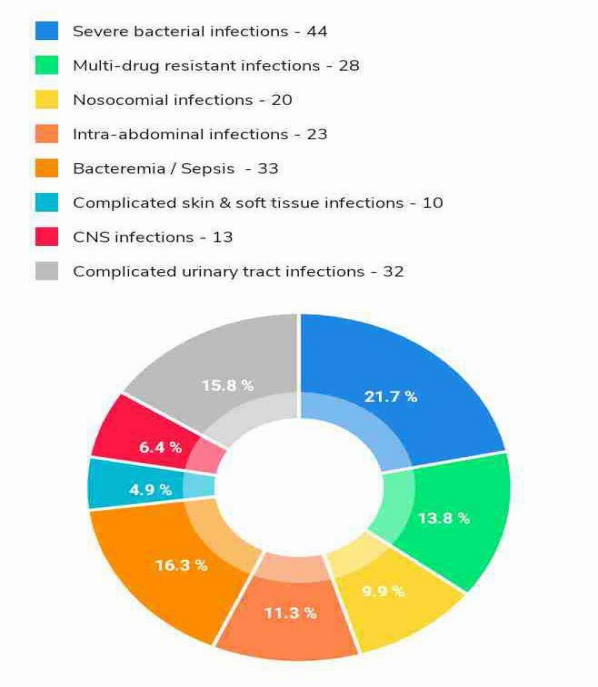

Figure: 3

Q.No:3- Specific carbapenem agent used:

a) Meropenem

b) Imipenem

c) Doripenem

d) Ertapenem

e) Others

Received answer: Based on the survey conducted among clinical pharmacists and physicians,

- **56.3%** of meropenem is prescribed
- **26.1%** of imipenem is prescribed
- **8%** of Ertapenem is prescribed
- **1.1%** of other carbapenems are prescribed.

Expected answer: Meropenem

According to this article, ***"Meropenem, A Review of its use in patients in Intensive care", by Miriam Hurst et al.,*** meropenem is the most commonly prescribed carbapenem, especially compared to imipenem. Meropenem carries a lower risk of inducing seizures, particularly in patients with central nervous system conditions. Its broad spectrum of activity, lower risk of CNS side effects, better tissue penetration, and flexible dosing make it the preferred carbapenem antibiotic in many clinical settings.

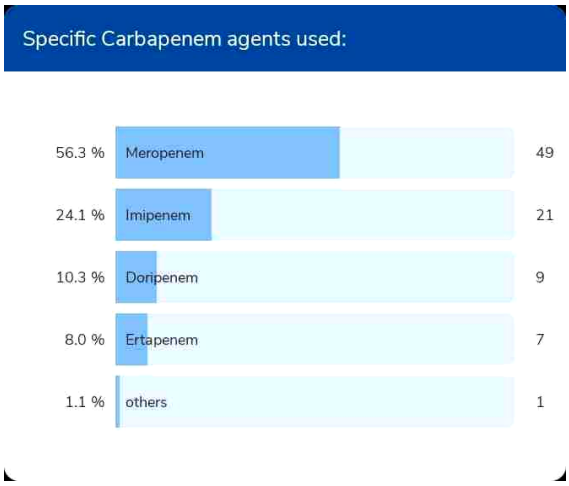

Figure: 4

Q.No:4- In your hospital setting, which combinations of carbapenem antibiotics are used?

Received answer: Based on the survey conducted among clinical pharmacists and physicians, the following combinations are used:

- Imipenem + cilastatin
- Meropenem + vaborbactam
- Meropenem + colistin

- Meropenem + tazobactam
- Meropenem + gentamicin
- Amoxicillin + clavulanate

Expected answer: Meropenem + vaborbactam and Imipenem + cilastatin + relebactam

According to the article, ***"The Role of New Carbapenem Combinations in the Treatment of Multidrug-Resistant Gram-Negative infections", by Emilio Bouza,*** these combinations enhance the effectiveness of carbapenems against resistant organisms, especially in the treatment of carbapenem-resistant *Enterbacteriacea* (CRE) and gram-negative bacteria.

Figure: 5

Q.No:5- Do you adjust dosing for special populations?

a) Yes

b) No

Received answer: Based on the survey conducted, **78%** of respondents reported that they are adjusting dose for special populations and **22%** of respondents said that they are not adjusting dose.

Expected answer: Yes

According to the article, ***"Optimization of Dosing Regimens and Dosing in Special Populations", by F.B. Sime et al.,***

- **Renal impairment:** Carbapenem antibiotics are primarily excreted by the kidney, so dose adjustment are essential in patient with renal impairment to avoid drug accumulation and toxicity.
- **Pediatric population:** Dosing in paediatric patients is typically weight based and may also need adjustment based on the child's renal function.
- **Geriatric population:** Geriatric patients may have reduced renal function due to age related changes. Renal function should be assessed, and dose adjustment should be made if necessary.
- **Pregnancy and lactation:** Carbapenems are classified as category B in pregnancy, indicating no evidence of risk in humans.

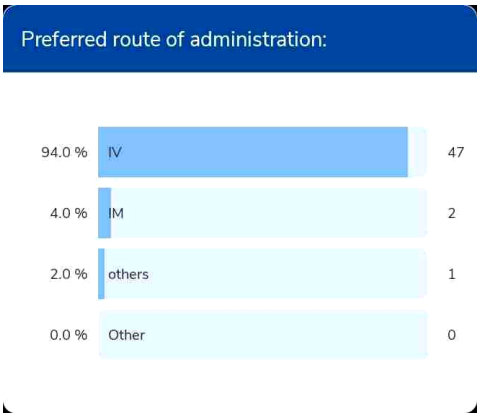

Figure: 6

Q.No:6- Preferred route of administration:

a) IV

b) IM

c) Others

Received answer: IV

Based on the survey results, the preferred route of administration of carbapenem antibiotics is intravenous (IV), with 94% of respondents choosing this option. Additionally, 4% preferred the intramuscular (IM) route, while 2% opted for other routes, such as oral administration.

Expected answer: IV

According to the article, ***"Carbapenems: a broad-spectrum antibiotic", by Tom Armstrong et al.,*** carbapenems typically exhibit low bioavailability, necessitating intravenous administration. However, imipenem-cilastatin and ertapenem can be given intramuscularly. Additionally, tebipenem, which is available only in Japan, can be taken orally. Faropenem, which is used in both India and Japan, is another carbapenem that can also be administered orally.

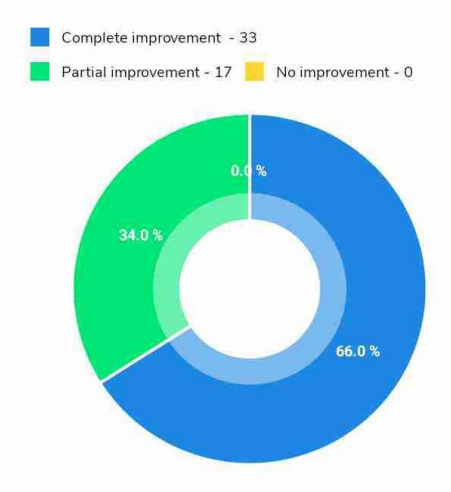

Figure: 7

Q.No:7- What is the curation rate of infectious people with carbapenems?

a) Complete improvement

b) Partial improvement

c) No improvement

Received answer: Complete improvement

The survey data indicates that carbapenem antibiotics show great promise in treating infections. A substantial **66%** of respondents reported complete improvement, while **34%** experienced partial improvement. Importantly, no patients reported a lack of improvement. This highlights the high rate of complete recovery and underscores the significant impact that carbapenem antibiotics have on effectively curing infections.

Expected answer: Partial improvement

According to several studies, these treatments can be effective in treating infections caused by susceptible organisms, with success rates often exceeding **70% to 80%.** However, in cases of extensively drug-resistant infections, the cure rate may be significantly lower, sometimes **falling below 50%.** These resistant infections pose a significant challenge in clinical settings, often necessitating the use of last-resort antibiotics, which may have limited efficacy and higher toxicity. Factors contributing to lower cure rates in resistant infections included the lack of effective treatment options, prolonged hospitalization, and increased mortality rates.

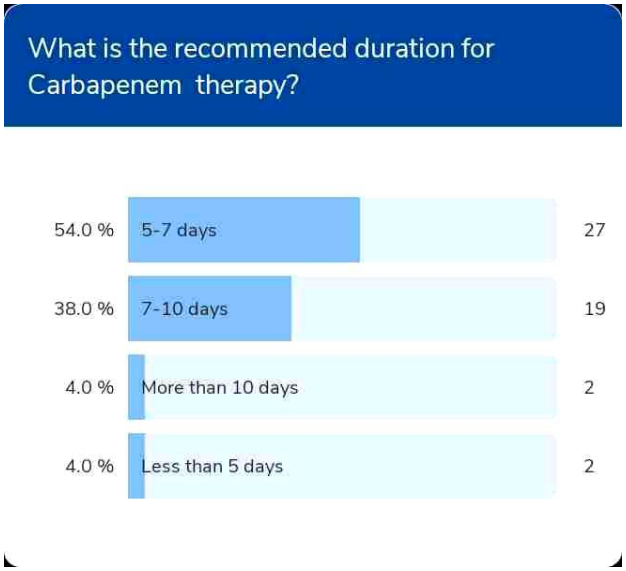

Figure: 8

Q.No:8- What is the recommended duration for carbapenem therapy?

a) < 5 days

b) 5 – 7 days

c) 7-10 days

d) > 10 days

Received answer: 5-7 days

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Based on the survey regarding the recommended duration for Carbapenem therapy, a clear majority of **54%** of respondents favor a treatment period of 5 to 7 days. Following that, **38%** suggest extending therapy to 7 to 10 days. A small group, just **4%,** believes treatment should last less than 5 days, while another **4%** think it should exceed 10 days. This data shows a strong consensus towards a 5 to 7-day regimen, indicating it might be the most effective and preferred duration among the practitioners surveyed.

Expected answer: 7-10 days

According to the article, ***"Carbapenem antibiotics for serious infections", by Peter M Hawkey,*** an 81 year-old woman with a urinary catheter and septicemia from a UTI was initially treated with cefotaxime and gentamicin, but her condition worsened due to ESBL-producing *Escherichia coli.* Her treatment was switched to meropenem, leading to a successful recovery after **7 days.**

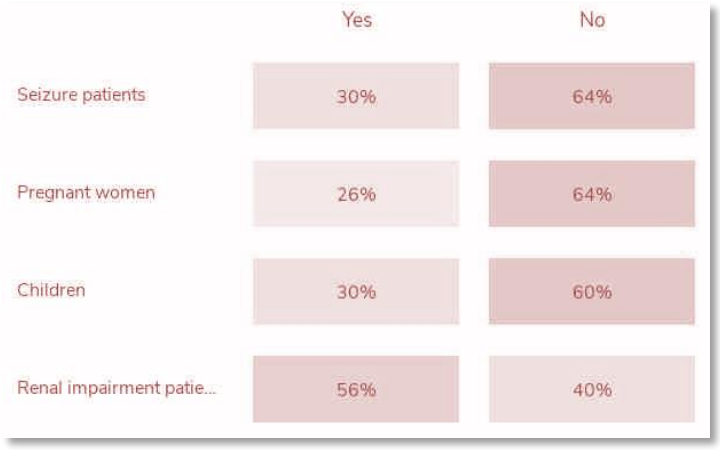

Figure: 9

Q.No:9- Is this carbapenem antibiotics, prescribing for following conditions?

a) Seizure patients

b) Pregnant women

c) Children

d) Renal impairment

a) Seizure patients:

Received answer: Based on the survey conducted among clinical pharmacists and physicians, the prescribing patterns of carbapenem antibiotics for seizure patients reveal that **30%** of respondents indicated that these antibiotics are prescribed in such cases, while **64 %** reported that they are not. This shows that most healthcare professionals are not prescribing carbapenems to seizure patients, because they concerns about side effects like worsening seizures.

Expected answer: No

According to the article, *"**The risk of seizures among the carbapenems: a meta- analysis", by J.Cannon et al.,*** the absolute risk of seizures with carbapenems is low, but imipenem was more **epileptogenic** than non-carbapenem antibiotics. Due to the risk of worsening seizures in patients with a seizure history, it should not be prescribed.

Alternative therapy:

According to the article ***"Epileptogenic Potential of Carbapenem Agents: Mechanism of Action, Seizure Rates, and Clinical Considerations", by April D. Miller,*** they have an epileptogenic potential, particularly with high-dose therapy. The article suggests that these medications should be **managed with benzodiazepines** and **avoided in combination with valproic acid** to mitigate the risk of seizures.

b) Pregnant women:

Received answer: According to the survey, **26%** of clinicians prescribing carbapenem antibiotics and the **64%** of them are not prescribing. They are typically not recommended for pregnant women due to potential risks to both the mother and the developing fetus. They are highly effective in the treatment of severe bacterial infections, but their safety during pregnancy is not well-established. It may cross the placenta, and without enough conclusive studies on their effects, doctors often choose safer alternatives to minimize the risk of teratogenecity or harmful effects. Physicians typically weigh the risks and benefits carefully, reserving carbapenem use for situation where no other effective treatment is available and the infection poses a greater danger to the mother's health.

Expected answer: Yes

According to the article, ***"Carbapenem use in critically ill patients", by Juliette Patrier et al.,*** the use of carbapenems in critically ill patients, does not address teratogenicity.

c) Children:

Received answer: In our survey on carbapenem antibiotic prescribing patterns among healthcare professionals, **30%** reported prescribing carbapenem antibiotic to paediatric patients, while **60%** stated they do not prescribe them to paediatric patients.

Expected answer: Yes

According to the article, ***"Clinical pharmacology of carbapenems in infants and children", by Gian Maria Pacifici et al.,*** the efficacy and safety of carbapenems in the treatment of severe bacterial infections in infants and children.

d) Renal impairment patients:

Received answer: 56% of health care professionals reported prescribing carbapenem antibiotics for patients with renal impairment, while 40% chose not to prescribe them in such cases.

The decision often depends on the severity of the renal condition and the need for dose adjustments. For patients with renal impairment, they require careful dose modification of avoid toxicity while ensuring efficacy. The adjustment help balance the drug's therapeutic benefits with the reduced renal clearance, ensuring patients safety.

Expected answer: Yes

According to the article ***"Meropenem in Elderly and Renally Impaired Patients", by B.A. Cunha et al.,*** patients with renal impairment can use carbapenem antibiotics, such as meropenem, but caution is warranted. The study highlights that while renal impairment complicates treatment meropenem has demonstrated a good safety profile and is well tolerated, even at higher doses. Since meropenem is primarily eliminated through the kidneys, careful evaluation of dosage and monitoring is essential in this patient population to ensure safety and efficacy.

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Table 2: RENAL DOSAGE ADJUSTMENTS (ADULTS)

IMIPENEM/ CILASTATIN	MEROPENEM	DORIPENEM	ERTAPENEM
▪ CrCl at least 90 mL/min: 500 mg (imipenem component) IV every 6 hours or 1 g (imipenem component) IV every 8 hours ▪ CrCl 60 to less than 90 mL/min: 400 mg (imipenem component) IV every 6 hours or 500 mg (imipenem component) IV every 6 hours ▪ CrCl 30 to less than 60 mL/min: 300 mg (imipenem component) IV every 6 hours or 500mg (imipenem component) IV every 8 hours ▪ CrCl 15 to less than 30 mL/min: 200 mg (imipenem component) IV every 6 hours or 500mg (imipenem component) IV every 12 hours ▪ CrCl less than 15 mL/min (not undergoing hemodialysis): Not recommended.	▪ Greater than 50 mL/min: Recommended dose every 8 hours ▪ CrCl greater than 25 to 50mL/min: Recommended dose every 12 hours ▪ CrCl 10 to 25 mL/min: One-half recommended dose every 12 hours ▪ CrCl less than 10 mL/min: One-half recommended dose every 24 hours	▪ CrCl greater than 50 mL/min: No adjustment recommended ▪ CrCl 30 to 50mL/min: 250 mg via IV infusion every 8 hours ▪ CrCl greater than 10 to less than 30 mL/min: 250mg via IV infusion every 12 hours	▪ CrCl greater than 30mL/min/1.73 m2: No adjustment recommended. ▪ Severe renal dysfunction (CrCl up to 30 mL/min/1.73m^2) & ESRD (CrCl up to 10 mL/min/1.73 m^2): 500 mg IV or IM once a day

Q.No:10- Challenges encountered in carbapenem use:

a) Drug resistance

b) High cost of therapy

c) Adverse effects

d) Drug interactions

e) Limited availability

f) Other

Received answer: It's evident that the high cost of therapy is a major concern, making up 43.3% with 45 occurrences. Drug resistance represents 27.9% of cases, with a total of 29 occurrences. Adverse effects are also significant, representing 16.3% with 17 occurrences.

Expected answer: Drug-resistance

According to the article, ***"Clinical Review: Balancing the Therapeutic, Safety, and Economic issues Underlying Effective Anti-pseudomonal Carbapenem use," by Thomas G. Slama et al.,*** drug resistance is a significant challenge in carbapenem use. Careful

monitoring is required to balance therapeutic effectiveness with safety and cost concerns. Ensuring appropriate use of carbapenems is essential to mitigate the development of resistance while maintaining clinical outcomes.

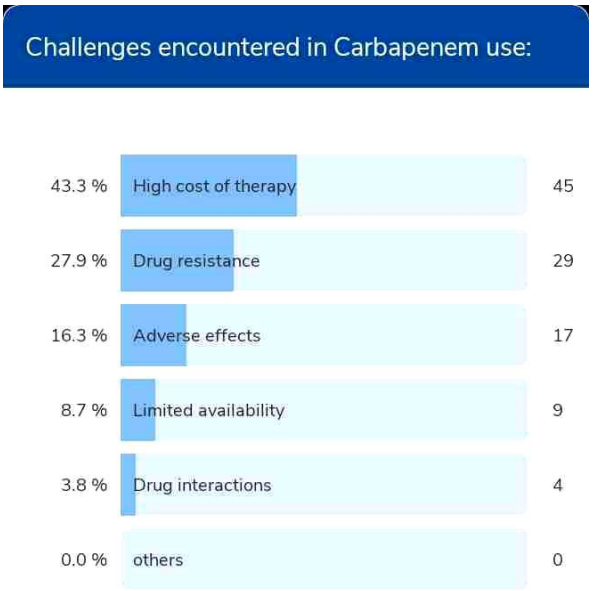

Figure: 10

Q.No: 11- How does resistance to carbapenems affect your clinical practice?

a) Limited treatment options

b) Prolongs patient hospital stay

c) Leads to use of more toxic or

less effective alternatives

d) Increases treatment cost

e) Others

Received answer: From our survey on the impact of carbapenem antibiotics usage, **35.4%** respondents highlighted an increase in treatment cost. Prolonged patient hospital stay was noted by **31.8%,** while **20%** felt it limited treatment options. Furthermore, **13.6%** indicated that it led to the use of more toxic or less effective alternatives. There were no responses in the 'Others' category. The data highlights serious concerns regarding the impact of carbapenem antibiotics usage, which could shape future healthcare practices and policies.

Expected answer: Limited treatment options

According to the article, ***"Infections caused by Carbapenem-resistant Enterobacteriaceae: An update on therapeutic options," by Chau-Chyun Sheu et al.,*** carbapenem resistance limits treatment options to a few alternatives like polymixins and tigecycline, which are often less effective and more toxic. This makes infections harder to treat, prolongs hospital stays, and increases healthcare costs.

Alternative therapy for carbapenem-resistance: Alternative therapies for carbapenem-resistance infections include colistin, aminoglycosides, tigecycline, fosfomycin, ceftriaxone+sulbactam+EDTA, ceftazidime/avibactam and ceftolozane/tazobactam as well as combinations of these drugs.

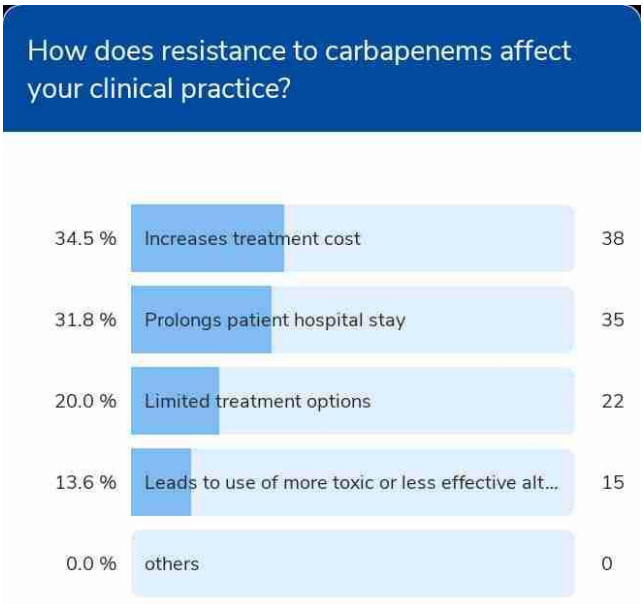

Figure: 11

Q. No: 12- Does your hospital have specific guidelines for carbapenem use?

a) Yes

b) No

c) Not sure

Received answer: Out of 50 respondents, 48% indicated that their hospital has specific guidelines for carbapenem use, while 12.0% stated there were no guidelines, and 40.0% were unsure.

Expected answer: Yes

According to the article, ***"Compliance with Carbapenem Guidelines in a University Hospital", by Van Hollebeke et al.,*** compliance with carbapenem guidelines was reported to be 76.3%, highlighting the need for a stronger carbapenem stewardship program. Inappropriate use of carbapenems can lead to increased resistance, emphasizing the importance of strict adherence to these guidelines.

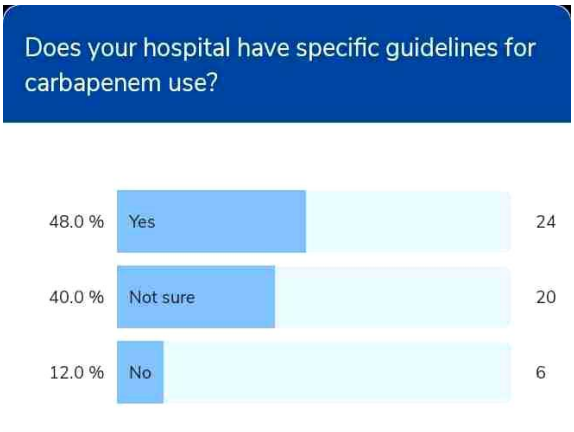

Figure: 12

Q. No: 13- How often do you consult with an infectious disease specialist or clinical pharmacist before prescribing carbapenems?

a) Always

b) Usually

c) Sometimes

d) Rarely

e) Never

Received answer: Sometimes

Out of the total 50 responses, **52%** of participants indicated "Sometimes," **18%** responded with "Always," **16%** selected "Rarely," **10%** chose "Usually," and **4%** answered "Never".

Expected answer: Always

According to the article, ***"Compliance with Carbapenem Guidelines in a University Hospitals", by Van Hollebeke et al.,*** it is essential that all healthcare professionals consult with an infectious disease specialist or clinical pharmacist before prescribing carbapenem antibiotics to ensure appropriate usage and reduce the risk of resistance.

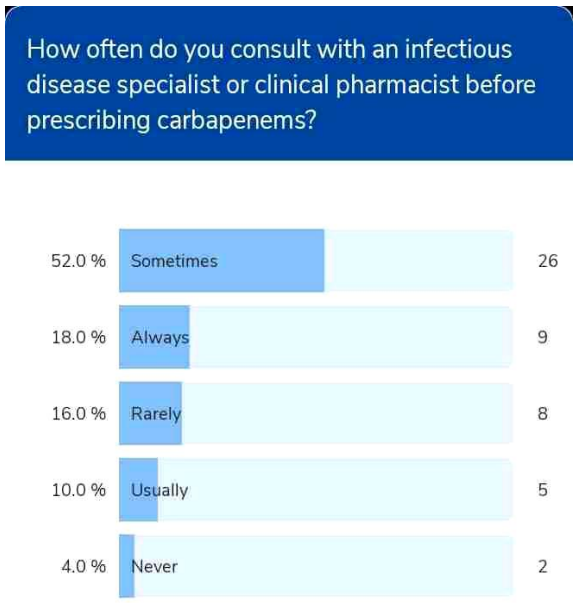

Figure: 13

Q. No: 14- Can you describe a situation where the use of carbapenem antibiotics significantly impacted the patient's outcome?

Received Answer:

1. Carbapenem management can drastically improve patients' survival rates in critical care.
2. Improve
3. Significant reduction in mortality rate.

4. Recently a patient with severe pyelonephritis with severe shock, dual **vasopressors**, lactate 70, severe acidosis got improved with meropenem 1g 8th hourly in 2 dajys where shock resolved lactate dropped, cultures grew *E.coli ESBL*.

5. When a patient in a complicated blood stream infection caused by an *E.coli ESBL* the choice is carbapenem, in that cases we have a good outcome. Or a patient suspected CNS infection like meningitis with post a neuro-surgery culture positive Gram-negative bacteria use of carbapenem.

6. Not using routinely

7. I often encountered MDR-gram negative sepsis in my patients. Carbapenem has significantly reduced mortality and hospital stay in majority of population

8. In complicated UTI and septic shock.

9. In severe UTI

10. Patient had sepsis due to non healing diabetic foot ulcer

11. Multidrug-resistant infections

12. Bacterial sepsis

13. RTA with open fracture

14. Patients with septicemia caused by MDR *Klebsiella pneumonia* responded well to meropenem, reducing mortility rates.

15. Meropenem is used to treat osteomyelitis, significantly improved outcomes against resistant pathogens like MRSA and *Pseudomonas aeruginosa*.

16. Sepsis due to a complicated UTI from Carbapenem resistant bacteria.This condition is treated with **imipenem+cilastatin** leads to rapid stabilization of the patient's condition and significant reduction in mortality risk.

17. It is used to treat the patient with prophylaxis of colorectal surgery.

18. Meropenem crosses BBB and highly effective to treat bacterial meningitis which improved neurological outcomes.

19. Decreased mortality in the treatment of severe infections caused during the surgery.

20. In cases of septic shock, complicated meningitis.

Q.NO: 15- Any other special comments on carbapenem antibiotics?

Received Answer:

1. Carbapenem resistance, mainly among Gram-negative pathogens, is an ongoing public-health problem of global dimensions. This type of antimicrobial resistance, especially when mediated by transferable carbapenemase-encoding genes, is spreading rapidly causing serious outbreaks and dramatically limiting treatment options.

2. Excellent antibiotics for ESBL infection, but resistant to it are rapidly developing specially in hospital acquired infections.

3. Misuse and overuse of carbapenem and it may be always consult by ID physician / ID pharmacist and should be monitor.

4. Septic shock patients are treated with carbapenem antibiotics (major antibiotic).

5. Therapy should always be preceded by culture and sensitivity. Full course of therapy, irrespective of marginal improvement in symptoms.

6. Very effective.
7. More rigid policies and regulations advised
8. Excellent activity against *streptococci, enterococci, staphylococci, listeria. Enterobacteriaceae, and pseudomonas.*
9. Higher antibiotics as of now.
10. It is a major antibiotic used for severe septic shock.
11. Carbapenem antibiotics are most effective against both gram positive and negative bacteria.
12. People who have an allergic reaction to penicillin are advised not to take carbapenem.
13. Therapy should be started only after culture and sensitivity test.
14. Patients should be advised to follow full course of antibiotic therapy.
15. May cause allergies in some patients.
16. More expensive compared to other antibiotics.
17. High cost of therapy.
18. Effective empirical monotherapy for conditions with complicated UTI. Community-acquired pneumoniae complicated intra-abdominal infection.
19. These are expensive and have short half-life.
20. A light at the end of the tunnel, when used ethically.
21. Rarely prescribed

The following table indicates the evidence based framed guidelines based on the answers obtained and drug databases.

Table 3:

CATEGORY	Renal dose adjustment	Pregnancy category	Types of infections treated	Adverse Drug Reactions
Meropenem	Required for CrCl < 50 mL/min	Category B	Intra-abdominal infections, bacterial meningitis, skin infections	Seizures, hypersensitivity reactions, pseudo membranous colitis, anaphylaxis
Imipenem	Required for CrCl < 90 mL/min	Category C	Respiratory tract infections, urinary tract infections, intra-abdominal infections	Pseudo membranous colitis, anaphylaxis, hypotension, seizures(higher risk), dizziness, pruritus, phlebitis, urticaria and somnolence.
Doripenem	Required for CrCl < 50 mL/min	Category B	Complicated urinary tract infections, intra-abdominal infections	Phlebitis, seizures, hypersensitivity reactions, pseudo membranous colitis, anaphylaxis
Ertapenem	Required for CrCl < 30 mL/min	Category B	Community-acquired pneumonia, intra-abdominal infections, skin infections	Seizures, leucopenia, thrombocytopenia, anaphylaxis

Table 4:

DRUGS → INFECTIONS ↓	MEROPENEM	IMIPENEM/ CILASTATIN	DORIPENEM	ERTAPENEM
Severe bacterial infections	1-2 g IV every 8 hours	500 mg to 1 g IV every 6 hours	500 mg IV every 8 hours	1 g IV once daily
Multi-drug resistant infection	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Not recommended due to potential for resistance selection
Nosocomial infection	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Not recommended due to potential for resistance selection
Complicated intra-abdominal infections	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Not recommended due to potential for resistance selection
Bacteremia/ sepsis	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Refer to susceptibility testing for specific recommendations	Not recommended due to potential for resistance selection
Complicated skin & Soft tissue infection	1-2 g IV every 8 hours	500 mg IV every 6 hours	500 mg IV every 8 hours	Not recommended due to broader spectrum agents being more appropriate
CNS infections	Refer to specialist for specific recommendations	Refer to specialist for specific recommendations	Refer to specialist for specific recommendations	Not recommended due to limited CNS penetration
Complicated UTIs	500 mg IV every 8 hours	Not recommended due to insufficient data	500 mg IV every 8 hours	Can be considered based on susceptibility

Table 5:

DRUGS → INFECTIONS ↓	IMIPENEM/ CILASTATIN	MEROPENEM	DORIPENEM	ERTAPENEM
Paediatric dose	15-25 mg/kg IV every 6 hours, max 1g/dose.	20-40 mg/kg IV every 8 hours, max 2g/dose.	10-20 mg/kg IV every 8 hours.	15 mg/kg IV every 12 hours (children >3 months).
Geriatric dose	Dose adjustment based on renal function.	Dose adjustment based on renal function.	Dose adjustment may be required depending on renal function.	Dose adjustment may be necessary.

Table 6:

Q.no	Question	Expected Answer	Answer from Collected data
1.	Frequency of prescribing / administering carbapenem antibiotics in a day. ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ More than 5	3 (TID)	1
2.	Common indications for carbapenem use ☐Severe bacterial infections ☐Multi-drug resistant infections ☐Nosocomial infections ☐Intra-abdominal infections ☐Bacteremia/Sepsis ☐Complicated skin & soft tissue infections ☐CNS infections ☐Complicated UTIs	Intra-abdominal infection	Severe bacterial infections
3.	Specific carbapenem agents used ☐ Meropenem ☐ Imipenem ☐ Ertapenem ☐ Doripenem ☐ Others	Meropenem	Meropenem
4.	In your hospital setting which combination of carbapenem antibiotics are used?	Meropenem+vaborbactam Imipenem+cilastatin+ relebactam	Meropenem + colistin Meropenem+vaborbactam Imipenem+cilastatin
5.	Do you adjust dosing for special populations? ☐ Yes ☐ No	Yes	Yes
6.	Preferred route of administration: ☐ IV ☐ IM ☐ Others	I.V	I.V
7.	What is the curation rate of infection people with carbapenem antibiotic? ☐ Complete improvement ☐ Partial improvement ☐ No improvement	Partial improvement	Complete improvement
8.	What is the recommended duration for carbapenem therapy? ☐ <5 days ☐ 5-7 days ☐ 7-10 days ☐ >10days	7 days	5-7 days
9.	Is this carbapenem antibiotic, prescribed for the following conditions? a) Seizure patients (Yes/No) b) Pregnant women (Yes/No) c) Children (Yes/No) d) Renal impairment (Yes/No)	a) No b) Yes c) Yes d) Yes	a) No b) No c) No d) Yes
10.	Challenges encountered in carbapenem use ☐ Drug resistance ☐ High cost of therapy ☐ Adverse effects ☐ Drug interactions ☐ Limited availability ☐ Others	Drug resistance	High cost of therapy
11.	How does resistance to carbapenems affect your clinical practice? ☐ Limited treatment options ☐ Prolongs patient hospital stay ☐ Leads to use of more toxic or less effective alternatives ☐ Increases treatment costs	Limited treatment options	Increases treatment cost & Prolongs patient hospital stay

	☐ Others		
12.	Does your hospital have specific guidelines for carbapenem use? ☐ Yes ☐ No ☐ Not sure	Yes	Yes
13.	How often do you consult with an infectious disease specialist or clinical pharmacist before prescribing carbapenems? ☐ Always ☐ Often ☐ Sometimes ☐ Rarely ☐ Never	Always	Sometimes
14.	Can you describe a situation where the use of carbapenem antibiotics significantly impacted the patient's outcome?	No comparative answer	
15.	Any other special comments on carbapenem antibiotics.	No comparative answer	

CONCLUSION:

This study emphasizes the important role of antibiotics play in treating infections, especially carbapenems, which are a strong group of beta-lactam antibiotics. Drugs like imipenem, meropenem, doripenem, and ertapenem are crucial for fighting severe infections that don't respond to other treatments.

However, we face a significant challenge with drug resistance, where bacteria evolve mechanisms to withstand the effects of even the most powerful antibiotics, including carbapenems. This alarming trend highlights the need for careful use of antibiotics and ongoing research to develop new strategies and treatments to combat resistant infections effectively.

It's also important to understand how these antibiotics work in the body, their possible side effects, and when to use each one to get the best results for patients. New drugs like tebipenem, biapenem, faropenem, and sulopenem are being developed to help fight infections that are hard to treat, showing that there is still hope in the fight against resistant bacteria.

In summary, while carbapenems are vital for treating serious bacterial infections, we must continue to address the problem of antibiotic resistance by using these drugs wisely and supporting research for better treatments. Additionally, implementing Antibiotic Stewardship Programs (ASPs) within healthcare settings is essential for optimizing antibiotic use, reducing resistance, and improving patient outcomes. By promoting responsible prescribing practices and educating both healthcare providers and patients, ASPs play a critical role in preserving the effectiveness of antibiotics for future generations.

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