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Original Research Article

Expert perspectives on the clinical use of meropenem monotherapy in the management of various antibiotic-resistant pathogens in Indian settings

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ABSTRACT

Background: To gather expert perspectives on the clinical use of meropenem monotherapy in managing multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) pathogens in Indian settings.
Methods: This cross-sectional study used a 20-item questionnaire to gather clinician opinions on prescription practices, clinical observations, and preferences regarding meropenem monotherapy. Descriptive statistics were employed to analyze the responses, presenting frequencies as percentages.
Results: A total of 353 clinicians participated in this study, with 37% reporting a 6-10% prevalence of MDR, XDR, and PDR pathogens in their practice. Complicated intra-abdominal infections (cIAIs) were the most common conditions treated with meropenem, reported by 54.96% of respondents. The majority (91.5%) of the respondents preferred combination therapy for resistant infections, with tigecycline (54%) and colistin (33.43%) being common choices. Key pathogens included Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii, Escherichia coli, and Staphylococcus aureus. Most participants (58%) favored administering 1g of IV meropenem in 2 to 3 divided doses. Bloodstream infections, meningitis, and ventilator-associated pneumonia (VAP) were noted as primary indications for meropenem use. Additionally, 68% of participants stated meropenem was the most prescribed antibiotic for complicated urinary tract infections (cUTIs), while 77% indicated it as the preferred treatment for Gram-negative MDR pathogens.
Conclusion: Meropenem remains a critical option for treating MDR, XDR, and PDR infections in India, particularly in combination with tigecycline or colistin. Clinicians preferred its use in cIAIs and VAP, especially in elderly patients. The findings highlight the importance of continuously monitoring resistance patterns to optimize treatment strategies.

Keywords: Meropenem, Antibiotic resistance, Meningitis, Complicated urinary tract infections, Multidrug-resistant pathogens

INTRODUCTION

Antibiotic resistance has long been recognized as a critical global problem, significantly impacting morbidity, mortality, and economic costs. The extensive literature documents the negative consequences, including longer and more expensive hospital stays.[1] Globally, antibiotic-resistant infections contribute to approximately 700,000 deaths annually due to multidrug-resistant (MDR) infections.[2] The centers for disease control and prevention has reported a rapid increase in infections caused by antibiotic-resistant bacteria, emphasizing the urgency of addressing this public health crisis.[3] The evidence suggests that the attributable cost of resistant infections per patient episode varies from US $2,371.4 to+US $29,289.1. On average, these infections

extend the length of stay by 7.4 days. Additionally, the odds ratio for mortality associated with resistant infections is 1.844, and the odds ratio for readmission is 1.492.[4] Furthermore, India ranks highest globally in human antibiotic consumption, a major contributor to antimicrobial resistance, with a usage rate of 10.7 units per person.[5] MDR is defined as resistance to at least one drug in three or more antimicrobial categories. Extensively drug-resistant (XDR) bacteria are resistant to all but one or two classes, while pan-drug-resistant (PDR) bacteria exhibit resistance to all available antimicrobial agents.[6]

Meropenem, a broad-spectrum β-lactam antibiotic, plays a key role in treating severe infections, particularly those caused by MDR bacteria. As a member of the carbapenem class, meropenem is highly effective against gram-negative and gram-positive bacteria, including resistant strains. It works by inhibiting bacterial cell wall synthesis, a mechanism shared by other β-lactam antibiotics, making it a powerful option in managing infections where other antibiotics fail.7 It is reported to be effective against resistant strains of Pseudomonas aeruginosa, *Escherichia coli*, and *Klebsiella pneumoniae*.[8]

The survey aims to gather clinicians' opinions on the use of meropenem monotherapy for managing antibiotic-resistant pathogens, specifically MDR, XDR, and PDR, in Indian settings. The findings will support clinical decision-making and enhance understanding of trends in the clinical application of meropenem for treating these resistant infections.

METHODS

We carried out a cross-sectional, multiple-response questionnaire-based study among clinicians specialized in managing antibiotic resistance, specifically MDR, XDR, and PDR pathogens in the major Indian cities from June 2023 to December 2023.

Convenience sampling method was adopted where an invitation was sent to leading clinicians who are expertise in managing infections in the month of March 2023 for participation in this Indian survey. About 353 clinicians from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provided necessary data were included. Clinicians were provided the option to skip any questions they did not wish to answer and were instructed to complete the questionnaire independently, without consulting their colleagues. Prior to the initiation of the study, written informed consent was obtained from all study participants.

The questionnaire booklet titled FAME (Facts on Meropenem: An Expert Opinion Study) study was sent to the clinicians who were interested to participate. The FAME study questionnaire consists of 20 questions focused on current prescription practices, clinical observations, and preferences regarding meropenem monotherapy in managing antibiotic resistance. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

Statistical analysis

Descriptive statistics were employed for data analysis with categorical variables presented as percentages. The frequency of each variable and corresponding percentage was calculated to illustrate its distribution. Graphs and pie charts were created using Microsoft Excel 2013 (version 16.0.13901.20400) to visually depict the distribution of categorical variables.

RESULTS

Out of 353 participants, 37% reported a 6-10% prevalence of antibiotic-resistant pathogens such as MDR, XDR, and PDR in clinical practice. More than half of the respondents (54.96%) stated that complicated intra-abdominal infections (cIAIs) are the most common conditions for meropenem prescription (Table 1). Approximately 51% reported that elderly patients are most affected by MDR, XDR, and PDR pathogens (Table 2). About 46% identified Pseudomonas aeruginosa, *Klebsiella pneumoniae*, *A. baumannii*, *E. coli*, and Staphylococcus aureus as the common strains of MDR, XDR, and PDR pathogens in their practice. Most participants (91.5%) indicated that combination antibiotic therapy is the preferred treatment for MDR, XDR, and PDR infections (Table 3). Around 33% of the clinicians noted that 25-50% of patients require combination therapy for these infections, and 54% preferred tigecycline in combination with IV meropenem for treatment (Table 4). About 80% of the participants identified bloodstream infections, meningitis, and VAP as key indications for meropenem use (Figure 1).

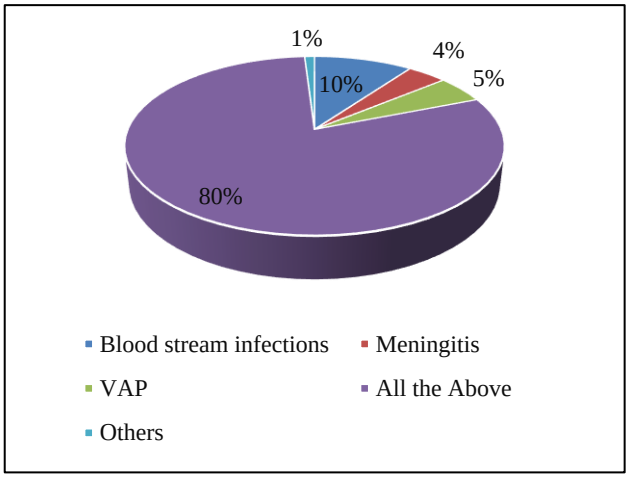

Figure 1: Distribution of response to indications for the use of meropenem in clinical practice.

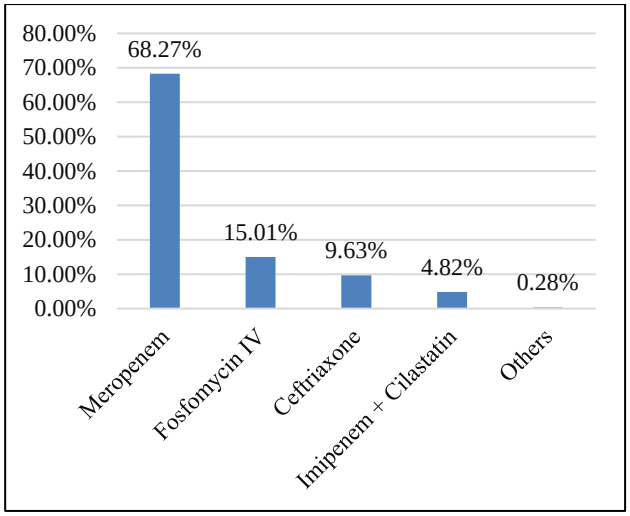

Figure 2: Distribution of response on most prescribed antibiotics for cUTIs.

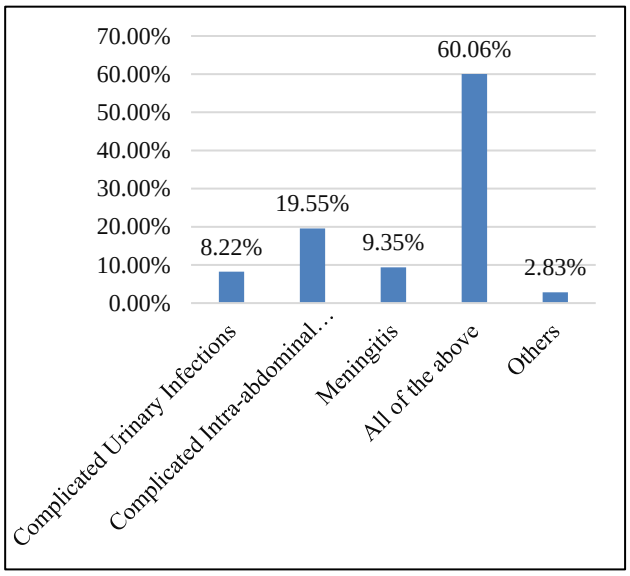

Figure 3: Distribution of response to indications for the use of meropenem+sulbactam in clinical practice.

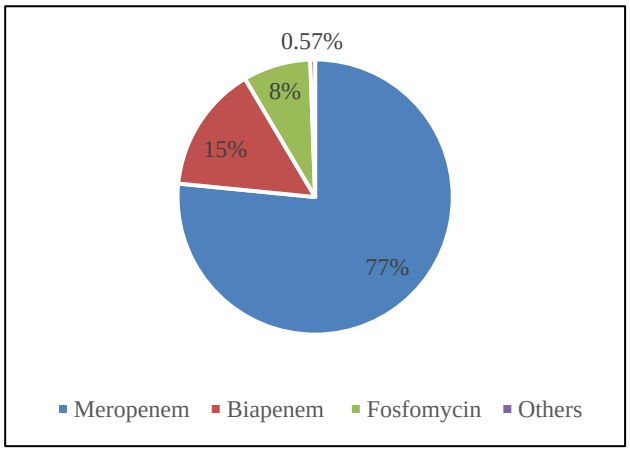

Figure 4: Distribution of response to preferred drug of choice for Gram-negative MDR pathogens.

Approximately 58% of respondents reported that the preferred dosage of IV meropenem is 1 g in 2 to 3 divided doses for treating MDR, XDR, and PDR infections. Likewise, 58% noted that IV meropenem, when combined with beta-lactams, aminoglycosides, tigecycline, colistin, and other agents, achieves an 80% clinical cure rate.

Around 43% of participants reported handling 6-10 sepsis cases monthly, while 44% preferred tigecycline combinations for treating carbapenem-resistant Enterobacteriaceae (CRE). Additionally, 45% reported managing 6-10 cases of complicated urinary tract infections (cUTIs) weekly, with 68% stating that meropenem is the most prescribed antibiotic for cUTIs (Figure 2).

Half of the participants (50.99%) reported meropenem as the preferred drug for nosocomial pneumonia. Around 33% stated that bacterial meningitis cases are most frequently seen in middle-aged patients. Approximately 44% of participants reported that 11-20% of patients have cIAIs, and 60% noted that cUTIs, cIAIs, and meningitis are key indications for meropenem+sulbactam use (Figure 3). Finally, 77% reported that meropenem was the preferred drug for treating Gram-negative MDR pathogens (Figure 4).

Table 1: Distribution of response to most common conditions for meropenem prescription in clinical practice (n=353).

Indications	Response rate (%)
Complicated skin and its infection	8.5
Bacterial meningitis >3 months	25.5
Complicated intra-abdominal infection	54.96
All of the above	1.13
Others	9.92

Table 2: Distribution of response to MDR, XDR, and PDR pathogens by age group in clinical practice (n=353).

Subset of population	Response rate (%)
Children	8.5
Young adults	7.37
Middle-aged	32.29
Elderly	51.84

Table 3: Distribution of response to preferred lines of treatment for MDR, XDR, and PDR infections in clinical practice (n=353).

Treatment choice	Response rate (%)
Monotherapy	8.22
Combination of antibiotics therapy	91.5
Others	0.28

Table 4: Distribution of response to preferred antibiotics for combination therapy with IV meropenem in clinical practice (n=353).

Antibiotic choice	Response rate (%)
Fosfomycin	9.07
Colistin	54.39
Tigecycline	33.43
Others	3.12

DISCUSSION

The survey provided valuable insights into real-world practices regarding meropenem monotherapy. The findings highlight meropenem's role in treating severe infections, with clinicians favoring its use in combination therapies for MDR, XDR, and PDR pathogens, especially in elderly patients. More than half of the current survey respondents reported cIAIs as the most common condition for meropenem prescription.

This aligns with findings from Lowe et al, who concluded that extensive comparative clinical data demonstrate meropenem to be an effective option for empirical monotherapy in treating moderate to severe intra-abdominal infections.[9] Similarly, Geroulanos found that meropenem monotherapy was equally effective and well-tolerated as the combination therapy of imipenem/ cilastatin for these conditions. The survey further emphasized the critical role of meropenem in treating severe infections, with clinicians favoring its use in combination therapies for MDR, XDR, and PDR pathogens, particularly in elderly patients, due to its reliable efficacy and safety profile.[10]

Antibiotic resistance presents a major challenge in the elderly due to higher comorbidity prevalence, age-related immune system decline, and increased exposure to pathogens from frequent hospitalizations or living in residential care facilities.[11] The survey participants indicated that elderly patients are particularly affected by MDR, XDR, and PDR pathogens. This observation aligns with findings by Mohapatra et al, who noted that elderly patients hospitalized were at a high risk of infections caused by XDR and PDR bacteria.[12] Additionally, Denkinger et al. concluded that elderly patients significantly contribute to the influx of MDR organisms into hospital settings, further complicating treatment options in these environments.[13]

Most survey participants indicated that combination antibiotic therapy is the preferred approach for treating MDR, XDR, and PDR infections. This preference is supported by Umemura et al, who noted that combination therapies, such as pairing β-lactam antibiotics with β-lactamase inhibitors or using other antibiotic combinations, offer a therapeutic strategy to combat MDR bacteria. In recent years, treatment options have expanded with several combination drugs gaining approval in more countries, broadening the therapeutic choices against resistant infections.[14] Additionally, Schmid et al, found that combination antimicrobial therapy for MDR Gram-negative bacteria was more effective than monotherapy in reducing mortality.[15] Many of the respondents preferred tigecycline in combination with IV meropenem for treatment. Tsala et al, noted that the triple combination of meropenem, tigecycline, and colistin exhibited bactericidal activity in a dynamic model against highly resistant Klebsiella pneumoniae (CP-Kp) isolates. This effect was more significant when meropenem was administered via prolonged infusion and tigecycline was given at high doses.[16]

The majority of the participants identified bloodstream infections, meningitis, and VAP as key indications for meropenem use. Baldwin et al. noted that meropenem was not only well-tolerated but also offered the advantage of flexible administration, either as an intravenous bolus or infusion. Its low risk of inducing seizures makes it particularly suitable for treating bacterial meningitis, a condition where seizure risk can complicate treatment. Moreover, meropenem stands out as the only carbapenem approved specifically for bacterial meningitis, further solidifying its role in managing this severe infection. In addition to meningitis, its broad spectrum of activity against Gram-negative organisms makes it a critical choice for treating VAP and bloodstream infections, especially in patients at high risk for MDR bacterial infections.[17]

Many of the respondents stated that meropenem was the most prescribed antibiotic for cUTIs. Shohita Dhill noted that IV meropenem/vaborbactam was the first carbapenem/β-lactamase inhibitor combination to be approved in the USA for treating patients with cUTIs.18 More than half of the respondents noted that cUTIs, cIAIs and meningitis were key indications for the use of meropenem in combination with sulbactam. Baldwin et al. stated that meropenem was approved in the U.S for treating cIAIs, complicated skin and skin structure infections (cSSSIs), and bacterial meningitis in pediatric patients aged 3 months and older.

In most other countries, it was also approved for treating nosocomial pneumonia, cIAIs, septicemia, febrile neutropenia, cSSSIs, bacterial meningitis, cUTIs, obstetric and gynecological infections, pulmonary exacerbations in cystic fibrosis patients, and severe community-acquired pneumonia (CAP).[17]

Ko et al, concluded that the combination of meropenem and sulbactam showed stronger antimicrobial activity against *Acinetobacter baumannii* strain Ab-153 compared to using either meropenem or sulbactam alone. This enhanced efficacy was particularly significant given the rising prevalence of MDR infections in clinical settings.[19] Moreover, the combination of sulbactam and meropenem may be considered as an alternative treatment option for multi-resistant and extremely resistant bacteria, offering a potential lifeline in cases where standard therapies fail.[20]

Most of the respondents reported that meropenem was the preferred drug for treating gram-negative MDR pathogens. Fish emphasized that meropenem exhibits strong activity against a wide spectrum of bacteria, including numerous gram-positive and gram-negative pathogens, many of which were potentially resistant strains like Pseudomonas aeruginosa, as well as anaerobic organisms.[21] Bassetti et al, highlighted that ceftazidime-avibactam, imipenem-relebactam, and meropenem-vaborbactam exhibit strong activity against certain CRE particularly *Klebsiella pneumoniae* carbapenemase producers.[22]

The robust sample size of the survey strengthens its findings by providing a comprehensive view of clinician perspectives on meropenem use in India, covering a wide range of prescription practices and preferences. However, limitations such as potential biases in self-reported data and recall bias impair the objectivity of the results. The lack of direct patient data also limits the ability to correlate clinical outcomes with prescribed therapies. Despite these limitations, the study underscores the need for ongoing research and updated treatment guidelines to combat rising antibiotic resistance. Future research should include patient data to better assess clinical outcomes and inform more actionable strategies for managing resistant infections.

CONCLUSION

This study highlighted key insights into meropenem prescribing patterns in India, with cIAIs being the primary indication, especially in elderly patients. Combination therapy, particularly tigecycline with IV meropenem, was preferred for managing MDR pathogens. Bloodstream infections, meningitis, and ventilator-associated pneumonia were also identified as key indications for meropenem use. These findings emphasized the crucial role of meropenem in treating severe infections caused by resistant organisms.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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