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Expert Perspectives on the Diagnosis and Management of Multidrug-Resistant Gram-Negative Infections: Findings from a Cross-Sectional Survey of Indian Clinicians

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A B S T R A C T

To assess clinical practice patterns in the diagnosis and management of multidrug-resistant Gram-negative bacterial (MDR-GNB) infections among clinicians in India, including microbiological diagnosis, empirical antibiotic selection, antimicrobial stewardship practices, usage of ceftazidime + avibactam, and clinicians' perceptions of its efficacy, safety, and clinical outcomes. This nationwide, cross-sectional, questionnaire-based survey was conducted among practicing clinicians across India. A structured 23-item multiple-choice questionnaire evaluated microbiological diagnostic practices, empirical antibiotic selection, antimicrobial stewardship, prescribing patterns of ceftazidime + avibactam, and clinicians' perceptions of its efficacy, safety, and clinical outcomes. Participation was voluntary with written informed consent. Responses were analyzed descriptively and are presented as frequencies and percentages. Among the 94 clinicians who participated in the survey, approximately 64% identified *Klebsiella pneumoniae* as the most frequently encountered Gram-negative pathogen. About 54% of respondents reported urinary tract infections as the most common source of MDR infections. Most clinicians (90.43%) preferred blood, urine, or sputum cultures for the identification of MDR organisms. The majority (71.28%) preferred carbapenems as empirical therapy for suspected MDR infections. Compared with colistin-based regimens, approximately 70% considered ceftazidime + avibactam to provide superior efficacy and safety. More than half (51.06%) of clinicians agreed that ceftazidime + avibactam should be used as first-line therapy for confirmed *Klebsiella pneumoniae* carbapenemase (KPC)-producing carbapenem-resistant *Enterobacteriaceae* (CRE). Most respondents (60.64%) reported routinely monitoring patients for potential adverse effects or complications associated with ceftazidime + avibactam therapy. The survey highlights current clinical practice patterns in the management of MDR Gram-negative infections, emphasizing the predominance of *Klebsiella pneumoniae*, culture-guided diagnosis, and the use of carbapenems as empirical therapy. Clinicians perceived ceftazidime + avibactam as an effective and safe treatment option for CRE infections, supporting its growing role in antimicrobial stewardship and improving clinical outcomes.

Introduction

Multidrug-resistant Gram-negative bacterial (MDR-GNB) infections are a major global health concern, contributing substantially to morbidity, mortality, and healthcare costs.[1] Recent surveillance studies indicate that up to 40% of common bacterial infections in some regions are resistant to first-line antibiotics, with neonates, older adults, and immunocompromised individuals disproportionately affected. Furthermore, antimicrobial resistance (AMR)-related healthcare costs exceed USD 100 billion annually and are projected to rise to nearly USD 300 billion by 2030.[2] In India, MDR-GNB represent a significant cause of bloodstream infections. Surveillance data from September 2022 to June 2023 showed that Gram-negative bacteria accounted for 71.8%-80.0% of positive blood cultures, of which 27.1%–35.0% were MDR. The predominant MDR pathogens included *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter* spp., *Pseudomonas aeruginosa*, and *Enterobacter* spp., all of which are associated with high levels of AMR, morbidity, and mortality.[3]

The increasing prevalence of MDR Gram-negative pathogens has significantly limited the effectiveness of conventional antimicrobial agents, creating an urgent need for newer therapeutic options with activity against resistant organisms. Ceftazidime–avibactam, a combination of a third-generation cephalosporin and a non-β-lactam β-lactamase inhibitor, has emerged as an important treatment option for infections caused by carbapenem-resistant and other β-lactamase-producing Gram-negative bacteria. Ceftazidime exerts bactericidal activity by binding to penicillin-binding proteins and inhibiting bacterial cell wall synthesis, whereas avibactam inhibits class A, class C, and some class D β-lactamases, thereby protecting ceftazidime from enzymatic degradation and restoring its activity against resistant Gram-negative pathogens. Owing to its broad spectrum of activity and favourable clinical outcomes, ceftazidime–avibactam has been increasingly incorporated into antimicrobial stewardship strategies for the management of MDR Gram-negative infections.[4]

Despite growing evidence supporting the efficacy of ceftazidime–avibactam, variations in microbiological diagnostic approaches, empirical antibiotic selection, antimicrobial stewardship practices, and antibiotic usage patterns continue to influence the management of MDR Gram-negative infections in routine clinical practice. Therefore, the present survey aimed to evaluate current clinical practice patterns in the diagnosis and management of MDR-GNB infection among clinicians in India, with a particular focus on microbiological diagnosis, empirical antibiotic selection, antimicrobial stewardship practices, usage patterns of ceftazidime–avibactam, and clinicians' perceptions of its efficacy, safety, and clinical outcomes.

Materials and Methods

A cross-sectional study was carried out among practicing clinicians across India involved in the diagnosis and management of MDR-GNB infection across various clinical settings in India from June 2025 to December 2025. The study was performed in accordance with Bangalore Ethics, an Independent Ethics Committee (ECR/355/Indt/KA/2022), which was recognized by the Indian Regulatory Authority, the Drug Controller General of India.

Questionnaire

The questionnaire booklet titled PROCARE (Physician Response Over critical and Recurrent Infection) was sent to clinicians who were interested in participating in the study. A structured 23-item multiple-choice questionnaire was designed to capture current clinical practices in the diagnosis and management of MDR-GNB infection. The questionnaire collected information on the epidemiology and burden of MDR-GNB infections, commonly encountered pathogens, major sources of infection, patient demographics, in-hospital mortality, microbiological diagnostic approaches, culture and antimicrobial susceptibility testing practices, empirical antibiotic selection, and preferred treatment strategies for carbapenem-resistant *Enterobacteriaceae* (CRE). It further assessed antimicrobial stewardship practices, including antibiotic de-escalation, clinicians' perceptions of antimicrobial stewardship programs, familiarity with ceftazidime–avibactam, and prescribing patterns for hospital-acquired bacterial pneumonia, ventilator-associated bacterial pneumonia, complicated urinary tract infections, and complicated intra-abdominal infections (cIAIs).

Participants

A convenient sampling technique was used, and an invitation was sent to professionals across India based on their expertise and experience in treating MDR-GNB infection in the month of March 2025 for participation in

this Indian survey. About 94 clinicians from major cities of all Indian states, representing the geographical distribution, shared their willingness to participate and provide necessary data. Clinicians were instructed to complete the questionnaire independently without consulting colleagues. Written informed consent was obtained from each participant before the study began.

Statistical analysis

Survey responses were analysed using descriptive statistical methods. Categorical variables were summarized as frequencies and percentages. The findings were presented using tables and figures generated in Microsoft Excel.

Results and Discussion

A total of 94 clinicians participated in the survey. More than half (53.19%) of the respondents reported that 10–25% of their admitted patients had infections caused by MDR-GNB organisms. Approximately 64% of participants identified *Klebsiella pneumoniae* as the most frequently encountered Gram-negative pathogen (Table 1). About 54% of respondents reported urinary tract infections as the most common source of MDR infections (Table 2).

Around 55% of respondents indicated that patients aged 41–60 years were the age group most commonly affected by MDR infections. Approximately 41% of clinicians estimated an in-hospital mortality rate of 10–20% among patients with MDR-GNB infections. More than two-thirds (69.15%) reported always performing culture and antimicrobial susceptibility testing before initiating antibiotic therapy in suspected MDR infections. Most respondents (90.43%) preferred blood, urine, or sputum cultures for the identification of MDR organisms (Table 3).

Nearly two-thirds (61.70%) reported waiting 24–48 hours for antimicrobial susceptibility reports before modifying therapy. The majority (71.28%) of clinicians preferred carbapenems as empirical therapy for suspected MDR infections (Figure 1). About 49% of participants preferred colistin-based combination therapy for the treatment of CRE. Approximately 40% reported often de-escalating antibiotic therapy based on culture results. Most respondents (82.98%) believed that antimicrobial stewardship programs are effective in reducing MDR infections. Around half (53.19%) of the clinicians reported being very familiar with ceftazidime + avibactam and using it frequently. Approximately 60% preferred ceftazidime + avibactam in 11–25% of patients with hospital-acquired bacterial pneumonia or ventilator-associated bacterial pneumonia. Similarly, 43% prescribed the agent in 11–25% of patients with complicated urinary tract infections (cUTIs), while about 39% reported similar prescribing frequencies for patients with complicated intra-abdominal infections (cIAIs). Approximately 31% of respondents reported occasionally encountering resistance to ceftazidime + avibactam.

Compared with colistin-based regimens, 70% of respondents considered ceftazidime + avibactam to provide superior efficacy and safety (Table 4). Approximately 51% of clinicians agreed that ceftazidime + avibactam should be used as first-line therapy for confirmed *Klebsiella pneumoniae* carbapenemase (KPC)-producing CRE (Figure 2). The majority (60.64%) of respondents reported regularly monitoring patients for potential adverse effects or complications associated with ceftazidime + avibactam.

Most respondents (93.62%) had not encountered adverse drug reactions associated with ceftazidime + avibactam. Based on the 5-point Global Improvement Scale, 55% of respondents reported marked improvement in clinical outcomes following treatment with ceftazidime + avibactam (Figure 3).

As observed in the current survey, many participants identified *Klebsiella pneumoniae* as the most frequently encountered Gram-negative pathogen. This finding reflects the growing burden of *K. pneumoniae* in healthcare-associated infections, particularly among hospitalized and critically ill patients. These findings are consistent with previous reports. Wattal *et al.,* reported that Gram-negative bacteria, particularly *Klebsiella pneumoniae*, were among the most frequently isolated pathogens causing bloodstream infections and were commonly associated with MDR, highlighting their high prevalence in critically ill pediatric patients.[5] Similarly, Shao *et al.,* demonstrated that *Klebsiella pneumoniae* was one of the predominant Gram-negative pathogens isolated from bloodstream infections in pediatric intensive care units and exhibited high rates of extended-spectrum β-lactamase (ESBL) production and AMR, underscoring its important role in severe pediatric infections.[6]

More than half of the respondents identified urinary tract

infections as the most common source of MDR infections. McMahony *et al.,* reported that MDR organisms are increasingly responsible for pediatric urinary tract infections worldwide, with ESBL-producing *Enterobacterales* and other resistant pathogens representing a major cause of MDR UTIs, particularly among children with prior antibiotic exposure, hospitalization, or underlying urinary tract abnormalities.[7] Similarly, Bryce *et al.,* in a systematic review of 58 studies involving 77,783 pediatric urinary isolates, demonstrated a high prevalence of AMR among childhood urinary tract infections, particularly in non-Organisation for Economic Co-operation and Development countries. The study further showed that previous antibiotic exposure was strongly associated with an increased risk of resistant urinary pathogens.[8]

Most clinicians preferred blood, urine, or sputum cultures as the primary diagnostic tools for identifying MDR organisms. This finding is consistent with current clinical recommendations. Miller *et al.,* in the Infectious Diseases Society of America (IDSA) and American Society for Microbiology (ASM) guidelines, recommend obtaining appropriate clinical specimens, including blood, urine, respiratory secretions (sputum or endotracheal aspirates), and other site-specific cultures, for the microbiological diagnosis of bacterial infections.

They further emphasize that culture and antimicrobial susceptibility testing remain the gold standard for pathogen identification and detection of AMR, enabling targeted antimicrobial therapy.[9] Similarly, Kalil *et al.,* in the ATS/IDSA guidelines for hospital-acquired and ventilator-associated pneumonia, recommend obtaining respiratory secretion and blood cultures to identify causative pathogens, including MDR organisms, and to facilitate antimicrobial de-escalation.[10] Furthermore, the Indian Council of Medical Research (ICMR) advocates obtaining appropriate microbiological cultures before initiating antibiotic therapy whenever feasible to guide antimicrobial selection and support antimicrobial stewardship.[11]

The majority of clinicians preferred carbapenems as empirical therapy for suspected MDR infections. This finding is consistent with current clinical recommendations. The IDSA recommends carbapenems, including meropenem, imipenem-cilastatin, and ertapenem, as the preferred empirical and definitive therapy for patients at high risk of infections caused by ESBL-producing *Enterobacterales*, particularly in severe infections, until antimicrobial susceptibility results become available.[12] Similarly, Weiss *et al.,* in the *Surviving Sepsis Campaign* guidelines, recommend the early initiation of broad-spectrum empirical antibiotics in children with septic shock, with antimicrobial selection guided by patient-specific risk factors for resistant pathogens. The guidelines further support the use of carbapenem-containing regimens as appropriate empirical therapy in children at high risk of MDR Gram-negative infections, followed by de-escalation based on culture and susceptibility findings.[13]

Compared with colistin-based regimens, many respondents considered ceftazidime–avibactam to provide superior efficacy and safety. In addition, more than half of the clinicians agreed that ceftazidime–avibactam should be used as first-line therapy for confirmed KPC-producing CRE. These findings reflect the increasing acceptance of ceftazidime–avibactam as a preferred treatment option for CRE infections in routine clinical practice. Van Duin *et al.,* demonstrated that patients with CRE infections treated with ceftazidime-avibactam had significantly lower 30-day mortality, better overall clinical outcomes, and a more favourable benefit-risk profile than those receiving colistin-based therapy.[14] Similarly, Yang *et al.,* in a systematic review and meta-analysis, reported that ceftazidime-avibactam was associated with lower 30-day mortality, higher clinical success, and significantly reduced nephrotoxicity compared with polymyxin/colistin-based regimens for the treatment of carbapenem-resistant *Enterobacterales* infections.[15]

The survey findings are also consistent with current international treatment guidelines. The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) recommends newer β-lactam/β-lactamase inhibitor combinations, including ceftazidime–avibactam, as first-line targeted therapy for infections caused by KPC-producing CRE.[16] Likewise, the National Institute for Health and Care Excellence (NICE) recommends ceftazidime–avibactam for severe drug-resistant Gram-negative infections when susceptibility testing confirms activity and appropriate alternative agents are unavailable. The guideline also highlights its role in the management of MDR infections, including those caused by OXA-48-producing *Enterobacterales*, while emphasizing microbiology-guided therapy and antimicrobial stewardship to optimize clinical outcomes.[17]

Table.1 Distribution of responses on the most frequently encountered Gram-negative pathogens

Pathogens	Response rate (n = 94)
Klebsiella pneumoniae	63.83%
Pseudomonas aeruginosa	6.38%
Acinetobacter baumannii	2.13%
All of the above	27.66%

Table.2 Distribution of responses on the most common sources of MDR infections

Source	Response rate (n = 94)
Urinary tract infections	54.26%
Hospital-acquired pneumonia	23.4%
Intra-abdominal infections	1.06%
All of the above	21.28%

Table.3 Distribution of responses on the most frequently used diagnostic tools for identifying MDR organisms

Diagnostic tool	Response rate (n = 94)
Blood/urine/sputum cultures	90.43%
Molecular testing (PCR GeneXpert)	1.06%
All of the above	8.51%

Table.4 Distribution of responses comparing ceftazidime + avibactam with colistin-based regimens.

Comparison	Response rate (n = 94)
Better efficacy and safety	70.21%
Similar efficacy but better safety	22.34%
Similar efficacy and safety	4.26%
Less effective but better tolerated	2.13%
Not comparable	1.06%

Figure.1 Distribution of responses on the preferred class of antibiotics used for empirical therapy in suspected MDR infections

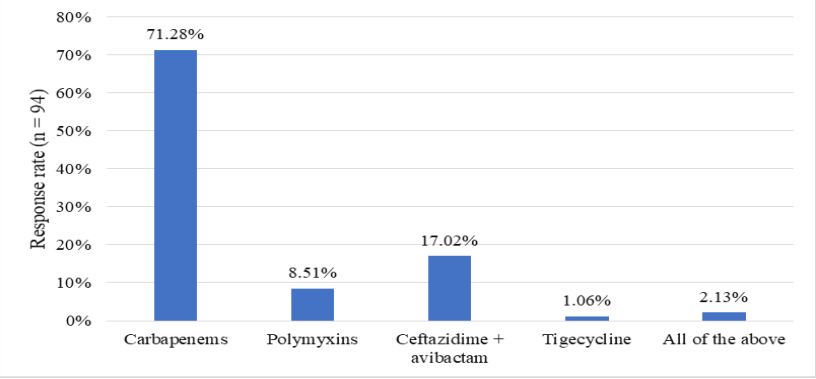


Figure.2 Distribution of responses on the use of ceftazidime + avibactam as first-line therapy for confirmed KPC-producing CRE.

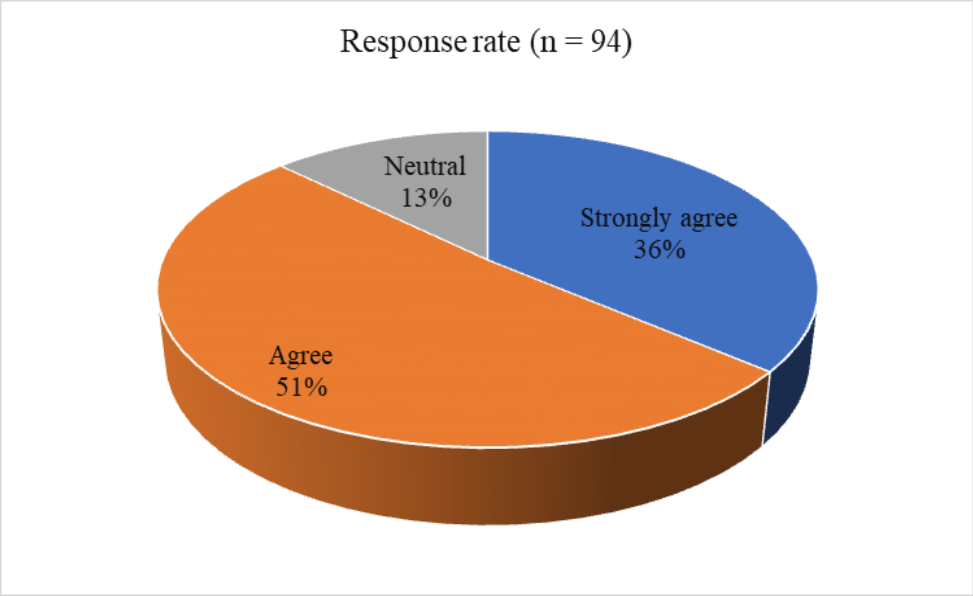
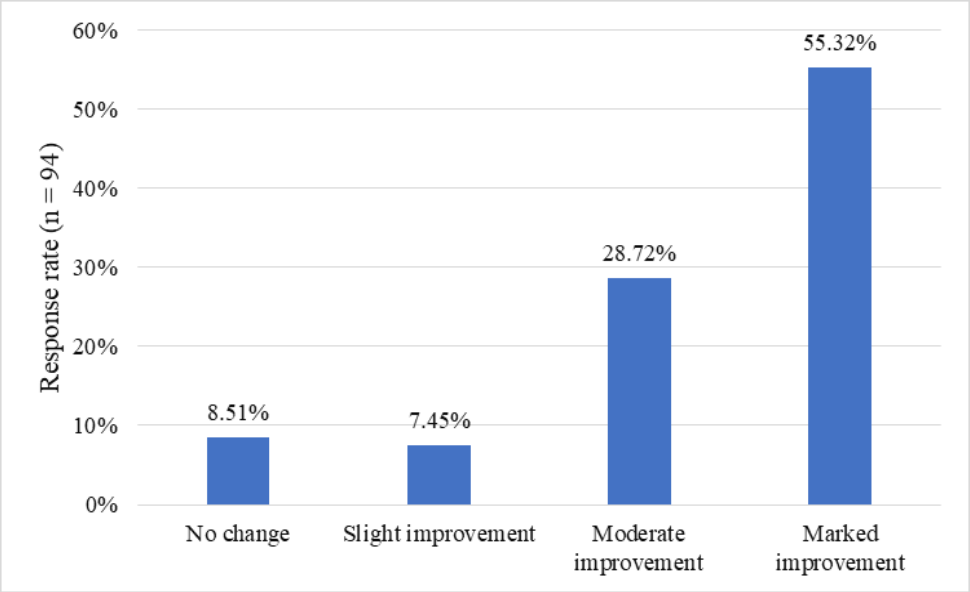


Figure.3 Distribution of responses on rating clinical outcomes with ceftazidime + avibactam based on a 5-point global improvement scale



Many respondents advised against the routine use of colistin when active newer β-lactam/β-lactamase inhibitor agents are available because of their superior efficacy and lower toxicity. This finding is consistent with current guideline recommendations. Tamma *et al.,* in the IDSA guidance, recommend newer β-lactam/β-lactamase inhibitor agents, including ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-cilastatin-relebactam, over polymyxin-based regimens for susceptible MDR gram-negative infections.

The guidance further advises against the routine use of polymyxins, including colistin, because of their inferior clinical outcomes and significant risk of nephrotoxicity.[12] Similarly, the European Society of Clinical Microbiology and Infectious Diseases

(ESCMID) recommends ceftazidime-avibactam and other newer β-lactam/β-lactamase inhibitor combinations as first-line therapy for susceptible CRE infections and discourages the routine use of colistin owing to its greater toxicity and comparatively lower efficacy.[16]

The majority of respondents reported regularly monitoring patients for potential adverse effects or complications associated with ceftazidime-avibactam therapy. This finding is consistent with previous studies. Shields *et al.,* reported that ceftazidime-avibactam was generally well tolerated but emphasized the importance of close clinical and microbiological monitoring during therapy to detect treatment failure, adverse events, and the emergence of AMR, particularly during prolonged treatment.[18]

Similarly, Duin *et al.,* demonstrated that although ceftazidime-avibactam was associated with significantly fewer adverse events, particularly nephrotoxicity, than colistin-based therapy, routine monitoring of renal function and clinical response remained an integral component of patient management throughout treatment.[14]

Based on the 5-point Global Improvement Scale, more than half of the respondents reported marked improvement in clinical outcomes following treatment with ceftazidime-avibactam. This finding is supported by previous studies. Duin *et al.,* demonstrated that ceftazidime-avibactam was associated with significantly lower 30-day mortality, higher clinical success, better overall clinical outcomes, and reduced nephrotoxicity compared with colistin-based therapy in patients with CRE infections.[14] Similarly, Jorgensen *et al.,* reported clinical cure rates exceeding 70–80%, high microbiological eradication rates, improved survival among patients with CRE infections, and a low incidence of treatment-related adverse events, supporting the favorable clinical efficacy and safety profile of ceftazidime-avibactam.[19]

The present survey provides valuable insights into current clinical practice patterns in the diagnosis and management of MDR Gram-negative infections among clinicians across India, highlighting contemporary approaches to microbiological diagnosis, empirical antibiotic selection, antimicrobial stewardship practices, and the use of ceftazidime–avibactam in routine clinical practice.

However, the study has certain limitations. The findings are based on self-reported responses and are therefore subject to recall and reporting bias. Additionally, variations in microbiological diagnostic approaches, antimicrobial stewardship implementation, and treatment practices across institutions and geographic regions may limit the generalizability of the findings. Further prospective, multicentre studies incorporating patient-level clinical and microbiological outcomes are needed to validate these observations.

The survey demonstrates that clinicians strongly support culture-guided diagnosis and antimicrobial stewardship in the management of MDR Gram-negative infections, with carbapenems remaining the preferred empirical therapy. Ceftazidime–avibactam is perceived as an effective and well-tolerated treatment option, particularly for CRE infections, with most clinicians endorsing its use as first-line therapy for confirmed KPC-producing CRE.

These findings highlight the growing clinical acceptance of ceftazidime–avibactam and reinforce its role in optimizing the management of MDR Gram-negative infections while supporting antimicrobial stewardship.

Author Contributions

S. Manjula: Investigation, formal analysis, writing—original draft. M. Krishna Kumar: Validation, methodology, writing—reviewing.

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Conflict of Interest

The authors are employees of Micro Labs Limited. The study was designed and conducted as part of a scientific initiative. The authors declare that no undue influence was exerted on data collection, analysis, or interpretation.

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interpretation of results.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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