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MICROBIOLOGICAL PROFILE OF MULTIDRUG-RESISTANT ORGANISMS IN A TERTIARY CARE HOSPITAL AND IN VITRO ACTIVITY OF NEWER ANTIBIOTICS AGAINST CLINICAL ISOLATES

Clinical Microbiology

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ABSTRACT

Antimicrobial resistance (AMR) represents a growing global health crisis. Multidrug-resistant organisms (MDROs) increasingly compromise the efficacy of standard antibiotic regimens, necessitating rigorous local surveillance and evaluation of newer therapeutic agents.The Objective of this study is to determine the microbiological profile of MDROs isolated from clinical samples in a tertiary care hospital and to evaluate the in vitro activity of newer antimicrobial agents — tigecycline, teicoplanin, quinupristin–dalfopristin, cefiderocol, and ceftazidime–avibactam — against them. A prospective cohort study was conducted over one and a half years at the Department of Microbiology, Government Medical College, Amritsar. A total of 200 non-duplicate MDRO isolates from hospitalized patients were analyzed. Antimicrobial susceptibility testing was performed using Kirby–Bauer disk diffusion and E-test (epsilometer strip) methods per CLSI guidelines. Resistance mechanisms (ESBL, AmpC, carbapenemase) were assessed phenotypically. Gram-negative bacilli predominated (64%), with Escherichia coli (30%), Klebsiella pneumoniae (20.5%), and Pseudomonas aeruginosa (13%) as the most common organisms. Cefiderocol demonstrated the highest overall susceptibility (90–95%) across all Gram-negative isolates including ESBL, AmpC, and carbapenemase producers. Ceftazidime–avibactam showed good efficacy against ESBL (85%) and AmpC producers (80%) but markedly reduced activity (40%) against carbapenemase producers. Gram-positive organisms retained complete susceptibility to linezolid, vancomycin, and teicoplanin. The study highlights a substantial MDRO burden in a tertiary care setting, with cefiderocol demonstrating superior and consistent in vitro activity across resistance phenotypes. Continuous local surveillance and evidence-based antibiotic stewardship are essential for guiding empirical therapy.

KEYWORDS

Multidrug-Resistant Organisms; Antimicrobial Resistance; Cefiderocol; Ceftazidime-Avibactam; ESBL; Carbapenemase; Antibiotic Susceptibility Testing; India

INTRODUCTION

Antimicrobial resistance (AMR) is among the most pressing threats to global public health. In 2019, approximately 4.95 million deaths were associated with drug-resistant infections worldwide, with AMR directly contributing to 1.27 million fatalities; projections suggest this burden may reach 10 million annual deaths by 2050.[1,2] . According to the WHO Global Surveillance Report 2025 (GLASS), antibiotic-resistant organisms cause around 1 in 6 bacterial infections globally, rising to 1 in 3 urinary tract infections. Methicillin-resistant Staphylococcus aureus (MRSA) prevalence stands at approximately 27%, while fluoroquinolone and third-generation cephalosporin resistance in Escherichia coli and Klebsiella pneumoniae approaches 40–70% across many regions. India, among the largest consumers of antibiotics globally, bears a disproportionate share of this burden. In 2019, AMR-attributable deaths in India numbered approximately 297,000 — exceeding mortality from several major diseases — and the country ranks 145th globally in age-standardized AMR-related mortality.[3]

The rampant utilization of broad-spectrum antibiotics has driven the proliferation of MDROs in both community and hospital settings. Clinically significant pathogens such as Methicillin-resistant Staphylococcus aureus (MRSA), Vancomycin-resistant enterococci (VRE), carbapenem-resistant Enterobacterales, and non-fermenters including Pseudomonas aeruginosa and Acinetobacter baumannii pose substantial therapeutic challenges.[4,5] These organisms deploy multiple resistance mechanisms — including beta-lactamase production (ESBL, AmpC, carbapenemases), efflux pumps, and porin loss — often in combination.

Against this backdrop, newer antimicrobial agents have been developed with enhanced activity against MDROs. This study evaluates the microbiological profile of MDROs at a tertiary care hospital in North India and assesses the in vitro activity of five such agents: tigecycline (glycylcycline), teicoplanin (glycopeptide), quinupristin–dalfopristin (streptogramin), cefiderocol (siderophore cephalosporin), and ceftazidime–avibactam (β-lactam/β-lactamase inhibitor combination).[6,7]

MATERIALS AND METHODS

A prospective cohort study including 200 patients was conducted in the Department of Microbiology, Government Medical College, Amritsar, over a period of eighteen months following approval from the Institutional Ethics Committee. All hospitalized patients with clinically suspected bacterial infections across Surgery, Orthopaedics, Obstetrics and Gynaecology, Medicine, and related wards of Guru Nanak Dev Hospital, Amritsar were included. Inclusion criteria were clinical isolates from patients with suspected infective conditions confirmed as multidrug-resistant (resistant to ≥3 classes of antibiotics) were included. Exclusion criteria included isolates not meeting MDR criteria, from non-clinical or environmental sources, or with incomplete identification/susceptibility data were excluded. Written informed consent was obtained from all enrolled patients. Samples (Urine, pus, wound swabs, vaginal secretions, respiratory secretions, body fluids, and blood samples) were collected aseptically following standard microbiological protocols. Samples were cultured on MacConkey and blood agar. Blood cultures were incubated at 37°C with daily subcultures for seven days. All isolates were identified by conventional biochemical methods. Antimicrobial susceptibility testing was performed by Kirby–Bauer disk diffusion and minimum inhibitory concentration (MIC) by E-test (epsilometer strip diffusion) per CLSI guidelines. Antibiotics tested for Gram-positive organisms and Gram-negative organisms were as per CLSI recommendations. Resistance mechanisms were evaluated phenotypically using disc diffusion: In Enetrobacterales ESBL production was inferred from resistance to third-generation cephalosporins; AmpC production was assessed using amoxicillin-clavulanate as an inducer; carbapenemase production was inferred from resistance to carbapenems. In contrast, Pseudomonas spp., and Klebsiella spp., AmpC production was assessd using Imipenem as an inducer. No molecular characterization was performed.

Data were analyzed using SPSS v20. Categorical variables were expressed as frequencies and percentages. Chi-square tests were used for association analyses, with $p < 0.05$ considered statistically significant.

RESULTS

Demographic and Clinical Distribution

A total of 200 non-duplicate clinical MDRO isolates were analyzed. The majority of patients belonged to the 21–40 years age group (60.5%), followed by the 41–60 years group (32.0%). Females constituted 57.5% of the study population. Most patients were from rural areas (60%). The surgery/orthopaedics/ENT wards accounted for the highest proportion of isolates (31%), followed by gynaecology (26%) and medicine/chest/TB wards (25.5%).

Sample type and Organism Distribution

Urine samples constituted the largest proportion (40%), followed by pus (30.5%) and wound swabs (11%). Gram-negative bacilli (GNB) predominated (64%). Escherichia coli was the most common organism (30%), followed by Klebsiella pneumoniae (20.5%), Enterococcus spp. (15%), Pseudomonas aeruginosa (13%), MSSA (12%), MRSA (9%), and Acinetobacter baumannii (0.5%).

Table 3: Distribution of Sample Types (n=200)

Sample Type	Frequency	Percentage
Urine	80	40.0%
Pus	61	30.5%
Wound	22	11.0%
Vaginal secretions	17	8.5%
Respiratory secretions	11	5.5%
Body fluid/Ascitic fluid/Suction tip	7	3.5%
Blood	2	1.0%
Total	200	100%

Table 4: Distribution of Organisms Isolated (n=200)

Organism	Number	Percentage
Escherichia coli	60	30.0%
Klebsiella pneumoniae	41	20.5%
Enterococcus spp.	30	15.0%
Pseudomonas aeruginosa	26	13.0%
MSSA	24	12.0%
MRSA	18	9.0%
Acinetobacter baumannii	1	0.5%
Total	200	100%

Prior Antibiotic Exposure

36% of patients had a history of antimicrobial use in the preceding three months. A statistically significant association was observed between prior antibiotic exposure and resistance to cefiderocol (p=0.003) and ceftazidime–avibactam (p=0.001), while no significant association was found for tigecycline, teicoplanin, or quinupristin–dalfopristin according to this study.

Antimicrobial Susceptibility Patterns

Enterococcus Spp. :

Complete susceptibility was observed with linezolid, vancomycin, and teicoplanin (100%). Tigecycline and high-dose gentamicin showed high sensitivity (93.3%). Quinupristin–dalfopristin was active in 86.7% of isolates. Resistance was notable for tetracycline (54.5%) and fluoroquinolones.

Table 5: Antimicrobial Susceptibility of Enterococcus spp. (n=30)

Antibiotic	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Linezolid (30µg) (n=30)	30 (100%)	0	0
Vancomycin (30µg) (n=30)	30 (100%)	0	0
Teicoplanin (30µg)(n=30)	30 (100%)	0	0
Tigecycline (15µg)(n=30)	28 (93.3%)	0	2 (6.7%)
Quinupristin–Dalfopristin (15µg)(n=30)	26 (86.7%)	0	4 (13.3%)
Gentamicin high-level (120µg) (n=30)	28 (93.3%)	0	2 (6.7%)
Ampicillin (10µg)(n=30)	20 (66.7%)	0	10 (33.3%)
Tetracycline-urine (15µg) (n=11)	5 (45.4%)	0	6 (54.5%)
Norfloxacin-urine (10µg)(n=11)	5 (45.4%)	0	6 (54.5%)
Nitrofurantoin-urine (300µg)(n=11)	7 (63.6%)	0	4 (36.3%)

MRSA :

All MRSA isolates showed complete susceptibility to linezolid, vancomycin, and teicoplanin. Moderate activity was seen with clindamycin and tetracycline (55.5% each). Significant resistance was recorded for fluoroquinolones (55.5%), erythromycin (55.5%), and cotrimoxazole (33.3%).

Table 6: Antimicrobial Susceptibility of Methicillin-resistant Staphylococcus Aureus (n=18)

Antibiotic	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Linezolid (30µg) (n=30)	30 (100%)	0	0
Vancomycin (30µg) (n=30)	30 (100%)	0	0
Teicoplanin (30µg)(n=30)	30 (100%)	0	0
Tigecycline (15µg)(n=30)	28 (93.3%)	0	2 (6.7%)
Quinupristin–Dalfopristin (15µg)(n=30)	26 (86.7%)	0	4 (13.3%)
Gentamicin high-level (120µg) (n=30)	28 (93.3%)	0	2 (6.7%)
Ampicillin (10µg)(n=30)	20 (66.7%)	0	10 (33.3%)
Tetracycline-urine (15µg) (n=11)	5 (45.4%)	0	6 (54.5%)
Norfloxacin-urine (10µg)(n=11)	5 (45.4%)	0	6 (54.5%)
Nitrofurantoin-urine (300µg)(n=11)	7 (63.6%)	0	4 (36.3%)

Escherichia Coli :

Cefiderocol demonstrated the highest sensitivity (95%), followed by imipenem (83.3%), cefepime (81.7%), and piperacillin–tazobactam (78.3%). Ceftazidime–avibactam and amoxicillin–clavulanate showed 66.7% sensitivity. Significant resistance was observed with norfloxacin (57.1%) and ceftriaxone (50%).

Table 7: Antimicrobial Susceptibility of Escherichia Coli (n=60)

Antibiotic	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Cefiderocol (30µg) (n=60)	57 (95%)	0	3 (5%)
Imipenem (10µg) (n=60)	50 (83.3%)	0	10 (16.6%)
Cefepime (30µg)(n=60)	49 (81.7%)	0	30 (50%)
Piperacillin–Tazobactam (100/10µg) (n=60)	47 (78.3%)	0	13 (21.7%)
Ampicillin–Sulbactam (10/10µg)(n=60)	42 (70%)	0	18 (30%)
Ceftazidime–Avibactam(30/20µg) (n=60)	40 (66.7%)	0	20 (33.3%)
Amoxicillin–Clavulanate(20/10µg) (n=60)	40 (66.7%)	0	20 (33.3%)
Nitrofurantoin-urine(300µg) (n=35)	20 (57.1%)	0	15 (42.8%)
Ceftriaxone(30µg) (n=60)	30 (50%)	0	25 (41.7%)
Norfloxacin-urine(10µg) (n=35)	15 (42.8%)	0	20 (57.1%)

Klebsiella Pneumoniae:

Cefiderocol retained the highest activity (90%), followed by ceftazidime–avibactam (78%) and imipenem (75.6%). Higher resistance was noted compared to E. coli, with ceftriaxone showing only 46.3% sensitivity and norfloxacin 30.7%.

Table 8: Antimicrobial Susceptibility of Klebsiella Spp. (n=41)

Antibiotic	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Cefiderocol((n=41)	37 (90%)	0	4 (9.7%)
Ceftazidime–Avibactam (n=41)	32 (78%)	0	9 (21.9%)
Imipenem (n=41)	31 (75.6%)	0	10 (24.3%)
Cefepime (n=41)	25 (60.9%)	0	16 (39%)
Piperacillin–Tazobactam (n=41)	25 (60.9%)	0	16 (39%)
Amikacin (n=41)	22 (53.6%)	0	19 (46.3%)
Ceftriaxone (n=41)	19 (46.3%)	0	22 (53.6%)
Nitrofurantoin-urine (n=13)	6 (46.1%)	0	7 (53.8%)
Norfloxacin-urine (n=13)	4 (30.7%)	0	9 (69%)

Pseudomonas Aeruginosa :

Cefiderocol showed the highest sensitivity (92.3%), followed by ceftazidime–avibactam (84.6%). Piperacillin–tazobactam and tobramycin demonstrated good activity (76.9%). Considerable resistance was observed with levofloxacin (53.8%) and piperacillin alone (61.5% resistant).

Table 9: Antimicrobial Susceptibility of Pseudomonas Aeruginosa (n=26)

Antibiotic	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Cefiderocol (n=26)	24 (92.3%)	0	2 (7.6%)
Ceftazidime–Avibactam (n=26)	22 (84.6%)	0	4 (15.4%)
Piperacillin–Tazobactam (n=26)	20 (76.9%)	0	6 (23.1%)

Tobramycin (n=26)	20 (76.9%)	0	6 (23.1%)
Imipenem (n=26)	16 (61.5%)	0	10 (38.4%)
Cefepime (n=26)	16 (61.5%)	0	10 (38.4%)
Ceftazidime (n=26)	16 (61.5%)	0	10 (38.4%)
Levofloxacin (n=26)	12 (46.1%)	0	14 (53.8%)

Resistance Mechanisms and Newer Antibiotic Efficacy

ESBL production was the most prevalent mechanism among Enterobacterales (E. coli: 60%; Klebsiella: 50%), followed by AmpC (E. coli: 20%; Klebsiella: 25%) and carbapenemase production (both: 15%). In Pseudomonas, AmpC predominated (35%). Cefiderocol maintained ~95% susceptibility across all resistance phenotypes. Ceftazidime–avibactam showed good activity against ESBL (85%) and AmpC (80%) producers but markedly reduced efficacy against carbapenemase producers (40%), attributable to the high prevalence of metallo-β-lactamases (notably NDM) against which avibactam has no inhibitory activity.

Table 10: Distribution of Resistance Mechanisms Among Gram-negative Isolates

Organism	ESBL (%)	AmpC (%)	Carbapenemase (%)
Escherichia coli	60%	20%	15%
Klebsiella spp.	50%	25%	15%
Pseudomonas spp.	20%	35%	20%

Table 11: Activity of Ceftazidime–avibactam and Cefiderocol by Resistance Mechanism

Resistance Mechanism	Antibiotic	Susceptible (%)	Intermediate (%)	Resistant (%)
ESBL Producers	Ceftazidime-Avibactam	85%	0	15%
	Cefiderocol	95%	0	5%
AmpC Producers	Ceftazidime-Avibactam	80%	0	20%
	Cefiderocol	95%	0	5%
Carbapenemase Producers	Ceftazidime-Avibactam	40%	0	60%
	Cefiderocol	95%	0	5%

DISCUSSION

The present study systematically evaluated the microbiological profile of MDROs and the in vitro efficacy of newer antimicrobials in a tertiary care setting in North India. Several key findings merit discussion in context of the global and national literature.

The predominance of patients in the 21–40 years age group aligns with studies by Chakrabarti et al. and Singh et al., likely reflecting greater healthcare exposure and antibiotic consumption in this economically active cohort.[8,9] The slight female predominance is consistent with the high burden of urinary tract infections in women. The higher rural representation reflects limited access to primary care, over-the-counter antibiotic misuse, and delayed presentation — patterns well-described in Indian hospital-based studies.[10]

Gram-negative organisms dominated the isolate profile, consistent with global surveillance data. E. coli, as the primary uropathogen, predictably led organism distribution — a finding mirrored in multiple Indian studies.[11,12] The comparatively low prevalence of Acinetobacter baumannii (0.5%) relative to ICU-focused studies reflects the broader, multi-ward sampling strategy of this study.

The preserved susceptibility of Enterococcus spp., MSSA, and MRSA to glycopeptides (vancomycin, teicoplanin) and linezolid is reassuring and concordant with existing literature from India and globally.[13] No vancomycin-resistant Enterococcus (VRE) or VISA/VRSA strains were identified, though this warrants ongoing monitoring. The high resistance to fluoroquinolones and macrolides among Gram-positive organisms reflects selective pressure from their widespread empirical use.

Among Gram-negative isolates, ESBL production was the predominant resistance mechanism, consistent with reports from Indian tertiary centers.[14] Carbapenemase prevalence remained comparatively modest (E. coli: 15%, Klebsiella spp.: 15%, Pseudomonas spp.: 20%). Notably, in this study, ICU isolates demonstrated higher sensitivity to most antibiotics compared to general ward isolates (ceftazidime–avibactam resistance: 0% in ICU vs 38% in Surgery/Ortho/ENT wards; p<0.001), contrasting with ICU-dominant published studies where carbapenemase prevalence frequently exceeds 30–40%. This reversal likely reflects stricter infection control practices and antibiotic stewardship protocols in the ICU of this institution, combined with a higher burden of healthcare-associated MDROs in surgical and gynaecological wards due to procedural interventions and prolonged antibiotic prophylaxis. Notably, cefiderocol demonstrated the highest and most consistent in vitro activity across all Gram-negative organisms and resistance phenotypes (~90–95%), including carbapenemase producers — a finding strongly supported by multiple international studies.[15,16] Its unique mechanism of siderophore-mediated iron transport enables it to bypass conventional resistance pathways including porin loss and efflux pump overexpression.

Ceftazidime–avibactam showed good efficacy against ESBL and AmpC producers but substantially reduced activity against carbapenemase producers (40%). This reduced efficacy is attributable to the prevalence of NDM-type metallo-β-lactamases in India, against which avibactam has no inhibitory activity — a limitation well-documented in the literature.[17,18] This distinction has significant clinical implications for empirical therapy in settings with high NDM prevalence.

This study has several strengths, including systematic evaluation of both conventional and newer agents, phenotypic resistance mechanism analysis, and association analyses with clinical variables. Limitations include the single-centre design, the relatively small number of isolates for some organisms (particularly Acinetobacter), and the absence of molecular characterization of resistance genes, which would permit more precise mechanistic interpretation.

CONCLUSION

The study documents a substantial MDRO burden in a tertiary care hospital in North India, with Gram-negative pathogens — particularly E. coli and Klebsiella pneumoniae — predominating. High resistance to commonly used antibiotics was observed, while newer agents retained strong in vitro activity. Cefiderocol demonstrated superior and consistent activity across resistance phenotypes, including carbapenemase producers, supporting its role as a therapeutic option in difficult-to-treat infections. Ceftazidime–avibactam showed good activity against ESBL and AmpC producers but limited efficacy against metallo-β-lactamase producers. Gram-positive MDROs remained fully susceptible to glycopeptides and linezolid. Continuous local microbiological surveillance and evidence-based antibiotic stewardship are essential to inform empirical therapy and curb the spread of resistance.

Ethical Approval: Institutional Ethics Committee approval was obtained prior to study commencement. Written informed consent was obtained from all participants.

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