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ANTIBIOTIC SUSCEPTIBILITY PROFILE OF BURKHOLDERIA CEPACIA COMPLEX AT A TERTIARY CARE HOSPITAL: CHANGING TRENDS OVER 6 YEARS

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ABSTRACT

Background: Burkholderia cepacia complex (BCC) is a group of non-fermentative Gram-negative bacilli that pose a significant therapeutic challenge due to intrinsic and acquired resistance to multiple antibiotics. BCC has emerged as a notable cause of opportunistic and nosocomial infections, especially in immunocompromised patients. Limited longitudinal data from India on antimicrobial susceptibility trends of BCC prompted this study. **Objectives:** To evaluate the changing trends in antibiotic susceptibility of clinical isolates of BCC over a six-year period in a tertiary care hospital in western Uttar Pradesh. **Methods:** A retrospective analysis was conducted from January 2019 to December 2024. A total of 231 BCC isolates from various clinical samples were included. Isolates were identified using standard biochemical tests and confirmed by the VITEK 2 GN card. Antibiotic susceptibility testing was performed by Kirby-Bauer disk diffusion method and interpreted using CLSI guidelines. The antibiotics tested included ceftazidime, meropenem, levofloxacin, minocycline and co-trimoxazole. The minimum inhibitory concentration of certain antibiotics was determined by VITEK 2 AST-N281 card. **Results:** The number of BCC isolates showed an overall increasing trend, rising from 22 in 2019 to 67 in 2024. Antibiotic susceptibility patterns revealed significant changes over the study period. Levofloxacin maintained high susceptibility, declining gradually from 89% to 76%. Minocycline showed the highest susceptibility in 2019 (97%), falling to 71% by 2024. Ceftazidime susceptibility decreased markedly from 75% to 52%, while meropenem exhibited a variable pattern with a sharp decline to 45% in 2024. In contrast, co-trimoxazole susceptibility, initially declining, showed a revival from 54% in 2023 to 73% in 2024. These trends were statistically significant ($p<0.001$). **Conclusion:** The study highlights dynamic resistance patterns in BCC over six years, with concerning declines in susceptibility to ceftazidime, minocycline and meropenem. The resurgence in co-trimoxazole susceptibility is promising and may reestablish its role in empirical therapy. Continued surveillance and antibiotic stewardship are imperative to curb emerging resistance in this difficult-to-treat pathogen.

KEYWORDS : : Burkholderia Cepacia Complex, Antimicrobial Susceptibility, Multidrug Resistance

INTRODUCTION

Burkholderia cepacia complex is a group of non-fermentative Gram-negative bacteria, comprising more than 20 closely related species, namely B. cepacia, B. multivorans, B. cenocepacia, B. vietnamiensis, B. stabilis, B. ambifaria, B. dolosa, B. anthina, B. pyrrocinia, B. ubonensis etc.[1,2,3] Owing to their exceptional metabolic adaptability, they are found ubiquitously in environmental habitats such as soil, water and various sources within healthcare settings, posing a intimidating challenge to infection control measures.[4,5] Over the last two decades, Burkholderia cepacia complex (BCC) has emerged as an opportunistic pathogen in patients with impaired immune status and underlying illnesses, causing life-threatening infections. BCC has gained importance as a devastating pulmonary pathogen, particularly in patients with cystic fibrosis and chronic granulomatous diseases.[4,6,7] BCC has emerged as a cause of various healthcare-associated infections including bloodstream infections, respiratory tract infections, urinary tract infections, septic arthritis, peritonitis and infections associated with indwelling medical devices.[8] BCC is known for its resilience to disinfectants and antseptics. BCC exhibits a distinctive antimicrobial profile with intrinsic resistance to polymyxins, aminoglycosides, first-generation cephalosporins, second-generation cephalosporins and traditional antipseudomonal penicillins, thereby posing therapeutic challenges.[2,9,10,11,12] The multiple antibiotic resistance of BCC has been assigned to an impermeable selective outer membrane, efflux pump mechanism and production of an inducible chromosomal beta-lactamase.[11] Given the limited treatment options and its potential to cause severe infections in vulnerable populations, surveillance of antibiotic susceptibility trends in BCC is crucial. To the best of our knowledge, long-term data on the antimicrobial resistance patterns of BCC in the Indian healthcare context remain scarce. Despite the clinical relevance, limited studies from India have documented the antibiogram data of BCC that had either reflected cross-sectional view of the contemporary susceptibility patterns or had not included a sufficient number of isolates. Hence, this present study was planned to provide a comprehensive data regarding the antibiotic susceptibility patterns of BCC isolates over a period of six years from our health-care setup. The study aims to highlight changing resistance trends and guide empirical therapy and antimicrobial stewardship efforts.

MATERIALS AND METHOD

The retrospective observational study was carried out in a tertiary care teaching hospital after approval from the institutional ethical committee in western region Uttar Pradesh, India, over a period of six years (January 2019 - December 2024). An analysis of laboratory records over 6 years for antimicrobial susceptibility patterns of Burkholderia cepacia complex isolates was carried out. A total of 231 BCC isolates obtained from various clinical specimens such as blood, respiratory samples, pus, urine, ascitic fluid and other sterile body fluids were included in the study. Samples were subjected to culture by conventional methods as per standard bacteriological techniques.[1] All the isolates producing non-lactose fermenting colonies on Mac Conkey's agar were identified by conventional tests such cytochrome oxidase test, motility, amino acid decarboxylase tests, triple sugar iron test, urea hydrolysis, and Hugh and Leifson's oxidation fermentation test for glucose.[1] The antibiotic sensitivity pattern was determined using Muller Hilton agar by Kirby-Bauer disk diffusion method. Antibiotics tested were ceftazidime (30µg), meropenem (10µg), levofloxacin (5µg), minocycline (30µg) and co-trimoxazole (trimethoprim 1.25µg /sulfamethoxazole 23.75µg), amikacin (30µg), gentamicin (10µg), tobramycin (10µg) and colistin (10µg). Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 were used as quality controls. Results of zone diameter were interpreted according to contemporary Clinical and Laboratory Standards Institute (CLSI) guidelines[10] over the six years, and breakpoints remained the same during this period. Isolates with intermediate susceptibility in disk diffusion were considered

as resistant. BCC isolate was picked up as non-lactose fermenting, oxidase positive, motile, Gram-negative bacillus which was resistant to colistin and aminoglycosides but sensitive to cotrimoxazole. Identification was further confirmed by an automated VITEK 2 system by GN card (Biomerieux, France). The minimum inhibitory concentration (MIC) of certain antibiotics was determined by VITEK 2 AST-N281 card.

Statistical Analysis

The data was analyzed statistically by using Z-test for proportions. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 231 clinical isolates of Burkholderia cepacia complex (BCC) were recovered over a six-year period from 2019 to 2024. The year-wise isolation showed a fluctuating but overall increasing trend [Table-1]. The number of isolates rose from 22 in 2019 to 67 in 2024, indicating a significant rise in isolation rates in recent years. Notably, the highest number of isolates was recorded in 2024 (67 isolates), followed by 2023 (58 isolates), while the lowest was in 2021 (17 isolates) [Table-1]. The antibiotic susceptibility patterns revealed varying resistance trends across the studied years [Table-2, Figure-1]. Ceftazidime susceptibility declined initially from 75% in 2019 to 45% in 2023, with a slight rebound to 52% in 2024. Co-trimoxazole susceptibility declined slightly from 62% in 2019 to 54% in 2023, but a notable increase to 73% was observed in 2024. Meropenem demonstrated variable trends, increasing from 66% in 2019 to a peak of 76% in 2022, followed by a sharp decline to 45% in 2024. The variations observed in the trend of susceptibility of BCC isolates to ceftazidime, co-trimoxazole and meropenem during the study period were statistically significant ($p<0.001$). Levofloxacin maintained relatively high susceptibility but showed a gradual decline from 89% in 2019 to 76% in 2024 ($p<0.001$). Minocycline exhibited the highest susceptibility in 2019 (97%) but showed a consistent downward trend to 71% by 2024 ($p<0.001$). As reflected in our data, by 2024, BCC isolates exhibited highest susceptibility to levofloxacin (76%) followed by co-trimoxazole (73%) and minocycline (71%), however the lowest susceptibility was seen with meropenem (45%) [Table-2, Figure-1]. These findings suggest evolving resistance patterns, with particular concern regarding ceftazidime, meropenem and minocycline, while co-trimoxazole showed a resurgence in susceptibility in the most recent year.

Table-1: Year-wise Isolation of Burkholderia Cepacia Complex

Year	Number of Isolates
2019	22
2020	38
2021	17
2022	29
2023	58
2024	67
Total no of isolates	231

Table 2: Year-wise Antibiotic Susceptibility Pattern of Clinical Isolates of Burkholderia Cepacia Complex (n=231)

Antibiotic	Antibiotic sensitivity profile (Percent susceptible)					
	2019	2020	2021	2022	2023	2024
Ceftazidime	75	72	48	46	45	52
Levofloxacin	89	86	84	81	79	76
Minocycline	97	89	82	74	77	71
Co-trimoxazole	62	60	58	56	54	73
Meropenem	66	64	72	76	71	45

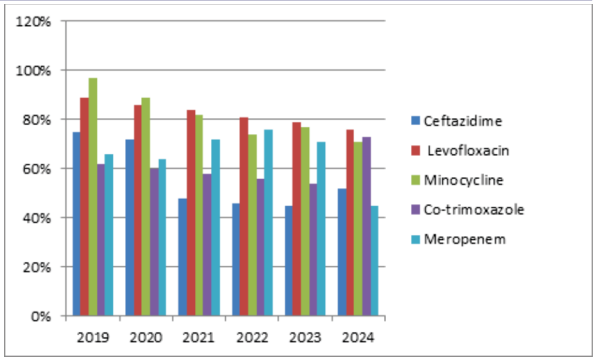

Figure-1: Year-wise Antibiotic Susceptibility Pattern of Burkholderia Cepacia Complex Isolates

Discussion

Burkholderia cepacia complex has gained importance as an emerging group of bacteria responsible for serious nosocomial infections, especially in critically ill and immunocompromised patients.[4,6-8] BCC proposes a notable therapeutic threat owing to its pervasive resistance to multifarious classes of antibiotics. The intrinsic resistance of BCC to various antibiotics including amoxicillin, ampicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin, ticarcillin, first-generation cephalosporins, second-generation cephalosporins, aminoglycosides, fosfomycin, ertapenem and polymyxin B and colistin, leaves the clinician with limited options for treatment.[10,11,13,14] Thus, the therapeutic choices for the infections caused by intrinsically multidrug-resistant BCC are narrowed to carbapenems, ceftazidime and trimethoprim-sulfamethoxazole.[12]It has been documented that an outer membrane of BCC serves as a barrier which controls the entry of antibiotics within the cell. Resistance is also remarkably influenced by role of efflux pumps. Resistance to beta-lactams has been ascribed to the presence of inducible chromosomal beta-lactamases and altered penicillin-binding proteins.[11] Intrinsic resistance to polymyxins is credited to altered lipopolysaccharide, whereas drug penetration is reduced by restrictive porin proteins.[12]

We present the retrospective data that provides insights into the evolving antimicrobial susceptibility trends of Burkholderia cepacia complex over a period of six years (2019-2024) at our tertiary care hospital (Figure-1). Our findings revealed the varying resistance trends with particular attention to five tested antibiotics: ceftazidime, levofloxacin, minocycline, co-trimoxazole and meropenem. Looking at the observations made in our study, by the year 2024, BCC isolates exhibited highest susceptibility to levofloxacin (76%) followed by co-trimoxazole (73%) and minocycline (71%). Levofloxacin has shown to maintain good susceptibility throughout the study period (from 89% to 76% over the six years), though the downward trend is concerning. This trend reflects growing resistance pressure, likely due to the widespread use of fluoroquinolones in clinical settings. Similar gradual reductions in susceptibility were noted in earlier Indian studies.[9,15]

In the present study, sensitivity to co-trimoxazole varied from 62% in 2019, with a notable increase from 54% in 2023 to 73% in 2024. In agreement to our finding, a study done in north India by Sethi S et al. had also observed the similar trend over the earlier decade (2007-2016), where the susceptibility of BCC to co-trimoxazole showed an upsurge, increasing from 70% mid-decade to 89% by 2016.[9] This finding pinpoints that co-trimoxazole could be considered as the drug of choice. As documented by various authors, co-trimoxazole has consistently shown favorable activity, making it a dependable choice for empirical therapy when supported by susceptibility results.[15-17] This reinforces co-trimoxazole's position as a frontline agent for BCC infections among the antibiotics,

which could be ascribed to its reintroduction into clinical use following a period of reduced prescribing, or due to plasmid loss contributing to renewed or restored bacterial susceptibility over time.[9,18]

In our hospital setting, minocycline which was highly effective initially (97% in 2019), showed reduced susceptibility to 71% by 2024. This is consistent with findings from the earlier study where minocycline susceptibility declined from 100 per cent in 2012 to 74 per cent by 2016.[9] This downturn also aligns with study showing decreasing minocycline activity, particularly in strains isolated from critically ill patients.[19]The declining trend may be linked to adaptive resistance mechanisms, including efflux pumps and target site mutations.[16]

In our setup, a marked drop in susceptibility to ceftazidime was observed, varying from 75% in 2019 to a low of 45% in 2023, slightly recovering to 52% in 2024. This decreasing trend is consistent with prior data from north India that reported a fall from 83% to 65% over a decade.[9] The waning efficacy of ceftazidime may be attributed to the production of inducible beta-lactamases and overexpression of efflux pumps in BCC.[15]

As per our data, meropenem showed an inconsistent pattern with a peak susceptibility of 76% in 2022, dropping sharply to 45% in 2024. This pattern suggests the sporadic emergence of resistant clones, possibly ascribed to widespread empirical carbapenem usage. Given that carbapenems are often used as last-resort agents, this finding underscores the need for judicious use and alternative therapeutic options.[9,19] BCC is known to exhibit resistance to carbapenems through altered outer membrane proteins and efflux mechanisms.[16]

The emerging antimicrobial resistance profile of BCC over a recent 6-year surveillance period emphasizes the need of regular antibiogram monitoring and individualized therapy guided by susceptibility results. Encouraging the rational use of antimicrobials and adhering to good clinical practices becomes essential to curb the rising threat of multidrug-resistant BCC in healthcare settings.

CONCLUSION

Burkholderia cepacia complex has continued to pose significant clinical challenges due to its intrinsic and acquired resistance to multiple antimicrobials. The six-year analysis of BCC isolates from a tertiary care hospital reveals dynamic shifts in antibiotic susceptibility patterns. The study highlights the concerning declines in susceptibility to ceftazidime, minocycline and meropenem. An encouraging sign is the recent resurgence in co-trimoxazole susceptibility, which could restore its potential as a preferred agent in managing BCC infections. These findings underscore the need for continuous surveillance and strict antimicrobial stewardship to guide empirical therapy and mitigate resistance development in this notoriously drug-resistant pathogen. Future research should be done to explore the genetic mechanisms of resistance and evaluate alternative treatment strategies, including combination therapies and novel antimicrobials.

Limitations

Due to resource constraints, the study did not include molecular typing of isolates to determine strain diversity or resistance mechanisms, which could provide deeper insight into resistance trends.

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