Assessing the Impact of *Burkholderia cepacia* in Critical Care: Insights into Clinical Outcomes, Resistance Patterns, and Contamination Sources

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Background and study aim: *Burkholderia cepacia* is known for causing severe infections in immunocompromised individuals. The bacteria's ability to form biofilms, secrete virulence factors, and resist multiple antibiotics exacerbates its pathogenicity. Despite the rising prevalence of *B. cepacia* infections in healthcare settings, particularly in critical care units, knowledge about its clinical profile, antimicrobial resistance patterns, and contamination sources in India remains limited. This study aimed to investigate the clinical characteristics, antibiotic susceptibility patterns, mortality rates, and potential sources of *B. cepacia* contamination in the critical care unit of G.B. Pant Hospital, Delhi.

Patients and Methods: This cross-sectional study was conducted between January and July 2023. Blood samples from critically ill patients were cultured for *B. cepacia* identification and antimicrobial susceptibility testing using the Vitek 2 system. Environmental sampling (n=200) was performed to assess possible contamination sources. Data were analyzed using descriptive statistics, and associations were tested with chi-square and multivariate analyses.

Results: Twenty-five patients with *B. cepacia* infections were included, with a 60% male predominance and an average age of 58.4 years. Diabetes (44%) and hypertension (40%) were common comorbidities. Ciprofloxacin (88%) and trimethoprim-sulfamethoxazole (88%) were the most effective antibiotics. The mortality rate was 40%, with chronic liver disease and prolonged ICU stay significantly associated with poor outcomes. Environmental sampling failed to identify a specific contamination source.

Conclusion: *B. cepacia* poses a significant risk in critical care settings, with high antibiotic resistance and mortality. Tailored antibiotic therapy and stringent infection control measures are critical for managing infections and improving outcomes.

INTRODUCTION

Burkholderia cepacia, a Gram-negative bacterium, has evolved from its origins as a plant pathogen to become a significant opportunistic human pathogen, particularly affecting individuals with compromised immune systems [1,2]. *B. cepacia* infections present clinically in a wide range, from asymptomatic colonization to life-threatening systemic infections [3]. The severity of infection is influenced by various factors, including the patient's underlying health status, immune system, and the specific strain of bacteria involved [4,5].

Recent studies have highlighted the growing concern about *B. cepacia's* propensity to cause bloodstream infections, often resulting in septicaemia [6]. Additionally, it can lead to urinary tract, skin, and soft tissue infections, with manifestations ranging from cellulitis to necrotizing fasciitis [7,8]. A 2019 study by Devanga Ragupathi and Veeraraghavan emphasized the importance of accurate identification and epidemiological characterization of the *B. cepacia* complex in clinical settings [9].

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Contaminated medical equipment, intravenous fluids, and environmental reservoirs within hospitals have been implicated in outbreaks [10,11]. A 2020 case series by Bharara et al. highlighted the potential for *B. cepacia* to cause outbreaks in neonatal intensive care units, underscoring the vulnerability of certain patient populations [12]. Vulnerable groups; including those undergoing chemotherapy, organ transplants, or using immunosuppressive drugs, are at higher risk, with neonates and geriatrics being particularly susceptible [13]. Understanding *B. cepacia's* pathogenicity is crucial. Surface structures such as pili, flagella, and adhesins facilitate its adherence to host cells, promoting colonization in various body sites [14]. Biofilm formation, enabled by exopolysaccharides like cepacian, plays a pivotal role in chronic infections, particularly in cystic fibrosis patients [15]. *B. cepacia* secretes virulence factors such as proteases, lipases, and phospholipases that contribute to tissue damage and immune evasion, making it a formidable pathogen [16]. The treatment of *B. cepacia* infections is complicated by its intrinsic and acquired resistance to multiple classes of antibiotics [14,15]. Efflux pumps, enzymatic degradation, and alterations in target sites contribute to its multidrug resistance. This necessitates a tailored approach based on antimicrobial susceptibility testing [17]. However, the limited treatment options underscore the importance of antimicrobial stewardship and the urgent need for alternative therapeutic strategies.

Despite the growing body of research on *B. cepacia* infections, there remains a significant knowledge gap regarding its clinical profile, antibiotic susceptibility patterns, and mortality rates in tertiary care settings in India. Furthermore, the specific sources of *B. cepacia* contamination in hospital environments often remain elusive, hampering effective infection control measures.

This study aims to address these knowledge gaps by investigating the clinical profile, antibiotic susceptibility patterns, mortality rates, and potential sources of *B. cepacia* contamination in the critical care unit of G.B Pant Hospital in Delhi. By providing comprehensive data on these aspects, we seek to inform more effective treatment strategies and infection control measures, ultimately improving patient outcomes in critical care settings.

MATERIALS AND METHODS

Study Design and Setting:

This hospital-based cross-sectional study was conducted in the critical care unit and Department of Microbiology at G.B Pant Hospital, Delhi, from January 1 to July 31, 2023. The study aimed to investigate *Burkholderia cepacia* infections detected in blood samples from patients admitted to the critical care unit.

Patient selection criteria :

Inclusion criteria:

- Patients who were admitted to the critical care unit with suspected septicemia during the study period.
- Patients with at least one blood culture positive for *B. cepacia*.
- Patients of all age groups and both genders.

Exclusion criteria:

- Patients with polymicrobial bacteremia.
- Patients with incomplete medical records.
- Patients who were transferred from other hospitals with a known *B. cepacia* infection.

Sample collection and processing:

As part of routine investigations, blood samples were collected from patients admitted to the critical care unit and sent for culture and sensitivity analysis to the hospital's Microbiology laboratory. Blood cultures were performed using the automated blood culture system BACT/Alert 3D (BioMérieux). Only blood bottle-flagged positive results were further processed.

Subculturing from positive blood cultures:

Subculturing was carried out by inoculating the positive blood cultures onto 5% sheep blood agar and MacConkey agar plates, which were then incubated overnight aerobically at 37°C. After 24 hours of incubation, the colonies grown on the 5% sheep blood agar were typically non-hemolytic, measuring 2-3mm in diameter, circular, low convex, and exhibited a metallic sheen. Non-lactose fermenting colonies were observed on MacConkey agar, and all isolates were oxidase-positive and resistant to colistin. Gram staining revealed the presence of Gram-negative bacilli that exhibited motility.

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Identification and antimicrobial susceptibility testing:
To confirm the identification and antimicrobial susceptibility of *Burkholderia cepacia* isolates, the Vitek 2 compact system (BioMérieux) was used according to the manufacturer's instructions. The antimicrobial susceptibility results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Environmental Sampling:
To investigate potential sources of *B. cepacia* contamination, we conducted extensive environmental sampling in the critical care unit. A total of 200 samples were collected from various sites, including:

- **Water Sources**: Tap water and sink drains.
- **Patient Environment:** Bed linens, operating table surfaces, and medical devices.
- **Respiratory Devices and Equipment**: Oxygen masks, respiratory tubes, and ventilators.
- **Suction Machines and Catheters.**
- **Medical Solutions**: Intravenous solutions like normal saline and Ringer lactate.
- **Surfaces:** Doorknobs, handrails, and medical equipment touchscreens.
- **Antiseptic Solutions:** Solutions used for disinfection in the critical care unit.

Environmental samples were processed using standard microbiological techniques for isolation and identification of *B. cepacia*.
Data Collection: Demographic data, clinical information, and laboratory results were collected from patients' medical records using a standardized data collection form. Information gathered included age, gender, underlying diseases, clinical diagnoses, risk factors, antibiotic susceptibility patterns, and patient outcomes.
Statistical Analysis: Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize patient characteristics, clinical features, and antibiotic susceptibility patterns. Continuous variables were expressed as mean ± standard deviation or median (interquartile range) based on the distribution of data. Categorical variables were presented as frequencies and percentages.
The chi-square test or Fisher's exact test was used to compare categorical variables between groups (e.g., survivors vs. non-survivors). Student's t-test or Mann-Whitney U test was used for continuous variables, depending on the normality of data distribution. A p-value < 0.05 was considered statistically significant. Variables with a p-value < 0.1 in univariate analysis were included in the multivariate model.

RESULTS

Patient Demographics and Clinical Characteristics
Our study comprised 25 critically ill patients with *Burkholderia cepacia* infections admitted to various critical care units at GB Pant Hospital. The mean age was 58.4 ± 17.2 years (range: 5-92 years). Fifteen patients (60%) were male, and 10 (40%) were female.

Underlying Conditions and Risk Factors
The most common underlying illnesses were:

- Diabetes Mellitus: 11 patients (44%)
- Hypertension: 10 patients (40%)
- Chronic liver disease: 5 patients (20%)

Significant risk factors included:

- Intravenous catheter use: 25 patients (100%)
- Central line use: 24 patients (96%)
- Prolonged ICU stay (>7 days): 15 patients (60%)

Clinical Diagnoses
The most frequent clinical diagnoses were:

- Pneumonia: 7 patients (28%)
- Septicemia: 6 patients (24%)
- Urinary tract infections: 4 patients (16%)

Antibiotic Susceptibility Patterns
Analysis of *B. cepacia* isolates revealed the following susceptibility patterns:

- Ciprofloxacin: 88% susceptible

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- Trimethoprim/Sulfamethoxazole: 88% susceptible
- Meropenem: 84% susceptible
- Cefoperazone + Sulbactam: 8% susceptible (92% resistant)
- Ceftazidime: 52% susceptible (48% resistant)

The difference in susceptibility between ciprofloxacin and cefoperazone + sulbactam was statistically significant ($p < 0.001$, Fisher's exact test).

Patient Outcomes

The overall mortality rate was 40% (10 patients). Univariate analysis showed that chronic liver disease (OR: 3.5, 95% CI: 1.2-10.1, $p = 0.02$) and prolonged ICU stay (OR: 2.8, 95% CI: 1.1-7.3, $p = 0.03$) were significantly associated with higher mortality.

Environmental Sampling

Despite extensive environmental sampling (200 samples), the specific source of *B. cepacia* contamination remained unidentified during the study period.

Table 1: This table shows the prevalence of key risk factors among the 25 patients with *B. cepacia* infections in our study.

Table 1: Risk Factors for *Burkholderia cepacia* infection	
Risk factor	**Number of patients**
Intravenous Catheter	25 (100%)
Central Line	24(96%)
Prolonged ICU Stay	15(60%)

Table 2: This table presents the antibiotic susceptibility patterns of the 25 *B. cepacia* isolates from our study, showing the percentage of isolates sensitive or resistant to each antibiotic.

Table 2: Antibiotic susceptibility patterns of *B. cepacia* isolates		
Antibiotics	**Sensitive %**	**Resistance %**
Ciprofloxacin	88	12
Trimethoprim / Sulfamethoxazole	88	12
Meropenem	84	16
Cefoperazone + Sulbactam	8	92
Ceftazidime	52	48

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DISCUSSION

Our study provides valuable insights into the clinical profile, antibiotic susceptibility patterns, and outcomes of *B. cepacia* infections in a tertiary care setting in Delhi. The findings have important implications for clinical practice and infection control.

The prevalence of underlying conditions in our study, particularly diabetes mellitus (44%) and hypertension (40%), aligns with recent studies. For instance, Bhat et al. (2021) reported a significant association between *B. cepacia* infections and diabetes mellitus in their case series [17]. Our findings reinforce the vulnerability of patients with chronic conditions to opportunistic pathogens like *B. cepacia*.

The antibiotic susceptibility patterns observed in our study are concerning, particularly the high resistance to cefoperazone + sulbactam (92%). This is higher than the rates reported by Bharara et al. (2020) in their neonatal ICU outbreak investigation, where resistance to cephalosporins ranged from 60-80% [12]. However, our findings of high susceptibility to ciprofloxacin (88%) and trimethoprim/sulfamethoxazole (88%) are more encouraging and consistent with the study by Devanga Ragupathi and Veeraraghavan [9].

The mortality rate of 40% in our study is concerning but comparable to other recent reports. Bilgin et al. (2021) reported a mortality rate of 33% in their outbreak investigation, while Gangaram et al. (2020) observed a mortality rate of 45% in their ICU-based study [6,11]. Despite conducting extensive environmental sampling, encompassing over 200 samples from various sources in the critical care unit, we were unable to identify the specific source of *Burkholderia cepacia* contamination during the study period. This is a common challenge faced in outbreak investigations, where the environmental reservoir harboring the pathogen may not be readily apparent [18]. As highlighted in the outbreak investigation literature, several factors can contribute to the difficulty in tracing the source of *Burkholderia* infections:

1. Persistence in the Environment: *Burkholderia species* are known to survive and persist in a wide range of environmental niches, from water sources to medical equipment. Their ability to form biofilms further enhances their environmental resilience, making them difficult to eradicate.
2. Versatile Transmission Pathways: *Burkholderia* can be transmitted through multiple routes, including contaminated medical devices, intravenous solutions, respiratory equipment, and even person-to-person spread. The complex interplay of these transmission modes can obscure the primary source.

These findings collectively underscore the significant threat posed by *B. cepacia* infections in critical care settings.

Limitations of the Study

Several limitations should be considered when interpreting our results:

- Small sample size: With only 25 patients, our statistical power is limited, and some associations may not have reached significance due to type II error.
- Single-center study: Our findings may not be generalizable to other settings or geographical regions.
- Retrospective design: This limits our ability to establish causal relationships and may introduce bias due to missing data or inconsistencies in documentation.
- Lack of molecular typing: We were unable to perform genetic analysis to determine the clonality of the isolates, which could have provided insights into potential transmission patterns.
- Unidentified environmental source: Despite extensive sampling, we could not pinpoint the source of *B. cepacia*, highlighting the challenges in controlling this pathogen in healthcare settings.

Future studies with larger sample sizes, multi-center designs, and molecular typing methods are needed to further elucidate the epidemiology and clinical impact of *B. cepacia* infections in critical care settings.

CONCLUSION:

The clinical and epidemiological characteristics of *Burkholderia cepacia* infections in critical care patients are clarified by our investigation. Our study highlights three key findings:

- High prevalence of underlying conditions: Diabetes mellitus (44%) and hypertension (40%) were common comorbidities, emphasizing the vulnerability of patients with chronic diseases to *B. cepacia* infections.
- Alarming antibiotic resistance patterns: We observed high resistance rates to cefoperazone + sulbactam (92%) and ceftazidime (48%), while ciprofloxacin and trimethoprim/sulfamethoxazole showed better efficacy (88%) susceptibility each.
- Significant mortality rate: The 40% mortality rate underscores the severity of *B. cepacia* infections in critical care settings.

These findings have important implications for clinical practice and infection control:

- They emphasize the need for enhanced surveillance and screening for *B. cepacia*, particularly in high-risk patients.
- They guide empiric antibiotic therapy, suggesting the potential use of ciprofloxacin or trimethoprim/sulfamethoxazole as first-line options, pending susceptibility results.

They highlight the urgent need for stringent infection control measures to prevent the spread of *B. cepacia* in healthcare settings.

In conclusion, our study provides valuable insights into the challenges posed by *B. cepacia* infections in critical care units. To tackle this ongoing threat and protect vulnerable patients, future research should focus on identifying environmental reservoirs, developing rapid diagnostic methods, and exploring novel therapeutic approaches. A multidisciplinary approach involving microbiologists, infectious disease specialists, and critical care teams is crucial for optimal management of *B. cepacia* infections and improvement of patient outcomes.

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Ethical considerations: This study was conducted as part of routine infection control and surveillance activities in our hospital. As it involved retrospective analysis of routinely collected, anonymized clinical and microbiological data, with no additional interventions or patient contact, formal ethical approval was not required as per our institutional guidelines .

Author Contributions:

Author contribution: We declare that all listed authors have made substantial contributions to all of the following three parts of the manuscript:

-research design, or acquisition, analysis, or interpretation of data؛

-drafting the paper or revising it critically؛

-approving the submitted version.

We also declare that no one who qualifies for authorship has been excluded from the list of authors.

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HIGHLIGHTS

Our results highlight the need for:

- Enhanced surveillance and screening for *B. cepacia*, particularly in high-risk patients with diabetes or prolonged ICU stays.
- Tailored antibiotic therapy based on local susceptibility patterns, with consideration of ciprofloxacin and trimethoprim/sulfamethoxazole as potential first-line options.
- Stringent infection control measures, including strict hand hygiene, proper disinfection of medical equipment, and regular environmental sampling.

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