Original Article

Nosocomial *Burkholderia cepacia* infections in a Turkish university hospital: a five-year surveillance

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Abstract

Background: *Burkholderia cepacia* has the potential to cause fatal infections in ICUs, and multidrug resistance makes them a serious threat in hospital settings. The aim of this study was to evaluate the epidemiology of *B. cepacia* infections in our hospital.

Methodology: The incidence, clinical characteristics, antimicrobial susceptibility, and outcomes of nosocomial *B. cepacia* infections during a five-year period were retrospectively analysed according to the infection control committee records.

Results: A total of 39 cases with nosocomial *B. cepacia* infection were included in the study. *B. cepacia* was identified from 0.7% of the nosocomial isolates. Its incidence was 0.26 per 1,000 admissions with 53.8% crude mortality rate. The most frequent nosocomial *B. cepacia* infection was pneumonia (58.9%), followed by bloodstream infections (25.6%), surgical site infections (7.6%), urinary tract infections, (5.1%), and skin-soft tissue infections (2.5%). Nosocomial *B. cepacia* infections were most commonly observed in intensive care units (61.5%). The most active antimicrobial agents were piperacillin-tazobactam, cefoperazone-sulbactam, and carbapenems.

Conclusions: The incidence of nosocomial *B. cepacia* infections was rare in our hospital, and no outbreak was detected during the study period. However, infections caused by *B. cepacia* should be taken into consideration because of their high mortality due to multidrug resistance in ICU settings.

Key words: Nosocomial, *Burkholderia cepacia*, surveillance

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Introduction

Burkholderia cepacia, formerly *Pseudomonas cepacia*, is an aerobic, motile, glucose-nonfermenting, multidrug resistant Gram-negative bacillus that proliferates under conditions of minimal nutrition and can survive in the presence of certain disinfectants. It is widely distributed in the natural environment and has been isolated from water, soil, fruits, and vegetables. *B. cepacia* has emerged as an serious human pathogen in the last two decades, causing fatal necrotizing pneumonia and bacteremia, especially in patients with cystic fibrosis (CF) or chronic granulomatous disease [1-4]. *B. cepacia* was isolated in 0.2-0.6% of all ventilator-associated pneumonias reported to the National Nosocomial Infections Surveillance System (NNIS) in the United States between 1998 and 2004 [2,5]. *B. cepacia* has been associated with outbreaks involving infections of the bloodstream, respiratory tract, and urinary tract inintensive care unit (ICU) settings [4]. Early detection and treatment with appropriate antibiotics of this organism is important because of its high transmissibility in the hospital setting, intrinsic resistance to many antibiotics, and association with a poor prognosis. Though infrequent, *B. cepacia* infections can be severe, with reported mortality rates as high as 83% among patients with lower respiratory tract infections [6,7].

In this retrospective study, we analyzed the incidence, clinical characteristics, antimicrobial susceptibility, and outcomes of nosocomial *B. cepacia* infections during the period 2003 to 2007 in our institution.

Materials and Methods

Gazi University School of Medicine is a 1,000-bed tertiary care teaching hospital in Ankara, Turkey. From January 2003 to December 2007, all patients with nosocomial infections (NI) due to *B. cepacia* were included in the study. The patients colonized with *B. cepacia* were excluded from the study. The data were obtained from infection control committee records. NI surveillance was performed actively, based on both laboratory and patient records, during

the period. The diagnosis of NI was made according to Centers for Diseases Control and Prevention (CDC) criteria [8]. The following data of the patients were collected and analyzed: age, sex, wards, duration of hospitalization, presence of prior antibiotic treatment, risk factors and underlying diseases of the patients, site of NI, microbiological data, and outcome.

Microorganisms were identified by the BBL Crystal Enteric/Nonfermenter ID Kit (Becton Dickinson, USA). The *in vitro* activities of antimicrobial agents were tested against the clinical isolates of *B. cepacia* by a disk diffusion method according to the Clinical and Laboratory Standards Institute (CLSI) standards [9]. Mueller-Hinton agar plates were inoculated with a bacterial suspension equivalent to a 0.5 McFarland Standard and then antibiotic susceptibility disks (Oxoid) were applied. Zones of growth inhibition were recorded in milimeters after overnight incubation at 35^{o}C.

Results

During the study period, *B. cepacia* was isolated from various clinical specimens of 48 patients. Only 39 of them (81.2%) were accepted as a causative agent of nosocomial infection. *B. cepacia*, as an aetiological agent, constituted 0.7% of NI isolates and 1.0% of Gram negative microorganisms. Nosocomial infection incidence was 30.5 per 1,000 admissions. Nosocomial *B. cepacia* infection incidence was 0.26 per 1,000 admissions. There was no acummulation of *B. cepacia* infections according to the occurrence time and the wards during the study period. The incidence of *B. cepacia* infections, its percentage among nosocomial pathogens, wards, and sites of NIs by years are shown in table 1.

The male/female ratio was 1.29 with the mean age 54.4 ± 23.4 years (median 54 years). Mean duration of hospitalization was 15.2 ± 9.9 days (median 15 days). Prior antibiotic use due to various infections was observed in only 15 (38.5%) of the patients. The crude mortality rate was 24.3% for all nosocomial infections and 53.8% for *B. cepacia* infections. *B. cepacia* infections were seen mostly in intensive care units. The most frequent infection was pneumonia (58.9%). The demographic and clinical characteristics of patients are shown in table 2.

The antimicrobial susceptibility of *B. cepacia* isolates is summarized in table 3. The most active antimicrobial agents were piperacillin-tazobactam, cefoperazone-sulbactam, and carbapenems.

Discussion

Non-fermentative Gram negative rods are opportunistic pathogens responsible for nosocomial infections. *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Stenotrophomonas maltophilia* are the most frequent non-fermentative agents of nosocomial infections in intensive care units. Multidrug resistance among these species can cause serious problems in the clinical setting. *B. cepacia* can now be added to this list because of its high transmissibility between hospitalized patients and multiple drug resistance. *B. cepacia* is virtually nonpathogenic in healthy hosts. It is commonly associated with colonization and pulmonary infection in CF patients [1,10,11]. However, the pathogenicity of *B. cepacia* is not always limited to individuals with CF. *B. cepacia* has also been recognised, albeit rarely, as causing fatal disease in healthy individuals [12,13]. This microorganism is associated with a wide variety of infections, including pneumonia, bacteremia, skin and soft tissue infection, genitourinary tract infection secondary to urethral instrumentation, or through exposure to contaminated solutions in hospitalized patients [4,14]. In hospitals, *B. cepacia* has been found to contaminate antiseptics, disinfectants, nebuliser solution, and dextrose solution [15]. Holmes *et al.* reported a large hospital outbreak that appeared to involve both CF and non-CF patients [16]. A phylogenetic analysis revealed a cross-infection by a single dominant clone of *B. cepacia* between patients with and without cystic fibrosis.

In the literature, reports of nosocomial *B. cepacia* infections are restricted to the epidemics [1-3,5,19]. Consistent with the nature of nosocomial epidemics, breaks in infection control as well as the high transmissibily of the microroganism are mostly responsible for the *B. Cepacia* epidemics. Our data do not show any epidemics, but all sporadic cases of *B. cepacia* infections. Though not included in the study, one can consider the rapid identification of the cases and the strict infection control measures and apply them to avoid epidemics.

The isolation and identification of *B. cepacia* can be difficult in the laboratory. The correct identification of this organism is important because of the high rate of cross-infection and associated virulence. Accurate identification of *B. cepacia* is difficult, and there are a few strains which are known

Table 1. Incidence of *Burkholderia cepacia* infections, isolation percentages, wards, and infection sites between 2003-2007.

Characteristic	**Value**
No. of *Burkholderia cepacia* isolates	39
Incidence (per 1000 admission)	0.26
% of *Burkholderia cepacia* among NI isolates	0.7
% of *Burkholderia cepacia* among Gram negative isolates 1.0	1.0
Wards	**No. (%) of patients**
Medical wards	10/39 (25.6)
Surgical wards	5/39 (12.8)
Intensive care units	24/39 (61.5)
Infection site	
Pneumonia (included VAP)	23/39 (58.9)
Bloodstream (included catheter related BSI)	10/39 (25.6)
Urinary tract	2/39 (5.1)
Surgical site	3/39 (7.6)
Skin-soft tissue	1/39(2.5)

NI = nosocomial infection, VAP = ventilator-associated pneumonia, BSI = Bloodstream infections

Table 2. Demographic and clinical characteristics of 39 patients with *Burkholderia cepacia* infection

Charasteristic	**Value**
Gender, male/female	22/17 (1.29)
Crude mortality rate (%)	53.8
Age, mean+SD (year)	54.4±23.4
Setting, ICU/non-ICU	24/15
Duration of hospitalization (days)	15.2±9.9
Underlying diseases / risk factors	**No. (%) of patients**
Central venous catheter	34 (87.1)
Urinary catheter	30 (76.9)
Antiacid	29 (74.3)
Mechanical ventilation	25 (64.1)
Endoscopy	22 (56.4)
Prior antibiotic use	15 (38.4)
Tracheostomy	14 (35.8)
Blood transfusion	13 (33.3)
Malignancy	11 (28.2)
Drainage catheter	11 (28.2)
Diabetes mellitus	6 (15.3)
Immunsupressive therapy	5 (12.8)
Hemodialysis	5 (12.8)

as the *B. cepacia* complex. The molecular taxonomic analyses placed different *B. cepacia* strains into groups known as genomovars. Although genotypic identification with molecular tests is more accurate for definitive identification, a few genomovars can be excluded according to the phenotypic characteristics [17]. As this study was a retrospective analysis and the cases were not cummulative, we could not identify genomovars of *B. cepacia* strains. Antimicrobial susceptibility tests were performed by the disk diffusion method in the study. Ideally, the susceptibility testing should have been done by the Etest or microbroth dilution method; this is a limitation for our retrospective study.

Table 3. Antimicrobial resistance rates of *Burkholderia cepacia* isolates (n:39)

Antibiotics	**Resistance, n (%)**
Amikacin	21 (53.8)
İmipenem	18 (46.1)
Meropenem	19 (48.7)
Netilmicin	21 (53.8)
Piperacillin-tazobactam	15 (38.4)
Ceftazidime	24 (61.5)
Cefotaxime	30 (76.9)
Cefepime	22 (56.4)
Ciprofloxacin	21 (53.8)
Cefoperazone-sulbactam	17 (43.5)
Trimethoprim-sulfamethoxazole	22 (56.4)

The incidence of nosocomial *B. cepacia* infections was very low in our hospital (0.26 per 1000 admission). The ICUs (61.5%) were the wards in which nosocomial *B. cepacia* infections occurred more frequently. The crude mortality was found to be 53.8% in nosocomial *B. cepacia* infections. The most frequent risk factors in these patients were invasive procedures such as mechanical ventilation and urinary and central venous catheterization, which were mostly related to the severity of the underlying diseases of patients in the ICU. There is no data about its incidence among nosocomial infections in surveillance studies in the literature. Most of the reports are focused on its potential to cause nosocomial outbreaks and of resistance to commonly used antibiotics. The outbreaks due to *B. cepacia* have frequently occurred in ICUs, and have been traced to sources related to the respiratory route, nebulised medication, mouthwash and the disinfectant [2,3,5]. Contaminated products, including tap, distilled, or deionized water; contaminated chlorhexidine; topical anesthetic agents; benzalkonium chloride; povidone iodine solution; and quarternary ammonium solutions were responsible for numerous outbreaks in a hospital

setting [1,4]. *B. cepacia* has been associated with outbreaks involving infections of the bloodstream, respiratory tract, and urinary tract [4].

In our hospital, the most frequent *B. cepacia* infection was pneumonia (58.9%), and 64.1% of the patients were under mechanical ventilation. Mechanical ventilation is a major risk factor for *B. cepacia* respiratory acquisition, and association has been described in *B. cepacia* outbreaks. Oropharyngeal bacterial colonization during intubation, poor cough reflex, and direct inhalation of contaminated aerosols into the lower respiratory tract have been involved in the higher risk for pneumonia of patients receiving mechanical ventilation [2,10].

Bloodstream infections, including catheter related BSI, were the second most common (25.6%) *B. cepacia* infection in our hospital. *B. cepacia* bacteremia, most often in association with polymicrobial catheter-related infection, has been reported in patients with cancer who are undergoing hemodialysis [4]. Two outbreaks of *B. cepacia* nosocomial infection in a neonatal intensive care unit were reported by Lee [18]. Prior long duration of an intravascular line was found to be associated with the first septicaemic episode in a case control analysis of the first outbreak. Another nosocomial outbreak of intravenous catheter-related *B. cepacia* bloodstream infections was reported by Nasser *et al*. [3].

B. cepacia is a well-known nosocomial pathogen that is intrinsically resistant to aminoglycosides and first- and second-generation cephalosporins. The multiple-antibiotic resistance of *B. cepacia* has been attributed to an impermeable selective outer membrane, an efflux pump mechanism, and/or the production of an inducible chromosomal beta-lactamase [19-21]. The antimicrobial resistance rates among *B. cepacia* strains were found to be high in our study. The most active antimicrobial agents against *B. cepacia* isolates were piperacillin-tazobactam, cefoperazone-sulbactam and carbapenems. Carbapenem resistance is reported to be as high as 48-89% among *B. cepacia* isolated from nosocomial infections with cystic fibrosis [22-24]. Carbapenem resistance rate in our study was approximately at the lower end of this range.

In conclusion, the incidence of nosocomial infections due to *B. cepacia* was rare in our hospital. No outbreak was detected during the study period. Nosocomial *B.cepacia* infections occured mostly in intensive care unit patients associated with invasive procedures. Its potential to cause fatal infections in the ICUs and its multidrug resistance makes its presence dangerous in hospital settings. The surveillance of *B. cepacia* infections should not be neglected, especially in the ICUs. Given the high transmissibility of the microorganism and previous epidemic reports, strict infection control measures should be applied in the case of a *B. cepacia* infection diagnosis.

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