Major Aspects of *Burkholderia gladioli* and *Burkholderia cepacia* Infections in Children

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Background: *Burkholderia cepacia* complex is an aerobic, non–spore-forming, catalase-positive, nonfermentative, Gram-negative bacterium common in environment. It is a serious pathogen especially for patients with cystic fibrosis (CF). But pathogenicity of *Burkholderia* is not limited to patients with CF. Herein, we aimed to reveal clinical patterns and outcomes of *Burkholderia* infections in pediatric patients in our hospital and also antimicrobial susceptibility of the isolated strain.

Methods: This retrospective study was conducted in Ankara Hematology Oncology Children's Training and Research Hospital. Patients with isolates of *Burkholderia* spp. between January 6, 2013, and January 12, 2018, were included in the study.

Results: *Burkholderia* spp. was isolated from 55 patients. 94.6% of these patients had underlying diseases and had prior hospitalization within a year. *Burkholderia gladioli* grew in 15 patients' samples (27.3%); 38 patients grew *B. cepacia* (69.1%). None of the patients that *B. gladioli* was isolated was diagnosed as CF;. all had nosocomial infections. *B. gladioli* seemed to be more susceptible to aminoglycosides, piperacillin-tazobactam, carbapenems and ciprofloxacin than *B. cepacia* ($P = 0.00$), whereas *B. cepacia* seemed to be more susceptible to ceftazidime than *B. gladioli* ($P = 0.032$). In addition, *B. cepacia* was more susceptible to trimethoprim-sulfamethoxazole and levofloxacin than *B. gladioli*, but this difference was not statistically significant ($P = 0.76$).

Conclusions: The incidence of nosocomial infections caused by *Burkholderia* spp. is rare especially in pediatric literature. In our study, nosocomial *Burkholderia* infections occurred mostly in intensive care unit patients. The surveillance of *Burkholderia* infections is still very important, and the clinicians should be aware of changing epidemiology and increasing resistance of the microorganism. Besides, there are no internationally agreed minimal inhibitory concentration breakpoints and disk-diffusion test thresholds for susceptibility testing for *Burkholderia*. Thus, the methods which were used for antibiotic susceptibility testing in our center might cause uncertainty about the results and internationally agreed minimal inhibitory concentration breakpoints and disk-diffusion test thresholds for susceptibility testing for *Burkholderia* is still a gap to fill for the current literature.

Key Words: *Burkholderia* spp., antibiotic susceptibility, nosocomial infection

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Burkholderia cepacia complex (Bcc) is an aerobic, catalase-positive, non–spore-forming, nonfermentative, Gram-negative bacterium commonly found in soil and moist environments.[1] *Burkholderia* spp. is a serious pathogen especially seen in patients with cystic fibrosis (CF),[2] and it can survive even in the presence of certain disinfectants.[3] Nevertheless, pathogenicity of *Burkholderia* is not limited to patients with CF.[4] Bcc is commonly found in fluid environments in healthcare settings. It can colonize and cause infection in hospitalized, immunocompromised patients. This might result in respiratory tract, bloodstream and urinary tract infections in these patients.[5] It can sometimes lead to outbreaks by means of different sources such as contaminated intravenous medications/fluids, medical devices or skin disinfectants.[6] There are >21 genotypes of Bcc. *B. cepacia* predominantly infects non-CF patients, whereas *Burkholderia multivorans*, *Burkholderia cenocepacia* and *Burkholderia gladioli* (non-cepacia group) are more common in patients with CF. *B. gladioli* is very similar to Bcc; however, following advanced molecular identification, it is classified as an independent species.[7] *B. gladioli* is more related to transient infection, less antibiotic resistance and absence of patient-to-patient transmission when compared with Bcc.[7] Main clinical presentations of *B. gladioli* are pulmonary disease especially in patients with CF before[8] and after lung transplantation,[9] chronic granulomatous disease[10] and acquired immune deficiency syndrome.[11] Extrapulmonary infection has also been identified in patients with CF[11] in immunocompromised hosts and patients with diabetes mellitus.[12]

In this study, we aimed to document clinical patterns and outcomes of pediatric patients infected with *Burkholderia* spp. in our hospital, as well as the antimicrobial susceptibility of the isolated strain from these patients.

METHODS

Study Design

This retrospective study was conducted in Ankara Children's Hematology and Oncology, Training and Research Hospital which is a tertiary children's care hospital. Patients with isolates of *Burkholderia* between January 6, 2013, and January 12, 2018, were included in the study. The body fluid samples collected were endotracheal aspirate, blood (either from a peripheral vein or through central venous catheter), cerebrospinal fluid, sputum and urine. Culture results as colonized, were also included in the study, to not only determine clinical properties but also analyze antimicrobial susceptibility. The following types of data were sourced from the patient records and analyzed: age, sex, unit, duration of hospitalization, presence of prior antibiotic treatment, risk factors (such as central venous catheter, mechanical ventilation and urinary catheterization) and underlying diseases of the patients, prior hospitalization with the same symptoms, site of NI, microbiologic data and outcome. In infected patients, after the detection of *Burkholderia* spp., empiric treatment was changed according to the antibiotic susceptibility test results. Signs and symptoms of patients recovered under therapy. Duration of treatment was focused on the diagnosis (like bloodstream infection, ventilator-associated pneumonia). Clinical improvement and decline in acute phase reactants were also used in terms of ending the therapy. Repetitive culture testing was not planned for ventilated patients, in case of detection of colonization.

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Definitions

Colonization was defined as the first stage of microbial infection at the appropriate portal of entry. It is the presence of microorganisms in or on a host with growth and multiplication but without tissue invasion or damage.[13,14] Therefore, in our study, cases without clinical symptoms of infection were accepted as cases of colonization. For patients with CF, an exacerbation was defined as the need for additional antibiotic treatment as indicated by a recent change in sputum volume or color; increased cough; increased malaise, fatigue or lethargy; anorexia or weight loss; decrease in pulmonary function by 10% or radiographic changes; increased dyspnea.[15] Therefore, CF cases with clinical findings were accepted as exacerbation of pneumonia in our study, while patients without these findings were accepted as colonized.

Sepsis was defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[16] In our study, sepsis was identified according to clinical findings as well as laboratory test results. Catheter-related bloodstream infection, nosocomial pneumonia, urinary tract infection, surgical site infection and skin and soft tissue infection were defined according to Centers for Disease Control and Prevention guidelines. Nosocomial infection was considered as definition when site-specific infection criteria occurred on or after third calendar day of admission.[17]

Microbiologic Identification

Samples were inoculated to BD Columbia Agar with 5% Sheep Blood-Becton Dickinson agar. Oxidase and catalase tests were made if necessary. After observing Bcc grew, bacterial subtyping and susceptibility tests were done with BD Phoenix automated identification and susceptibility testing system. If resistance occurred, Mueller–Hinton agar plates were inoculated with a bacterial suspension equivalent to a 0.5 McFarland Standard, and then the antibiotic susceptibility disks (Oxoid) were applied. Zones of growth inhibition were recorded in millimeters after overnight incubation at 35°C.

Antibiotic susceptibility test interpretation was determined using Clinical and Laboratory Standard Institute guidelines; Clinical and Laboratory Standard Institute recommended testing with ceftazidime, minocycline, meropenem and trimethoprim-sulfamethoxazole (TMP-SMX), in 2010.[18] European Society of Clinical Microbiology and Infectious Diseases does not determine minimal inhibitory concentration (MIC) values for Bcc antibiotic susceptibility tests.[19] In our study, because no European Society of Clinical Microbiology and Infectious Diseases species-specific breakpoints were available, non–species-related breakpoints were used. When considering the MIC values given for colistin (MIC ≤2), gentamicin (MIC ≤4), imipenem (MIC ≤4), meropenem (MIC ≤2), piperacillin-tazobactam (MIC ≤16/4), ciprofloxacin (MIC ≤0.5), levofloxacin (MIC ≤1) and amikacin (MIC ≤8), MIC values defined for *Pseudomonas* spp. were used as reference, and when considering MIC values for tigecycline (MIC ≤0.5), ceftriaxone (MIC ≤1), ampicillin-sulbactam (MIC ≤8), ceftazidime (MIC ≤8) and TMP-SMX (MIC ≤4), MIC values defined for Enterobacteriaceae were used.[20,21].

Ethical Approval

Ankara Hematology Oncology Children's Training and Research Hospital Ethics Committee approved the study, with the reference number: 2018/185.

Statistical Analyses

Patients' data were collected from hospital records retrospectively, and data entry was completed for statistical analyses. All statistical analyses were conducted using SPSS software (version 22; IBM, Chicago, IL). Continuous data that did not follow a normal distribution were reported using medians with minimum and maximum and compared using the Mann-Whitney *U* test, as appropriate. For the whole group, one sample χ^2 test was used to compare the subgroups (like wards, risk factors, underlying diseases) of the patients. χ^2 test was also used for comparison of the *Burkholderia* strains in terms of antibiotic susceptibility, ward, underlying disease, etc., and precise *P* values were reported.

RESULTS

Burkholderia spp. was isolated in 55 patients. Twenty-two of these patients were female (40%), and 33 were male (60%). Median age was 40.8 months (0.23–172 months). These patients were hospitalized for minimum 2, maximum 8 days (median, 3). Forty-seven (94.6%) of these patients had underlying diseases and had prior hospitalization within the last year. These underlying diseases were neuromotor disorders and cerebral palsy in 14 patients, malignancies in 12 patients, CF in 5 patients and other conditions in 17 patients. All patients in our study, who were treated for *Burkholderia* infection, responded well to treatment, and none of the patients died. No repetitive culture positivity was observed in the study group. There were no coinfections with other bacteria in the entire study group. Patient characteristics, underlying diseases and risk factors are shown in Table 1.

The body fluid specimens of patients where *Burkholderia* isolated were blood (n = 27), endotracheal aspirate (n = 13), pus (n = 5), sputum (n = 5), urine (n = 3), cerebrospinal fluid (n = 1) and bronchoalveolar lavage (n = 1). Twenty-two patients had central venous catheter; 13 patients, who were hospitalized in intensive care units (ICUs), were mechanically ventilated. The clinical presentation was sepsis in 24 patients, ventilatory-associated pneumonia in 11 patients and pneumonia in 3 patients (all were CF). Because there were no clinical symptoms or signs of infection, 13 of these results were assumed as colonization. Eight of the patients who had sepsis also needed circulatory support like dopamine or milrinone. The patients' distribution from different pediatric wards is shown in Table 2. The number of patients in ICU was significantly higher than the number of patients from other wards ($P = 0.017$).

TABLE 1. Incidence of *Burkholderia cepacia* Infections, Isolation Percentages, Wards and Infection Sites Between 2003 and 2007

Characteristic	Value
Gender, male/female, n	33/22
Age (mo), median + SD	40.8 (0.23–192.43)
Duration of hospitalization (d) (before culture positivity)	3 (2–8)
Duration of hospitalization (d) (after culture positivity)	14 (7–30)
Prior hospitalization, n (%)	47 (94.6)
Risk factors,* n (%) of patients	
None	11 (22)
Central venous catheter	22 (44)
Other	4 (8)
Mechanical ventilation	13 (26)
Underlying disease,† n (%) of patients	
Neuromotor disorder	14 (25.4)
Cystic fibrosis	5 (9.0)
Malignancy	12 (21.8)
None	4 (7.2)
Other	17 (30.9)

*Data of 5 patients could not be reached.
†Data of 3 patients could not be reached.

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TABLE 2. Demographic and Clinical Characteristics of 39 Patients With *Burkholderia cepacia* Infection

Characteristic	Value
No. of *Burkholderia cepacia* isolates	55
Wards, n (%) of patients	
Medical wards	46 (83)
Pediatric intensive care unit	13 (23.6)
Infant unit	7 (12.7)
Hematology oncology department	9 (16.3)
Bone marrow transplantation	4 (7.27)
Toddler unit	2 (3.6)
Neonatal intensive care unit	6 (10.9)
Infectious disease unit	3 (5.45)
Outpatient	2 (3.6)
Surgical wards	9 (16.3)
Infection site,* n (%) of patients	
Pneumonia (included VAP)	14 (25.9)
Bloodstream (included catheter-related BSI)	24 (43.6)
Urinary tract	3 (5.5)
Surgical site	0
Skin-soft tissue	0
Colonization site, n (%) of patients	13 (27.6)
Sputum	2 (3.6)
Endotracheal aspirate	2 (3.6)
Pus	5 (9.0)
Central venous catheter	3 (5.4)
Ventriculoperitoneal shunt	1 (1.8)

*Data of 1 patient could not be reached.

Forty-two patients (76.3%) were treated with different clinical presentations of *Burkholderia* infection. Colonized patients were not treated, and sampling was not repeated. Median treatment duration was 14 days (7–30). Median C-reactive protein level was 6.45 mg/dL (0–22), and median leukocyte count was 11,300 (100–38,300). Carbapenem was used in 68.8% of patients (24.1% carbapenem alone, 10.3% was used after piperacillin-tazobactam consecutively, 13.8% combination with colistin, 3.4% combination with aminoglycosides and 17.2% combination with ciprofloxacin). The other antibiotics used were TMP-SMX (6.9%), ceftriaxone (6.9%), piperacillin-tazobactam (3.4%), cefepime (3.4%), ceftazidime (3.4%), ciprofloxacin (3.4%) and linezolid (3.4%). Combination therapy was used when there was no clinical improvement after 72 hours of treatment.

B. gladioli grew in 15 patients' samples (27.3%) and *B. cepacia* grew in 38 (69.1%). Two of these samples were nontypable (3.6%). No difference was found between *B. gladioli* and *B. cepacia* due to pediatric wards, clinical outcome, the body part of the sample or the risk factors and underlying diseases (Table 3). C-reactive protein and leukocyte counts were also similar in both serotypes ($P = 0.67$). None of the patients, in whose samples *B. gladioli* were isolated, was diagnosed as CF; all were nosocomial infections.

Antibiotic susceptibility of *B. gladioli* and *B. cepacia* is shown in Table 4. According to these findings, *Burkholderia* spp. were accepted as susceptible to TMP-SMX (MIC ≤2) (20/34), followed by meropenem (MIC ≤4) (12/31) and piperacillin-tazobactam (MIC ≤16) (13/34). Levofloxacin (MIC ≤0.5) and tigecycline (MIC ≤0.5) seemed to be effective, but the number of samples was not as much as meropenem, TMP-SMX and piperacillin-tazobactam. According to χ^2 test, 75% of samples which were susceptible to meropenem were also susceptible to piperacillin-tazobactam and aminoglycosides ($P = 0.02$).

When the evaluations of antibiotic susceptibility for *B. cepacia* and *B. gladioli* were performed separately, *B. gladioli* isolates seemed to be more susceptible to aminoglycosides, piperacillin-tazobactam, carbapenems and ciprofloxacin than *B. cepacia* isolates ($P = 0.00$), whereas *B. cepacia* isolates were found to be more susceptible to ceftazidime than *B. gladioli* isolates ($P = 0.032$). In addition, *B. cepacia* isolates were found to be more susceptible to TMP-SMX and levofloxacin than *B. gladioli* isolates, but this difference was not statistically significant ($P = 0.76$) (Table 5).

TABLE 3. *Burkholderia* spp. and Distribution in Pediatric Wards

	Burkholderia Gladioli, n (%)	Burkholderia cepacia, n (%)	P
Pediatric intensive care unit	1 (6.7)	11 (28)	
Hematology oncology department	5 (33.3)	4 (10.5)	
Bone marrow transplantation	0 (0)	4 (10.5)	0.43
Toddlers ward	1 (6.7)	1 (2.6)	
Infantile clinic	3 (20)	4 (10.5)	
Infectious disease unit	2 (13.3)	1 (2.6)	
Burn wound clinic	2 (13.3)	4 (10.5)	
Neonatal intensive care unit	0 (0)	5 (13.2)	
Pediatric surgery	1 (6.7)	2 (5.3)	

DISCUSSION

Bcc is a newly emerging nonfermenting Gram-negative bacteria that cause nosocomial infections.[22] To the best of our knowledge, this is the largest reported pediatric data with 55 patients, of which 24 were sepsis patients due to *Burkholderia* infections. There was no outbreak during our study period. The most common species was *B. cepacia* (n = 38) followed by *B. gladioli* (n = 15). This is a new finding because *B. gladioli* is not that common in pediatric literature, especially as the reason of nosocomial infections. Generally, *B. gladioli* is presented with case reports or series.[23] Only 5 of our patients had CF, and *B. gladioli* was isolated from none. Clinicians should be aware of the increasing prevalence of *B. gladioli*–associated nosocomial infections in non-CF patients.

The reports about Bcc infections are generally limited to outbreaks, and surveillance studies that include sporadic cases are rare. Our study provides a sample that fills this research gap.

The clinical presentation of *Burkholderia* infection varies in different studies. In the study by Srinivasan et al,[22] the most frequent isolation of *B. cepacia* was from blood cultures. This was followed by pus, central line catheter tip, urine, sputum and tracheal

TABLE 4. Antimicrobial Susceptibility Rates of *Burkholderia* Isolates (n = 39)

Antibiotics	Sensitive*	Resistant†	Total	%
Amikacin	13	32	45	28.9
Gentamicin	12	33	45	26.7
Ampicillin-sulbactam	6	34	40	15
İmipenem	8	24	32	25
Meropenem	12	19	31	38.7
Piperacillin-tazobactam	13	21	42	38.2
Ceftazidime	8	21	29	21.6
Ceftriaxone	3	37	40	7.5
Ciprofloxacin	12	32	44	27.3
Trimethoprim-sulfamethoxazole	20	14	34	58.8
Ticarcillin-clavulanate	4	5	9	44.4
Levofloxacin	10	3	13	76.9
Tigecycline	9	7	16	56.3
Colistin	2	35	37	5.4

*Under the estimated MIC values.
†Over the estimated MIC values.

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TABLE 5. Comparison of Antibiotic Susceptibility Between *Burkholderia* spp.*

Antibiotics	Burkholderia Gladioli, n (%)	Burkholderia Cepacia, n (%)	P
Amikacin			0.00
MIC ≤8	10 (76.9)	3 (9.3)	
MIC >16	3 (23.1)	29 (90.7)	
Gentamicin			0.00
MIC ≤4	10 (76.9)	2 (6.2)	
MIC >4	3 (23.1)	30 (93.8)	
Ampicillin-sulbactam			0.08
MIC ≤8	3 (37.5)	3 (9.3)	
MIC >8	5 (62.5)	29 (90.7)	
İmipenem			0.00
MIC ≤4	6 (85.7)	2 (8)	
MIC >4	1 (14.3)	23 (92)	
Meropenem			0.04
MIC ≤2	5 (71.6)	7 (29.1)	
MIC >8	2 (28.4)	17 (70.9)	
Piperacillin-tazobactam			0.04
MIC ≤16/4	8 (72.7)	5 (21.7)	
MIC >16/4	3 (27.3)	18 (78.3)	
Ceftazidime			0.032
MIC ≤8	0	8 (33.3)	
MIC >8	5 (100)	16 (66.7)	
Ceftriaxone			0.12
MIC ≤1	2 (22.2)	1 (32.2)	
MIC >2	7 (77.8)	30 (67.8)	
Ciprofloxacin			0.008
MIC ≤0.5	7 (58.3)	5 (15.6)	
MIC >0.5	5 (41.7)	27 (84.4)	
Trimethoprim-sulfamethoxazole			0.34
MIC ≤2	3 (42.8)	17 (62.9)	
MIC >4	4 (57.2)	10 (37.1)	
Levofloxacin			0.76
MIC ≤1	1 (100)	9 (75)	
MIC >1	0	3 (25)	
Tigecycline			0.91
MIC ≤0.5	5 (83.3)	4 (40)	
MIC >0.5	1 (16.7)	6 (60)	
Colistin			0.37
MIC ≤2	0	2 (7.4)	
MIC >2	10 (100)	25 (92.6)	

*Indeterminated MIC values were accepted as resistant.

aspirate.[22] In the study by Dizbay et al,[3] pneumonia (58.9%) was the most common clinical presentation of Bcc, followed by bloodstream infection, surgical site infection and urinary tract infections.[3] In our study, 37% of patients had blood stream infections, and 25.9% of patients had pneumonia (including ventilator-associated pneumonia).

In the study by Kim et al,[24] there were 10 pediatric sepsis patients due to *Burkholderia* in 10-year period. He reported that *Burkholderia* may cause hospital infections in immunocompromised patients and in previously healthy pediatric patients with a history of hospitalization in ICU.[24] 94.6% of our patients had a history of prior hospitalization, 13 (23.6%) of them were hospitalized in ICU and the number of patients with sepsis was 24 in our study.

As many strains of *B. cepacia* are highly resistant to many antibiotics, options for treatment of *B. cepacia* are limited. In reports where *B. cepacia* show up to 50.4% resistance to every antibiotic tested, multidrug-resistant isolates are not indicated as uncommon.[25,26] Similarly, in our study, *B. cepacia* was resistant >90% to aminoglycosides, 78.2% to piperacillin-tazobactam, 70.8% to meropenem, 84.3% to ciprofloxacin and 92.5% to colistin. Interestingly, 62.9% of this species was susceptible to TMP-SMX, and 75% seem to be susceptible to levofloxacin. Unlike *B. cepacia*, *B. gladioli* was 76.9% susceptible to aminoglycosides, >70% to carbapenems, 72.7% to piperacillin-tazobactam and 58.8% to ciprofloxacin, whereas 57.1% resistant to TMP-SMX. In the study by Kennedy et al,[27] *B. gladioli* resistance to ≥2 antipseudomonal antibiotic groups was 33%. Resistance was found higher in chronic infection but as low as 6% in transient infection. Resistance was more prevalent to third-generation cephalosporins (28%) and quinolones (20%).[27] Our results show that *B. gladioli* was more susceptible than *B. cepacia* overall, so we can say that when dealing with *B. cepacia*, clinicians should be more careful. Besides, in our study, *B. cepacia* was found more susceptible to TMP-SMX, whereas *B. gladioli* was found more susceptible to piperacillin-tazobactam, aminoglycosides and carbapenems. Considering the proximity of MIC values found in this study and if supported with more studies, these MIC values can be reconsidered to be acceptable in future studies.

Antibiotics that may be effective against *B. cepacia* include TMP-SMX, minocycline, ceftazidime, antipseudomonal penicillins, antipseudomonal quinolones and carbapenems (meropenem has greater in vitro activity against *B. cepacia* than imipenem).[28] In a current review, Sfeir[29] reports that meropenem, ceftazidime, TMP-SMX and doripenem remain the most effective empiric treatment for Bcc infections based on in vitro susceptibility data. In the report by Kim et al,[24] *B. cepacia* cultures of 14 pediatric patients were mostly susceptible to meropenem, levofloxacin, ceftazidime and TMP-SMX.[22] In the report by Srinivasan et al,[22] *B. cepacia* was 71% susceptible to TMP-SMX, 60% to cefoperazone/sulbactam, 69% to cefepime, 93% to colistin and 41% to imipenem.[22] In the study by Mazer et al,[30] it was mentioned that some of the agents that retain activities against the *B. cepacia* strains included ceftazidime, meropenem, piperacillin-tazobactam and TMP-SMX. He also showed that 90% of *B. gladioli* strains were piperacillin/tazobactam susceptible.[30] According to the study by Segonds et al,[7] the activities of the aminoglycoside antibiotics against *B. gladioli* are very high. This contrasts the very poor activities of this class of antibiotics against Bcc species. Research in Turkey shows that quinolones, aminoglycosides, piperacillin-tazobactam, TMP-SMX and carbapenems were effective against Bcc.[3] Our data support some of these research, like meropenem is better suited than imipenem in treating *B. cepacia*, and TMP-SMX and quinolones were options to choose in empiric treatment of *B. cepacia*. But in contrast to this knowledge, *B. cepacia* seemed to be seriously resistant to carbapenems and 50% to ceftazidime. This an important finding, which may be because of our local susceptibility patterns, but still this resistance should be considered when treating *B. cepacia* patients.

The limitation of this study is that it was a retrospective study from a single center. Clinical information was gathered only via patient records, and some of the data needed for this study were not reachable. In addition, the methods which were used for antibiotic susceptibility testing in our center might cause uncertainty about the results and internationally agreed MIC breakpoints and disk-diffusion test thresholds for susceptibility testing for *Burkholderia* is still a gap to fill for the current literature.

The strength of this study is that we reviewed data for a 5-year period including not only outbreaks but also sporadic cases. Another important strength is that this is the largest series studied with pediatric patients. Because not much data exist regarding *B. cepacia* and *B. gladioli* in Turkey, especially in pediatric patients, more data should be collected and analyzed. Besides, more studies about treatment modalities of *Burkholderia* infections are still needed, and internationally agreed MIC breakpoints and disk-diffusion test thresholds for susceptibility test for *Burkholderia* are needed to be established.

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In conclusion, *Burkholderia* infections influence morbidity and mortality among pediatric patients. Bcc species have innate resistance to many antibiotics, which makes their treatment more difficult. They are known to cause outbreaks in various ICUs. The incidence of nosocomial infections due to *Burkholderia* spp. is rare especially in pediatric literature. In our study, nosocomial *Burkholderia* infections occurred mostly in ICU patients associated with invasive procedures. The surveillance of *Burkholderia* infections is still very important, especially in the ICUs. Awareness of colonization and effective therapy of *B. cepacia* infection is crucial. Also, infection control and monitoring are important, especially in patients under prolonged hospital admission.

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