Emergence of *Burkholderia cepacia* in ICU Setting

Suneeta Meena¹, Raunak Bir², Seema Sood³, Bimal Kumar Das⁴, Arti Kapil⁵

**ABSTRACT**

**Background:** *B. cepacia* is metabolically versatile organism which is not only resistant to many antibiotics but also disinfectants. This makes their survival easy even in restricted areas like intensive care unit (ICU) and management difficult.

**Aims and objectives:** To describe sudden emergence of *Burkholderia* at a tertiary care centre ICU setting in milieu of colistin usage

**Materials and methods:** Cases were patients with culture proven *B. cepacia*. They were picked up as non-lactose fermenting, oxidase positive, motile, gram-negative bacilli which was resistant to colistin and aminoglycosides and sensitive to cotrimoxazole. These isolates were further confirmed by both VITEK-2 compact system (Biomerieux, France) and standard bacterial techniques.

Colistin consumption data were retrospectively collected from medical store records of hospitals and individual ICU pharmacy records from January 2016 to June 2016, and were expressed as total daily doses in a month per 1000 patient days (DDD/1000PD)

**Results:** An increase was observed in *B. cepacia* infection linked to increased consumption of colistin in ICU.

**Conclusion:** Based on these results an increase was observed in *B. cepacia* infection which correlated with increased consumption of colistin in ICU. We speculate that extensive use of colistin may lead to selection of intrinsically resistant *B. cepacia* and may facilitate their spread as nosocomial pathogens.

**Keywords:** *Burkholderia cepacia*, Colistin, ICU

**Indian Journal of Critical Care Medicine** (2019): 10.5005/jp-journals-10071-23237

---

**INTRODUCTION**

*B. cepacia* is widely distributed in the natural environment and has been isolated from water, soil, fruits, and vegetables. It is an aerobic, motile, glucose-nonfermenting, multidrug resistant gram-negative bacillus that is also resistant to many disinfectants. These bacteria exhibit an extraordinary metabolic versatility, allowing their adaptation to a wide range of environments. Over the last 2 decades, *B. cepacia* complex has emerged as a serious human pathogen. It can cause fatal necrotizing pneumonia and bacteremia, especially in patients with cystic fibrosis or chronic granulomatous diseases. It is an opportunistic pathogen that causes disease in immunocompromised individuals and has been associated with outbreaks in intensive care unit (ICU) settings.

However, *Burkholderia cepacia* detection from clinical samples is very infrequent in All India Institute of Medical Sciences, Delhi. But, an upsurge of pneumonia caused by this organism which is intrinsically resistant to colistin, was observed for last six months from January 2016 to June 2016 at a tertiary care referral hospital in various ICU. Unfortunately in this context increased use of colistin as a last line therapeutic drug for patients infected with multidrug resistant (MDR) gram-negative bacteria has led to the recent emergence of colistin-resistant bacteria (CRB) among bacterial species. The present study endeavours to describe sudden emergence of *Burkholderia* at a tertiary care centre ICU setting in milieu of colistin usage.

**MATERIAL AND METHODS**

Our center is a tertiary care referral hospital in northern India. We isolated and identified *B. cepacia* isolates from clinical samples, such as endotracheal (ET) aspirate, bronchoalveolar lavage (BAL), blood, drain fluid and blood who were admitted between January 2016 and June 2016.
Emergence of *Burkholderia cepacia* in ICU Setting

**Decarboxylases**, aerobic low-peptone basal medium containing glucose.8

**Colistin Consumption**

Colistin consumption data were retrospectively collected from medical store records of hospitals and individual ICU pharmacy records from January 2016 to June 2016, and were expressed as total dialy doses in a month per 1000 patient days (DDD/1000PD).

**Results**

From Jan 2016 to May 2016, a total of 15 patients had cultures positive for *B. cepacia*. Four of the positive cultures came from tracheal aspirates, 9 from bronchoalveolar lavage (BAL), 1 from blood 1 from chest drain fluid. There was no accumulation of *B. cepacia* infection according to occurrence time and wards or ICU during the study period. Infections caused by *B. cepacia* included pneumonia (n = 14) and bacteremia (n = 3). Two patients had both bacteremia and pneumonia. One isolate was obtained from chest drain fluid of one patient who also had concurrent pneumonia.

All the isolates were from various ICUs of the institution. Most of the infections were hospital acquired due to various risk factors like tracheostomy and intravenous line. *Burkholderia* being a contaminant was considered infectious agent only when it was repeatedly isolated and correlated with clinical features. The demographic and clinical characteristics of the patients are given in Table 1.

The correlation between colistin consumption and prevalence of *B. cepacia* infection is shown in Figure 1. A scatter plot was also plotted to show association between colistin usage and emergence of *B. cepacia* in Figure 2.

By disk diffusion method all the isolates were susceptible to cefoperazone/sulbactam (100%), Piperacillin/tazobactam (100%), levofloxacin (100%). Maximum resistance was observed against ceftazidime (93%) followed by meropenam (53%).

**Discussion**

As stated previously *Burkholderia cepacia* is ubiquitously present in environment, has been isolated from water, soil. It is frequently recovered from hospital water sources.3,10 Moreover it can survive in the presence of certain disinfectants.2,11 It is non-pathogenic in healthy hosts and is commonly associated with colonization and pulmonary infection, especially in cystic fibrosis patients.12 However, it is increasingly being recognised as a newly nonfermenting gram-negative bacteria causing nosocomial infections in hospital setting. It is associated with a wide variety of infections, including pneumonia, bacteremia, skin and soft tissue infection, genitourinary tract infection secondary to urethral instrumentation. Outbreaks have occurred through exposure to contaminated solutions such as antisepsics, disinfectants, nebulizer solution, and dextrose solution in hospitalized patients.13 After January 2016 number of patients with *B. cepacia* infections increased, which correlated well with increased consumption of colistin. However, all the cases were sporadic and there was no accumulation according to occurrence time and location. Moreover, regular periodic environmental sampling of all the ICU could not isolate *B. cepacia*

| Characteristic                                      | Value |
|----------------------------------------------------|-------|
| Total no. *B. cepacia*                             | 15    |
| Patient distribution in intensive care unit        |       |
| Medical ICU                                        | 4     |
| Surgery ICU                                        | 2     |
| Neurosurgery ICU                                   | 3     |
| AB8 ICU                                            | 6     |
| Demographic and clinical characteristics            |       |
| Male/female                                        | 8/7   |
| Age mean                                           | 51.8  |
| Duration of hospitalization                        | 47.2  |
| No. of patients who died                           | 5/15(33.3%) |
| Tracheostomy                                       | 7/15  |
| Hematological malignancy                           | 1/15  |
| Diabetes mellitus                                  | 2/15  |
| Pneumonia                                          | 14/15 |

![Fig. 1: Correlation between colistin consumption (DDD/1000PD) and no. of patients infected with *B. cepacia*](image1)

![Fig. 2: Scatter plot depicting association between colistin usage and emergence *B. cepacia*](image2)
**Emergence of Burkholderia cepacia in ICU Setting**

*B. cepacia* complex has intrinsic resistance to many antimicrobials. It has been well documented to have intrinsic resistance to aminoglycosides, first- and second-generation cephalosporins, traditional antipseudomonal penicillins and polymyxins. The multiple antibiotic resistance of *Burkholderia* has been ascribed to an impermeable selective outer membrane, efflux pump mechanism and/or production of an inducible chromosomal beta-lactamase.\(^1\) In our study also, isolates were resistant to amoxicillin-clavulanic acid (100%) and ceftazidime (100%). It is possible that it may potentially survive well in the environment if there is frequent exposure to broad spectrum antibiotics. Increased use of colistin can cause collateral damage and increased healthcare associated *B. Cepacia* infections. The most active antimicrobial agent against *B. cepacia* isolates were piperacillin-tazobactam and cefoperazone-sulbactam. Based on these results an increase was observed in *B. cepacia* infection linked to increased consumption of colistin in ICU. Resistance to carbapenem compounds is now endemic in several countries worldwide and has led to an increased use of colistin. This result can be further explained by the fact that colistin has been extensively used as a treatment of last resort for patients of ventilator associated pneumonia due to carbapenemase-producing bacteria mainly in *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *K. pneumoniae*. We speculate that extensive use of colistin may lead to selection of intrinsically resistant *B. cepacia* and may facilitate their spread as nosocomial pathogens. This phenomenon has been previously observed in cystic fibrosis where colistin use by aerosols occasionally has led to the selection of intrinsic CRB (colistin resistant bacteria) including *Inquilinus limosus*, *Brevundimonas diminuta*, *Ochrobactrum anthropi*, *Pandoraea spp.*, *Chryseobacterium indolgenes* and *Burkholderia spp.*\(^5\)–\(^11\)

Nosocomial pneumonia (n = 12) accounted for most of the *B. cepacia* infections and 75% (n = 9) were under mechanical ventilation. All the patients were admitted in various ICU (Table 1). Several predisposing factors have been suggested as the major determinants for developing pneumonia. These include permanence in ICU, having undergone major surgery, and having an intravenous catheter.\(^14\) It is difficult to point out at a predisposing factor in this short study with small number of isolates. So far during the study period crude mortality rate was 33.3% (n = 5). But patients were already admitted in ICU for severe underlying condition.

Our study had several limitations. Firstly, it was a retrospective short duration study where sample size was small so risk factor analysis could not be done. Secondly *Burkholderia* isolates were picked up on the basis of antibiotic susceptibility. So, isolates which were cotrimoxazole resistant could have been missed. Lastly, simutaneous emergence of other colistin resistant bacteria (CRB) of genera *Proteus*, *Providencia*, *Morganella* and *Serratia* was not looked for. Nevertheless, this short report does highlight emergence of *B. cepacia* in era of increased usage of colistin as last resort for multidrug resistant bacteria (MDR) gram-negative bacteria. However, other factors could have been responsible for the same which could not be identified in this study.

Use of colistin, also known as the ‘antibiotic of last resort’ should be restricted. Clinicians should avoid using it as initial empirical therapy. It may be used in combination with other antibiotics to increase antibacterial efficacy and to maintain usefulness against MDR gram-negative infections.

**Conclusion**

Use of colistin as last resort for MDR organisms is acting as grounds for emergence of CRB like *B. cepacia*. Colistin should definitely not be used empirically rather in combination with other antibiotics as per the antibiotic policy. It is in this context that hospital should update its antibiogram and make it readily available to clinicians managing patients in such setting.

**References**

1. Mortensen JE, Fisher MC, LiPuma JJ. Recovery of *Pseudomonas cepacia* and other *Pseudomonas* species from the environment. Infect Control Hosp Epidemiol 1995;16:30–32.
2. Huang CH, Jang TN, Liu CY, Fung CP, Yu KW, Wong WW. Characteristics of patients with *Burkholderia cepacia* bacteremia. J Microbiol Immunol Infect 2001;34:215–219.
3. Siddiqui AH, Mulligan ME, Mahenthiralingam E, Hebben J, Brewrink J, Qaiyumi S, et al. An episodic outbreak of genetically related *Burkholderia cepacia* among non-cystic fibrosis patients. J Infect Dis 2001;186:944–948.
4. Estivariz CF, Bhatti LI, Pati R, Jensen B, Arduino MJ, Jeremiah D, et al. An outbreak of *Burkholderia cepacia* associated with contamination of albuterol and nasal spray. Chest 2006;130:1346–1353.
5. Nasser RM, Rahi AC, Haddad MF, Daoud Z, Irani-Hakime N, Almawi WY. Outbreak of *Burkholderia cepacia* bacteremia traced to contaminated hospital water used for dilution of an alcohol skin antiseptic. Infect Control Hosp Epidemiol 2004;25:231–239.
6. Zurita J, Mejia L, Zapata S, Trueba G, Vargas AC, Aguirre S, et al. Healthcare-associated respiratory tract infection and colonization in an intensive care unit caused by *Burkholderia cepacia* isolated in mouthwash. Int J Infect Dis. 2014 Dec;29:96–99.
7. Abat C, Desboves G, Olatan AO, Chaudet H, Roattino N, Fournier PE, et al. Increasing burden of urinary tract infections due to intrinsically colistin-resistant bacteria in hospitals in Marseille, France. Int J Antimicrob Agents. 2015 Feb;45(2):144–150.
8. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twenty-sixth informational supplement M100-S26. Wayne PA: Clinical and Laboratory Standards Institute; 2016.
9. The nonfermentative gram negative bacilli In: Winn W AS, Jande K, Jorgensen JH, Pfaller MA, and Yolken RH, editors. Manual of clinical microbiology, ASM Press, Washington, DC 2007: 749–769.
10. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twenty-sixth informational supplement M100-S26. Wayne PA: Clinical and Laboratory Standards Institute; 2016.
11. Mortensen J, Qaiyumi S, et al. An episodic outbreak of genetically related *Burkholderia cepacia* bacteremia traced to contaminated hospital water used for dilution of an alcohol skin antiseptic. Infect Control Hosp Epidemiol 2004;25:231–239.
12. Oie S, Kamiya A. Microbial contamination of antiseptics and disinfectants. Am J Infect Control;1996;24: 389–395.
13. LiPuma JJ, Currie BJ, Lum G, Vandamme P, Burkeholderia, Porton-entophomonas, Ralstonia, et al. In Murray PR, Baron EJ, Jorgensen JH, Pfaffer MA, and Yolkken RH, editors. Manual of clinical microbiology, ASM Press, Washington, DC 2007: 749–769.
14. Mahenthiralingam E, Baldwin A, Dowson CG. *Burkholderia cepacia* complex bacteria opportunistic pathogens with important natural biology. J Appl Microbiol 2008;104:1539–1551.
15. Burns JL, Wadsworth CD, Barry JJ, Goodall CP. Nucleotide sequence analysis of a gene from *Burkholderia (Pseudomonas)* cepacia encoding an outer membrane lipoprotein involved in multiple antibiotic resistance. Antimicrob Agents Chemother 1996; 40: 307–313. 20.
15. Menuet M, Bittar F, Stremler N, Dubus JC, Sarles J, Raoult D, et al. First isolation of two colistin-resistant emerging pathogens, Brevundimonas diminuta and Ochrobactrum anthropi, in a woman with cystic fibrosis: a case report. J Med Case Rep. 2008;2:373.

16. Chen FL, Wang GC, Teng SO, Ou TY, Yu FL, Lee WS. Clinical and epidemiological of Chryseobacterium indologenes infections: analysis of 215 cases. J Microbiol Immunol Infect. 2013;46(6):425–432.

17. Biswas S, Brunel JM, Dubus JC, Reynaud-Gaubert M, Rolain JM. Colistin: an update on the antibiotic of the 21st century. Expert Rev Anti Infect Ther. 2012;10(8):917–934.

18. Dizbay M, Tunccan OG, Sezer BE, Aktas F, Arman D. Nosocomial Burkholderia cepacia infections in a Turkish university hospital: a five-year surveillance. J Infect Dev Ctries. 2009;3(4):273-7.