Research Article

Pseudo-outbreak of *Burkholderia cepacia* blood stream infections in intensive care units of a super-speciality hospital: A cross-sectional study

Mohit Bhatia, Poonam Sood Loomba, Bibhabati Mishra, Vinita Dogra

Department of Microbiology, Govind Ballabh Pant Institute of Post Graduate Medical Education and Research, New Delhi, India

Correspondence to: Mohit Bhatia, E-mail: docmb1984@gmail.com

Received: March 02, 2017; **Accepted:** March 23, 2017

ABSTRACT

Background: Multiple nosocomial outbreaks caused by *Burkholderia cepacia* involving contaminated water, contaminated medication, nebulization solution, etc., have been reported. **Objectives:** This study was conducted with the aim of tracing the most likely causes of sudden increase in isolation rates of *B. cepacia* from blood samples of patients admitted in different intensive care units (ICUs) of a super-speciality hospital. **Materials and Methods:** A cross-sectional study was conducted in a super-specialty hospital located in New Delhi, India, from August 2015 to July 2016. Blood samples from 600 non-consecutive patients admitted in various ICUs were received for culture and sensitivity testing during the study period. Blood samples of 147 of these non-consecutive inpatients yielded *B. cepacia* in culture. Relevant details of all patients were obtained as per the pro forma formulated. Environmental sampling was also performed at regular intervals to trace the possible sources of infection. Chi-square test was used to calculate *P* value. **Results:** The study period was divided into three-quarters and the difference in the proportion of cases isolated from the ICUs under study during each of these quarters was not found to be statistically significant ($0.05 < P < 0.1$). A statistically significant association ($P < 0.001$ using Chi-square test) was found between afebrile status and simultaneous isolation of *B. cepacia* from blood samples of patients. *B. cepacia* could not be consistently isolated from any source during the study period. **Conclusions:** Nursing staff and doctors working in wards and ICUs should work in liaison with a diagnostic laboratory to assure swift communication of healthcare-associated infection alerts. Isolation of *B. cepacia* from clinical samples should always be correlated clinically to avoid inadvertent use of antimicrobials.

KEY WORDS: *Burkholderia cepacia*; Pseudo-outbreak; Intensive Care Units

INTRODUCTION

Burkholderia cepacia is a catalase-producing, non-lactose-fermenting, aerobic Gram-negative bacterium found in various aquatic environments. It is classified as 10 serovars, collectively termed as *B. cepacia* complex (BCC).[1,2] BCC species have often been reported from outbreaks in both immunocompetent and immunocompromised patients admitted in hospitals. Nosocomial infections caused by BCC include blood stream infections (BSI), pneumonia, surgical wound infections, and genitourinary tract infections.[3] Multiple healthcare-associated outbreaks have been described involving contaminated water, prefabricated moist washcloths, contaminated medication, nebulization solution, antiseptic solution, heparin, moisturizing body milk, and mouthwash solution.[4] In a systematic review of nosocomial infections related to contaminated substances, BCC along with *Enterobacter* spp. ranked first as contaminating pathogen in substances other than blood.[3] Both intrinsic contamination (during manufacturing) and extrinsic contamination (after opening) of medical solutions and equipment have been reported.[5-8]

Access this article online	
Website: http://www.ijmsph.com	**Quick** Response code
DOI: 10.5455/ijmsph.2017.0305723032017	

In July 2015, there was a dramatic increase in the number of *B. cepacia* being isolated from blood samples of patients admitted in different intensive care units (ICUs) of a super-speciality hospital. This study was conducted with the aim of investigating this unusual occurrence to implement appropriate infection control measures.

MATERIALS AND METHODS

A cross-sectional study was conducted in a super-speciality hospital located in New Delhi, India, from August 2015 to July 2016 to trace the most likely causes of sudden increase in isolation rates of *B. cepacia* from blood samples of patients admitted in general ICU and ICUs belonging to cardiothoracic and vascular surgery (CTVS) and Neurosurgery Departments, respectively. Blood samples from six hundred non-consecutive patients admitted in aforementioned ICUs were received for culture and sensitivity testing during the study period. Blood samples of one hundred and forty seven of these non-consecutive inpatients yielded *B. cepacia* in culture. Relevant details of all patients were obtained as per the pro forma formulated. Majority of the blood samples obtained from these patients were processed using BACTEC FX (Becton Dickinson International, New Delhi, India) automated blood culture system during the study period. However, few blood samples had to be processed manually as per standard guidelines due to non-availability of readymade enrichment broth bottles compatible with BACTEC FX automated blood culture system. The bacterial isolates obtained from these blood samples were identified as *B. cepacia* using VITEK-2 (BioMerieux, New Delhi, India, Pvt. Ltd.,) automated system. *In vitro* susceptibility testing for three antibiotics recommended for BCC was performed only for isolates obtained from febrile patients as per Clinical and Laboratory Standards Institute guidelines 2015. Susceptibility to trimethoprim/sulfamethoxazole and meropenem was determined in the form of minimum inhibitory concentration values using VITEK-2 automated system. Susceptibility to ceftazidime was determined by modified Kirby-Bauer disc diffusion method.[9] Environmental sampling was also performed at regular intervals (every 15-30 days) to trace the possible sources of infection. Random samples were collected from the following sites: Lid (inner and outer surfaces), rim, and water of condensation present on inner surface of blood culture bottles; water of condensation present on the walls of refrigerator used to store blood culture bottles containing sterile enrichment broth; neurosurgery and CTVS operation theater (OT) tables; ventilators, bed railings and intravenous (IV) stands, bed linen, humidifier water, central venous catheter (CVC) hubs (inner and outer surfaces) and skin swab samples of area around the site of insertion of CVC of patients, hand swabs of nursing staff and doctors, tap and reverse osmosis water, sinks, cotton gauze pieces used for dressing, disposable rubber gloves, IV injection needles and syringes, multidose vials, in-use disinfectants, namely betadine and absolute alcohol, swabs obtained from rim of bottles of disinfectants in all aforementioned ICUs under study. Organisms isolated from these sites were identified using VITEK-2 automated system. Antibiotic susceptibility testing was performed only for *B. cepacia* isolates obtained from these sites.

RESULTS

The colony morphology of *B. cepacia* on blood agar and MacConkey agar has been depicted in Figure 1a and b, respectively. The study population consisted of 93 males and 54 females. The mean age (±standard deviation) was 37.2 ± 21 years.

Blood samples obtained from 403 out of 600 non-consecutive inpatients during the study period were either reported as "sterile" or "contaminants grown" based on the organisms isolated in culture and clinical history. Blood samples obtained from 147 out of the remaining 197 nonconsecutive inpatients yielded *B. cepacia* in culture. Only one blood sample each could be obtained from 83 of these patients, of whom 43 were afebrile at the time of sample collection. Paired blood samples collected 3-4 days apart were obtained from the remaining 64 patients. *B. cepacia* was repeatedly isolated from blood of 64 patients of whom 54 were afebrile at the time of sample collection. However, *B. cepacia* was not isolated from any other clinical specimen obtained from 147 patients. Blood samples obtained from the remaining 50 inpatients yielded organisms other than *B. cepacia* and were reported in accordance with their clinical history of fever and/or raised total leukocyte count.

Isolation of *B. cepacia* from blood samples of afebrile patients was found to be statistically significant ($P < 0.001$) using Chi-square test.

Table 1 and Figure 2 depict the ICU-wise distribution of the study population during the study period. 80, 42, and 25 out of 147 of these patients were admitted in CTVS ICU, neurosurgery ICU, and general ICU, respectively, during the study period. The study period was divided into three-quarters, namely, Quarter 1 (August 2015- November 2015), Quarter 2 (December 2015-March 2016), and Quarter 3 (April 2016-July 2016). The difference in the proportion of cases isolated from the ICUs under study during these three-quarters was evaluated using Chi-square test and was not found to be statistically significant ($0.05 < P < 0.1$).

The antibiotic susceptibility profile of *B. cepacia* isolated from blood samples of 50 febrile patients has been depicted in Table 2. 25 of these patients were admitted in CTVS ICU,

15 in general ICU, and 10 in neurosurgery ICU, respectively, during the study period. Isolates with different antibiotic susceptibility profiles were isolated from all ICUs under study during the study period.

Table 3 depicts the list of organisms isolated from different environmental samples. *B. cepacia* could not be consistently isolated from any source. This organism was isolated only on four occasions during the study period from different sources which are as follows: Inner surface of hub of CVC line of a patient admitted in general ICU, multidose heparin vial in general ICU, CTVS OT table, and tap water obtained from the same OT. The antibiotic susceptibility profile of these environmental *B. cepacia* isolates has been depicted in Table 4.

DISCUSSION

Several peculiar observations were made during the study period. *B. cepacia* was isolated from blood samples of patients admitted in ICUs managed by three different departments. Isolation of *B. cepacia* from blood samples was increasingly reported initially from patients admitted in CTVS ICU, and later neurosurgery and general ICUs were also involved. No seasonal trend was observed. Since there was no significant difference in the proportion of cases reported from CTVS, neurosurgery and general ICUs, respectively, during the study period, hence, isolation of *B. cepacia* from blood samples of patients admitted in these patients can be considered as independent events. *B. cepacia* was not isolated from any other specimen obtained from these patients. A statistically significant association was found between afebrile status and simultaneous isolation of *B. cepacia* from blood samples of patients. This finding points toward the fact that it was a pseudo-outbreak of *B. cepacia* BSI indicating a breach in infection control practices.

Antibiotic susceptibility profile of *B. cepacia* isolates revealed a high level of resistance to trimethoprim/sulfamethoxazole, meropenem, and ceftazidime. *B. cepacia* is generally resistant to most of the antibiotics, and it

Table 1: ICU wise distribution of patients whose blood samples yielded *B. cepacia* in culture during the study period

Month	CTVS ICU	General ICU	Neurosurgery ICU
August-2015	1	1	1
Septembr-2015	3	0	0
October-2015	7	0	0
Novenber-2015	4	1	0
December-2015	15	2	2
January-2016	10	1	8
February-2016	5	9	1
March-2016	18	6	16
April-2016	0	2	4
May-2016	1	0	5
Junuary-2016	6	1	3
July-2016	10	2	2
Total	80	25	42

B. cepacia: Burkholderia cepacia, ICU: Intensive care units, CTVS: Cardiothoracic and vascular surgery

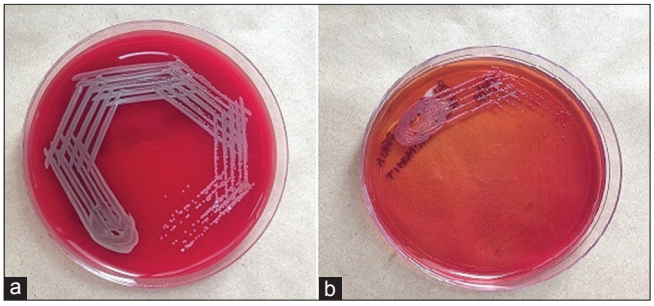

Figure 1: (a and b) Colony morphology of *Burkholderia cepacia* on blood and MacConkey agar plates, respectively

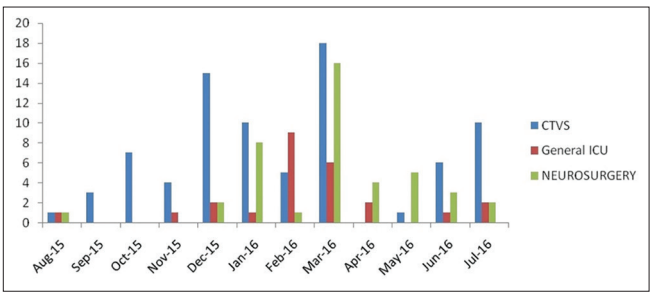

Figure 2: Intensive care units-wise distribution of *Burkholderia cepacia* isolated from blood samples of admitted patients during the study period

Table 2: Antibiotic susceptibility profile of *B. cepacia* isolated from blood samples of 50 febrile patients admitted in different ICUs during the study period

ICU from which isolated	*n* (%)		
	Trimethoprim/sulfamethoxazole	Meropenem	Ceftazidime
CTVS ICU *N1=25	10 (40)	15 (60)	10 (40)
General ICU #N2=15	2 (13.3)	2 (13.3)	3 (20)
Neurosurgery ICU @N3=10	2 (20)	3 (30)	2 (20)

*N1: Number of febrile patients in CTVS ICU, #N2: Number of febrile patients in general ICU, @N3: Number of febrile patients in neurosurgery ICU, *B. cepacia*: *Burkholderia cepacia*, ICU: Intensive care unit, CTVS: Cardiothoracic and vascular surgery

Table 3: List of organisms isolated from different environmental samples

Type of environmental sample	Organisms isolated
Lid (inner and outer surfaces) of blood culture bottles	Coagulase negative *Staphylococci*, *Enterococcus* spp.
Rim of blood culture bottles	Coagulase negative *Staphylococci*
Water of condensation present on inner surface of blood culture bottles	Sterile
Water of condensation present on the walls of refrigerator used to store blood culture bottles containing sterile enrichment broth	Aerobic spore-bearing bacilli
Ventilators	*E. coli*, Acinetobacter spp., *Klebsiella* spp., *Morganella* spp., Coagulase negative *Staphylococci, Enterobacter* spp.
Bed railings and IV stands	*E. coli, Acinetobacter* spp., coagulase negative *Staphylococci*
Bed linen	Coagulase negative *Staphylococci, E. coli, Acinetobacter spp.*
Humidifier water	*R. pickettii*, *Sphingomonas* spp., coagulase negative *Staphylococci,* aerobic spore-bearing bacilli
CVC hubs (inner and outer surfaces)	*B. cepacia* isolated once from general ICU, coagulase negative *Staphylococci*, *E. coli, Acinetobacter* spp., *Klebsiella* spp., *Morganella* spp.
Skin swab samples of area around the site of insertion of CVC of patients	*E. coli*, coagulase negative *Staphylococci, Acinetobacter* spp.,
Hand swabs of nursing staff and doctors posted in ICUs under study	Coagulase negative *Staphylococci*
Tap water	*Klebsiella* spp., *P. aeruginosa, B. cepacia* isolated once from CTVS OT
RO water	*P. aeruginosa, Klebsiella* spp.,
Sinks	Aerobic spore-bearing bacilli
OT table	*B. cepacia* isolated once from CTVS OT table
Cotton gauze pieces used for dressing	Aerobic spore-bearing bacilli, coagulase negative *Staphylococci*
Disposable rubber gloves	Aerobic spore-bearing bacilli
IV injection needles and syringes	Sterile
Multi-dose vial	*B. cepacia* isolated only once from heparin multi-dose vial used in general ICU
In-use disinfectants namely betadine and absolute alcohol used in ICUs under study	Sterile
Swabs obtained from rim of bottles of disinfectants used in ICUs under study	Aerobic spore-bearing bacilli

B. cepacia: Burkholderia cepacia, E. coli: Escherichia coli, R. pickettii: Ralstonia pickettii, P. aeruginosa: Pseudomonas aeruginosa, IV: Intravenous, ICU: Intensive care unit, CVC: Central venous catheter, CTVS: Cardiothoracic and vascular surgery, RO: Reverse osmosis, OT: Operation theater

Table 4: Antibiotic susceptibility profile of four environmental *B. cepacia* isolates

Source	Trimethoprim/sulfamethoxazole	Meropenem	Ceftazidime
Inner surface of hub of CVC line of a patient admitted in general ICU	R	R	S
Multi-dose heparin vial in general ICU	R	R	S
CTVS OT table	S	S	R
Tap water obtained from CTVS OT	R	S	R

B. cepacia: Burkholderia cepacia, ICU: Intensive care unit, CTVS: Cardiothoracic and vascular surgery, OT: Operation theatre, CVC: Central venous catheter, IV: Intravenous

should be treated with a combination of antimicrobials.[10,11] Most of the strains are susceptible to ceftazidime (95%), piperacillin, minocycline, and cefotaxime and resistant to aminoglycosides, tetracycline, carbenicillin, and ticarcillin. The drug of choice for the empirical treatment of *B. cepacia* bacteremia is ceftazidime and trimethoprim/sulfamethoxazole, unless *B. cepacia* is proved to be resistant to these.[10,12]

Another important observation was that all *B. cepacia* isolates obtained from blood samples of patients and environmental samples of same or different ICUs exhibited variable antibiotic susceptibility pattern, thus indicating circulation of different bacterial strains. However, a drawback of this study was that molecular typing of *B. cepacia* isolates obtained from blood and environmental samples could not be done due to non-availability of facility.

Environmental sampling from all possible sources was done, but no consistent source of contamination could be elucidated. *B. cepacia* was isolated only four times during the study period from different sources, namely, inner surface of CVC hub, multidose heparin vial, CTVS OT table, and tap water in CTVS OT. Previous outbreaks of *B. cepacia* have been linked to extrinsic contamination of antiseptics including alcohol/chlorhexidine, multidose vials of ringer lactate used as water for injection, and mannitol.[13-15] Intrinsic contamination of medication causing BCC bacteremias has also been reported. These include contamination of ultrasound gel, albuterol solution for nebulization, water for injection, moisturizing body milk and IV bromopride, and antiemetic drug granisetron.[12,16-20]

Despite the fact that no source could specifically be found as the cause of this pseudo-outbreak, some infection control measures were implemented which included the following: Hand hygiene, chlorination of water supplied to ICUs and OTs, and proper cleaning of ICUs and OTs. Another practice which was specifically targeted was the use of a common needle inserted into rubber caps of multidose heparin vials through which separate sterile syringes were loaded. With sustained efforts of hospital infection control team, the number of *B. cepacia* isolates reduced substantially after July 2016.

CONCLUSION

B. cepacia is an emerging nosocomial pathogen capable of causing outbreaks. Appropriate infection control measures should be implemented and reviewed at regular intervals to avoid such situations. Infection control training of nursing staff and doctors, especially new inductees should be conducted at regular intervals. Nursing staff and doctors working in wards and ICUs should work in liaison with a diagnostic laboratory to assure swift communication of healthcare-associated infection alerts. Isolation of *B. cepacia* from samples obtained from patients should always be correlated clinically to avoid the inadvertent use of antimicrobials.

ACKNOWLEDGMENTS

The authors would like to acknowledge Nursing staff of Hospital Infection Control Team, Govind Ballabh Pant Institute of Post Graduate Medical Education & Research, New Delhi, India.

REFERENCES

1. Gautam V, Singhal L, Ray P. *Burkholderia cepacia* complex: Beyond pseudomonas and acinetobacter. Indian J Med Microbiol. 2011;29(6):4-12.
2. Lipuma JJ. Update on the *Burkholderia cepacia* complex. Curr Opin Pulm Med. 2005;11(6):528-33.
3. Vonberg RP, Gastmeier P. Hospital-acquired infections related to contaminated substances. J Hosp Infect. 2007;65(1):15-23.
4. Boszczowski I, do Prado GV, Dalben MF, Telles RC, Freire MP, Guimarães T, et al. Polyclonal outbreak of bloodstream infections caused by *Burkholderia cepacia* complex in hematology and bone marrow transplant outpatient units. Rev Inst Med Trop Sao Paulo. 2014;56(1):71-6.
5. Mangram A, Jarvis WR. Nosocomial *Burkholderia cepacia* outbreaks and pseudo-outbreaks. Infect Control Hosp Epidemiol. 1996;17(11):718-20.
6. Govan JR, Hughes JE, Vandamme P. *Burkholderia cepacia*: Medical, taxonomic and ecological issues. J Med Microbiol. 1996;45(6):395-407.
7. Van Laer F, Raes D, Vandamme P, Lammens C, Sion JP, Vrints C, et al. An outbreak of *Burkholderia cepacia* with septicemia on a cardiology ward. Infect Control Hosp Epidemiol. 1998;19(2):112-3.
8. Gravel-Tropper D, Sample ML, Oxley C, Toye B, Wood DE, Garber GE. Three-year outbreak of pseudobacteremia with *Burkholderia cepacia* traced to a contaminated blood gas analyzer. Infect Control Hosp Epidemiol. 1996;17(11):737-40.
9. Miles RS, Amyes SG. Laboratory control of antimicrobial therapy. In: Collee JG, Fraser AG, Marimon BP, Simmons A, editors. Mackie and McCartney Practical Medical Microbiology. Reprint. 14th ed. New Delhi: Elsevier; 2007. p. 151-78.
10. Lu DC, Chang SC, Chen YC, Luh KT, Lee CY, Hsieh WC. *Burkholderia cepacia* bacteremia: A retrospective analysis of 70 episodes. J Formos Med Assoc. 1997;96(12):972-8.
11. Coutinho HD. *Burkholderia cepacia* complex: Virulence characteristics, importance and relationship with cystic fibrosis. Indian J Med Sci. 2007;61(7):422-9.
12. Douce RW, Zurita J, Sanchez O, Cardenas Aldaz P. Investigation of an outbreak of central venous catheter-associated bloodstream infection due to contaminated water. Infect Control Hosp Epidemiol. 2008;29(4):364-6.
13. Lee S, Han SW, Kim G, Song DY, Lee JC, Kwon KT. An outbreak of *Burkholderia cenocepacia* associated with contaminated chlorhexidine solutions prepared in the hospital. Am J Infect Control. 2013;41(9):e93-6.
14. De Smet B, Veng C, Kruy L, Kham C, van Griensven J, Peeters C, et al. Outbreak of *Burkholderia cepacia* bloodstream infections traced to the use of Ringer lactate solution as multiple-dose vial for catheter flushing, Phnom Penh, Cambodia. Clin Microbiol Infect. 2013;19(9):832-7.
15. Souza Dias MB, Cavassin LG, Stempliuk V, Xavier LS, Lobo RD, Sampaio JL, et al. Multi-institutional outbreak of *Burkholderia cepacia* complex associated with contaminated mannitol solution prepared in compounding pharmacy. Am J Infect Control. 2013;41(11):1038-42.
16. Hutchinson J, Runge W, Mulvey M, Norris G, Yetman M, Valkova N, et al. *Burkholderia cepacia* infections associated with intrinsically contaminated ultrasound gel: The role of microbial degradation of parabens. Infect Control Hosp Epidemiol. 2004;25(4):291-6.
17. Martins IS, Pellegrino FL, Freitas Ad, Santos Mda S, Ferraiuoli GI, Vasques MR, et al. Case-crossover study of *Burkholderia cepacia* complex bloodstream infection associated with contaminated intravenous bromopride. Infect Control Hosp Epidemiol. 2010;31(5):516-21.
18. Alvarez-Lerma F, Maull E, Terradas R, Segura C, Planells I,

Coll P, et al. Moisturizing body milk as a reservoir of *Burkholderia cepacia*: Outbreak of nosocomial infection in a multidisciplinary intensive care unit. Crit Care. 2008;12(1):R10.
19. Ghazal SS, Al-Mudaimeegh K, Al Fakihi EM, Asery AT. Outbreak of *Burkholderia cepacia* bacteremia in immunocompetent children caused by contaminated nebulized sulbutamol in Saudi Arabia. Am J Infect Control. 2006;34(6):394-8.
20. Singhal T, Shah S, Naik R. Outbreak of *Burkholderia cepacia* complex bacteremia in a chemotherapy day care unit due to intrinsic contamination of an antiemetic drug. Indian J Med Microbiol. 2015;33(1):117-9.

How to cite this article: Bhatia M, Loomba PS, Mishra B, Dogra V. Pseudo-outbreak of *Burkholderia cepacia* blood stream infections in intensive care units of a super-speciality hospital: A cross-sectional study. Int J Med Sci Public Health 2017;6(7):1139-1144.

Source of Support: Nil, **Conflict of Interest:** None declared.