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AN OUTBREAK OF BURKHOLDERIA CEPACIA COMPLEX IN THE PAEDIATRIC UNIT OF A TERTIARY CARE HOSPITAL

Microbiology

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ABSTRACT

Introduction: Burkholderia cepacia complex (Bcc) is a non fermentative Gram-negative bacillus, now increasingly recognized as an important human pathogen causing hospital acquired infections. Bcc is a common contaminant in pharmaceutical products. We have described an outbreak of Bcc bacteraemia amongst children admitted in paediatric ICU and paediatric ward of tertiary care hospital in North India.

Materials and Methods: The study was conducted in a department of microbiology in a tertiary care hospital of North India for a period of 6 months from 1 July 2019 to 31 December 2019. Blood culture samples from paediatric patients yielded growth of non fermenting , oxidase positive, motile, gram negative bacilli which were sent to the department of Medical Microbiology, Post Graduate Institute of Medical Education and Research Chandigarh for identification by Matrix - assisted laser desorption /ionization –Time of flight- Mass Spectrometry(MALDI-TOF MS). Antimicrobial susceptibility of the clinical isolates was performed on Muller-Hinton agar by modified Kirby-Bauer's disc diffusion method in accordance with Clinical Laboratory Standards Institute 2019 guidelines. Additional samples were collected from paediatric unit to identify the source.

Results: The study involved 31(7.7%) cases of blood culture proven septicemia due to Bcc among patients admitted in paediatric ICU and ward. All the Bcc isolates showed a similar antibiogram with resistance to Amikacin, Gentamicin, Ceftazidime, Cefipime, Levofloxacin and Colistin and 100% sensitivity to Piperacillin -Tazobactam, Meropenem, Imipenem and Cotrimoxazole. Source of the outbreak could not be identified despite active surveillance.

Conclusion: Early diagnosis and appropriate therapy, along with impementation of essential hospital infection control practices is required for successful containment of this pathogen.

KEYWORDS

Burkholderia Cepacia Complex, Outbreak, Bacteremia, Pediatric Unit

INTRODUCTION

Burkholderia cepacia (Bc) is an aerobic Gram negative bacillus commonly found in soil and moist environment1. Recently it has emerged as an important opportunistic pathogen in hospitalised and immunocompromised patients resulting in significant morbidity and mortality, this is because of its ability to survive in the environment for prolonged period with limited nutrition and its increasing resistance to most antibiotics and inherent resistance to polymyxin B and colistin2. Various host and environmental factors such as immune suppression, clinical co-morbidities, prolonged hospital stay, use of central venous access and exposure to medical devices make the patients susceptible to infection by Bcc. Small hospital outbreaks are frequent and are usually due to a contaminated source such as disinfectant, intravenous solutions, nebuliser solutions, mouthwash and medical devices including respiratory therapy equipment[3,4,5,6].

Worldwide, outbreaks by Bcc have been reported in Intensive care units (ICU's), dialysis, transplant and paediatric patients. In these outbreaks, diverse sources like contaminated parenteral fluids, disinfectants such as chlorhexidine, antiemetic drug vials, lipid emulsion stoppers, nasal spray, mouthwash have been identified. A few outbreaks have been reported from India too, which include reports from Paediatric Intensive Care Unit (PICU)7, haematology unit8 and a neurotrauma intensive care unit[9].

Here we describe an outbreak of Bcc bacteraemia that affected children admitted in neonatal ICU and paediatric ward of a tertiary care hospital occurring between July 2019 and Dec 2019.

MATERIALAND METHODS :

The study was conducted from July 2019 to December 2019 in the microbiology department of a tertiary care hospital when an outbreak was suspected with five subsequent cases of bacteraemia caused by Bcc which occurred over a period of ten days in neonatal ICU and paediatric ward. This unusually high isolation of Bcc in blood cultures in neonatal ICU and paediatric ward prompted a detailed microbiological investigation.

Blood samples of children admitted in ICU and paediatric ward showing signs and symptoms of sepsis or any other relevant indication were collected aseptically in BACTEC blood culture bottles(Becton Dickinson, USA) and incubated in BACTEC 9120 and monitored regularly. All bottles with positive signals were removed from the instrument, Gram stained and subcultured on blood agar and MacConkey's agar plates. Isolates were identified based on colony morphology, Gram staining characteristics, motility, oxidase and a panel of other biochemical tests. Antimicrobial susceptibility of the clinical isolates was performed on Muller-Hinton agar by modified Kirby-Bauer's disc diffusion method in accordance with Clinical Laboratory Standards Institute 2019 guidelines[10]. The antibiotics used were Amikacin (30µg), Gentamicin (10µg), Ceftazidime (10µg), Cefipime (30µg), Piperacillin-Tazobactam (100/10µg), Imipenem (10µg), Meropenem (10µg), Levofloxacin (5µg), Colistin (10µg) and Cotrimoxazole (1.25/23.75 µg). All the isolates were sent to department of Medical Microbiology, Post Graduate Institute of Medical Education and Research Chandigarh for identification and characterization by Matrix - assisted laser desorption /ionization –Time of flight- Mass Spectrometry(MALDI-TOF MS).

Environmental sampling and culture:

As part of the outbreak investigation, microbiological cultures were collected from environmental surfaces, tap water, nebuliser solution, intravenous solutions, disinfectants, injections (in use and unopened), instruments, syringes, IV fluids administration sets, antibiotic solutions and vial stoppers. Pre moistened sterile swabs were used to collect samples from surfaces such as injection preparation area, ambubag, nebuliser, injection stoppers, hands of healthcare workers,stethoscopes, TPN feeds, bed rails (head end and foot end) and bed linen. The samples were inoculated on blood agar and MacConkey agar plates which were incubated for 48 hours at 37°C.

Tap water samples were centrifuged at 3000 rpm for 15 minutes and the sediments were processed. All liquid samples were inoculated directly on blood agar, MacConkey agar and in brain heart infusion (BHI) broth and were incubated at 37°C for 2 days. BHI was incubated at 37°C for 5 days and checked for turbidity daily. Subculture from BHI was made on blood agar and MacConkey agar plates in case of turbidity.

RESULTS:

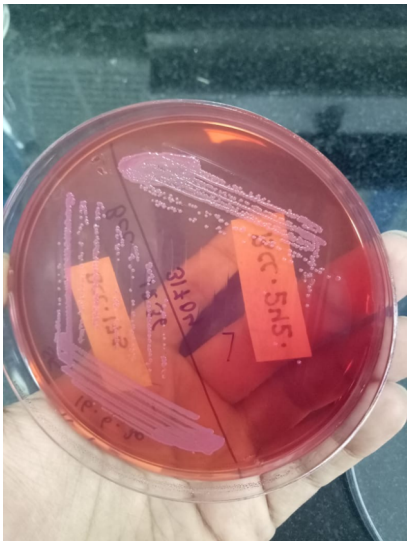
In the present study a total of 402 isolates were recovered from 4796 blood culture samples over a period of six months and out of these 31(7.7%) were Bcc. Since the incidence of Bcc over the last year in NICU and paediatric ward was 0-1 cases/month, this sudden increase in Bcc infections was identified as an outbreak. All the Bcc isolates (31) were subjected to antimicrobial susceptibility testing and all showed a similar antibiogram with resistance to Amikacin, Gentamicin, Ceftazidime, Cefipime, Levofloxacin and Colistin and 100% sensitivity to Piperacillin -Tazobactam, Meropenem, Imipenem and Cotrimoxazole.

It was observed that all the patients were between 0-8 years of age and males were more in number (n=19) than the females (n=12) . These patients had been provisionally diagnosed as cases of lower respiratory tract infection, cerebral palsy, congenital heart disease, low birth weight, preterm delivery with or without sepsis. Common invasive procedures such as peripheral IV catheterisation have been performed in all these children. Emperically all these children were put on IV Piperacillin-Tazobactam and IV Netilmicin. It was observed that 29 of 31 patients with Bcc positive improved after receiving antimicrobial therapy based on the antimicrobial susceptibility testing report. Overall mortality was 6.4%(2/31). The study of environmental samples failed to show culture growth for Bcc (Table 1). Results of the MALDI-TOF MS showed that the blood isolates belonged to different clads which showed that the isolates were of different genera and may not be from the same source (Figure 1).

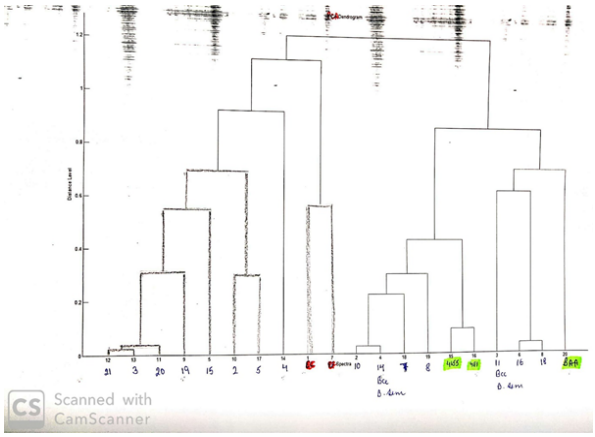
Table 1 Results Of Environmental Sampling

SAMPLE	RESULT
1.Tap water	No growth of Bcc
2.Distilled water, Normal saline, sterile saline for injections	No growth of Bcc
3.Nebuliser solution	No growth of Bcc
4.Disinfectants	No growth of Bcc
5.Injections (in-use & unopened)	No growth of Bcc
6.Ventilator tubes, suction tubes, Ambu-bags	No growth of Bcc
7.Sealed injection vial rubber stoppers (amikacin, netilmicin, meropenem, gentamicin, ceftriaxone)	No growth of Bcc
8.Finger impressions of healthcare workers	No growth of Bcc
9.Stethoscope	No growth of Bcc
10.Swabs from bed rails, bed linen, patient trolley	No growth of Bcc
11.TPN feed	No growth of Bcc

Growth of BCC on Mac conkey agar



DANDROGRAM



DISCUSSION :

Bcc are opportunistic Gram negative nosocomial pathogens that can cause life threatening disease and have propensity to produce serious outbreaks within clinical settings[11]. They have innate potential to survive and proliferate in the hospital environment, growing on moist surfaces. Its multi-drug resistance adds onto the overall morbidity and mortality of the patients[12].

The present outbreak was observed in the paediatric unit of tertiary care hospital where 7.7% (31/404) blood culture were found to be positive for Bcc over a period of six months. Recently several outbreaks of Bcc in paediatric unit heve been reported. Bhise et al from Nagpur reported an outbreak affecting 10 neonates, however the source could not be traced in this outbreak[13]. In 2017; 76 (20.37%) isolates recovered from blood culture was found to be positive for Bcc over a period of 8 months in a study of Mali S et al[7]. In 2019 Kirmani S et al observed the presence of Bcc in 30 blood cultures of patients admitted to PICU over a period of 8 months [14]. This indicates that Bcc is an important cause of bacteremia in PICU. Few outbreaks have been reported from other departments such as haematology, oncology, haemodialysis and neurotrauma intensive care unit.

In most of the outbreaks reported worldwide Polymerase chain reaction (PCR), ribotyping, and random amplified polymorphic DNA analysis, Expanded multilocus sequence typing (EMLST) have been used as tools for epidemiological typing. In a study by Mali et al , the isolates were confirmed by recA PCR and the source was traced by EMLST. Magalhaes et al have reported a polyclonal outbreak of Bcc affecting 24 haemodialysis patients[15]. Another outbreak was reported by N Rastogi et al., in neurotrauma intensive care unit affecting 48 patients with Bcc which were identified by using automated Vitek 2.0systems. Multilocus sequence typing (MLST) were performed for extensive source tracking which was found to be tap water[9].

A study was done by Adrian Egli et al , they re- analysed six isolates of ESBL producing E.coli by performing MALDI-TOF MS based typing and comparing results to those obtained by pulsed fielded gel electrophoresis (PGFE) and it was found that the PGFE and MALDI-TOF MS based dendrograms showed similar results[16].

In our study, we could not trace the source of infection despite active surveillance and environmental sampling. MALDI-TOFF based dendrograms of BCC isolates recovered during the outbreak suggested that the isolates fell under different clads which means that they may not be from the same source.

Bcc have a unique and challenging antimicrobial profile. They are resistant to multiple antimicrobials especially to the common used antibiotics such as aminoglycosides, cephalosporins and Polymyxin B. Different resistant patterns have been reported in different outbreaks that have occurred worldwide. In the present outbreak all the strains were resistant to Amikacin, Gentamicin, Ceftazidime, Cefipime, Levofloxacin and Colistin. However the studies have shown sensitivity to ceftazidime and other 3rd generation cephalosporins. In some of the studies, the organism has been reported to be resistant to imipenem and aminoglycosides, while our isolates showed excellent sensitivity to imipenem and meropenem. These variations in antibiotic susceptibility pattern could probably be due to the different antibiotic policiesused in different institutions.

The limitation of present study is that PCR and Extended multi-locus sequence typing (eMLST) have not been performed due to resource limitation in our laboratory.

CONCLUSION:

BCC is an emerging pathogen which can cause high morbidity and mortality in immunocompromised patients. Burkholderia sepsis in any clinical ward is a matter of concern and early and effective diagnosis, appropriate therapy along with implementation of effective hospital infection control practices are required for the successful management of this pathogen. Prompt thorough investigations along with molecular confirmation and typing of isolates are recommended to confirm and control the outbreak

ETHICS STATEMENT:

This study did not require any ethical clearance as it dealt with a hospital outbreak. Clinical samples were received in the microbiology laboratory as a part of routine patient care.

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Nil.

Conflict of interest:
There are no conflicts of interest.

REFERENCES

1. Goldmann DA, Klinger JD. Pseudomonas cepacia: biology, mechanisms of virulence, epidemiology. J Pediatr. 1986 May;108(5 Pt 2):806-12.
2. Gautam V, Singhal L, Ray P. Burkholderia cepacia complex: beyond pseudomonas and acinetobacter. Indian J Med Microbiol. 2011 Jan-Mar;29(1):4-12.
3. Panlilio AL, Beck-Sague CM, Siegel JD, Anderson RL, Yetts SY, Clark NC, et al. Infections and pseudoinfections due to povidone-iodine solution contaminated with Pseudomonas cepacia. Clin Infect Dis. 1992 May;14(5):1078-83.
4. 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 Epidemi-ol. 1998 Feb;19(2):112-3.
5. Centers for Disease Control and Prevention (CDC). Nosocomial Burkholderia cepacia infection and colonization associated with intrinsically contaminated mouthwash-Arizona, 1998. MMWR Morb Mortal Wkly Rep. 1998 Nov 6;47(43):926-8.
6. Weems JJ Jr. Nosocomial outbreak of Pseudomonas cepacia associated with contamination of reusable electronic ventilator temperature probes. Infect Control Hosp Epidemi-ol. 1993 Oct;14(10):583-6.
7. Mali S, Dash L, Gautam V, Shastri J, Kumar S. An outbreak of Burkholderia cepacia complex in the paediatric unit of a tertiary care hospital. Indian J Med Microbiol. 2017 Apr-Jun;35(2):216-20.
8. Shuvra Neel Baul, Rajib De, Prakas Kumar Mandal, Swagnik Roy, Tuphan Kanti Dolai, Prantar Chakrabarti. Outbreak of Burkholderia Cepacia Infection: a Systematic Study in a Hematolooncology Unit of a Tertiary Care Hospital from Eastern India. Mediterr J Hematol Infect Dis. 2018; 10(1): e2018051.
9. Rastogi N, Khurana S, Veeraraghavan B, Yesurajan Inbanathan F, Rajamani Sekar SK, Gupta D, et al. Epidemiological investigation and suc-cessful management of a Burkholderia cepacia outbreak in a neurotrauma intensive care unit. Int J Infect Dis. 2019 Feb;79:4-11.
10. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing. 29th. Wayne, PA:CLSI;2019.
11. Sousa SA, Ramos CG, Leitão JH. Burkholderia cepacia Complex: Emerging Multihost Pathogens Equipped with a Wide Range of Virulence Factors and Determinants. Int J Microbiol. 2011;2011. pii: 607575.
12. Memish ZA, Stephens G, Balkhy HH, Cunningham G, Francis C, Poff G, et al. Outbreak of Burkholderia cepacia bacteremia in immunocompetent children caused by contaminated nebulized sulbutamol in Saudi Arabia. Am J Infect Control. 2009 Jun;37(5):431-2.
13. Bhise SM, Rahangdale V, Qazi MS. Burkholderi cepacia an emerging cause of septicemia- An outbreak in a neonatal intensive care unit from a tertiary care hospital of central India. Int Organ Sci Res J Dent Med Sci 2013;10:41-3.
14. Kirmani S, Khan F, Kaushal N, Shahid M, Taneja N, Ahmad A. Burkholderia cepacia complex bacteremia in paediatric intensive care unit in a tertiary care hospital in North In-dia. CHRISMED J Health Res 2019;6:232-6.
15. Magalhaes M, Doherty C, Govan JR, Vandamme P. Polyclonal outbreak of Burkhold-eria cepacia complex bacteraemia in hemodialysis patients. J Hosp Infect 2003;54;120-3.
16. Egli A, Tschudin-Sutter S, Oberle M, Goldenberger D, Frei R, Widmer AF. MALDI-TOF MS basrd typing of extended spectrum beta lactamase producing E.coli- A novel tool for real time outbreak investigation . PLOS ONE 2015;10(4):1371-6