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ORIGINAL ARTICLE

# An Outbreak of *Burkholderia cepacia* Bacteremia in a Neonatal Intensive Care Unit

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**Abstract**
*Objectives* To identify the source of infection, to study the clinical profile and outcomes of neonates with Burkholderia septicemia and to determine the antimicrobial susceptibility patterns of the isolates.
*Methods* The authors describe a 3 mo outbreak of nosocomial *Burkholderia cepacia* bacteremia involving 12 neonates. During the outbreak, ventilator humidifier water, intravenous solutions and other possible sources were taken from the concerned neonatal intensive care units (NICUs); cultured and isolates identified by standard microbiological techniques and VITEK system. Clinical details of affected babies were also obtained to ascertain the clinical significance of the isolates.
*Results* All neonates had clinical and biochemical evidence of sepsis and the source could be tracked to intravenous solutions of 5 % dextrose, normal saline (opened bottles) and continuous positive airway pressure humidifier water. Strain relatedness of the environmental isolates with the clinical isolates is likely as antibiotic susceptibility patterns were similar.
*Conclusions* The investigations revealed the source of the nosocomial outbreak which is crucial for initiating appropriate control measures.

**Keywords** Burkholderia · Bacteremia · Neonate · Outbreak

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## Introduction

*Burkholderia cepacia*, formerly *Pseudomonas cepacia* is a motile gram negative bacillus which is aerobic and glucose non-fermenting. It proliferates under conditions of minimal nutrition and can survive in the presence of certain disinfectants. It has a wide distribution in the natural environment *viz* water, soil, fruits, and vegetables. In the last two decades, *B. cepacia* has emerged as a serious human pathogen causing fatal necrotizing pneumonia and bacteremia, especially in patients with cystic fibrosis (CF) or chronic granulomatous disease. Cross-transmission, frequent pulmonary procedures, and central venous access facilitates the nosocomial spread of this organism and various such nosocomial outbreaks in neonates have been reported. High transmissibility in the hospital setting, intrinsic resistance to many antibiotics and association with a poor prognosis highlights the need for early detection and treatment of *B. cepacia* infections [1, 2].

The *B. cepacia* complex comprises 17 phenotypically similar but genetically distinct species. The species with most medical relevance are *B. cenocepacia, B. multivorans, B. dolosa, B. gladioli.* Around 90 % of human infections are caused by *B. cenocepacia* and *B. multivorans* [3, 4].

Small hospital outbreaks are frequent and are usually due to a single contaminated source such as disinfectants, intravenous solutions, nebulizer solutions, mouthwash and medical devices, including respiratory therapy equipment. False positive bacteremia or pseudo-outbreaks of *B. cepacia* have been reported with contamination traced to medical equipment and disinfectants, so significance of the isolate has to be correlated with clinical aspects of the patient [5].

Appropriate antimicrobial therapy is challenging as the organisms are intrinsically resistant to most antibiotics, including polymixins. The carbapenem, meropenem appears to be the most active agent. Unfortunately, human infections are

usually intractable to therapy unless combinations of three or four antibiotics are used. Strict infection control measures, including segregation are necessary to limit the spread of highly transmissible strains [1].

This study was conducted to investigate into an outbreak of *B. cepacia* septicemia which occurred in the neonatal intensive care units of two hospitals affecting 12 neonates. This included conducting environmental and epidemiological investigations to identify the source of infection, study of the clinical profile and outcomes of neonates with *Burkholderia* septicemia and determining the antimicrobial susceptibility patterns of the isolates.

## Material and Methods

It was a retrospective study done over a period of one month (April 2014). Study subjects were neonates with septicemia admitted in the period January 2014 to March 2014. Sepsis was determined if two or more of the following criteria associated with positive blood culture were met: (a) fever or hypothermia, (b) tachycardia, (c) tachypnea or apnea and (d) leukocytosis or leukopenia or an increase in immature forms. The symptoms included lethargy; feed intolerance and clinical shock with metabolic acidosis which lack specificity. Blood cultures were done by automated blood culture system BACTEC 9040 and isolates, if any, were identified by standard microbiological techniques [6] and VITEK system. Antibiotic susceptibility was done by Kirby Bauer disk diffusion method. Clinical details of the affected babies were collected from Medical Records Department using a proforma.

Samples from sources previously reported potential reservoirs of *B. cepacia,* like water reservoir of incubator humidifiers, heated humidifier water from respiratory devices, tap water, incubator surfaces, antiseptic products and intravenous solutions were taken from the concerned neonatal intensive care units (NICUs). The samples were inoculated into BHI broth and incubated at 37 °C for 5 d and then subcultured onto chocolate agar and Mac Conkeys agar. Isolates, if any, were identified by standard microbiological techniques and VITEK system [6, 7].

Antibiotic susceptibility testing was done by Kirby Bauer's disk diffusion method on Muller Hinton agar and interpreted based on Clinical Laboratory Standard Institute (CLSI) guidelines [8]. Antibiotic sensitivity was done using disks of cotrimoxazole, ceftazidime, chloramphenicol, levofloxacin, meropenem, tetracycline and ticarcillin clavulanic acid. The antibiotic susceptibility pattern of clinical isolates were compared with that of environmental isolates to establish their relatedness. Ethical clearance was obtained from the institutional ethics committee.

## Results

A total of 12 babies were found to have *B. cepacia* bacteremia in the specified period.

Seven out of the 12 babies were boys (58.33 %). Majority of the babies were preterm 10(83 %), mean age being 34.3 wk of gestation and range being 30–40 wk. Mean birth weight was 1.72 kg and lowest birth weight was 1.4 kg.

All except one baby had clinical signs of sepsis and elevated CRP levels (≥6 mg/dl). Hence, Burkholderia pseudobacteremia was diagnosed in this baby. Leukopenia as well as leukocytosis was observed, the range of leukocyte counts being 5,700–41,000/cu mm. Mean leukocyte count was 18,908/cu mm which is marginally above the upper limit of normal (Normal : 5,000–18,000/cu mm) for this age group. Mean CRP level was 26.21 mg/dl and highest CRP level was 80 mg/dl.

Antibiotic susceptibility pattern of clinical isolates is given in Table 1.

Maximum susceptibility was seen to ceftazidime (100 %) and cotrimoxazole (100 %) followed by chloramphenicol (91.6 %). The isolates showed maximum resistance to ciprofloxacin.

Nine out of the 12 babies had a good outcome; they improved and were discharged. Two of the babies expired, one was the baby with Burkholderia pseudobacteremia who died as a result of disseminated intravascular coagulation and antecedent causes being low birth weight, respiratory distress syndrome and pneumothorax. The cause of death of the second baby was sepsis with intraventricular hemorrhage. This baby had acyanotic congenital heart disease and tracheoesophageal fistula as well.

All clinical isolates of *B. cepacia* were from a single hospital NICU, however four out of these babies were outborn in a sister institution and referred; hence screening samples were obtained from both NICUs. Screening samples and swabs for source tracking included tap water, IV fluids (fresh and opened), distilled water for humidifiers, boiled water for feeds and swabs from incubator surfaces. *B. cepacia complex* was

**Table 1** Antibiotic susceptibility pattern of clinical isolates of *B. cepacia* complex

| Antibiotic | Susceptibility n (%) |
|---|---|
| Amikacin | 10 (83.3) |
| Ceftazidime | 12 (100) |
| Cotrimoxazole | 12 (100) |
| Chloramphenicol | 11 (91.6) |
| Ciprofloxacin | 9 (75) |
| Meropenem | 10 (83.3) |
| Piperacillin-tazobactam | 10 (83.3) |

isolated from opened IV fluid bottles of 5 % dextrose and sodium chloride as well as from continuous positive airway pressure humidifier water of the outbreak NICU and cultures from the other NICU were negative for *B. cepacia.* The isolates had antibiotic susceptibility pattern similar to the clinical isolates. Unopened IV fluid showed no growth on culturing.

## Discussion

Non-fermentative gram negative rods like *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Stenotrophomonas maltophilia* are important causes of opportunistic infections in hospitalised patients and are frequently isolated in intensive care units [9]. Multidrug resistance is commonly seen among these species and treating infections caused by these organisms can be a serious problem. *B. cepacia* is also a non-fermentative gram negative bacilli that 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 [10, 11]. It has been commonly associated with colonization and pulmonary infection in patients with cystic fibrosis [12, 13] and there are reports of fatal disease in healthy individuals as well [14]. In hospitals, *B. cepacia* has been found to contaminate antiseptics, disinfectants, nebuliser solution, and dextrose solution [15]. Holmes et al. have reported a large hospital outbreak that involved both cystic fibrosis and non-cystic fibrosis patients attributed to cross-infection by a single dominant clone of *B. cepacia* [16].

In the index study *B. cepacia* was isolated from 12 neonates, majority of them (83.3 %) were preterm babies with lower limit of gestation being 30 wk and mean birth weight 1.72 kg. In similar studies conducted in Paris and Malaysia on Burkholderia septicemia in neonates, median birth weight was 1.67 kg, which supports the fact that Burkholderia is an opportunistic pathogen causing disease in patients with definite pre-disposing factors [5, 7]. To rule out possibility of possible contamination, clinical features and blood investigations of affected babies were also obtained in the present study. All except one baby had clinical signs of sepsis like fever, hypothermia, tachypnea and leukocytosis/leukopenia. The same baby had a normal CRP value as well, so was defined as a case of Burkholderia pseudobacteremia. All the other babies had high CRP values, highest being 80 mg/dl.

An unusual increase in incidence of cases of Burkholderia sepsis in hospitalised babies hinted towards a probable nosocomial outbreak which led to an investigation into the same. The source of infection was tracked to opened IV fluid bottles (which were being used for multiple babies) and ventilator humidifier water. A study from Paris describes an outbreak of nosocomial *B. cepacia* bacteremia in which a *B. cepacia* strain, genotypically identical to the blood isolates was recovered from the upper surface of capped rubber stoppers of bottles of a commercial lipid emulsion used for parenteral nutrition [7]. In a Malaysian hospital, *Burkholderia cepacia* was isolated from the water of an oxygen humidifier in the delivery room, ventilator water traps and humidifier water trap in the neonatal unit which had led to two nosocomial outbreaks. They also found association between prior long line and septicemic episode ($P$ 0.019) but assisted ventilation did not show any such association [5]. In a study presented at the 15th International Congress on Infectious Diseases, an outbreak of hospital-acquired *B. cepacia* bloodstream infections was traced to the use of intravenous solution as multiple-dose for catheter flushing in Cambodia [17]. *Burkholderia cepacia*, as a cause of nosocomial outbreaks has also been isolated from unused antiemetic for IV use [18], moisturizing body milk used in ICUs [19], mannitol solution used for irrigation in urologic surgery [20], sink drains [21], water for injection [22] and ultrasound gel [23].

The strain relatedness of the clinical and environmental isolates in the index study was suggested by similar antibiotic susceptibility patterns. Though the organism is well known for multidrug resistance, the isolates in the index showed good susceptibility to various classes of drugs including a third generation cephalosporin, aminoglycoside, cotrimoxazole, fluoroquinolone and carbapenem. However, Dizbay et al. from Turkey in their study on various nosocomial *B. cepacia* infections (predominantly pneumonia) reported 50 % resistance towards amikacin, carbapenems, cefepime, ciprofloxacin and cotrimoxazole; 61 % resistance was noted towards ceftazidime [2]. Kuzumoto et al. from Japan found carbapenems as the most active agents against *B. cepacia* isolated from neonates in a similar outbreak [24].

Nosocomial outbreaks, like the concerned one create dilemma especially in the NICU setting and require prompt investigation. The investigation reports aid in implementing specific control measures and re-inforce aseptic precautions in all invasive procedures. Standard precautions to be followed for prevention of all nosocomial infections include hand washing, use of personal protective equipment like sterile gloves, mask, gown and eye guard depending on the procedure involved, proper waste management and environmental control.

## Conclusions

The present nosocomial outbreak originated from intravenous fluids which were used for parenteral nutrition of neonates as well as from ventilator water trap. It is a serious issue of concern and prompt control measures like single use of IV fluids, care of intravenous lines, cleaning of ventilator circuits were implemented. Outbreak investigations are absolutely

essential to keep a check on nosocomial pathogens. A limitation of the index study is that the relatedness of isolates though highly likely by the antibiograms, should have been confirmed by genotyping.

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**Conflict of Interest** None.

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