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**Original Research Article**

# Pattern of clinical manifestation and antibiotics sensitivity of *Burkholderia Cepacia* sepsis in Neonatal Intensive Care Unit of tertiary care centre of North India

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## ABSTRACT

**Background:** Neonatal sepsis is a major cause of morbidity and mortality worldwide. Now a days, neonatal sepsis due to *Burkholderia cepacia* is on rise. This study was conducted to delineate clinical presentation and antibiotic sensitivity pattern from blood culture proven *Burkholderia* sepsis. Methods: In this retrospective analytical study, thirty-six neonates admitted to Neonatal Intensive Care Unit of a tertiary care hospital with blood culture proven *Burkholderia* sepsis were included. Clinical manifestation, laboratory findings and antibiotic sensitivity patterns of blood culture proven *Burkholderia* sepsis were analyzed.
**Results:** : All neonates were inborn and were admitted within 24 hours of birth. Difficulty in breathing was most common presenting symptom and seizure was second in number. There was no association with mode of delivery. Male to female ratio is 1.4:1. Progressive thrombocytopenia was the most consistent feature and in 6 patients also associated with anaemia. Average hospital stay was increased and more in preterm neonates. In this setup piperacillin + tazobactem was found to be most sensitive against *Burkholderia cepacia* and cotrimoxazole was 2nd in sensitivity.
**Conclusions:** Proper and timely identification of Non Fermentative Gram Negative Bacilli (NFGNB) other than Pseudomonas can help confine morbidity due to such infections. High degree of suspicion helps in early recognition. Efficient housekeeping is necessary to prevent nosocomial infections due to these pathogens.

**Keywords:** Antibiotic Sensitivity, *Burkholderia* , Neonatal, Nosocomial ,Septicemia

## INTRODUCTION

Neonatal sepsis (NNS) is a major cause of morbidity and mortality worldwide and one of the three important causes of 2.7 million deaths every year.[1] Its incidence is more in developing countries compared with developed countries.[2]

Neonatal sepsis is defined as a disseminated disease with positive blood culture during the neonatal period (28 days of life), and involvement of various systemic infections of the newborn such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infection.[3] NNS is responsible for about 30-50% of the neonatal deaths.[4]

*Burkholderia cepacia* (*B. cepacia*) is saprophytic and phytopathogenic, glucose non-fermenting, motile and multidrug resistant gram negative bacilli which are not considered a part of the normal human flora.[5] *B. cepacia* has emerged as an important opportunistic as well as multidrug resistant pathogen in hospitalized and immunocompromised patients.[6] The most common risk factors in neonates of nosocomial sepsis are prematurity,

very low birth weight, exposure to invasive procedures, receiving parenteral nutrition with lipid emulsions, frequent use of broad spectrum antibiotics and indwelling catheter related infections.[7]

*B. cepacia* can cause serious clinical problem because of its resistance to many antimicrobial drugs and its ability to survive in antiseptic solutions and in hospital environment.[8] The present study was therefore designed to evaluate clinical presentation as well as blood culture sensitivity pattern of *B. cepacia* so can limit morbidity and mortality by using appropriate antibiotics.

## METHODS

The current study is a retrospective analytical study conducted in Department of Pediatrics and neonatal intensive care unit of pandit deen dayal upadhaya hospital, an associated hospital of SMS medical college, Jaipur, working under Janani Suraksha Yojana (JSY) by Government of India. Study conducted from 1st April 2018 to 31 March 2019. From the aforementioned NICU, a total 690 blood samples of neonates with signs and symptoms suggestive of septicemia were sent for culture and antimicrobial sensitivity to the Department of Microbiology over a period of approximately 1 year. Neonates with blood culture proven of *B. cepacia* were included in this study.

### *Inclusion criteria*

- Newborns ≤ 28 days of age.
- Inborn newborns.
- Newborns with *Burkholderia cepacia* proven culture positive.
- Newborn with clinical features suggestive of sepsis like difficulty breathing, seizures, dullness, hypo/hyperthermia, apnoea, cyanosis etc.
- Newborn whose parents gave consent to participate in study.

### *Exclusion criteria*

- Newborn > 28 days age
- Outborn babies
- Newborn with culture negative or culture positive other than *burkholderia cepacia* sepsis.
- Newborn whose parents does not gave consent to participate in study.

Blood samples were drawn at the time of admission before instituting antimicrobial therapy and were followed using standard microbiological laboratory protocol. *Burkholderia cepacia* was isolated from 36 samples. Antimicrobial sensitivity was determined using Kirby Bauer disc diffusion method as per CLSI guidelines. These 36 neonates with clinical and blood culture proven septicemia due to *Burkholderia cepacia* were included in the study and various clinical and microbiological data were compiled like, gestational age at birth, body weight, mode of delivery, age at admission, presenting features, routine blood investigation results, culture and antimicrobial sensitivity pattern and outcome at discharge.

## RESULTS

Authors had sent blood culture for 690 subjects and out of which 270 cases were found to be culture positive, with in culture positive cases 36 were positive for *Burkholderia cepacia*. Among cases male to female ratio is 1.4:1 (Table 1). The ratio of normal vaginal delivery to operative mode of delivery was 0.89:1 (Table 2). All 36 patients were inborn 25 were preterm and 11 were full term (Table 3). Most of neonates were admitted within 24 hours of birth and respiratory distress was present in approximately all. Progressive thrombocytopenia was seen in 28 subjects and anaemia was seen in 6 patients though leucocytosis was seen only in one. CRP was detected positive in 24 subjects.

**Table 1: Sex distribution of cases.**

| Sex | Percentage |
|---|---|
| Male | 21(58.33) |
| Female | 15(41.67) |

**Table 2: Distribution of cases according to type of delivery.**

| Type of delivery | Percentage |
|---|---|
| NVD | 17(47.22) |
| LSCS | 19(52.78) |

**Table 3: Distribution of cases according to gestational age.**

| Gestation | Percentage |
|---|---|
| Term | 11(30.55) |
| Preterm | 25(69.45) |

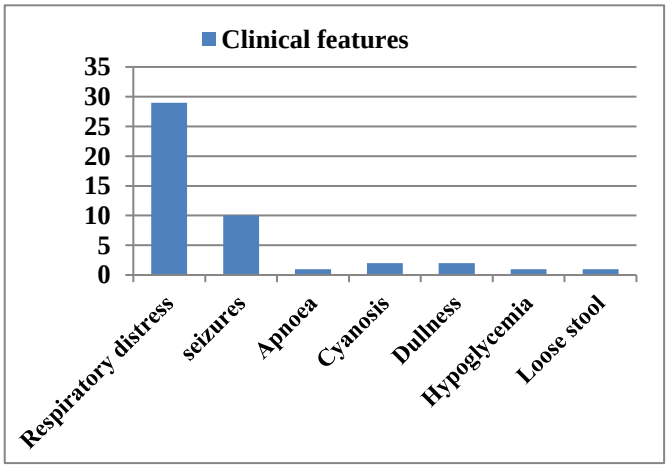


**Figure 1: Pattern of presentation of cases.**

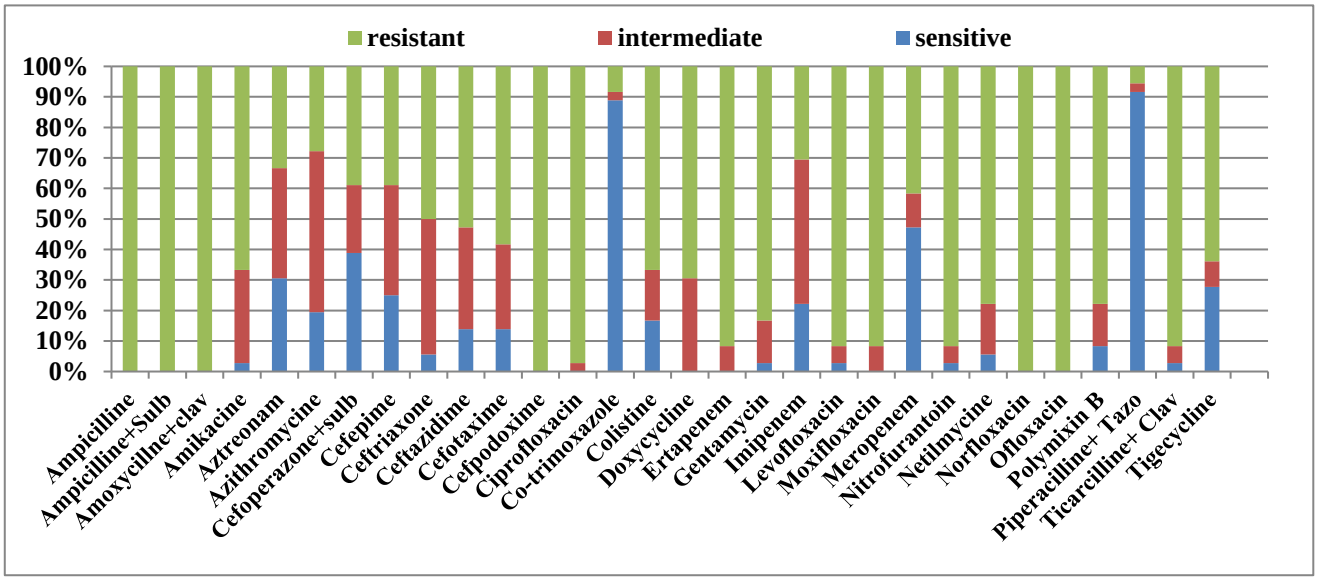


**Figure 2: Antibiotic sensitivity pattern of *B. Cepacia* species in cases.**

Nearly all patients admitted with respiratory distress, seizure was second most common manifestation develop in 10 patients, cyanosis in 2, dullness in 2, loose stool in 1, hypoglycemia in 1 and apnoea in 1 subject (Figure 1). Mean duration of hospital stay for all cases is 19.36 days while in preterm it is 21.2 days and in term babies it is 15.18 days suggest that preterm babies have longer duration of hospital stay and are more prone for complications. Out of 36 newborns 2 were referred to higher centres due to associated other co morbidities and 1 was taken LAMA, 2 expired and 31 were successfully discharged.

In this study authors have also assessed about antibiotic sensitivity pattern of *B. cepacia* species due to its recent development of multidrug resistance against new antibiotics. Authors found that piperacilline+tazobactem is most sensitive iv antibiotic and cotrimoxazole is most sensitive oral antibiotic against *Burkholderia cepacia* species (Figure 2).

## DISCUSSION

*Burkholderia cepacia* is a difficult pathogen microbiologically as it is not easily identified and clinically as it possesses intrinsic resistance to many potent antimicrobial agents. Infections of blood, urinary tract, and respiratory tract usually result from exposure to contaminated medical solutions or devices but are rarely fatal. Unlike Pseudomonas aeruginosa which may be carried by around 10% humans (e.g. as a gut colonizer), *Burkholderia* has not yet been recovered from human sources other than the sites of infection.

In this study involved 36 cases of blood culture proven septicemia due to *Burkholderia cepacia* in neonates admitted in Neonatal Intensive Care Unit (NICU). Since all the neonates were inborn and developed early neonatal septicemia, they probably acquired it from the environment. The pathogenicity of this complex is suggested by the clinical picture of these neonates, all of whom had signs and symptoms suggestive of sepsis and nearly 77.78% had thrombocytopenia which correlates with the study by Bhise et al. and Patra et al.[9,10]

Although the ratio of preterm and term neonates is significantly indicative of increased propensity of preterm babies developing *Burkholderia sepsis*, and preterm neonates had increased average hospital stay and poorer prognosis. There was also no significant correlation with operative mode of delivery as more than half of the neonates were born of normal vaginal delivery and this is in synchronization with findings of Patra et al.[10]

A diagnostic clinching feature was development of progressive thrombocytopenia which was found in nearly 78% neonates with *Burkholderia sepsis.* Seizures were observed in approximately 28% neonates with *burkholderia sepsis*.

In general, *Burkholderia* manifests innate resistance to aminoglycoside antibiotics and widespread resistance to many beta-lactam agents, including extended-spectrum penicillins such as piperacillin and the 4th generation cephalosporin cefepime. The 2010 Sanford Guide recommends co-trimoxazole as the treatment of choice for this infection.

In addition, it lists 5 antibiotics to which more than 60% of clinical isolates of *B. cepacia* are susceptible or that are clinically effective: Meropenem, ceftazidime, ceftibuten, chloramphenicol and trimethoprim.[11] Trimethoprim-Sulfamethoxazole and Doxycycline or minocycline are potential oral therapies for *B. Cepacia* complex. For intravenous therapy Meropenem along with a second agent such as trimethoprim-sulfamethoxazole,

doxycycline, minocycline, ceftazidime, or amikacine are potential options.[12] However study by Priyamvada Roy13 found that all the isolates of *burkholderia* cepacia were uniformly susceptible to piperacillin, piperacillin-tazobactam and cefepime. So, the antibiogram of *Burkholderia spp*. isolated from patients, by retaining susceptibility to these three antibiotics, seemed to be slightly different from those isolated from other studies.

In this study authors found that piperacillin+tazobactem was most sensitive against *burkholderia cepacia* and cotrimoxazole was 2nd in sensitivity. Piperacilline+ tazobactem was sensitive in 92% cases, Trimethoprim-Sulfamethoxazole was sensitive in 90% cases and meropenem was sensitive in only 47% cases.

## CONCLUSION

Proper and timely identification of Non-Fermentative Gram Negative Bacilli (NFGNB) other than Pseudomonas can help confine morbidity due to such infections. High degree of suspicion helps in early recognition. Efficient housekeeping is necessary to prevent nosocomial infections due to these pathogens.

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