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Neonatal septicemia caused by *Burkholderia cepacia* in a tertiary care hospital in north India

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Abstract
Aims: Nosocomial infections due to non fermentative Gram negative bacilli is on rise. This study was conducted to delineate the microbiological parameters and compile the clinic-demographic data of ten neonates suffering from blood culture proven *Burkholderia* sepsis.
Material and Methods: In this retrospective analytical study, ten neonates admitted to Neonatal Intensive Care Unit of a tertiary care hospital with blood culture proven *Burkholderia* sepsis were included. Relevant microbiological, clinical and demographic data was collected and analysed. Further, samples were collected from the environment to trace the source of this pathogen.
Results: All neonates were inborn and were admitted within 24 hours of birth. Respiratory distress was most common presenting symptom. There was no association with operative mode of delivery. Progressive leucopenia and thrombocytopenia was the most consistent feature. Two neonates had to be intubated and mechanically ventilated. Average hospital stay was increased and more so in preterm neonates.
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.

Keywords: Septicemia, Neonatal, *Burkholderia*, Nosocomial

1. Introduction
Burkholderia cepacia is a known saprophytic and phytopathogenic bacterium causing opportunistic human infections specially in patients of cystic fibrosis and chronic granulomatous disease [1, 2]. *Burkholderia* are a genus containing non-fermentative Gram negative bacteria with slow oxidase positivity and are often misdiagnosed as *Pseudomonads* or *Acinetobacter* [3]. There have been reports of outbreaks in hospital settings including sepsis in hospitalized neonates [4]. Its ability to survive in antiseptic solutions and other moist surfaces in hospital environments like intravenous fluids, nebulizer solutions and respiratory therapy equipments and its intrinsic resistance to many antimicrobials poses a serious clinical problem [1, 2]. Therefore early diagnosis by culture and sensitivity and subsequent appropriate therapy can limit morbidity and mortality.

2. Materials and Methods
The current study is a retrospective analytical study conducted in Department of Microbiology, and a neonatal intensive care unit of an associated hospital working under Janani Suraksha Yojana (JSY) by Government of India. From the aforementioned NICU, a total 68 blood samples of neonates with signs and symptoms suggestive of septicemia were received for culture and antimicrobial sensitivity to the Department of Microbiology within a span of 11 days (From 29-08-2015 to 09-09-2015). 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 ten samples. Antimicrobial sensitivity was determined using Kirby Bauer disc diffusion method as per

CLSI guidelines. The identity and sensitivity of the pathogen was confirmed using the automated microbial identification and antimicrobial sensitivity testing system Vitek 2 developed by Biomerieux USA. [1, 2].

These ten 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.

Samples were also taken from the probable sources of pathogen in the hospital environment to isolate *Burkholderia sp*. Such samples included chlorhexidine hand rub solution, tap water, refrigerator, soap, suction apparatus, i.v. fluid (D-10%), trolley, vials of dehydrated antibiotic, and thermometer [1, 4-6].

3. Results

{Table 1}

All ten patients were inborn and four out of ten were preterm. The ratio of normal vaginal delivery to operative mode of delivery was six to four. All neonates were admitted within 24 hours of birth and respiratory distress in one form or another was present in all. Two neonates had to be intubated and mechanically ventilated. All neonates had intravenous catheter. Progressive thrombocytopenia and/or leucopenia were seen in eight patients though relative neutropenia was seen only in one.

The average hospital stay in neonates suffering from sepsis due to pathogens other than Burkholderia was 13-15 days while in these cases it was more than 20 days. In preterm neonates it was as high as 36 days.

The antimicrobial sensitivity testing was performed on all the isolates and revealed the following: [7]

{Insert Table 2}

Table 1: Compiled clinical data and demographic information of the ten neonates included in the study. (NVD: Normal Vaginal Delivery, LSCS: Lower Segment Caesarean Section

Case no.	Gestational Age (in weeks)	Body weight at birth (in Kg)	Mode of Delivery	Age at admission	Relevant clinical history	Relevant Blood Investigations	Sample from which organism isolated	Hospital Stay (days)	Outcome at discharge
1.	32	1.5	NVD	1 day	Respiratory distress, cyanosis	Within Normal Limits	Blood	30	Normal
2.	32	0.750	LSCS	1 day	Respiratory distress, Twin pregnancy, meconium stained liquor	Thrombocytopenia, Leucopenia	Blood	22	Expired
3.	40	3	NVD	14 hours	Respiratory distress, seizures	Hypoglycemia, hypocalcemia, Normal cell counts	Blood	21	Normal
4.	40	2.75	LSCS	3 hours	Respiratory distress, Pneumonia, Jaundice	Within Normal Limits	Blood	24	Normal
5.	41	2.5	NVD	1 hour	Apnea, Meconium stained liquor, mechanical ventilation, extubated after 6 hours.	Persistent Thrombocytopenia, Normal leucocyte counts with relative neutropenia	Blood	36	Normal
6.	39	2.5	NVD	1 hour	Respiratory distress	Persistent thrombocytopenia, progressive leucopenia	Blood	23	Normal
7.	34	1.25	LSCS	1 day	Respiratory distress, Cyanosis	Thrombocytopenia	Blood	27	Normal
8.	39	2.5	LSCS	1 day	Respiratory distress	Progressive thrombocytopenia, Leucopenia	Blood	25	Normal
9.	40	3	NVD	1 hour	Asphyxia, Meconium stained liquor, Mechanical ventilation, extubated after 7 days	Thrombocytopenia	Blood and Endotracheal tube tip	28	Normal
10.	32	1.25	NVD	1 hour	Respiratory distress	Progressive thrombocytopenia and leucopenia	Blood	28	Normal

Table 2: Antibiogram of isolated pathogen (*Burkholderia* sp).

S.no.	Antibiotic	Sensitivity
1	Ceftazidime	Sensitive
2	Colistin	Resistant
3	Cotrimoxazole	Sensitive
4	Gentamicin	Resistant
5	Levofloxacin	Sensitive
6	Meropenem	Sensitive
7	Piperacillin-Tazobactam	Sensitive
8	Polymyxin B	Resistant

4. 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 [8].

Our study involved ten 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 80% had

leucopenia and thrombocytopenia which correlates with the study by Bhise *et al.* and Patra *et al* [4, 5]. Although the ratio of preterm and term neonates is not significantly indicative of increased propensity of preterm babies developing *Burkholderia* sepsis, but 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* [5].

Two neonates had to be mechanically ventilated and the culture of Endotracheal tube tip was cultured for bacterial growth in both the cases. Though we could isolate *Burkholderia sp* in one case, we could not isolate it in another.

A clinching feature was development of progressive leucopenia and thrombocytopenia which was much more consistently associated with *Burkholderia* septic neonates rather than sepsis due to other pathogens.

One baby expired but since the baby was born of a preterm, twin pregnancy with meconium stained liquor and was very low birth weight, the mortality cannot be attributed to the virulence of pathogenic bacteria (*Burkholderia* sp) alone. The other baby of this twin pregnancy did not develop sepsis suggesting the infection being probably acquired from the environment and not mother and the predilection of *Burkholderia* to affect immunocompromised patients.

The gravity of *Burkholderia* sp infections amplifies due to its intrinsic resistance to most available antimicrobial agents. It is resistant to aminoglycosides, polymyxin B and colistin which are usually considered the last-resort antibiotics [1, 9]. An *in vitro* susceptibility study by Daniel *et al*. reported susceptibility to minocycline (94.4%), ceftazidime (86.1%), ciprofloxacin (83.3%), and trimethoprim-sulfamethoxazole (83.3%) [10]. Co-trimoxazole has been reported as drug of choice [1, 11]. But intravenous cotrimoxazole is not available in most parts of India [5]. The antimicrobial sensitivity pattern of the *Burkholderia cepacia* strain in our study reasserts the obvious. The fact that all isolates presented same antimicrobial sensitivity pattern establishes that they belong to a common strain and quite possibly a common source.

All isolates were sensitive to piperacillin-tazobactam, meropenem and ceftazidime and resistant to carbenicillin, gentamicin, polymyxin B and colistin as expected due to intrinsic resistance of this organism. The neonates in this study were effectively treated with meropenem and piperacillin – tazobactam thus reiterating the results of Patra *et al* [5].

Samples taken from the potential sources of the pathogen in NICU environment and medical devices or solutions were processed as per standard microbiological procedures. But despite extensive sampling, *Burkholderia* could not be isolated similar to the study by Patra *et al* and Kuzumoto *et al* [6, 12].

5. Conclusion

In India, the exact prevalence of *Burkholderia cepacia* infections is still unknown and there are very few reports of such outbreaks due to lack of appropriate resources and standard laboratory tests for identification causing misleading reports of such organisms as other nonfermentative Gram negative bacilli [13-16].

Our study highlights the importance of appropriate identification of Gram negative bacilli and adequate reporting of such nosocomial pathogens even when they are not associated with typical clinical scenarios. We also emphasize the significance of proper housekeeping in hospital setting to contain the hospital acquired infections.

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