DOI: https://doi.org/10.53350/pjmhs2023176466

ORIGINAL ARTICLE

Outbreak of Burkholderia Cepaciae Bacteremia in Neonatal Units of a Public Sector Hospital in Karachi, Pakistan

SHAMAILA TASLEEM[1], MADIHA SATTAR ANSARI[2], AZIZULLAH KHAN DHILLO[3], SADIA ISHAQUE[4], SOHAIMA MANZOOR[5], SHEHLA BAQI[6], HABIB UR REHMAN[7]

[1]*Fellow Infectious Disease, Civil Hospital Karachi And Shaheed Mohtarma Benazir Bhutto Institute of Trauma, Karachi*
[2]*Microbiologist, Pathology, Dr Ruth KM Pfau Civil Hospital, Karachi, Pakistan*
[3]*Assistant Professor, Consultant Infectious Diseases Asst Prof Dow University Of Health Sciences And Civil Hospital, Karachi, Pakistan*
[4]*Head of Department, Infectious Disease, SMBBIT*
[5]*Consultant, Infectious Diseases, Dr Ruth KM Pfau Civil Hospital, Karachi, Pakistan*
[6]*Professor, Infectious Disease, Shaheed Mohtarma Benazir Bhutto Institute of Trauma, Karachi*
[7]*Medical Doctor, Internal Medicine, Ziauddin University, Medical College, Karachi, Pakistan*
Correspondence to: Shamaila Tasleem, Email: drsham084@gmail.com, Cell: +92 333 3735778

ABSTRACT

Aim: This study aimed to determine the occurrence of Burkholderia cepaciae outbreak in neonatal units, identifying the source, defining the best therapy for B. Cepaciae, and enhancing infection control practices.

Methods: All neonates with BCC bacteremia during the study period were included. Data were gathered through the microbiology database, medical charts, laboratory data, and infection control surveys. Disk diffusion methodology was used in accordance with CLSI. Information from environmental cultures and feedback was included in the study.

Results: The results showed varying patient demographics across the three pediatric wards, with differences in weight, gender distribution, hospital stay duration, and diagnoses. Trends of outbreak were identified with varying patterns in different wards. An intervention was performed, leading to general improvements in infectious disease control practices, and Burkholderia cepaciae was found to be most sensitive to Levofloxacin and Trimethoprim-Sulfamethoxazole.

Conclusion: The study identified suspected sources and defined susceptibility profiles for empirical therapy for B. Cepaciae, contributing to the prevention of future outbreaks. Challenges in implementation underscore the need for proper administration and continuous emphasis on correct implementation of infection control practices.

Keywords: BCC bacteremia, neonates, outbreak, Burkholderia cepaciae, infection control practices, Civil Hospital Karachi.

INTRODUCTION

Burkholderia cepaciae is a gram negative, glucose non-fermenting bacillus that is ubiquitous in the environment and has been isolated from water, soil, fruits and vegetables[1]. However, it has now been identified as a human pathogen causing a wide spectrum of infections resulting in significant morbidity and mortality[2]. It is considered an opportunistic pathogen in the hospitalized immunocompromised population and has been responsible for outbreaks in intensive care settings and neonatal nurseries[3]. B cepaciae has been associated with infections of the bloodstream, respiratory and urinary tract[4].

Burkolderia is a very important pathogen in terms of affecting patients with immunocompromised status and lung diseases such as Cystic Fibrosis, chronic granulomatous lung disease, causing a decline in lung function. This species is a source of concern as it is an antibiotic resistant bug[5]. Therefore, BCC is now considered an important bug that is associated with nosocomial infections and a major risk factor for hospitalized patients with compromised immune systems due to its intrinsic resistance to many important classes of antibiotics and other commonly used antiseptics in hospital settings[6].

It has been observed that Bukholderia Cepaciae complex specie outbreaks have become commonly associated with non-CF patient population in intensive care units (ICUs) involving neonatal, pediatric and adult ICUs (NICU, PICU). Such outbreaks have BCC as a common culprit[7]. BCC can be an infrequent cause of neonatal sepsis in NICU and can lead to such outbreaks. Usually such affected newborns are usually the ones affected by any congenital anomaly or were preterm babies[8]. Neonatal infection with BCC specie can lead to multiple complications including sepsis in newborns, but the major neonatal population at risk with high mortality due to BCC infections are those infants affected by leukemia, neutropenia, lymphopenia, steroid therapy and candidemia[9]. The prevalence of BCC was found to be 9.4% with Burkholderia cepaciae specie being the most prevalent one at 67.3%[10]. The organism can first infect any immunocompromised newborn and subsequent infections in other newborns admitted in NICU can occur via any modes of transmission by the hospital stuff using any medical devices, catheters, or ventilators[11].

In this cross-sectional study, our aim was to determine the occurrence of Burkholderia cepaciae complex associated outbreak in neonatal units of a public sector hospital located in Karachi, Pakistan and to study associated risk factors that can lead to increased susceptibility to BCC infections, and to recognize methods that reduce transmission rate and hence decrease the occurrence of BCC bacteremia in neonatal hospital units.

MATERIAL AND METHODS

Civil Hospital Karachi (CHK), established in 1898, was one of the largest public sector hospitals in the country with 1900 Beds. It had 3 Pediatric Units, and although all the units were within the premises of CHK and affiliated facilities, they were distinctly separate in terms of location, faculty, and staff.

In April of 2021, the department of Infectious Diseases at CHK noted an increasing number of cases of BCC bacteremia in neonates from all three of the pediatric units of Civil Hospital, with a concomitant increase in requests for ID consultations for these patients. An outbreak of BCC in the pediatric units was suspected at that time.

The aim was to retrospectively review all cases of BCC bacteremia in neonates from when the first cases were reported until the cessation of the outbreak. Cases were first reported in September 2020, with a significant increase in January 2021. This was followed by a decline and cessation of the outbreak in September 2021.

The study period was therefore defined from September 2020 until September 2021.

Outbreak cases were defined as neonates from any of the 3 Pediatric Units with one or more BCC-positive blood cultures.

All neonates with BCC bacteremia identified during the study period were included. Patients that fit the inclusion criteria were identified through the microbiology database. Medical charts were reviewed for potential risk factors, management, clinical course, and outcome. Laboratory data was accessed from the HMIS system. Antimicrobial susceptibility of BCC was also documented.

For outbreak purposes, closely related species were defined as those that had a similar susceptibility profile with a discrepancy of no greater than 1 class of antimicrobial agent. Disk diffusion methodology, in accordance with Clinical and Laboratory

Standards Institute (CLSI), was used in the Microbiology Laboratory of the hospital. MICs were not available.

The hypothesis was that poor infection control practices and poor environmental cleaning and disinfection were the most likely risk factors for the outbreak. Data that was gathered during the outbreak by the Infectious Diseases department and the Infection Control nurses of Civil Hospital through infection control surveys was collated and included in this study. Survey forms routinely used by Infection Control included audits of environmental cleaning, hand hygiene, the availability, and proper use of personal protective equipment, injection safety, compliance with standard and transmission-based precautions.

Microbiological data of environmental cultures of the pediatric nurseries of all three units and the Labour Room that were obtained during the outbreak were retrieved from the database and included in this study. Feedback of the study findings was provided to the respective faculty and staff of the 3 units.

The aims and objectives of this study were to identify the source of the outbreak in the pediatric units of CHK, to use the data to prevent further outbreaks, and to reinforce among healthcare workers and hospital administration the importance of correct implementation of Infection Control practices. This study also aimed to determine the antimicrobial susceptibility of B. Cepaciae isolates during the outbreak to define the best empirical therapy for this pathogen in future cases and ultimately to reduce mortality and morbidity in the neonatal nurseries through recommendations and guidelines that arose from the findings. All data was entered in SPSS.

Approval of the IRB of Dow University of Health Sciences was requested. In all cases, confidentiality was maintained of all patient identifiers such as name, residence, and contact information. Patient data was maintained securely. Findings of the study were shared with the pediatric faculty for the prevention of further outbreaks of BCC. A meeting was held with hospital administration and pediatric faculty regarding the outbreak.

A consent form was not deemed necessary since this was a retrospective study of cases involving manual chart review and abstraction of data from the electronic medical system.

RESULTS

Background and Outbreak Overview: The report describes an outbreak of Burkholderia cepaciae bacteremia (BCC) in three pediatric wards (PEADS-I, PEADS-II, PEADS-III) of Civil Hospital (CHK) in Karachi, Pakistan, between September 2020 and September 2021. The trend showed an increasing number of cases in neonates, particularly notable in January and April 2021, before a decline and cessation in September 2021.

Patient Demographics: The report also provides demographic and medical data across the three pediatric wards (Table 1):

- PEADS-I: 49 patients, average weight 2.23 kg, gender distribution (49% male, 51% female).
- PEADS-II: 18 patients, average weight 2.02 kg, gender distribution (50% male, 50% female).
- PEADS-III: 41 patients, average weight 2.20 kg, gender distribution (68.3% male, 31.7% female).

Hospital Stay and Diagnosis: The Table 1 includes hospital stay duration, with differences among the three wards, and common diagnoses, including sepsis, low birth weight, transient tachypnea of newborns, and other neonatal issues.

Outcomes: Most patients were discharged, with PEADS-I and PEADS-II having higher discharge rates. There were some deaths reported, with PEADS-II having a higher mortality rate (16.7%). PEADS-III had a higher number of patients leaving against medical advice (LAMA) at 19.5% (Table 1).

Table 1: Demographic Characteristics of Patients among PEADS

Variable	Peads-I (n=49)	Peads-II (n=18)	Peads-III (n=41)	P-Value
Weight, kg	2.23±0.59	2.02±0.44	2.20±0.62	0.281
Gender				
Male, n(%)	24(49.0%)	9(50.0%)	28(68.3%)	0.000
Female, n(%)	25(51.0%)	9(50.0%)	13(31.7%)	
Hospital Stay, Days	15.41±9.96	18.94±11.48	11.61±5.66	0.000
Diagnosis				
Transient tachypnea of Newborn, n(%)	5(10.2%)	2(11.1%)	5(12.2%)	0.000
Sepsis, n(%)	22(44.9%)	6(33.3%)	11(26.8%)	
Low Birth Weight, n(%)	18(36.7%)	7(38.9%)	15(36.6%)	
Preterm, n(%)	22(44.9%)	7(38.9%)	18(43.9%)	
Respiratory Distress Syndrome, n(%)	18(36.7%)	5(27.8%)	15(36.6%)	
Intrauterine Growth Restriction, n(%)	0(0.0%)	0(0.0%)	8(19.5%)	
Hypoxic Ischemic Encephalopathy, n(%)	8(16.3%)	2(11.1%)	8(19.5%)	
Neonatal Jaundice, n(%)	2(4.1%)	2(11.1%)	4(9.8%)	
Chronic Heart Disease, n(%)	2(4.1%)	0(0.0%)	0(0.0%)	
Infant of Diabetic Mother, n(%)	1(2.0%)	1(5.6%)	0(0.0%)	
Meningitis, n(%)	2(4.1%)	0(0.0%)	0(0.0%)	
Hypoglycemia, n(%)	1(2.0%)	0(0.0%)	0(0.0%)	
Meconium Aspiration Syndrome, n(%)	6(12.2%)	1(5.6%)	7(17.1%)	
Outcome				
Admitted, n(%)	0(0.0%)	0(0.0%)	2(4.9%)	0.186
Discharged, n(%)	36(73.5%)	14(77.8%)	22(53.7%)	
Expired, n(%)	5(10.2%)	3(16.7%)	4(9.8%)	
LAMA, n(%)	4(8.2%)	0(0.0%)	8(19.5%)	
Referred, n(%)	4(8.2%)	1(5.6%)	5(12.2%)	

Applied Chi-Square/Fisher's Exact & ANOVA test

Trend of Outbreak (Figure 1):

- PEAD Ward I: The cases began here, increasing until January 2021, staying relatively constant until September 2021.
- PEAD Ward II: First reported in February 2021, peaked in April, and declined through September.
- PEADS Ward III: Surge in March, decline in April, a massive surge in May, and then a decline.

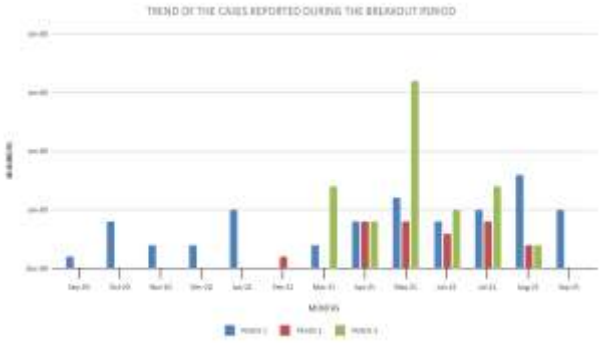

Figure 1: Trend of the Cases Reported During the Breakout

Culture Sensitivity Results: Burkholderia cepaciae was found to be most sensitive to Levofloxacin (96.3%) and Trimethoprim-Sulfamethoxazole (93.5%), with lower sensitivity to other antibiotics.

Table 2: Culture Susceptibility Patterns

Culture Sensitivity	n (%)
Levofloxacin, n(%)	104(96.3%)
Trimethoprim Sulfamethoxazole, n(%)	101(93.5%)
Ceftazidime, n(%)	31(28.7%)
Meropenem, n(%)	9(8.4%)
PAN, n(%)	2(1.9%)
PAN-R, n(%)	2(1.9%)

Intervention and Challenges: An intervention was performed, including the audit of cleaning practices, hand hygiene, proper use of PPE, injection safety, and more. Though the intervention generally improved infectious disease control practices, challenges were faced in PEADS-I due to administration issues (Supplemental Table).

Environmental Cultures: Environmental cultures were also performed to determine the source, but Burkholderia cepaciae could not be isolated. However, multiple organisms were isolated from suction bottles, which are considered a suspected source.

DISCUSSION

The recent findings from our research provide an in-depth perspective on the transmission dynamics and infection control mechanisms of Burkholderia cepacia in three pediatric wards. The pattern of the outbreak and its subsequent management strategies can be correlated and contrasted with previous studies on similar outbreaks, particularly those conducted in neonatal intensive care units (NICUs) and pediatric intensive care units (PICUs)[12-18].

Our demographic data indicates significant variability in gender distribution among the wards. PEADS-III notably had a male predominance at 68.3%[12]. Interestingly, while Paul et al. identified the source of Burkholderia cepacia infection being linked to intravenous solutions and ventilator humidifier water[12], we found no isolation of Burkholderia cepaciae from the environmental cultures, suggesting suction bottles as the suspected source.

A study by Doit et al. found a genotypically identical B. cepacia strain in lipid emulsion bottle stoppers used for parenteral nutrition[13]. This finding emphasizes the importance of rigorous infection control measures and sterilization practices for medical devices and solutions, which are consistent with our intervention strategies. Our results, combined with those from Nannini et al., further stress the need for caution regarding the use of ultrasound gels and other agents susceptible to bacterial contamination[14].

Another crucial finding of our research is the sensitivity pattern of Burkholderia cepaciae to antibiotics. A substantial sensitivity to Levofloxacin (96.3%) and Trimethoprim-Sulfamethoxazole (93.5%) was observed. These findings align with previous reports, signifying the importance of continuous monitoring and regular susceptibility testing during outbreaks[12].

The challenges faced in PEADS-I due to administrative issues highlight the crucial role of management and swift decision-making during nosocomial outbreaks. Bharara et al. reinforced the importance of timely infection control measures, as their rapid interventions led to the effective curtailing of an outbreak[15]. It's worth noting, however, that there appears to be a repetition of the Bharara et al. study in the provided references[15,16], which may indicate an oversight in our literature review.

Song JE et al. reported an outbreak caused by a contaminated 0.5% chlorhexidine solution in NICUs, which they identified through meticulous investigation[17]. Their approach stresses the importance of considering seemingly unlikely sources of contamination. Similarly, Loukil et al. reported an outbreak in NICU and PICU settings with B. cepacia being linked to respiratory therapy devices[18]. These studies, when considered alongside our findings, emphasize the multifaceted sources of potential B. cepacia infections in pediatric settings.

Limitations: Our study, like all research endeavors, comes with its limitations. One significant constraint is the difficulty in isolating Burkholderia cepacia. The bacteria's elusive nature complicates the detection and identification processes. The challenge in isolating the bacterium might have affected our ability to definitively identify all potential sources of contamination. Furthermore, our reliance on demographic and medical data, as comprehensive as they may be, might not capture all factors contributing to transmission dynamics, particularly socio-behavioral determinants not documented in our datasets.

CONCLUSION

The outbreak of Burkholderia cepaciae bacteremia in the pediatric wards of Civil Hospital in Karachi, Pakistan, underscores the importance of stringent infectious disease control measures. The intervention involving comprehensive audits of cleaning, hand hygiene, and proper use of protective equipment led to tangible improvements in practices, but challenges in one ward highlighted the need for proper administration and ownership. The critical lesson from this report is that adopting and rigorously implementing good infectious disease control practices is not an option but a necessity. By investing in training, monitoring, and strict adherence to infection control protocols, healthcare institutions can definitively prevent such outbreaks, thereby reducing morbidity and mortality. This commitment to excellence in infection control not only ensures the safety of vulnerable patients but fosters a culture of vigilance and responsiveness, emphasizing the need for relentless focus on safeguarding the well-being of both patients and healthcare workers.

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