

ORIGINAL ARTICLE

Surveillance of healthcare-associated bloodstream infections in neonatal intensive care unit of a tertiary care hospital

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Abstract

**Background and objective:** Healthcare-associated infections (HAIs) are a serious threat to patient safety. They cause substantial morbidity and mortality across various healthcare settings, including neonatal intensive care units (NICUs). This study was undertaken to determine the incidence of HA bloodstream infection (HA-BSI) in the NICU of a tertiary care hospital.

**Methodology:** Data were collected in a systematic manner based on the Centers for Disease Control and Prevention (CDC) guidelines for the surveillance of HAI for a period of 1 year (Jan–Dec, 2022). The HAI rate was calculated using the following formula: No. of cases/No. of patient days  $\times$  1,000.

**Result:** Among the 1,085 admitted neonates, the incidence of HA-BSI was 15.80/1,000 patient days. HAI was seen in neonates having mean birth weight  $1,722.5 \pm 113.906$  g, mean gestational age  $29.6 \pm 1.38$ , and mean duration of hospital stay  $13.8 \pm 4.081$  days. Among the 80 cases of HA-BSI, recognized pathogens were 22 (27.5%) *Klebsiella pneumoniae*, 16 (20%) non-albicans *Candida*, 13 (16.25%) methicillin-sensitive *Staphylococcus aureus*, 10 (12.5%) *Candida albicans*, 10 (12.5%) *Acinetobacter baumannii*, 4 coagulase-negative staphylococci, 3 (3.75%) methicillin-resistant *Staphylococcus aureus*, 1 (1.25%) *Escherichia coli*, and 1 (1.25%) *Enterococcus*. The mortality rate was 56.78%.

**Conclusion:** The predominance of *K. pneumoniae* and *A. baumannii* as causative pathogens suggests the need of stringent infection control measures and targeted antimicrobial strategies to reduce the burden of HAI and improve patient outcomes.

Keywords: healthcare-associated infection; bloodstream; NICU; infection rate

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Healthcare-associated infections (HAIs) pose a major threat to patient safety, thus causing significant morbidity and mortality globally (1). Standardized protocols of HAI surveillance across hospital networks can give significant data on the burden of HAI and also reveal gaps in implementation of infection control measures (2). To tackle these issues, it is crucial to develop and implement comprehensive hospital guidelines aimed at the prevention, monitoring, and management of HAIs within the Neonatal Intensive Care Unit (NICU). These guidelines are based on evidence-based practices and are specifically designed to meet the distinct physiological and clinical requirements of neonates. They offer a standardized framework for infection control practices, which encompass hand hygiene, antimicrobial stewardship, device care protocols, environmental disinfection, and staff training (3). We had previously studied several outbreaks of multidrug resistant organism (MDRO) in

the neonatal unit of the tertiary care hospital (4–6). However, we could not implement any HAI surveillance during these outbreaks. More recently, we studied an outbreak of Non albicans *Candida* (NAC) in the same neonatal unit and analyzed the gaps with implementation of a standardized HAI surveillance program (6). The present study was performed to analyze the trends of healthcare-associated bloodstream infection (HA-BSI) in NICU through this initiated surveillance protocol.

## Methods

### Study site and details

This cohort study was conducted in the Department of Microbiology, and the 40-bedded NICU of the 2,200-bedded tertiary care hospital, Varanasi, India. This study consisted of data collected during 1-year period (Jan 2022–Dec 2022) and analyzed after collection.

### Definitions

For the purpose of data collection, HAI was defined as infection with a date of event, > 2 calendar days after the hospital admission date. Date of event was considered as the date of first positive case occurs within the window period. HA-BSI was defined as a laboratory-confirmed HA-BSI. Recognized pathogens were defined as those enlisted as a cause of BSI in the Centers for Disease Control and Prevention (CDC) manual (7). An organism that commonly inhabits body surfaces as commensals was considered as contaminants as per the list of CDC manual.

### Data collection

This study included the data of the neonates admitted in the NICU. An active patient (neonate)-based surveillance was done prospectively by the identification of the blood culture positive cases from the laboratory investigation records in the NICU. Data were collected by the Infection Prevention and Control (IPC) team consisting of microbiologists, pediatricians, and infection control nurses trained in HAI surveillance. Surveillance was performed by regular review of the microbiological data from the record files of the NICU through daily visits to the NICU. Data were collected based on the modules from European Centre for Disease Prevention and Control (ECDC), CDC (2), and National Healthcare Safety Network (NHSN) for surveillance purpose provided by national surveillance network. Along with microbiological data, clinical data based on features of physician's suspicion of sepsis, in form of hypotension, hypothermia, respiratory distress, fever, apnea, and bradycardia were considered for selection of cases. Blood culture reports of probable contaminants were not considered.

### Infection control practices

During this period, the IPC members monitor hand hygiene practices of the staff of NICU through direct observation. They also provided monthly feedbacks on compliance to hand hygiene followed with a review meeting with the staff of the NICU. At the same time, the staff were also repeatedly trained on surface cleaning and disinfection as per the hospital guidelines. Periodic environmental surveillance was done to detect the source of contaminants in the NICU environment.

### Data analysis

The incidence of HA-BSI was calculated using the formula: No. of cases/No. of patient days  $\times$  1,000. To assess the effect of birthweight on the infection rate, all newborns were stratified to three categories: <1,500 g, 1,500–2,500 g, and > 2,500 g.

Statistical analysis was performed by the two-way chi square test using MedCalc Statistical Software version 19.2.6 (MedCalc Software bv, Ostend, Belgium) to show the association of BSI with HAI and non-HAI neonates. Results with a *P*-value  $\leq$  0.05 were considered statistically significant.

### Result

During the study period, 1,085 neonates were admitted in the NICU. The incidence of HA-BSI was 15.80/1,000 patient days. Neonates with birthweight <1,500 g, 1,500–2,500 g, and >2,500 g had HA-BSI incidence of 5.92, 6.12, and 3.75/1,000 patient days, respectively. The mean birth weight of neonates with HAI was  $1,722.5 \pm 113.90$  ( $P = 0.0001$ ), mean gestational age  $29.6 \pm 1.38$  ( $P = 0.0148$ ), and mean duration of hospital stay  $13.8 \pm 4.081$ . The mortality rate was 56.78%. The characteristics of the cases of HAI and non-HAI have been shown in Table 1. Mean birth weight of neonates and gestational age was significantly associated with HA-BSI.

Of the total neonates, 371 (34.19%) were diagnosed as cases of neonatal sepsis, with a positive blood culture. The following pathogens were isolated: *Klebsiella pneumoniae* 21.02% (78/371), non-albicans *Candida* (NAC) 16.98% (63/371), *Acinetobacter baumannii* 13.47% (50/371), methicillin-sensitive *Staphylococcus aureus* 12.66% (47/371), *Escherichia coli* 9.70% (36/371), *Candida albicans* 7.54% (28/371), methicillin-resistant *Staphylococcus aureus* (MRSA) 6.73% (25/371), coagulase negative staphylococci (CoNS) 6.46% (24/371), and *Enterococcus* spp. 3.50% (13/371). However, as only a single blood culture was considered, CoNS was considered as contaminants. Of the 371 cases of neonatal sepsis, 76 cases were diagnosed as HA-BSI. Recognized pathogens in HA-BSI were 22 (27.5%) *K. pneumoniae*, 16 (20%) NAC, 13 (16.25%) *S. aureus*, 10 (12.5%) *C. albicans*, 10 (12.5%) *A. baumannii*, 3 (3.75%) MRSA, 1 (1.25%) *E. coli*, and 1 (1.25%) *Enterococcus*. The distribution of organisms in HAI and non-HAI has been shown in Fig. 1, and the distribution

**Table 1.** Characteristics of HAI and non-HAI neonates, *N* = 371 (Jan 2022–Dec 2022)

Characteristics	HAI ( <i>n</i> = 76) <i>N</i> (%)	non-HAI ( <i>n</i> = 295) <i>N</i> (%)	<i>P</i>
Mean gestational age (weeks)	29.6 $\pm$ 1.38	30.13 $\pm$ 4.12	0.0148*
Mean birth weight (g)	1,722.5 $\pm$ 113.90	2080.95 $\pm$ 673.67	0.0001*
Gender (male)	47 (58.75)	177 (60)	0.7700
Low birth weight (<2,500 g)	56 (59.90)	218 (74)	0.9698
Mortality rate	53 (66.25)	178 (60.39)	0.1323

\**P*  $\leq$  0.05, significant.

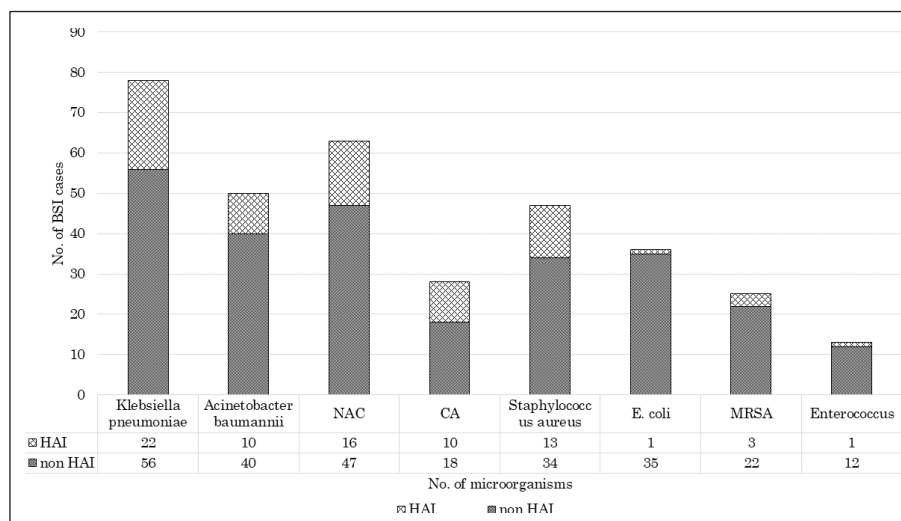


Fig 1. Distribution of microorganisms causing bloodstream infections in the NICU, both HAI and non-HAI.

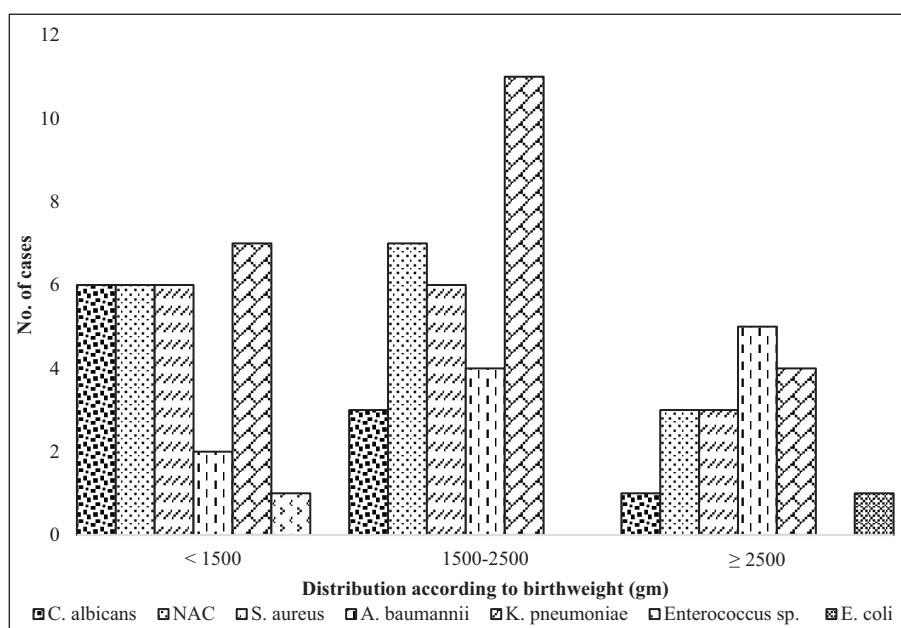


Fig 2. Distribution of organisms associated with HA-BSI based on birth weight of the neonates (<1,500 g, 1,500–2,500 g, and >2,500 g).

of organisms according to birthweight of neonates has been shown in Fig. 2.

Based on birth weight of the neonates, *K. pneumoniae* was the most common pathogen in neonates with <1,500 g, 30.84% (28/76) and 1,500–2,500 g, 40.78% (31/76) groups, while *A. baumannii* was commonest in the >2,500 g group, 22.36% (17/76).

For the organisms isolated from 76 HAI cases, susceptibility pattern for *K. pneumoniae* was for levofloxacin 71.42% (15/21), ciprofloxacin 61.90% (13/21), amikacin 70.58% (12/17), gentamicin 42.85% (9/21), meropenem 52.63% (10/19), imipenem 42.10% (8/19), while for *A. baumannii*,

it was amikacin 72.72% (8/11), ciprofloxacin 63.63% (7/11), levofloxacin 45.45% (5/11), imipenem 54.54% (6/11), and meropenem 45.45% (5/11). All the *Candida* isolates were 100% (26/26) susceptible for fluconazole, itraconazole, and voriconazole. For *S. aureus*, susceptibility shown against vancomycin 100% (13/13) and linezolid 100% (13/13).

Among the total cases of neonatal sepsis, during the study period, the empirically used antibiotics were amikacin 61.45% (228/371), levofloxacin 43.93% (163/371), vancomycin 50.67% (188/371), fluconazole 28.03% (104/371), meropenem 22.10% (82/371), and piperacillin/tazobactam 6.73% (25/371).

## Discussion

Over the past few decades, significant advances in NICU have led to remarkable improvements in the survival rates of neonates. These developments including better respiratory support, advance monitoring system, and refined nutritional support have undoubtedly contributed to saving countless lives and improving outcomes for these vulnerable populations.

Neonatal ICUs face alarmingly high rates of HA-BSIs particularly in low birthweight category, where rates reach 6.09/1,000 patient days (8). Neonates with a birthweight of < 1,500 g, 1,500–2,500 g, and > 2,500 g had HA-BSI incidence of 5.92, 6.12, and 3.75/1,000 patient days comparable to a multicentre study from India showing 21.00, 8.1, and 10.8/1,000 patient days, respectively, for the same birthweight categories in neonates (1). The overall incidence of HA-BSI was 15.80/1,000 patient days as compared with studies from India (13.2%) (9), Poland (7.32%) (10), and from Nepal (47%) (11). This can be due to poor maternal health, lack of skilled birth care, and weak healthcare access especially in rural areas. Neonates' mortality remains a significant global health challenge; however, there is hope for further reductions in neonates' mortality with continued progress in healthcare settings.

All the BSIs were primary, and none was associated with central line comparable to a study from India showing 74% BSIs were classified as primary BSI (1).

In the present study, *K. pneumoniae* was the most common pathogens associated with BSI in neonates, followed by *A. baumannii* and *S. aureus*, similar to a multicentre study from India, showing the same pattern of organisms that is *K. pneumoniae* (24.8%), *A. baumannii* (21.3%), and *S. aureus* (8.8%) (1). Another study from India showed that *K. pneumoniae* (39.39%) was the most common pathogen associated with HA-BSI (12), which is in line with studies from Italy showing *K. pneumoniae* as the most common pathogens, and the mortality rate of HA-BSI was higher with Gram-negative pathogens (36.4%) compared with Gram-positive (4.5%) (13). A study from South Korea showed that among the bacterial cases, *S. aureus* (65%) represented the majority cases of HA-BSI (14). Another study from Turkey showed that *K. pneumoniae* (25.9%) was the most common etiologic agents of HA-BSI (15), similar to that from Poland (29.3%) (10).

*Klebsiella* is a member of normal microbiota in the gastrointestinal and respiratory tracts. Additionally, hospital surfaces and high-touch equipment can act as reservoir for the bacteria. Another reason can be due to the immature immune system of the infants, which is less capable of defending against infections (16). A recent research on colonization of Carbapenem resistant *Klebsiella pneumoniae* (CRKP) on neonates has shown that CRKP can colonize skin and gut of neonates within 24–72 h of birth

(17). Similarly, *A. baumannii*, which is also known for its high resistance to multiple antibiotics, can survive on surfaces and equipment for prolonged periods. The combination of its environmental persistence, resistance to treatments, and the high vulnerability of NICU patients contributes to *A. baumannii*, which is a common and challenging pathogen in intensive care units (18).

Although empirical use of antibiotics was high in this study, compared to another study from USA where over 95% of infants admitted to the NICU receive empirical antibiotics in the first postnatal days, only 1–5% have positive initial blood cultures (19). This can be due to difficulty in distinguishing between bacterial infection and non-infectious conditions in newborns, especially preterm infants with undeveloped immune systems. Clinicians may initiate antibiotics as a precautionary measure because early signs of infection can be nonspecific and potentially life threatening if left untreated. Additionally, delays in obtaining definitive culture results can lead to prolonged empirical antibiotic use. The lack of standard guidelines and fear of negative outcomes contribute further overuse of antibiotics in NICU settings (20).

This study has some limitations. A single blood culture criteria was used to diagnose BSI. Additionally, this study was conducted on a single NICU setting, which limits the generalizability of the findings to other healthcare facilities with differing infection control practices. Nevertheless, it reinstates the importance of HAI surveillance based on standardized protocols in order to intervene with adequate measures. The strength of this study was attributed to the systematic surveillance of HA-BSI in an extensive NICU cohort, and the correlation of low birth weight and gestational age with the risk of infection. This study provides valuable insights into the distribution of pathogens and their resistance patterns, thereby providing significant guidance for empirical treatment and infection management in neonatal care.

## Conclusion

The increased occurrence of HA-BSI and the related mortality emphasize the urgent necessity for improved infection prevention measures in the NICU. The prevalence of multidrug-resistant organisms such as *K. pneumoniae* and *A. baumannii* underscores the significance of strong antimicrobial stewardship, prompt diagnosis, and focused treatment to reduce the effects of HAIs and enhance neonatal survival rates.

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**Conflict of interest and funding**

NA.

**Ethical approval**

This study was approved by the Institute Ethical Committee via letter No. Dean/2021/EC/2598, dated: 10-04-2021.

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