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Original Article

Central line-associated bloodstream infections (CLABSI): Microbiology and antimicrobial resistance pattern of isolates from the Pediatric ICU of a tertiary care Indian hospital

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ABSTRACT

Objectives: Central line-associated bloodstream infections (CLABSIs) are important and serious healthcare-associated infections (HAI), with a reported mortality of 12–25%. We conducted this study to determine incidence of CLABSI in our Pediatric Intensive Care Unit (PICU), and to study the profile (gram positive or negative) of organisms causing these infections and also their antimicrobial resistance pattern.

Methods: A prospective cohort study was conducted in our PICU for a period of one and a half years from 1st August 2011 to 31st January 2013. Blood samples were collected for culture when primary or secondary bacteremia was suspected. A CLABSI was defined as per CDC guidelines. Antimicrobial susceptibility testing was done by Disk diffusion Technique using Kirby Bauer's method and interpretation was as per CLSI guidelines.

Results: There were 13 episodes of CLABSI, of which, 5 (38.5%) were caused by *Klebsiella* spp., 3 (23.1%) by *Pseudomonas* spp., 1 (7.7%) by *Acinetobacter* spp., 1 (7.7%) by *Proteus* spp., 1 (7.7%) by *Enterococcus faecium*, and 2 (15.3%) by *Staphylococcus epidermidis*. All the *Pseudomonas* spp. isolates were sensitive to Ciprofloxacin whereas *Acinetobacter* spp. was resistant to it. Four of 5 *Klebsiella* spp. isolates were resistant to carbapenems and all were resistant to 3rd generation cephalosporins. Both the *S. epidermidis* isolates were methicillin resistant.

Conclusions: Gram-negative organisms continue to predominate HAIs in the developing countries, reflecting the suboptimal infection control. More worrisome is the rise of multi-drug-resistant gram-negative bacilli, which are resistant to quinolones, 3rd and 4th generation cephalosporins, and carbapenems. Preventive and control measures are the most cost-effective parameters to help contain the rising antimicrobial resistance.

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1. Introduction

Intravascular catheters are indispensable for modern day healthcare. They include short-term peripheral venous and arterial catheters, short-term central venous catheters (CVCs), long-term tunneled and cuffed CVCs, and long-term peripherally inserted CVCs.¹

Although such catheters provide necessary vascular access, their use puts patients at risk for local and systemic infectious complications, including local site infection, catheter-related bloodstream infection (CRBSI), septic thrombophlebitis, endocarditis, and other metastatic infections (e.g., lung abscess, brain abscess, osteomyelitis, and endophthalmitis).²

Central line-associated bloodstream infections (CLABSIs) are one of the most important HAIs associated with a high mortality rate of 12–25%.³ Multiple studies of the causative organisms for CRBSIs exist in the adult literature, but few such studies in the pediatric population exist. We conducted this study to determine incidence of CLABSI in our Pediatric ICU, and study the profile (gram positive or negative) of organisms causing these infections and also their antimicrobial resistance pattern.

2. Methods

2.1. Study design and setting

We conducted a prospective cohort study to measure the burden of CLABSIs in the Pediatric Intensive Care Unit (PICU) of All India Institute of Medical Sciences (AIIMS), New Delhi. We also aimed to study the profile of organisms causing these infections and their corresponding antimicrobial resistance pattern. This study was conducted in the PICU for a period of one and a half years from 1st August 2011 to 31st January 2013. Ethical clearance was taken from the Ethics Committee of AIIMS (Ref. No. IESC/T-282/01.07.2011).

2.2. Participants

Inclusion criteria

- All the children who stayed in PICU for ≥ 48 h.
- Patients with no infection incubating at the time of admission to PICU, i.e. samples collected on Day 1 of the patients stay were culture negative (blood, urine, and sputum/broncho-alveolar lavage).

Exclusion criteria

- All the children who stayed in PICU for < 48 h.
- Patients with any infection incubating at the time of admission to PICU, i.e. samples collected on Day 1 of patients stay were culture positive (blood, urine, and sputum/broncho-alveolar lavage).

2.3. Materials and methods

2.3.1. CLABSI

Case definition – This was defined as per CDC guidelines,³ i.e. a CLABSI is recovery of a pathogen from a blood culture (a single

blood culture for organisms not commonly present on the skin and two or more blood cultures for organisms commonly present on the skin) in a patient who had a central line at the time of infection or within the 48-h period before development of infection. The infection cannot be related to any other infection the patient might have and must not have been present or incubating when the patient was admitted to the facility.

2.3.2. Secondary bloodstream infection

Bloodstream infection (BSI), which is secondary to a primary infection site, i.e. related to an infection at another site, such that the primary site of infection may have seeded the bloodstream secondarily. If the criteria for the primary site infection require a culture, then at least one organism cultured from that site must match an organism in the blood culture.⁴

Blood samples were collected for culture when primary or secondary bacteremia was suspected. For children > 1 year age, 3–5 ml blood was drawn out and put in a blood culture bottle containing 50 ml of Brain Heart Infusion (BHI) broth, whereas for infants, 1 ml blood was put in a McCartney's bottle containing 10 ml BHI broth.

The sample in blood culture bottle was kept in the incubator at 37 °C. After 24 h, first subculture was done on Blood Agar (BA) and MacConkey Agar (MA). If negative, second subculture was done on BA and MA after 48 h. After 2 weeks, final subculture was done on BA and MA, before discarding the sample.

Interpretation – A single positive blood culture was considered significant for organisms not commonly present on the skin and two or more blood cultures for organisms commonly present on the skin.

2.3.3. Antimicrobial susceptibility testing

It was done by Disk diffusion Technique using Kirby Bauer's method and interpretation as per CLSI guidelines.⁵

3. Results

Out of 349 patients included in our study, 19 developed a BSI. All the patients who developed a BSI were on a central line during their stay in the PICU. Of these 19 patients, 13 (68.4%) had primary BSI due to the central line, i.e. they developed central line-associated bloodstream infection (CLABSI). The remaining 6 (31.6%) patients developed a secondary bloodstream infection, i.e. related to an infection at another site.

The incidence density of CLABSI was 5.03 per 1000 central line days calculated by the following formula:

$$\text{Incidence density of CLABSI} = \frac{\text{Episodes of CLABSI}}{\text{Central line days}} \times 1000$$

$$= 13/2580 \times 1000 = 5.03$$

When calculating incidence density of CLABSIs, the Centre for Disease Control and Prevention⁶ (CDC) guidelines recommend that we take “central-line days” as the denominator for the calculation. ‘Central line days’ is calculated by daily count of patients on a central line, admitted in a healthcare facility. This adjusts risk of CLABSI with respect to the duration the central line was in place.

3.1. Microbiology

The 13 episodes of CLABSI were predominantly caused by gram-negative organisms, as depicted by Table 1.

3.2. Antimicrobial susceptibility profile of bacterial isolates causing CLABSI

Of the 13 bacterial isolates of CLABSI, 10 were gram-negative bacilli (GNB) and 3 were gram-positive cocci (GPC).

1) Gram-negative organisms

a) Nil-fermenters

Of the 3 *Pseudomonas* spp. isolates causing CLABSI, 2 were sensitive to Amikacin. None were sensitive to Imipenem. One isolate was sensitive to Meropenem. All three isolates were sensitive to Ciprofloxacin, Cefoperazone-Sulbactam, and Piperacillin-Tazobactam. The single isolate of *Acinetobacter* spp. was sensitive to Meropenem, Cefoperazone-Sulbactam, and Piperacillin-Tazobactam and resistant to Amikacin and Imipenem.

b) Enterobacteriaceae family

i) *Klebsiella* spp. – Of the 5 *Klebsiella* spp. isolates, 3 were sensitive to Amikacin. Only one was sensitive to Imipenem and Meropenem. All isolates were sensitive to Ciprofloxacin and Cefoperazone-Sulbactam. Of the 5 isolates, four were sensitive to Piperacillin-Tazobactam.

ii) *Proteus* spp. – The only isolate of *Proteus* spp. was sensitive to all drugs except Ciprofloxacin.

2) Gram-positive organisms

i) *Staphylococcus epidermidis* – Both isolates of *S. epidermidis* were methicillin resistant. Of the two isolates, one was sensitive to Amikacin. Both isolates were sensitive to Vancomycin, Teicoplanin, and Linezolid and resistant to Erythromycin, Penicillin, and Rifampicin.

ii) *Enterococcus faecium* – The single isolate of *E. faecium* was resistant to Amikacin. It was sensitive to Gentamicin, Vancomycin, and Linezolid and resistant to Teicoplanin, Erythromycin, and Penicillin.

procedures in place. This information would also help in future development of protocols to reduce the incidence, and thus morbidity, mortality, and healthcare cost associated with CLABSI.

Multiple studies of the causative organisms for CRBSIs exist in the adult literature, but few such studies in the pediatric population exist. The National Nosocomial Infection Surveillance System survey (NNISS) of PICU patients identified coagulase-negative *Staphylococcus* spp. as the predominant organism associated, accounting for 37.8% of reported cases.⁷ The most commonly reported causative pathogens remain coagulase-negative staphylococci, *Staphylococcus aureus*, enterococci, and *Candida* spp.⁸ GNB accounted for 19% and 21% of CLABSIs reported to CDC and the Surveillance and Control of Pathogens of Epidemiological Importance (SCOPE) database, respectively.⁸

In our study, we found a predominance of GNBs causing CLABSI, in contrast to GPCs, which predominate in studies from developed countries.⁹ Similarly, in a previous study done in our PICU on HAIs, 96.5% of the bacterial isolates causing HAIs were GNBs, including BSIs.¹⁰ In another Indian study done in PGI, Chandigarh by Lakshmi¹¹ et al. in the PICU, it was also found that GNBs predominated as a causative factor for nosocomial BSI. Thus, GNBs continue to dominate in developing countries where infection control practices are not optimal.

Emerging multidrug-resistant GNBs are another major challenge in the treatment of these infections. The gram-negative bacteria resistant to quinolones and all 3rd and 4th generation cephalosporins, which are important drugs for empirical treatment in ICUs, are increasing. To this, added the emergence of carbapenem resistance, it leaves very limited choice for the treatment of the patient. We also found similar trends in the CLABSI isolates of our study. Nil-fermenters are now on the rise in the healthcare settings. Colistin is the only choice left in cases of multidrug-resistant BSI isolates. Tigecycline use is not a very good treatment option in BSI patients.

Antimicrobial resistance has now become a global challenge. Extensive use of antibiotics has led to selective pressure on bacteria and emergence of multidrug-resistant strains of bacteria, thus taking us back to almost the pre-antibiotic era.¹²

Limitations of our study include, not looking for fungi as the causative organism of CLABSI in each and every patient. Only in high-suspicion cases, where bacterial blood cultures were negative and the patients did not respond to antibiotics, fungal blood culture was performed. Also, our study lacks any statistical conclusion.

Prevention and control of infection is one of the most important and most cost-effective parameter to contain and reduce the burden of antimicrobial selective pressure. HAIs due to multidrug-resistant organisms are a major challenge in any healthcare facility.¹² For prevention of nosocomial infections, especially device-associated infections like CLABSI, education is an important and sustainable measure.

Conflicts of interest

The authors have none to declare.

4. Discussion

The present study was undertaken to obtain information on CLABSIs in our PICU, in an attempt to have all policies and care

Table 1 – Etiology of organisms causing CLABSI in PICU.

Etiology	CLABSI n = 13
<i>Klebsiella</i> spp	5 (38.5%)
<i>Pseudomonas</i> spp.	3 (23.1%)
<i>Acinetobacter</i> spp.	1 (7.7%)
<i>Proteus</i> spp.	1 (7.7%)
<i>Enterococcus faecium</i>	1 (7.7%)
<i>Staphylococcus epidermidis</i>	2 (15.3%)
Total	13

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