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Major Article

Infection with gram-negative bacteria among children in a tertiary pediatric hospital in Egypt

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Key Words:
healthcare-associated infection
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Background: Patients in pediatric intensive care units (PICUs) are susceptible to infections with gram-negative bacteria (GNB).
Methods: A prospective observational study was conducted in 2 PICUs at Cairo University Hospitals to determine the incidence and outcome of GNB infections over 1 year. Variables of interest included age, gender, isolated organism, susceptibility to antibiotics, and final outcome.
Results: During the study period, 1420 patients were admitted to the PICU; of these, 291 developed GNB infections. The median age of the studied GNB patients was 50 months (interquartile range [IQR], 22-80 months). The mortality rate was 37.1%. Organisms were isolated from blood in the majority (86.6%) of patients, with Klebsiella (36.0%) being the most frequently isolated organism. Among patients with GNB infection, 235 patients, one had a multidrug-resistant (MDR) infection. The length of hospital stay was statistically significantly longer in the MDR group (25 days; IQR, 20-30) than in the non-MDR group (15 days; IQR, 10-20) ($P < .01$). Mortality was similar in both groups (37.4% vs 35.7% in the MDR and non-MDR groups, respectively; $P = .88$).
Conclusion: This study highlights high rates of pediatric MDR-GNB infections and emphasizes the need for a continuous surveillance system in the management of these critically ill children.

BACKGROUND

Healthcare-associated infections (HAIs) are increasing worldwide, especially among children who are admitted to pediatric intensive care units (PICUs).[1] Patients in the PICU are highly vulnerable to infections because of impaired host defenses, administration of drugs (eg, muscle relaxants), and the use of invasive devices.[2] The burden of HAIs due to multidrug-resistant organisms (MDROs) varies widely according to geographic region, healthcare setting, type of pathogen, and antimicrobial substance.[3] Many of these HAIs are due to multidrug-resistant gram-negative bacteria (MDR-GNB).[4] Several studies have demonstrated that MDR-GNB infections are an important determinant of patient safety and represent a public health concern, with high patient morbidity and mortality, increased healthcare costs, and prolonged length of hospital stay.[5] However, studies in PICUs are rare, especially in Arab countries. Most pediatric studies have focused on specific HAIs and MDR-HAIs caused by specific etiologic agents.[6-8]

In Egypt, there is a gap in the literature with respect to MDROs, in particular MDR-GNB in PICUs. Although a few studies have been conducted, they tended to focus on prevalence and incidence, studied a single organism, or were designed to clarify financial costs.[9] Accordingly, this prospective observational study was conducted to determine the incidence and outcome of patients harboring hospital-acquired GNB infections, both MDR and non-MDR, at 2 PICUs at Cairo University Children Hospital in Egypt.

METHODS

Study design and setting

This 1-year prospective observational study was conducted in 2 PICUs at Cairo University Children Hospital, a university-affiliated teaching hospital in Egypt, in the period from June 2016 to June 2017. The PICUs included 23 and 14 beds and together receive

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approximately 1420 patients annually. They follow the same management protocol.

Study population

Children aged 1 month to 12 years (according to the hospital admission policy) were included in the study. For all patients admitted to the PICU, routine blood and urine cultures are taken, as well as sputum cultures when feasible. Patients were included if their initial cultures were negative, had no signs of infection on admission, and then developed a healthcare-associated GNB infection, proved by later positive culture and signs of infection. Patients who were admitted to the PICU with microbial infection, had positive initial cultures with no signs of infection (ie, colonized), or were immune-compromised (due to immunodeficiency or immunosuppressive therapy) were not considered to have a health care associated infection.

Working definitions

MDR is the resistance of microorganisms to at least 3 different groups of antibiotics with intrinsic activity against GNB (eg, beta-lactams, aminoglycosides, carbapenems, and quinolones).[10] **Colonization** was defined as any positive culture without clinical signs of infection.[11] **PICU-related HAI** was defined as any infection that was not present or incubating at the time of admission and that occurred 48 hours or more after admission to the PICU.[12]

Sepsis-related Organ Failure Assessment (SOFA) score

SOFA score was used for prediction of outcome and indirect assessment of disease severity on admission. Higher scores (range, 0-24) indicate more severe disease.[13]

Data collection tool

A data collection form was designed to collect and record the following data for children with GNB infections: age, gender, primary diagnosis, isolated organism, site of isolation, antibacterial susceptibility, length of PICU stay, types of invasive procedures performed (such as endotracheal intubation, central venous catheterization, parenteral nutrition, and blood transfusion), SOFA score, and final outcome of patients during their PICU stay (survived or died).

Microbiologic workup

One or 2 different samples were taken from each patient, depending on the infection site. All clinical samples—blood, sputum, cerebrospinal fluid, central venous line, stool, wound discharge, and urine—were inoculated on routine culture media (MacConkey agar, blood agar, and chocolate agar), and identification of the isolated organism was performed by biochemical tests and Vitek-2 compact system whenever required.

Antibacterial susceptibility testing

The susceptibility of the isolated GNB was tested against 8 antibiotics (ciprofloxacin, piperacillin/tazobactam, cefotaxime, ceftriaxone, amikacin, imipenem, meropenem, and polymixin) using the disk diffusion method following Clinical and Laboratory Standards[14] to evaluate the in vitro susceptibility of bacterial isolates to these antibiotics. Frequency of different MDR isolates was reported and further grouped by site of isolation among different isolate sites as well as different type of organism. Patients were divided into MDR and non-MDR groups to analyze the outcome of GNB infections.

Statistical analysis

Statistical analysis was done using Statistical Package for Social Science software (SPSS, version 21.0, IBM). Data were summarized using median and interquartile range (IQR) for quantitative variables and using frequency and percentage for qualitative variables. Comparison between groups was performed using the Mann-Whitney test for continuous variables and the chi-square or Fisher's exact test for categorical variables. *P* values less or equal to .05 were considered statistically significant.

Ethical considerations

The Ethical Review Committee in the Faculty of Medicine, Cairo University, revised and approved the study protocol. Informed consent was obtained directly from the legal guardian of each patient (mother, father, or other caregiver) before data collection and after explanation of the study objectives and importance. All procedures for data collection were treated with confidentiality according to Helsinki declarations of biomedical ethics.[15]

RESULTS

Of 1420 patients who were admitted to the PICU during the study period, 291 who developed GNB infections were enrolled in this study. The median age of the studied GNB patients was 50 months (IQR, 22-80 months). The mortality rate was 37.1% (108/291). Organisms were isolated from blood in the majority (86.6%) of patients,

Table 1
Clinical characteristics of the enrolled GNB patients at a tertiary pediatric hospital in Egypt

Variable	Total (n = 291)
Primary diagnosis *n, %*	
Sepsis	38, 13.1
CVS	46, 15.8
CNS	40, 13.7
Respiratory	71, 24.4
GE	13, 4.5
*Others	83, 28.5
SOFA score on admission *median, (IQR)*	8, (5-12)
Isolated organisms *n, %*	
Total no. of isolated organism	308
Pseudomonas	93, 30.1
Actinobacter	69, 22.4
Klebsilla	111, 36.0
E coli	19, 0.6
Enterobacter	16, 5.2
Site of isolation *n, %*	
Total no. of sites of isolation	306
Blood	265, 86.6
Sputum	85, 28.0
CSF	68, 22.2
Stool	42, 14.0
Urine	21, 6.8
Wound	9, 3.0
Medical procedures *n, %*	
Total no. of medical procedures	415
MV	123, 29.6
CVL	151, 36.3
TPN/PPN	93, 22.4
Blood transfusion	48, 16.5
LOS (days) *median, (IQR)*	15, (10-25)
Mortality rate *n, %*	108. 37.1

NOTE. Data are expressed as number and % for qualitative variables and median with (IQR) for quantitative variables.
CNS, Central nervous system; *CVL*, central venous line; *CVS*, cardiovascular system; *GE*, gastroenteritis; *IQR*, interquartile range; *LOS*, length of stay; *MV*, mechanical ventilation; *TPN/PPN*, total parenteral nutrition/partial parenteral nutrition.
*Others: skin and soft tissue infections/urinary.