IJID Regions 13 (2024) 100423

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

High rates of nosocomial infections and antimicrobial resistance in a Moroccan pediatric intensive care unit: A cause for alarm

Said Younous[1], Dounia Nadifiyine[1,*], Amal Yassine[1], Youssef Mouaffak[1], Houssam Eddine Sahraoui[1], Abdelaziz Sihami[1], Nabila Soraa[2]

[1] Pediatric anesthesia and Intensive care unit, University Hospital Mohammed VI of Marrakech, Marrakech, Morocco
[2] Laboratory of Microbiology, University Hospital Mohammed VI of Marrakech, Marrakech, Morocco

ARTICLE INFO

Keywords:
Nosocomial infections
Pediatric intensive care unit
Yeasts
GNB
Antibiotics
Resistance

ABSTRACT

Objectives: This study aimed to determine the epidemiology of nosocomial infections (NIs) in a pediatric intensive care unit and define the risk factors associated with NIs.
Methods: We performed a prospective descriptive and analytical monocentric study on the incidence of NIs in the pediatric intensive care unit between July 2021 and May 2022. Children with NIs (cases) were compared with matched controls without NIs.
Results: We analyzed 396 patients; 102 had NIs. The global incidence of NIs is 44.7% (incidence density of 10.6 per 1000 days of hospitalization). The incidence densities of blood stream infection, pneumonia associated with mechanical ventilation, and urinary tract infection were 10 per 1000 days of central venous catheter use, 7.2 per 1000 of mechanical ventilation use, and 11.1 per 1000 days urinary catheter use. The overall microbiological profile of NIs is dominated by gram-negative bacilli in 78%, followed by gram-positive cocci in 13%. The most common agents in sepsis were *Klebsiella pneumoniae*. In pneumonias, *Acinetobacter Baumanii* was the most common cause, and, in urinary tract infection, the most frequent agents were gram-negative bacteria, especially *Escherichia coli* (33.3%). The presence of NIs was associated with a long period of hospitalization, use of invasive devices (central venous catheter, mechanical ventilation, and bladder catheters), and use of antibiotics.
Conclusions: The incidence of NIs acquired in this unit was high and was associated with extrinsic and intrinsic factors.

Introduction

Nosocomial infection (NI) or health care–associated infection (HAI) is a systemic condition resulting from the adverse effect of the presence of infectious agents or their toxins. They are a major public health problem due to the cost and the morbidity and mortality they cause. They are particularly common in the intensive care unit (ICU) due to the patient's decreased immune defenses and the increasing number of invasive procedures. NIs remain a dreaded complication in children, especially in newborns, because they result in significant morbidity, considerable excess cost of care, and a non-negligible mortality rate.

The pediatric ICU (PICU) in Marrakech is composed of 12 boxes and 13 beds. Each box is equipped with a handwashing station and hydroalcoholic solutions.

The medical team of the service is composed of five senior doctors, interns, and residents. The paramedical team is composed of a head nurse, 12 nurses, a pharmacy manager, and a physiotherapist. The nurse-patient ratio is 1:3 in the morning, 1:4 in the afternoon, and 1:6 in the evening.

The service caters to infants and children under the age of 15 years who present with or are at risk of developing one or more acute organ failures related to a medical or surgical condition that directly threatens their vital prognosis and necessitates the use of supportive measures. The service also caters to newborns with surgical conditions requiring surgery to ensure optimal medical management during and after the surgical procedure.

This study aimed to describe the epidemiology of NIs in the PICU, describe the characteristics of the study population, analyze the microorganisms responsible and their resistance profiles, and determine the morbidity and mortality associated with NIs. The results of this study can contribute to the development of realistic, rapid, and adapted strategies for the prevention and control of NIs in the PICU.

* Corresponding author.
E-mail address: dounia.nadifiyine1997@gmail.com (D. Nadifiyine).

https://doi.org/10.1016/j.ijregi.2024.100423
Received 18 May 2024; Received in revised form 6 August 2024; Accepted 7 August 2024

Materials and methods

This is a prospective, descriptive, and analytical monocentric study conducted using the medical records of children hospitalized in the PICU over a period of 11 months, from July 2021 to May 2022. The study population includes all children admitted to the PICU in Marrakech during the study period. The study included children aged from birth to 14 years who stayed in the PICU for more than 48 hours and developed one or more NIs based on the diagnostic criteria defined by the modified Atlanta Centers for Disease Control and Prevention 2008 [1].

Patients transferred to the PICU for a severe infectious pathology (community or nosocomial) documented in the originating service were only included in the study if they developed an infection with other microorganisms during their stay in the PICU. Patients excluded from the study are those whose length of hospitalization was less than 48 hours and/or did not meet the selected diagnostic criteria.

For each patient, the following parameters were recorded: sociodemographic variables including age, gender (male or female), and source of admission (emergency, another hospital department, or another facility); clinical variables including comorbidities, reason for admission, technical procedures used for care (endotracheal intubation, urinary catheterization, central and/or peripheral venous access, drains), site of infection (respiratory, digestive, urinary, surgical site), microorganisms found in biological samples at the site of infection, and their antibiotic sensitivities; and patient outcomes, including length of stay in the ICU and clinical outcome (survival or death).

The data were recorded on a pre-established and pretexted collection form. The information was then entered into a spreadsheet (Excel) for preparation and analysis. Statistical analysis was performed using SPSS 26.0 software for Windows.

A *P*-value less than 0.05 was considered significant. Quantitative data were expressed as mean and SD, whereas qualitative data were presented as number and percentage of patients. The Pearson chi-squared test was performed for each categorical variable, and Student's *t*-test was used for continuous variables. Odds ratios and their 95% confidence intervals, obtained by Fisher's exact test, were used to establish the relationship between associated factors and NIs. The level of statistical significance was set at 0.05.

Results

Patient's characteristics

The results of the study conducted on 396 patients show that 102 patients had NIs. The highest rate of NIs was found in patients aged over 2 years, followed by those aged under 1 month (neonates). The median age was 2.5 years (2-4). Male patients were predominant, accounting for 57%, with a sex ratio of 1.32. The main reasons for admission were surgical pathologies, including esophageal atresia and acute abdomen, and traumatic pathologies, such as severe trauma and thermal burns.

Patients who had NIs had a significantly longer stay in the ICU than those without NIs (median of 13 days vs 2 days, with a significant P <0.005). Of the patients who had NIs, 21.6% were under antibiotic therapy for an infectious pathology before admission to the ICU (P <0.005).

NI sites

The incidence rate of NIs was 44.7%, with a density of incidence of 10.6 per 1000 hospitalization days. There were 177 episodes of NIs in the 102 infected patients, with a ratio of infection to infected of 1.73 and a total hospitalization period of 1658 days. Bacteremia was the most predominant NI, accounting for 44% of cases, followed by nosocomial pneumonia at 30%, then surgical site infections, infections in burned patients, and urinary tract infections (UTIs), with a percentage of 7% each.

The incidence of bacteremia was 19.9%, with a density of incidence of 20 per 1000 central venous catheter days. The incidence of catheter-related infections complicated with nosocomial bacteremia or not was 4.04%, and 67.6% of patients who had at least one episode of HAI had a central venous catheter, making it a risk factor for HAIs (P <0.005).

The incidence of nosocomial pneumonia in the series was 13.6%, with a density of incidence of 7.2 per 1000 mechanical ventilation days. Of the patients who had at least one episode of HAI, 82.4% were ventilated for more than 48 hours, making mechanical ventilation a risk factor for NIs (P <0.005).

The incidence of UTIs was 3.2%, with a density of incidence of 11.1 per 1000 urinary catheterization days. Furthermore, 84.3% of patients with a HAI were catheterized for more than 48 hours (P <0.005), making urinary catheterization a risk factor for HAIs. The incidence of skin infections in patients with burns was 3.53% and 4.3% for surgical site infections (the actual intraoperative surgical site cultures and wound swabs from infected surgical wounds).

Clinical symptoms

The clinical symptoms were fever in 90% of patients, and the hemodynamic signs were mainly marked by tachycardia in 80% of cases. Among the cutaneous manifestations of NIs, there were mottling in 60% of patients and scleroderma in neonates. In patients on mechanical ventilation, 92% had bronchial secretions that became purulent and abundant, and 43% of patients had an aggravation of ventilatory parameters. Patients with a central venous catheter and who developed a catheter-related NI had local signs at the insertion site. The chest X-ray performed on all patients on mechanical ventilation revealed the presence of an alveolar syndrome in 45% of cases and interstitial pneumonia in 18% of cases.

Microbiological data

Microbiological findings show 189 microorganisms, with gram-negative bacilli dominating the microbiological profile and representing 78% of the identified germs. Enterobacteria occupied the first place, mainly *Klebsiella pneumoniae* and *Enterobacter cloacae*, whereas non-fermenting gram-negative bacilli were mainly represented by *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (Figure 1).

The distribution of microorganisms according to the site of infection are presented in Tables 1–3.

Microbiological resistance

The resistance of Enterobacteriaceae strains to aminopenicillins was 45% for *Escherichia coli* and 100% for *E. cloacae* and *K. pneumoniae*. However, aminoglycosides maintained good activity on the isolated Enterobacteriaceae. No strain of *E. coli* resistant to aminoglycosides was

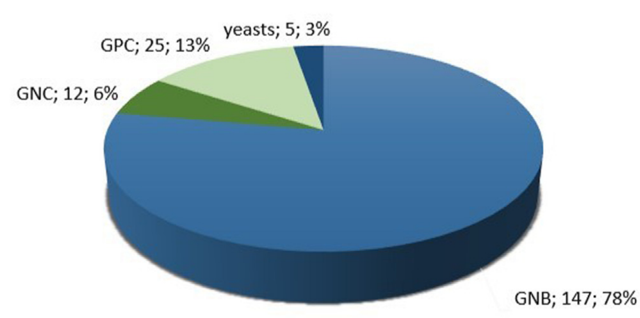

Figure 1. Distribution of microorganisms responsible for nosocomial infection. GNB, gram-negative bacilli; GNC, gram-negative cocci; GPC, gram-positive cocci.

Table 1
The distribution of microorganisms responsible for nosocomial bacteremia.

Germ	Number	Percentage
Gram-negative bacilli	**69**	**87.3%**
Enterobacteriaceae	**44**	
-*Klebsiella pneumoniae*	33	
-*Escherichia coli*	3	
-*Enterobacter cloacae*	13	
-*Enterobacter hormaichei*	1	
-*Enterobacter asburiae*	1	
-*Serratia marscesens*	3	
-*Citrobacter freundii*	1	
Non-Fermenting gram negative bacilli	**25**	
-*Acinetobacter baumanii*	15	
-*Acinetobacter jhonsonii*	1	
-*Pseudomonas aeruginosa*	8	
-*Stenotrophomonas maltofilia*	1	
Gram positive cocci	**8**	**10%**
-Staph coagulase negative	4	
-*Enterococcus feacium*	2	
-*Streptococcus pneumoniae*	2	
Yeasts	**3**	**3.75%**
-*Candida*	3	

Table 2
The distribution of microorganisms responsible for nosocomial pneumonia.

Germ	Number	Percentage
Gram-negative bacilli	**48**	**69.56%**
Enterobacteriaceae	**21**	
-*Klebsiella pneumoniae*	13	
-*Escherichia coli*	1	
-*Enterobacter cloacae*	4	
-*Enterobacter freundii*	1	
-*Enterobacter hormaichei*	2	
Non-fermenting gram negative bacilli	**27**	
-*Acinetobacter baumanii*	19	
-*Pseudomonas aeruginosa*	6	
-*Stenotrophomonas maltofilia*	2	
Gram positive cocci	**13**	**18.84%**
-*Staphylocoque aureus*	9	
-*Streptocoque pneumoniae*	4	
Gram negative bacilli	**8**	**11.6%**
Hemophilus influenzae	7	
Moraxella catharralis	1	

Table 3
The distribution of microorganisms responsible for urinary tract infections.

Germ	Number	Percentage
Gram-negative bacilli	**3**	**33.3%**
Enterobacteriaceae	**3**	
-*Escherichia coli*	3	
Gram-positive cocci	**4**	**44.5%**
-*Enterococcus feacium*	3	
-*Enterococcus fecalis*	1	
Yeasts	**2**	**22.2%**
-*Candida albicans*	1	
-*Candida tropicalis*	1	

described. All strains of *E. coli* were sensitive to imipenem, whereas 10% of *K. pneumoniae* and 30% of *E. cloacae* strains produced carbapenemase.

Regarding non-fermenting gram-negative bacteria (GNB), all isolated strains of *A. baumannii* were resistant to different classes of antibiotics. Furthermore, all isolated strains were sensitive to colistin in the standard antibiogram. For *P. aeruginosa*, in the family of aminoglycosides, this germ showed 56% resistance to amikacin. This resistance was lower for imipenem, which was only 12%.

All isolated strains of *Stenotrophomonas maltophilia* were multiresistant and only sensitive to trimethoprim-sulfamethoxazole.

Regarding gram-positive cocci, only 5% of methicillin-resistant *Staphylococcus aureus* were isolated in our study (View Table 4).

Treatment

Antibiotic therapy was prescribed for our patients empirically based on clinical and ecologic criteria. In 85%, the initial empirical antibiotic therapy was maintained because it was adapted to the isolated germ.

Morbidity and mortality

A total of 51% percent of deceased patients had at least one HAI; therefore, NIs are a factor of excess mortality (P <0.005). A total of 6.1% of deceased patients had at least one episode of catheter-related bloodstream infections (P <0.005). A total of 34.3% of deceased patients had at least one episode of nosocomial bloodstream infections during their stay in the ICU, with a significant P-value (P <0.005). A total of 24.2% of deceased patients had at least one episode of ventilator-associated pneumonia.

More than 50% of patients who had an NI, especially with multiresistant germs, experienced clinical worsening complicated by septic shock. A total of 50% of patients had an unfavorable outcome leading to death. A total of 45% of patients showed clinical improvement after receiving appropriate treatment and antibiotic therapy and were transferred to another hospital service. A total of 5% of our patients stayed in the ICU for more than 45 days, with clinical improvement, and were discharged home.

Discussion

NI is a concerning phenomenon in developing countries health care units, especially in ICUs, due to its frequency, additional cost, and potential impact on the prognosis of the initial condition. In recent years, NIs have become increasingly diverse and difficult to prevent, diagnose, and treat.

In this study, 102 cases of NIs were found, representing an incidence of 44.7%. NIs are frequent in neonatal and pediatric ICUs. In Europe, the incidence of NIs is 2.45% in a study conducted in Spain [2]. However, in most low-resource countries, this incidence remains high and close to the results of this study, such as 37% in Turkey [3] and 33.3% in Vietnam [4].

Regarding demographic data, a male predominance was observed in all studies [2–8]. The admission reasons for children who subsequently developed NIs vary widely and are mainly related to the recruitment habits of each ICU. In this study, surgical pathologies (esophageal atresia in 26 cases, acute abdomen in 17 cases) were the most common, especially in newborns, followed by traumatic pathologies (severe trauma and burns) in 26 cases.

The length of stay for patients with NIs differs between studies due to the specificities of each service [3,4,6,8]. In this study, the median stay for patients with NIs was 13 days, compared with 2 days for other hospitalized patients in the service (significant with P <0.005). The study by Garcia in Spain also noted a long average stay of 18 days (1), which remains high compared with other studies.

Our PICU encompasses a broader range of critically ill children than other studies, including newborns with complex surgical conditions and congenital anomalies that necessitate extended hospitalization.

Furthermore, our PICU manage patients with severe burns who require intensive care and prolonged hospitalization, unlike other centers with dedicated burn units. This unique population may contribute to the extended length of stay observed in our series.

Patients with NIs experienced a significantly longer stay in the PICU than those without infections. This extended stay increases the risk of exposure to pathogens and potential complications.

The sites of NIs include bacteremia as the predominant site, followed by pneumonia and UTIs. In contrast to NIs in adults, acquired pneumonia under mechanical ventilation is the most common [9]. In adults, bacteremia is mainly caused by central venous catheterization [10], whereas primary bacteremia is more common in newborns in this study,

Table 4
Bacterial resistance.

	NUMBER	AMX	AMX-CLAV	C3G	CAZ	AMK	CN	IPM /MEM /ERT	TMP-SMX	CST
Klebsiella Pneumoniae	28	100%	100%	80%	70%	20%	40%	10%	-	0%
Pseudomonas Aeruginosa	16	100%	100%	81%	81%	56%	51%	12%	-	0%
Acinetobacter Baumanii	28	100%	100%	95%	92%	78%	92%	12%	-	0%
Enterobacter Cloacae	20	100%	100%	96%	91%	0%	69%	30%	-	0%
E. Coli	9	45%	45%	22%	22%	0%	0%	0%	-	0%
Staph aureus	5					SARM	5%			
Pneumocoque	6	16%	16%	16%	0%	0%	0%	0%	0%	0%
Stenotrophomonas Maltophilia	2	100%	100%	100%	100%	100%	100%	100%	0%	100%

with an incidence close to that of Turkish and Vietnamese studies [3,4]. The microbial epidemiology of bacteremia varies widely between studies; however, in this study, GNB predominate, particularly, *K. pneumoniae* and *A. baumanii*, followed by *Enterococcus cloacae*. In the European network, the germs responsible for bacteremia are mainly coagulase-negative *Staphylococci* in Garcia's study and French pediatric ICU [5,6]. However, fungemia was the most common in Turkey and Vietnam [3,4].

Nosocomial pneumonia ranks second in this study, with a lower incidence than in other studies. The epidemiologic profile is represented by GNB (*A. baumanii, K. pneumoniae* and *P. aeruginosa*), as well as in the studies of Kepenekli *et al.* and Le *et al.* [3,4]. In the European network, pneumonia associated to mecanical ventilation (PAVM) is mainly due to gram negative cocci (GPCs) [5,11]. UTIs rank third in NIs; however, in this study, they ranked fifth, with an incidence of 3.2 and a density of incidence of 11.1 per 1000 days of urinary catheterization. According to the literature, *E. coli* and *Candida albicans* are the two main germs involved in nosocomial UTIs [12–14].

The high NI rate compels us to delve into potential contributing factors and explore avenues for improvement, the following are some hypotheses that may explain this discrepancy:

- Limited trained staff in our PICU could have led to lapses in infection control protocols due to increased workload and time constraints.
- Inadequate staffing or reduced monitoring during night shifts compared with day shifts due to the nurse-to-patient ratio might have created opportunities for lapses in hygiene practices.
- Inadequate cleaning and disinfection procedures for surfaces and equipment within the PICU might have allowed the persistence of infectious agents.
- Limited availability of materials could have compromised infection control efforts.

Bacterial resistance

The high prevalence of multidrug-resistant bacteria such as *K. pneumoniae* and *A. baumannii* suggests a potential breakdown in antibiotic stewardship practices or inadequate infection control measures.

The microbial resistance of GNB implicated in NIs reflects the severity of these infections and their prognosis, particularly, the multiresistance of some strains such as *K. pneumoniae* secreting β-lactamases (80% of Klebsiella Pneumonia in our study are extended-spectrum β-lactamase producers, 80% in the study by Benjaballah, and 90% in the study by Le) [4,7,15].

As for *A. baumannii*, which is classified as a super-resistant bacteria due to its enormous capacity to acquire multidrug resistance genes, it poses a real problem in terms of therapeutic choices [16–18]. All strains isolated in our study were multidrug-resistant, only sensitive to colistin, requiring an association of this molecule with carbapenems and aminoglycosides.

Despite therapeutic progress and progress in hygiene, *P. aeruginosa* remains frequently isolated in critically ill patients. The infections it causes are often severe and have a poor prognosis [19]. This bacterial species is characterized by moderate sensitivity to antibiotics and by an ease of acquiring resistance mechanisms that may occur during treatment [20]. Resistance to ceftazidime is slightly higher in our study (81% resistance). However, resistance to imipenem affected only 12% of the strains isolated in our work, which is less significant than other rates reported in other studies [21,22].

Given the emergence of multidrug-resistant bacteria and the difficulty in treating NIs caused by these bacteria, colistin has become increasingly important in the management of these infections. Its potential for developing acquired resistance is classically low, particularly, when used in combination with other antibacterials [23]. In our study, this problem of resistance to colistin has not yet arisen, and this molecule, thus, finds a strategic place in the treatment of severe multidrug-resistant GNB infections.

The fundamental element of the policy to improve the safety and quality of care in any health care facility is the fight against NIs. The main axes of this policy are epidemiologic surveillance, staff training, and preventive measures.

At the Mohamed VI Marrakech University Hospital, a committee to fight against NIs was created in 2007. Its mission is to inform and train the staff of the institution in hospital hygiene; invest in staff training and implement comprehensive training programs on infection control protocols for all staff; emphasizing proper hand hygiene, sterile technique, and appropriate use of personal protective equipment; evaluate staffing needs and ensure adequate coverage across all shifts to maintain rigorous infection control practices; review and strengthen environmental cleaning procedures, focusing on high-touch surfaces and equipment; and promote a culture of hand hygiene through readily available disinfectants and educational campaigns.

Conclusion

In conclusion, NI remain a major public health problem in PICUs, especially in newborns, and are associated with significant morbidity, mortality, and excess cost of care. This study provides important information on the epidemiologic profile of NIs in a PICU in Morocco.

The results of this study highlight the need to explore the impact of specific interventions and strategies on the prevention and control of NIs in PICUs, including the use of novel technologies and approaches, such as molecular epidemiology and machine learning algorithms. By improving our understanding of the epidemiology and pathogenesis of NIs in PICUs, we can take steps to reduce their burden and improve the quality of care for critically ill children.

Declarations of competing interest

The authors have no competing interests to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval and consent to participate

Not applicable.

Authors contributions

Said YOUNOUS: Conceptualization, Supervision, Validation, Resources. Dounia NADIFIYINE: Conceptualization, Data curation, Formal analysis, Resources, Software, Writing - original draft, Writing - review editing. Amal YASSINE: Data curation, Resources. Youssef MOUAFFAK: Management and coordination responsibility. Houssam Eddine SAHRAOUI: Management and coordination responsibility. Abdelaziz SIHAMI: Management and coordination responsibility. Nabila SORAA: Visualization.

References

[1] Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;**36**:309–32. doi:10.1016/j.ajic.2008.03.002.

[2] Campins M, Vaqué J, Rosselló J, Salcedo S, Durán M, Monge V, et al. Nosocomial infections in pediatric patients: a prevalence study in Spanish hospitals. EPINE Working Group. *Am J Infect Control* 1993;**21**:58–63. doi:10.1016/0196-6553(93)90225-s.

[3] Kepenekli E, Soysal A, Yalindag-Ozturk N, Ozgur O, Ozcan I, Devrim I, et al. A national pointprevalence survey of pediatric intensive care unit-acquired, health-careassociated infections in turkey, Japanese. *Jpn J Infect Dis* 2015;**68**:381–6. doi:10.7883/yoken.JJID.2014.385.

[4] Le NK, Hf W, Vu PD, Khu DTK, Le HT, Hoang BTN, et al. High prevalence of hospital-acquired infections caused by gram-negative carbapenem resistant strains in Vietnamese pediatric ICUs: a multi-centre point prevalence survey. *Medicine* 2016;**95**:e4099. doi:10.1097/MD.0000000000004099.

[5] Boyer S, Guyard M, Caseris M, Blanc T, Pinquier D, de Saint, Blanquat L, et al. Infections nosocomiales en r´eanimation p´ediatrique. In: *R´eanimation p´ediatrique*. Berlin: Springer; 2013. p. 323–37.

[6] Garcia IJ, Torn´e EE, Arriortua AB, de Carlos, Vicente JC, Soler PG, Torre JAC, et al. Trends in nosocomial infections and multidrugresistant microorganisms in Spanish pediatric intensive care units. *Enferm Infecc Microbiol Clin* 2016;**34**:286–92. doi:10.1016/j.eimc.2015.07.010.

[7] Jaballah B, Bouziri A, Kchaou W, Hamdi A, Mnif K, Belhadj S, et al. Epidemiology of nosocomial bacterial infections in a neonatal and pediatric Tunisian intensive care unit. *Med Mal Infect* 2006;**36**:379–85. doi:10.1016/j.medmal.2006.05.004.

[8] Porto JP, Mantese OC, Arantes A, Freitas C, Gontijo Filho PP, Ribas RM. Nosocomial infections in a pediatric intensive care unit of a developing country: Nhsn surveillance. *Rev Soc Bras Med Trop* 2012;**45**:475–9. doi:10.1590/s0037-86822012005000003.

[9] Mayhall CG. Ventilator-associated pneumonia or not? contemporary diagnosis. *Emerg Infect Dis* 2001;**7**:200–4. doi:10.3201/eid0702.010209.

[10] Arnoni MV, Berezin EN, Martino MDV. Risk factors for nosocomial bloodstream infection caused by multidrug resistant gram-negative bacilli in pediatrics. *Braz J Infect Dis* 2007;**11**:267–71. doi:10.1590/s1413-86702007000200020.

[11] Brook I. Pneumonia in mechanically ventilated children. *Scand J Infect Dis* 1995;**27**:619–22. doi:10.3109/00365549509047077.

[12] Laupland KB, Zygun DA, Davies HD, Church DL, Louie TJ, Doig CJ. Incidence and risk factors for acquiring nosocomial urinary tract infection in the critically ill. *J Crit Care* 2002;**17**:50–7. doi:10.1053/jcrc.2002.33029.

[13] Caron F. Physiopathologie des infections urinaires nosocomiales. *Med Mal Infect* 2003;**33**:438–46.

[14] Binelli CA, Moretti ML, Assis RS, Sauaia N, Menezes PR, Ribeiro E, et al. Investigation of the possible association between nosocomial candiduria and candidaemia. *Clin Microbiol Infect* 2006;**12**:538–43. doi:10.1111/j.1469-0691.2006.01435.x.

[15] Lecaillon E, Boixados M, Delpech N, Cabrol A, Gueudet P, Negre C, et al. Emergence de proteus mirabilis et Klebsiella pneumoniae poss´edant une blse: traitement et suivi. *Med Mal Infect* 1993;**23**:427–30. doi:10.1016/S0399-077X(05)80969-2.

[16] Ozdemir H, Kendirli T, Ergun H, Ciftci E, Tapisiz A, Guriz H, et al. Nosocomial infections due to Acinetobacter˙ baumannii in a pediatric intensive care unit in turkey. *Turk J Pediatr* 2011;**53**:255–60.

[17] Daniels TL, Deppen S, Arbogast PG, Griffin MR, Schaffner W, Talbot TR. Mortality rates associated with multidrug-resistant Acinetobacter baumannii infection in surgical intensive care units. *Infect Control Hosp Epidemiol* 2008;**29**:1080–3. doi:10.1086/591456.

[18] Cisneros JM, Rodríguez-Baño J. Nosocomial bacteremia due to Acinetobacter baumannii: epidemiology, clinical features and treatment. *Clin Microbiol Infect* 2002;**8**:687–93. doi:10.1046/j.1469-0691.2002.00487.x.

[19] Lepape A. Epidemiology of infections due to pseudomonas aeruginosa. *Ann Fr Anesth Reanim* 2003;**22**:520–2. doi:10.1016/s0750-7658(03)00169-2.

[20] Wang LJ, Sun Y, Song WL, Zhang ZJ, Liu CF. Changes of drug-resistance of Pseudomonas aeruginosa in pediatric intensive care unit. *Zhonghua Er Ke Za Zhi* 2012;**50**:657–63.

[21] Mesaros N, Nordmann P, Plésiat P, Roussel-Delvallez M, Van Eldere J, Glupczynski Y, et al. Pseudomonas aeruginosa: resistance and therapeutic options at the turn of the new millennium. *Clin Microbiol Infect* 2007;**13**:560–78. doi:10.1111/j.1469-0691.2007.01681.x.

[22] Geyik MF, Aldemir M, Hosoglu S, Tacyildiz HI. Epidemiology of burn unit infections in children. *Am J Infect Control* 2003;**31**:342–6. doi:10.1016/s0196-6553(02)48226-0.

[23] Li J, Rayner CR, Nation RL, Owen RJ, Spelman D, Tan KE, Liolios L. Heteroresistance to colistin in multidrug-resistant Acinetobacter baumannii. *Antimicrob Agents Chemother* 2006;**50**:2946–50. doi:10.1128/AAC.00103-06.