Article/Artigo

Nosocomial infections in a pediatric intensive care unit of a developing country: NHSN surveillance

Infecções hospitalares em unidade de terapia intensiva pediátrica de um país em desenvolvimento: vigilância NHSN

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ABSTRACT

Introduction: This study aimed to determine the epidemiology of the three most common nosocomial infections (NI), namely, sepsis, pneumonia, and urinary tract infection (UTI), in a pediatric intensive care unit (PICU) in a developing country and to define the risk factors associated with NI. **Methods**: We performed a prospective study on the incidence of NI in a single PICU, between August 2009 and August 2010. Active surveillance by National Healthcare Safety Network (NHSN) was conducted in the unit and in a case control approach, children with NI (cases) were compared with a matched controls without NI. **Results:** We analyzed 172 patients; 22.1% had NI, 71.1% of whom acquired it in the unit. The incidence densities of sepsis, pneumonia, and UTI per 1,000 patients/day were 17.9, 11.4, and 4.3, respectively. The most common agents in sepsis were *Enterococcus faecalis* and *Escherichia coli* (18% each); *Staphylococcus epidermidis* was isolated in 13% of cases. In pneumonias *Staphylococcus aureus* was the most common cause (3.2%), and in UTI the most frequent agents were yeasts (33.3%). The presence of NI was associated with a long period of hospitalization, use of invasive devices (central venous catheter, nasogastric tube), and use of antibiotics. The last two were independent factors for NI. **Conclusions**: The incidence of NI acquired in this unit was high and was associated with extrinsic factors.

Keywords: Nosocomial infections. Pediatric ICU. Surveillance system.

RESUMO

Introdução: O objetivo deste estudo foi determinar a epidemiologia das três infecções hospitalares (IH) mais comuns - sepse, pneumonia e infecção do trato urinário (ITU) - em uma unidade de terapia intensiva pediátrica (UTIP) de um país em desenvolvimento e definir os fatores de risco associados com IH. **Métodos**: Nós desenvolvemos um estudo prospectivo de incidência de IH em uma única UTIP, entre agosto/2009 e agosto/2010. Foi conduzida uma vigilância ativa pelo *National Healthcare Safety Network* (NHSN) na Unidade e as crianças com IH (casos) foram comparadas com um grupo (controles) em um estudo caso-controle. **Resultados**: Nós analisamos 172 pacientes, 22,1% com IH, 71,1% adquirida na Unidade. A densidade de incidência de sepse, pneumonia e ITU por 1.000 pacientes/dia foram 17,9, 11,4, e 4,3, respectivamente. Os agentes mais comuns na sepse foram *Enterococcus faecalis* e *Escherichia coli* (18% cada), e *Staphylococcus epidermidis* foram isolados em 13% dos casos. Nas pneumonias *Staphylococcus aureus* foram os agentes mais comuns (3,2%), e nas ITUs os agentes mais frequentes foram os fungos (33,3%). A presença de IH foi associada com tempo de hospitalização prolongado, uso de procedimentos invasivos (CVC, sonda nasogástrica) e uso de antibióticos. Os dois últimos foram fatores independentes para o desenvolvimento de IH. **Conclusões**: A incidência de IH adquirida na Unidade foi alta, associada a fatores de risco extrínsecos.

Palavras-chaves: Infecções hospitalares. UTI pediátrica. Sistema de vigilância.

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INTRODUCTION

Nosocomial infection (NI) constitutes a major health problem associated with high morbidity, mortality, and increase of healthcare costs, especially in pediatric intensive care units (PICU). Patients in these units, despite representing a small percentage of inpatients, contribute to over 20% of NI[1]. Bloodstream infections (BSI) are the most common NI in these units (28-52% of all)[2,3], followed by pneumonia and urinary tract infection (UTI)[3,4]. The first two are responsible for approximately 50% of NIs, with UTI causing an additional 12% to 22%[5]. A previous study developed in a Brazilian PICU showed sepsis as a major cause (18.6%) of death[6].

In Europe, incidence ranges from 1% in general pediatric wards to 23.6% in PICUs[7]. In Brazil, despite the lack of information about this issue in children there are many studies on adult patients, including NI risk factors and measures to prevent a patient from acquiring NI, and the work is extremely heterogeneous as far as number of beds, services available, and patients are concerned[8]. Studies have reported that less than 10% of beds are available to intensive care units in Brazilian hospitals, despite the fact that they represent 40% of NIs[9,10]. In this study, we investigated the epidemiological profile of the three most common NIs (sepsis, pneumonia, and UTI) in a PICU of a Brazilian university hospital and the risk factors associated with these infections.

METHODS

Hospital

The Hospital das Clínicas of the Universidade Federal de Uberlândia, State of Minas Gerais, Brazil, is a public teaching hospital of more than 500 beds, with the PICU presenting eight beds. The hospital offers tertiary care.

Design of the study

This survey was divided into two stages. The first stage entailed a prospective cohort study in the PICU

of the Hospital das Clínicas of the Universidade Federal de Uberlândia by the National Health Care Safety Network (NHSN) system[11]. The children were followed until discharged or death. Every inpatient hospitalized from August 2009 to August 2010 was initially considered a potential participant, and those with stays of >48h or longer were included. After the first phase, a nested case-control study was conducted to identify the associated factors for NI. The cases were children with NI, whereas the controls were children without infections. The medical records of patients were reviewed for demographic and risk factor data. Data collected included gender, length of stay, underlying diseases, invasive procedures, infection on admission, and PICU-acquired infection.

Definitions

PICU-acquired NIs were defined according to the Centers for Disease Control and Prevention (CDC)[12]. Infections that commenced at or after 48h after admission to the PICU were included as PICU-acquired infections.

Urinary tract infection: the patient must have at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, and positive urine culture with counts ≥105 colony-forming units per milliliter (CFU/ml).

Pneumonia: the criteria for the definition of pneumonia were chest radiograph with new pulmonary infiltrate or progression of an existing one, accompanied by two of the following signs or symptoms: leukocytosis (>0,000/mm^3) or leukopenia (<4,500/mm^3), hyperthermia (>38ºC) or hypothermia (<35ºC), purulent sputum, tracheal aspirate bacterial count of ≥106CFU/ml.

Bacteremia: this was defined as the biological documentation of infection, i.e., the result of a positive blood culture.

Sepsis: this was defined as a systemic response to an infection, followed by one or more of these conditions: a) temperature >38ºC or <36ºC; b) heart rate >90 beats/min; c) respiratory rate >20 breaths/min or PaCO2 <32mmHg; d) leukocyte count >12,000cells/mm^3, or >10% of juveniles; e) sepsis with hypotension, associated with the presence of perfusion abnormalities that may include lactic acidosis, oliguria, or acute alteration in mental status defined as septic shock; total patients per day was defined as the somatory of total time of hospitalization by the patients in PICU; epidemiological investigations' incidence rate was defined as the number of each infection as the numerator and the number of days those patients were at risk as the denominator per 1,000[13]; device-associated incidence rate was defined by dividing the number of each infection by the number of days those patients were exposed to risk factors per 1,000[13].

Statistical analysis

Significant differences between groups were determined using the X^2-test or Fisher exact test, where appropriate. Statistical significance was defined by $p \leq 0.05$. Association between variables and nosocomial infections were expressed as odds ratios (OR) with their respective 95% confidence intervals (95%CI) obtained by means of conditional logistic regression models. Statistical analyses were performed using Epi-Info (version 3.3.2) and Bioestat 5.0 (CDC, Atlanta).

Ethical considerations

Approval for the study was granted by the research ethics committee of the hospital. Patient names were not disclosed, and all the information about them was kept confidential. All the samples were analyzed by the hospital's microbiology laboratory and recovered to another's tests.

RESULTS

From August 2009 to August 2010 a total of 172 patients were hospitalized in the PICU with a mean stay of 8.1 days. Of these patients, 38 (22.1%) were infected at least once in the PICU, with 60 episodes, and 8.7% had community-acquired infection. The PICU mortality rate for the population during the study period was 8.1%. **Table 1** shows the demographic features, co-morbidities, use of devices, length of stay, and mortality of the patients.

The mean overall patient NI rate was 27.2 per 1,000 patients/day, with an incidence of 22.1% (patients with NI). The rates of primary BSI, pneumonia, and UTI per 1,000 device-days were 18.2, 17.8, and 7.0, respectively. **Table 2** shows the potential risk factors of NI associated with unvaried analyses. Risk factors significantly associated with NI included use of central venous catheter (CVC) [p=0.001, odds ratio (OR) = 8.77], length of stay (p<0.001), nasogastric tube (p=0.0002, OR=5.00), and use of antibiotics (p=0.0004, OR=7.89). These same factors, with the exception of length of hospitalization, were also independently associated with infection by multivariate analyses.

TABLE 1 - Characteristics of patients admitted to the PICU of the Hospital das Clínicas of the Universidade Federal de Uberlândia, Brazil, between August 2009 and August 2010.

	Patients (n = 172)	
Variables	**n**	**%**
Gender		
female	81	47.1
male	91	52.9
Time of hospitalization ≥ 7 days	71	41.3
Patients with nosocomial infection	38	22.1
PICU acquired	27	71.1
Community infection	15	8.7
Patients with sepsis	25	65.8
with microbiological criteria	15	60.0
Patients with pneumonia	16	30.2
with microbiological criteria	7	43.7
Patients with urinary tract infection	6	11.3
with microbiological criteria	5	83.3
Use of antibiotics		
yes	119	69.2
no ≥ 2	58	48.7
Patients with CVC	129	75.0
Patients with MV	91	53.0
Patients with urinary catheter	100	58.1
Patients with NT	89	51.8
Patients with parenteral nutrition	6	3.5
Underlying diseases		
heart	43	25.0
neoplasia	7	4.1
nephropathy	1	0.6
others*	7	4.1
Surgery	71	41.3
Mortality	14	8.1

PICU: pediatric intensive care unit; **CVC:** central venous catheter; **MV:** mechanical ventilation; **NT:** nasogastric tube; *hypertension, cerebral palsy, sickle cell disease, and short bowel syndrome.

TABLE 2 - Univariate analysis of associated factors presented by patients admitted to PICU of the Hospital das Clínicas of the Universidade Federal de Uberlândia, Brazil, between August 2009 and August 2010.

	Patients with NI (n=38)		Patients without infection (n=119)			
Variables	**n**	**%**	**n**	**%**	**P**	**OR (95%CI)**
Age (means/SD)	4.2	4.6	4.1	3.7	>0.05	-
Hospitalization/means ± SD	14.1	9.2	6.2	4.9	<0.05	-
Female	16	42.1	59	49.6	>0.05	0.74 (0.33-1.64)
male	22	57.9	60	50.4		
Underlying Disease						
heart	13	34.2	32	26.9	>0.05	1.41 (0.60-3.31)
neoplasia	-	-	6	5.0	>0.05	0.05 (0.05-2.95)
nephropathy	-	-	-	-	-	-
others*	3	7.9	1	0.8	>0.05	10.11 (0.89-260.80)
Invasive devices						
CVC	36	94.7	80	67.2	<0.05	8.77 (1.91-55.60)
MV	27	71.0	59	49.6	<0.05	2.50 (1.07-5.93)
urinary catheter	25	65.8	66	55.5	>0.05	1.54 (0.68-3.55)
NT	30	78.9	51	42.8	<0.05	5.00 (1.98-13.00)
parenteral nutrition	3	7.9	2	1.7	>0.05	5.01 (0.65-45.01)
tracheostomy	2	5.3	5	4.2	>0.05	1.27 (0.16-7.84)
drain	10	26.3	41	34.4	>0.05	0.68 (0.28-1.64)
Surgery	18	47.4	53	44.5	>0.05	1.12 (0.51-2.48)
Antibiotics						
yes	35	92.1	71	59.7	<0.05	7.89 (2.15-34.18)
no ≥ 2	27	77.1	22	30.1	<0.05	10.82 (4.34-27.52)

PICU: pediatric intensive care unit; **SD:** standard deviation; **OR:** odds ratio; **CVC:** central venous catheter; **MV**: mechanical ventilation; **NT:** nasogastric tube; *cystic fibrosis, cerebral palsy, sickle cell disease, and short bowel syndrome.

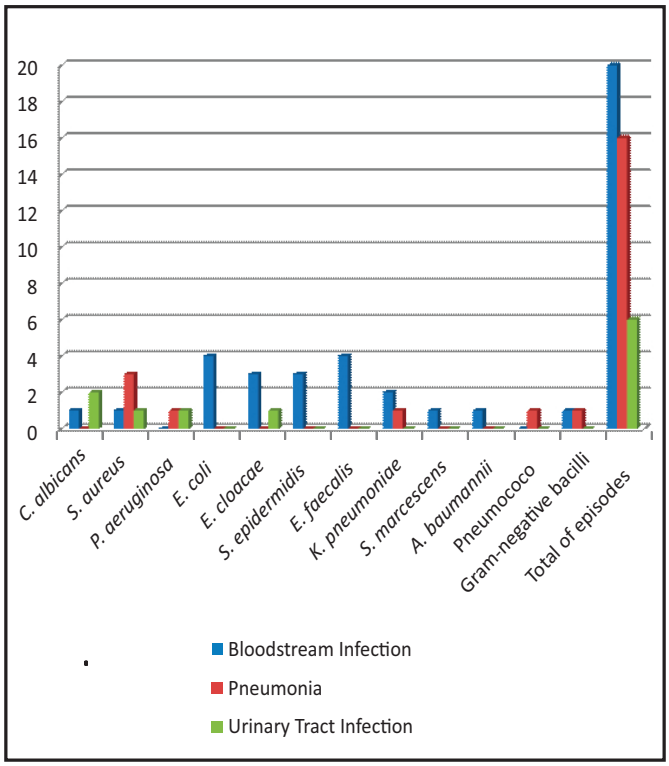

FIGURE 1 - Pathogens identified in nosocomial infections developed by children hospitalized in the PICU of the Hospital das Clínicas of the Universidade Federal de Uberlândia, Brazil, between August 2009 and August 2010.

C. albicans*:** *Candida albicans*; ***S. aureus: *Staphylococcus aureus*; ***P. aeruginosa***: *Pseudomonas aeruginosa*; ***E. coli***: *Escherichia coli*; ***E. cloacae***: *Enterobacter cloacae*; ***S. epidermidis:*** *Staphylococcus epidermidis*; ***E. faecalis*** *Enterococcus faecalis*; ***K. pneumoniae***: *Klebsiella pneumoniae*; ***S. marcescens:*** *Serratia marcescens*; ***A. baummanii:*** *Acinetobacter baummanii*. Others: clinical or radiologic signs.

Gram-negative bacilli were the most common pathogens identified in the NI in our PICU (47%), followed by Gram-positive cocci bacteria (44.1%). Sepsis was more commonly reported, and 60% of cases had at least one microorganism isolated in blood culture. The most common agents were *Enterococcus faecalis* (18%) and *Escherichia coli* (18%), and among non-fermenting bacilli only *Acinetobacter baumannii* was detected (4%). *Staphylococcus epidermidis* was isolated in 13% of cases. The pathogens isolated from pneumonia were *Staphylococcus aureus* as the most common cause (3.2%), and among isolates of Gram-negative bacilli, 1.5% were *Pseudomonas aeruginosa*. In three children, more than one microorganism was isolated. In UTI cases (83.3%) at least one microorganism was isolated. Yeasts were more commonly reported in UTI (33.3%), and *S. aureus* and *P. aeruginosa* were uncommon (**Figure 1**).

DISCUSSION

It is well established that NI is associated with high rates of morbidity, mortality, and significant economic cost that tend to represent a larger problem in hospitals in developing countries than in developed ones[14]. Although there are abundant data from epidemiological studies about these infections in PICU, most of the research has not come from developing countries such as Brazil, and has mainly been expressed in infection rates per hospital/day or device/day[15,16]. Analysis of data obtained in our study suggests that surveillance systems, like the NHSN, are important for providing feedback from individual PICUs, allowing comparison with other literature data.

In our investigation, the data showed a high frequency of these infections (27.2 per 1,000 patients/day; 22.1%), with a significant proportion (71.1%) of PICU-acquired infection, as also reported in the PICU of Hospital São Paulo, which showed an NI incidence rate of 18%[6]. Sepsis was considered as community-induced if it manifested up to 72h after the patient's confinement, and if the patient did not come from another hospital environment[12]. Due to underlying diseases of individuals and their need for long hospitalization, these patients can develop infection from some pathogens restricted to hospital environments, making the recovery of patients harder and making these patientesan infection source that spreads these infections to the community[17]. In our study only 8.7% of infections were acquired in the community.

In intensive care units where there is usually a high density of antibiotic use, resultant bacteria tend to be more common, isolates are often resistant and multi-resistant, and horizontal dissemination is common[18]. In this group the risk for acquiring NI is from five to ten times greater[19]. The major risk factors for the acquisition of NI in pediatric patients are the severity of the underlying disease, the presence of an invasive device, longer time of hospitalization in PICU, high population density, and use of antibiotics[20]. In this series, we verified as statistically significant the following risk factors: use of invasive devices such as CVC or nasogastric tubes, length of stay in PICU, and antibiotics use. However, only the use of antibiotics and the use of CVCs and nasogastric tubes were independently associated with NI, similar to results reported elsewhere[20-22]. The length of stay in our PICU was found to be the risk factor for NI by unvaried analyses, similar to other studies, and long stay reflects the severity of the underlying disease, requiring greater care[6,23].

No differences were found in the distribution of pathogens in PICU infections when compared with those observed in adults[19,24,25]. Gram-negative bacilli were predominant (47%), followed by Gram-positive cocci (44.1%) and yeasts (8.9%).

Bloodstream infections are the most common NI in PICUs (28-52% of all), followed by pneumonia (including ventilator-associated pneumonia), UTI, and enteric, surgical site, and skin infections[3,4,26].

As in adults, most BSI in PICU are associated with the use of a CVC[2,15,20]. Our data showed that the incidence of sepsis was 17.9/1,000 patient days, accounting for 65.8% of all NI. A higher proportion of all BSI was related to CVCs, with the incidence density rate (18.2/1,000 CVC days) observed in the present study higher than the NHSN data for a clinical-surgical PICU[27].

Enterococcus faecalis and *Escherichia coli* as etiological agents of infections (18% each), followed by *Enterobacter cloacae* and *S. epidermidis* (13% each), were the main agents of sepsis. Bloodstream infection is classified as primary or secondary based on the presence or the absence of knowledge focus outside the vascular system. The main focus of secondary infections is the lung, responsible for 50% of all cases[28]. Primary sepsis is usually (85%) related to a CVC, and shows a mortality rate between 12% and 25%, lengthening the patient's hospitalization time from ten to forty days[29,30]. In our investigation, primary and secondary sepsis rates were similar (53.3% and 46.6%, respectively). The CVC was the main origin in the first at about 50% of cases, with the lung the main origin in secondary sepsis at about 50% of cases.

Pneumonia associated with mechanical ventilation is considered the most common infection in adult diagnosis, but isolating a single type in children is difficult[31-33]. There are few studies on pediatric patients, and incidence rates range from 2% to 68%[34]. Surveillance studies in PICU patients have reported that pneumonia accounts for 2% to 17% of NI[27,35,36]. In this study pneumonia was the second most common infection (30.2%) with an incidence rate of 11.4 per 1,000 patients a day and 17.8 per 1,000 ventilation days.

According to the literature, Gram-negative bacilli are the most frequent pathogens in these infections, either in adults or in children, in developing countries[2,26,27,36-38]. Our results differed, with *S. aureus* as the most frequent agent.

The most common organisms in urinary tract infections are *Escherichia coli*[39-41] or, as in our study, *Candida albicans*. These data are in accordance with other Brazilian studies[42-45].

In our study the frequency of UTI/1,000 urinary catheter (UC) days was greater than in studies realized in developing countries[46], and although these infections are responsible for almost 40% of all NI, they continue to be unrepresentative in Brazilian hospitals, considering that the majority of them (80%) are associated with the use of urinary catheters[47,48]. Fifty-eight percent of our patients were using this invasive device, with an infection rate of 7.0/1,000 UC days.

Our data suggest that frequent surveillance systems, like the NHSN, were important to evaluate the association of these well-known risk factors with PICU risk factors and causative organisms, as a high frequency of these infections was associated with extrinsic risk factors and the predominance of Gram-negative bacilli followed by Gram-positive cocci.

This study has some limitations, particularly when it is to be compared with others. First, we studied only three types of infections. Second, we had a relatively small number of patients in the case group, thus reducing the statistical power and the ability to study subsets of patients. Furthermore, information on the management of the condition and on the severity of the underlying illness was unviable, and because all our study patients where hospitalized in a single tertiary hospital, our results may not be generalized to other institutions.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L, The Healthcare Infection Control Practices Advisiory Commitee. 2007 Guidelines for Isolation Precautions: Preventing Transmission of Infections Agents in Healthcare Settings [Internet]. Atlanta: CDC; 2008. 225 p. Available from: http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/isolation2007.pdf/.
2. Grohskpof L, Sinkowits-Cochran R, Garret D, Sohn A, Levine G, Siegel J, et al. The Pediatric Prevention Network. A national point-prevalence survey of pediatric intensive care unit-acquired infections in the United States. J Pediatr 2002; 140:432-438.
3. Urrea M, Pons M, Serra M, Latorre C, Palomeque A. Prospective incidence study of nosocomial infection in a pediatric intensive care unit. Pediatr Infect Dis J 2003; 22:490-493.
4. Stover B, Shulman S, Bratcher D. Nosocomial infection rates in US children's hospital neonatal and pediatric intensive care units. Am J Infect Control 2001; 29:152-157.
5. Huskins Ch, Goldmann D. Nosocomial Infections. *In:* Feigin RD, Cherry J, editors. Texbook of Pediatric Infectious Diseases. 4th ed. Philadelphia: Saunders; 2004; p. 2874-2925.
6. Einloft PR, Garcia PC, Piva JP, Bruno F, Kipper DJ, Fiori RM. Perfil epidemiológico de dezesseis anos de uma Unidade de Terapia Intensiva Pediátrica. Rev Saude Publica 2002; 36:728-733.

7. Raymond J, Aujard Y, Bekassi A, The European study group. Nosocomial infections in pediatric patients: a European, multicenter prospective study. Infect Control Hosp Epidemiol 2000; 21:260-263.
8. Prade SS. Estudo brasileiro de magnitude das Infecções Hospitalares em hospitais terciários. Rev Control Infec Hosp 1995; 2:11-23.
9. Dorawiche RO. Nosocomial bloodstream infections and second-generation vascular catheters. *In*: Wenzel RP, editor. Prevention and control of nosocomoal infections. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2003. p. 281-292.
10. Toufen Jr C, Hovanian ALD, France SA, Carvalho CRR. Prevalence rates of infection in intensive care units of the tertiary teaching hospital. Rev Hosp Med Optional Clin Sao Paulo 2003; 58:254-259.
11. Pratt RJ, Pellowe CM, Wilson JA, Loveday HP, Harper PJ, Jones SRLJ, et al. National evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. J Hosp Infect 2007; 65 (suppl I):1-64.
12. Horan TC. 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; 36:309-332.
13. Becerra MR, Tantalean JÁ, Suárez VJ, Alvarado MC, Candela JL, Urca FC. Epidemiologic surveillance of nosocomial infections in a pediatric intensive care unit of a developing country. BMC Pediatrics 2010; 10:66.
14. Gastimeier P, Kampf G, Wischnewski N, Hauer T, Schulgen G, Schumacher G, et al. Prevalence of nosocomial infection in representative German hospitals. J Hosp Infect 1998; 38:37-49.
15. Jarvis WR. Epidemiology of nosocomial infections in paediatric patients. Pediatr Infect Dis J 1987; 6:344-351.
16. Stover BH, Shulman ST, Bratcher DF, Brady MT, Levine GL, Jarvis WR. Paediatric Prevention Network. Nosocomial infection rates in US children's hospitals' neonatal and paediatric intensive care units. Am J Infect Control 2001; 29:152-157.
17. Harbarth S, Ferrieri K, Hugonnet S, Ricou B, Suter P, Pittet D. Epidemiology and prognostic determinants of bloodstream infections in surgical intensive care. Am Med Association 2007; 137:1353-1359.
18. Shlaes DM, Gerding DN, John JRJF, Craig WA, Bornstein DL, Duncan RA, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. Infect Control Hosp Epidemiol 1997; 18:275-291.
19. Moreira MR, Ribas RM, Rodrigues AAA, Gontijo Filho PP. Consumo de antibióticos e etiologia de pneumonia associada à ventilação em pacientes internados na Unidade de Terapia Intensiva do Hospital de Clínicas da Universidade Federal de Uberlândia. Rev Pan Infect 2009; 11:11-16.
20. Melo MJG, Albuquerque MFPM, Lacerda HR, Souza WV, Correia JB, Brito MCA. Risk factors for healthcare-associated infection in pediatric intensive care units: a systematic review. Cad Saude Publica 2009; 3:5373-5391.
21. Pratt RJ, Pellowe C, Loveday HP, Robinson N, Smith GW, Barrett S, et al. The epic project: developing national evidence-based guidelines for preventing healthcare associated infections. Phase I: guidelines for preventing hospital-acquired infections. Department of Health (England). J Hosp Infect 2001; 47:3-4.
22. Harris JA. Paediatric nosocomial infections: children are not little adults. Infect Control Hosp Epidemiol 1997; 18:739-742.
23. Agus D, Linde-Zwirble WT, Lidicker J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated cost of care. Critic Car Med 2001; 29:1303-1310.
24. Porto JP, Dantas RCC, Freitas C, Matoso DC, Almeida AB, Gontijo Filho PP, et al. Bloodstream Infection Associated/Related to the Central Venous Catheter in Mixed ICU of Adults from a Brazilian university Hospital: Etiology, pathogenesis and risk factors. Rev Pan Infect 2010; 12:24-29.
25. Brito DVD, Brito CS, Resende DS, Moreira-do-Ò J, Abdallah VOS, Gontijo Filho PP. Nosocomial Infection in Brazilian Neonatal Intensive Care Unit: a 4-year surveillance study. Rev Soc Bras Med Trop 2010; 43:633-637.
26. Raymond J, Aujard Y, Bekassi A, The European Study Group: Nosocomial infections in pediatric patients: a European, multicenter prospective study. Infect Control Hosp Epidemiol 2000; 21:260-263.
27. Elward A, Warren D, Fraser V. Ventilator-associated pneumonia in pediatric intensive care unit patients: Risk factors and outcomes. Pediatrics 2002; 109:758-764.
28. Munford RS. Sepsis, severe sepsis, and septic shock. *In*: Mandell GL, Bennett JE, Dolin R, editors. Princ & Pract Infectious Disease. Philadelphia: Elsevier; 2005; p. 906-926.
29. Safdar N, Kluger DM, Maki DG. A review of risk factors for CR-BSI caused by percutaveaously inserted, noncuffed central venous catheter. Medicine 2002; 81:466-479.
30. Vincent JL. Nosocomial Infections in Adult Intensive-Care Units. The Lancet 2003; 361: 2068-2077.
31. Brook I. Pneumonia in mechanically ventilated children. Scan J Infect Dis 1995; 27:619-622.
32. Mayhall CG. Ventilator-associated pneumonia or not? Contemporary diagnosis. Emerg Inf Dis 2001; 7:200-204.
33. Koema M, van der Ven AJ, Ramsay G, Hoepelman IM, Bonten MJ. Ventilator associated pneumonia: recent issues and pathogenesis, prevention and diagnosis. J Hosp Infect 2001; 49:155-162.
34. Salahuddin N, Zafar A, Sukhyani L, Rahim S, Noor MF, Hussain K, et al. Reducing ventilator-associated pneumonia rates through a staff education programme. J Hosp Infect 2004; 57:223-227.
35. Rivera R, Tiballs J. Complications of endotracheal intubation and mechanical ventilation in infants and children. Crit Care Med 1992; 20:193-199.
36. Almuneef M, Memish Z, Balkhy H, Alalem H, Abutaleb A. Ventilator-associated pneumonia in pediatric intensive care unit in Saudi Arabia: A 30 month prospective surveillance. Infect Control Hosp Epidemiol 2004; 25:753-758.
37. Foglia E, Meier M, Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. Clinic Microbiol Reviews 2007; 409-425.
38. Zar H, Cotton M. Nosocomial pneumonia in pediatric patients: practical problems and rational solutions. Pediatr Drugs 2002; 4:73-83.
39. Schaechter M, Engleberg NC, Eisenstein BI, Medoff G. Microbiologia: mecanismos das doenças infecciosas. 3rd ed. Rio de Janeiro: Guanabara Koogan; 2002.
40. Koneman EW, Allen SD, Janda WM, Schreckenberger PC, Winn Jr WC. Diagnóstico microbiológico. 5th ed. Buenos Aires: Editora Médica Panamericana SA; 1999.
41. Mims C, Playfair J, Roitt I, Wakelin D, Williams R. Microbiologia médica. 2nd ed. São Paulo: Manole ltda; 1999.
42. Binelli CA, Moretti ML, Assis RS, Sauaia N, Menezes PR, Ribeiro E, et al. Investigation of the possible association between nosocomial candiduria and candidaemia. Clinic Microbiol Infect 2006; 12:538-543.
43. Kobayashi CC, Fernandes OF, Miranda KC, Sousa ED, Silva MR. Candiduria in hospital patients: a study prospective. Mycopathologia 2004; 158:49-52.
44. Passos XS, Sales WS, Maciel PJ, Costa CR, Miranda KC, Lemos JA, et al. *Candida* colonization in intensive care unit patients' urine. Mem Inst Oswaldo Cruz 2005; 100:925-928.
45. Oliveira RD, Maffei CM, Martinez R. Nosocomial urinary tract infections by *Candida* species. Rev Assoc Med Bras 2001; 47:231-235.
46. Flores-González JC, Hernández-González A, Rodríguez-López C, Roldán-Cano V, Rubio-Quiñones F, Quintero-Otero S, et al. Infección nosocomial del tracto urinario en ni¯nos críticos. Med Intensiva 2011; 35:344-348.
47. Medeiros EAS, Machado A, Ferraz AAB, Ferraz E, Arruda E, Nobre J, et al. Projeto Diretrizes: Prevenção da infecção hospitalar [Internet]. Sociedade Brasileira de Infectologia; 2001. 23 p. Available from: http://alfa.epm.br/diretrizes/pd/PREVENCA.pdf/.
48. Sobel JD, Kaye D. Host factors in the pathogenesis of urinary tract infections. Am J Med 1984; 122-130.