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Prevalence and Anti-Microbial Susceptibility of Hospital Acquired Infections in Two Pediatric Intensive Care Units in Egypt

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Abstract

BACKGROUND: Hospital-acquired (nosocomial) infection is a common serious health problem worldwide, especially in pediatric intensive care units and is associated with high mortality and morbidity, prolonged hospital stays and high cost.

AIM: To determine the types of organisms involved in hospital-acquired an infection in two pediatric intensive care units during the one-year study and its anti-microbial susceptibility.

MATERIAL AND METHODS: This study was carried out in the pediatric intensive care units (PICU) of Ain Shams & Cairo Universities, where 86 pediatric patients were recruited. Their age ranged from 1 month to 156 months with mean 20.7 ± 25.8 months. Male to female ratio was 37:29. Four samples were collected from each child for culture and sensitivity: blood, endotracheal aspirate, urine and skin swab.

RESULTS: The most common microorganism was staphylococcus while Gram-negative bacteria were the commonest group. Amikacin and imipenem are the most sensitive antibiotics. Risk estimate for different risk factors among studied patients revealed no significance.

CONCLUSION: Staphylococcus was the commonest micro-organism while Gram-negative infections were the commonest group among PICU with a predominance of Acinetobacter and Klebsiella. Respiratory infections were the most common, followed by blood-borne infection. Risk factors for mortality were not significant.

Introduction

Hospital-acquired (nosocomial) infection is a common serious health problem worldwide especially in pediatric intensive care units and is associated with high mortality and morbidity, prolonged hospital stays and high cost [1], [2].

As regard hospital-acquired infections in pediatric intensive care, few data are available from a developing country where the majority of studies were done in adults and developed countries. The risk factors for these infections that common to vulnerable pediatric patients include age, primary disease, and intensive procedures commonly used in pediatric intensive care units [3], [4], [5].

The incidence of HAI ranged from 3% to 37%, where it is higher in developing countries than in developed countries. Pathogens and antibiotic sensitivity patterns vary significantly among countries and institutions and vary within an institution over years [6], [7], [8], [9], 10], [11], [12], [13], [14], [15], [16]. This study aimed to report the prevalence of hospital-acquired infection in the pediatric intensive care units, risk factors, and its anti-microbial susceptibility.

Subjects and Methods

This study was carried out in the pediatric ICU

of Ain Shams & Cairo Universities over one-year periods (2014-2015), where 86 pediatric patients were recruited but 20 patients were excluded for insufficient data (15.6% of total PICU admission). The pediatric ICU of Cairo University is 10 beds while that of Ain Shams University is 14 beds. Their age ranged from 1 month to 156 months with mean 20.7 ± 25.8 months. Male to female ratio was 37:29. The following variables were analysed including age, sex, underlying disease, mechanical ventilation, invasive manoeuvres, a period of hospital stays, outcome, infection screening including CBC, CRP, cultures (blood, endotracheal, urine, skin swab), liver and kidney functions, and anti-microbial therapy. Patients admitted less than 24 hours in PICU were excluded were hospital-acquired infection is considered after 48 hours of admission to ICU [17].

The study was approved by the Ethical Committee of the National Research Centre. Written consent was taken from the parents of the studied patients.

Four samples (Blood, throat swab or endotracheal aspirate, urine samples, skin swabs) were obtained for microbiological assay. The samples were collected in a sterile container and sent to the lab for assessment and study as follows:

1. Blood culture technique: All of the phlebotomies were performed with peripheral sticks, and the blood samples were drawn by a clinician by the bedside after cleansing the skin with 70% isopropyl alcohol and applying 10% povidone-iodine for 1 min. The blood samples were inoculated at a volume of 1 to 5 ml into BACTEC Peds Plus/F and were placed in the BACTEC 9050 blood culture instrument. Anaerobic blood cultures were not prepared. All study bottles were incubated for 7 days. Whenever there was a sign of microbial growth, the detection time was documented. The bottles that had a positive signal were smeared and stained with Gram stain. Subcultures on blood. Mac Conkey and chocolate agar plates were done. Subcultures were incubated at 35°C for a duration of 48 h. Instrument-negative bottles were Gram stained and subcultured at the end of the 7-day protocol to confirm negativity. False-positive cultures were defined as those that were indicated by the instrument to be positive but had revealed no microorganisms by Gram staining and subculture. All isolates were considered to be clinically significant.

2. Throat swabs and endotracheal aspirate: A Gram stain was performed on all swabs and aspirates for the identification of bacteria and measurement of the white blood cell count. White cells were counted from 20 high power fields, and the average was taken. All samples were plated immediately onto blood, chocolate, and Mac Conkey agars.

3. Urine samples: Routine urine cultures were done by plating the specimens on blood agar and MacConkey's agar using calibrated loops for the semiquantitative method. Colony counts of 10^2 or 10^3 CFU/mL were used to define probable infection [18], [19].

4. Skin swabs: Dry sterile cotton-tip swab was rubbed on the skin, collected in a sterile container and sent to the lab. All samples were plated immediately onto blood, chocolate, and Mac Conkey agars.

Identification of isolated bacteria: The isolated microorganisms were identified by standard microbiological techniques, including Gram staining, colony characteristics, and biochemical properties. [20], [21]. gram-negative bacilli, which are oxidase negative, were identified using API 20 E (biomerieux) and API (20 NE) kit for identification of non-fermenters.

Antimicrobial susceptibility testing (AST): Kirby performed AST – Bauer disc diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines [22]. All isolates were tested by the standard disk diffusion method against β-lactam and non-β-lactam agents, including ampicillin, amoxicillin-clavulanic, piperacillin, third-generation cephalosporins (cefoperazone – sulbactam, cefepime), carbapenems (Imipenem), amikacin, gentamicin, ciprofloxacin and the results were also interpreted based on the CLSI guidelines. All antimicrobial disks used for susceptibility testing were obtained from BD BBL Sensi-Disc (Becton Dickinson, Sparks, Maryland, USA).

Statistical analysis

Standard computer program SPSS for Windows, release 13.0 (SPSS Inc, Tulsa, USA) (23) was used for data entry and analysis. All qualitative variables were expressed as count and per cent. Chi-square (χ^2) test was used to compare the frequency of qualitative variables among the different groups. Continuous variables were evaluated using the Mann-Whitney test. Risk analysis was calculated as odds ratio and confidence intervals. For all tests, a probability (p) less than 0.05 was considered significant.

Results

Table one shows clinical laboratory descriptive data. The prevalence of HAIs in this study was 15.6% of PICUs admission. Thirty-one patients (47%) were suffering from anaemia (Hb less than 10gm/dl). Leucocytosis (↑11.000) was present in 45 patients (68%), while leucopenia (↓4000) was in 4 patients (6%). Twenty-one patients (32%) were suffering from thrombocytopenia (platelets less than

150.000). Renal impairment occurred in 4 patients (6%). SGOT and SGPT were elevated in 12 (18%) and 15 (23%) patients respectively. CRP was positive in all patients.

Table 1: Descriptive data of patients under study

Characteristic	PICU patients
Age (months)	20.7 ± 25.8
Sex (M/F)	37/29
Hb (gm/l)	9.94 ± 1.65
WBCs (x1000)	13.28 ± 5.85
Platelets (x1000)	241.4 ± 143.18
Urea (mg/dl)	27.3 ± 24.5
Creatinine (mg/dl)	0.5 ± 0.69
SGOT (mg/dl)	135.64 ± 524.68
SGPT (mg/dl)	95.52 ± 329.3
CRP	Positive for all patients
Period of PICU stay	15.2 ± 13.94

The prevalence rate of nosocomial infection was 24% among blood cultures, 33% among endobronchial cultures, 12% among urine cultures, and 16.5% among skin cultures (Table 2).

Table 2: Culture results among studied patients

Culture/Organism	Blood No %	Endobronchial No %	Urine No %	Skin No %	Total No infection %
No growth	50 76	44 67	58 88	55 83.5	
Gram +ve cocci					
Staph	8 12	3 4.5	0 0	4 6	15
Strept	0 0	1 1.5	1 1.5	0 0	26.3
Gram -ve bacilli					2 3.5
Klebsiella	2 3	8 12	1 1.5	1 1.5	
Acinetobacter	4 6	4 6	4 6	2 3	12 21
E. coli	1 1.5	2 3	0 0	0 0	14 24.6
Yersinia	0 0	1 1.5	0 0	0 0	3 5.3
Serratia	0 0	1 1.5	0 0	2 3	1 1.7
Enterobacter	1 1.5	1 1.5	0 0	2 3	3 5.3
Candida	0 0	0 0	2 3	0 0	4 7
Mixed	0 0	1 1.5	0 0	0 0	2 3.5
					1 1.7
Total	66 100	66 100	66 100	66 100	

The most common microorganism group was Gram-negative bacteria. The commonest micro-organisms isolated from infected patients were Staphylococcus aureus, Acinetobacter, and Klebsiella; each caused about a fifth of the infections with positive microbiological results (Table 3). According to cultural sensitivity, amikacin and imipenem are the most sensitive antibiotics whatever the type of the organism (Table 3).

Table 3: Antibiotic Sensitivity Among Studied Patients

Organism/Antibiotic	Staph No: 15	Strep No: 2	Kleb No: 12	Acinet-obacter No: 14	E. coli No: 3	Serratia No: 3	Yersenia No: 1	Entero No: 4	Candida No: 2
Amoxaclav	0	0	0	3	0	0	0	0	0
Amikacin	11	0	6	6	0	0	1	3	0
Imipenam	9	0	2	6	0	1	1	3	0
Cephalosporin	1	0	1	1	0	1	0	1	0
Ciprofloxacillin	3	1	5	3	0	1	0	2	0
Gentamycin	1	0	1	1	0	0	1	0	0
Piperacillin	0	1	0	0	1	0	0	0	0
Tobramycin	1	0	4	2	1	0	0	1	0
Vancomycin	3	0	0	0	0	0	0	0	0

As regards the common invasive procedure used among our patients, mechanical ventilation was used for 91% of patients (60 patients of them 24 died), a central venous catheter for 6% (4 patients), and nasogastric tube for 53% (35 patients). The mortality rate was 36% (24 patients). Considering seasonal variation, winter was the commonest season for infection (Table 4).

Table 4: Seasonal variation of infectious organisms in studied patients

Season	No of patients	Blood culture +ve	Endobronchial culture +ve	Urine culture +ve	Skin culture +ve
Spring	16	2	5	4	3
Summer	15	5	6	0	5
Autumn	11	1	4	1	2
Winter	24	8	7	3	1
Total	66	16	22	8	11

Risk estimate for infection as a risk factor for death revealed that it is not as regard type of organism, nosocomial infections, and pneumonia (Table 5).

Table 5: Risk estimate for infections among studied patients

Infections		Survival N (%)	Non-Survival N (%)	Fisher's exact test p-value
Staph	Negative	34 (81%) 8	18 (75%) 6	0.755 NS
	Positive	(19%)	(25%)	
Klebsiella	Negative	34 (81%) 8	22 (91.7%) 2	0.306 NS
	Positive	(19%)	(8.3%)	
Nosocomial	Negative	18 (42.9%) 24	8 (33.3%) 16	0.601 NS
infection	Positive	(57.1)	(66.7%)	
Pneumonia and	Negative	24 (57.1%) 18	11 (54.2%) 13	0.448 NS
Sepsis	Positive	(42.9%)	(45.8%)	

Risk estimate for other different risk factors among studied patients including age, a period of stay, invasive techniques revealed no significance where P value for age, a period of stay estimated by Mann-Whitney test were 0.7 and 0.19 respectively. Risk estimate for the other risk factors and invasive technique revealed no significance P-value < 0.05 (Table 6). By dividing the patients into two groups; group 1: pneumonia and septicemia (31 patients), group 2: others (35 patients); risk estimate for different risk factors using Odds ratio revealed no significance as regard anaemia, thrombocytopenia, renal impairment, and invasive techniques including CVP, urinary catheter, and mechanical ventilation (Table 6).

Table 6: Risk estimate for other risk factors including labs and invasive techniques among studied patients as a whole and in both groups

Risk Factors	All patients (66)		Group 1 (31)		Group 2 (35)	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Anemia	2.059	0.743-5.703	3.536	0.78-16.032	1.167	0.277-4.913
Thrombocytopenia	1.5	0.518-4.345	0.471	0.095-2.337	4.56	0.975-21.322
Renal impairment	5.857	0.574-59.808	0.379	0.238-0.604	2.3	0.130-40.545
CVP	1.667	0.599-4.641	1.018	0.235-4.407	2.45	0.562-10.68
Urinary Catheter	1.273	0.462-3.503	0.429	0.099-1.857	3.733	0.788-17.684
Mechanical ventilation	8.726	0.4698-162.064				

CI = Confidence Interval; CVP = Central Venous Line.

Discussion

Infection control and proper anti-microbial therapy in PICUs is a challenge for medical staffs working in it. This study was carried out in two pediatric intensive care units in Egypt to report the prevalence of HAIs. The prevalence of HAIs in this study was 15.6% of PICUs admission. The prevalence of HAIs varies in different PICUs from country to country, from institution to institution, and from season to season in the same institution according to age,

underlying disease, and other risk factors. The prevalence in other studies ranged from 3% to 27% where it is higher in developing countries than developed countries [6], [7], [9], [10], [11], [12], [13], [14], [15], [16]. A Turkish study in 50 PICUs to assess a national point-prevalence survey of PICUs HAIs reported the overall HAI rate as 37% [8].

The rate in our study is different from other studies wherein American study in 35 PICUs; the HAI rate was 11.9% [24]. A prevalence rate of HAI from 17 European PICUs was 23.6% [25]; while in a Spanish PICU study, the rate was 29.8% [26]. The incidence in developing countries was over 20% [27]. The prevalence was not high in our study compared to another Egyptian study done by El-Nawawy and his colleagues [6] because this study was conducted in two university hospitals with improved infection control programs.

In this study, the most common types of HAI in PICU were respiratory followed by blood borne infection, UTI, and skin. Similar to our study, many studied revealed that the most common infection was respiratory followed by blood [8], [13], [25], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40]. In other studies, the most frequent sites of infection were bloodstream, lower respiratory tract, or urinary tract [7], [9], [41], [42], [43], [44], [45]. Only one study revealed that UTI was the commonest followed by blood borne and lower respiratory tract infections [39].

The most common microorganisms in this study were Gram-negative bacteria. Although there was a controversy between studies as to regard causative organisms, many studies including this study reported that gram-negative organisms were more commonly isolated [5], [13], [39], [42], [44], [46]. The commonest micro-organisms isolated from our infected patients were Staphylococcus aureus, Acinetobacter, and Klebsiella. Many studies also revealed that Staphylococcus aureus was the commonest [5], [44], [46]. Lee et al., the study revealed that Staphylococcus aureus was the most common Gram-positive organism, while Pseudomonas aeruginosa, Escherichia coli, and Klebsiella pneumoniae were the commonest Gram-negative organisms [39]. In Becerra et al., study, Candida was the commonest bloodstream infection [7]. In Atıcı study, the most common organisms were Klebsiella spp. (19.4%), followed by Pseudomonas aeruginosa (13.8%), and Acinetobacter baumanii (12%) [9]. Vincent et al., study (2009) reported that S aureus was the most common organism, followed by Acinetobacter, and Klebsiella. Acinetobacter was found in high incidence (24% of all infected patients) [40]. One study found an increased incidence of gram-positive organisms [47] while the Sepsis Occurrence in Acutely Ill Patients (SOAP) study reported an equal frequency of gram-positive and gram-negative organisms [28]. In a study done by Vincent et al., 2006 [28], Acinetobacter was involved in 9% of all infected patients, which was similar to the rate reported in EPIC study 1996 [48]. Similar to our study, Acinetobacter was observed to be an increased incidence in recent studies [40]. Alotaibi et al., the study concluded that Klebsiella was the commonest organism isolated from respiratory infection and UTI, while Klebsiella and Candida were the most common organisms that affect the bloodstream [14].

The hospital-acquired infection has commonly been used to guide empirical antibiotic treatment based on the different pathogens circulating in the hospital environment. In our study, amikacin and imipenem are the most sensitive antibiotics whatever the type of the organism which is similar to Mireya study [49].

The mortality rate in our study was 36%, which is nearly the same as reported in developing countries and higher than that reported in developed counties. In developing counties, the mortality rate ranged from 20 to 38% [3], [7], [44], [50] while in developed countries it was 7.7 to 10% [25], [51].

In this study, we found that sepsis was not a risk factor for death. Studying different risk factors for mortality among the studied patients, including age, a period of stay, type of organism, invasive techniques including CVP, urinary catheter, and mechanical ventilation revealed no significance. The risk factors for HAI in PICU differ between studies according to the method of comparison where some studies compare between the patient in ICU and patients in the pediatric ward, number of patients in the study that use invasive devices. The limitation of this study was a small number of patients. The viral infection is underdiagnosis. Mireya et al., the study revealed that age under 1 year, the severity of the disease, and mechanical ventilation were significant risk factors [49]. Rasslan et al., the study found that device associated infection rates in PICU in Egypt was higher than in developed countries and was considered as a risk factor for HAI (52). Aktar et al., the study revealed that only mechanical ventilation was found to be a risk factor for mortality in multiple logistic regression analysis [44]. Also, María et al., the study showed that disease severity and candida infection were the main risk factor for mortality [7]. Few studies showed that type of organism is a risk factor as Ashkenazi et al., the study reported mortality rate of 60% in Acinetobacter sp. bacteremia and 42% yeast associated infection [53].

As regard seasonal variation, winter was the commonest season for nosocomial infection in this study. Few studies demonstrated the impact of seasonal variation on different organisms. Caldeira et al., [54] and Fortaleza et al., [55] studies revealed an increased incidence of Gram-negative bacilli in warm weather. This controversy may be referred to that most of our patients were suffering from a respiratory infection.

In conclusion, Staphylococcus was the

commonest micro-organism while Gram-negative infections were the commonest group among PICU with a predominance of Acinetobacter and Klebsiella. Respiratory infections were the most common, followed by blood-borne infection. Risk factors for mortality were not significant. The empirical antibiotic choice was made according to culture and sensitivity. Respiratory infections were the most common, followed by blood-borne infection. Risk factors for mortality were not significant. Infection control programs are required repetitively and periodically for proper choice of antibiotics and infection control.

References

1. Abramczyk ML, Carvalho WB, Carvalho ES, Medeiros EA. Nosocomial infection in a pediatric intensive care unit in a developing country. Braz J Infect Dis. 2003; 7:375-80. https://doi.org/10.1590/S1413-86702003000600004 PMid:14636476

2. Akash Deep, R. Ghildiyal, S. Kandian and N. Shinkre. Clinical and Microbiological Profile of Nosocomial Infections in the Pediatric Intensive Care Unit (PICU). Indian Pediatrics. 2004; 41:1238-1246.

3. Alotaibi MG, Rahman S, Al-Shalaan MA, Omair A. Frequency of Nosocomial Infections in Pediatric Intensive Care Unit at King Abdulaziz Medical City, Riyadh, Saudi Arabia. J Infect Dis Ther. 2015; 3(5):234-236. https://doi.org/10.4172/2332-0877.1000234

4. Campins M, Vaque J, Rosello J, Salcedo S, Duran M, Monge V, Garcia Caballero J, Saenz MC, Calbo F, Armadans L. Nosocomial infections in pediatric patients: a prevalence study in Spanish hospitals. Am J Infect Control. 1993; 21:8-63. https://doi.org/10.1016/0196-6553(93)90225-S

5. Choudhury J, Mohanty D, Routray S S. Microbiological profile of Nosocomial infections in the pediatric patients admitted to intensive care unit: Int J Pediatr Res. 2016; 3(2):100-104.

6. Correia M, Simao C, Lito LM, Cabecadas M, Almeida H, Carvalho A, et al. Nosocomial infections in a Pediatric Intensive Care Unit. Acta Med Port. 1997; 10:463-468.

7. Daniel WW. Biostatistics: A foundation for analysis in the health sciences. 7th (ed.) John Wiley and Sons. Inc., New York. 2000:166-7.

8. El-Nawawy AA, Abd El-Fattah MM, Metwally HA, Barakat SS, Hassan IA. One year study of bacterial and fungal nosocomial infections among patients in pediatric intensive care unit (PICU) in Alexandria. J Trop Pediatr. 2006; 52:185-191. https://doi.org/10.1093/tropej/fmi091 PMid:16186137

9. Garner JS, JarvisWR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. Am J Infect Control. 1988; 16:128-40. https://doi.org/10.1016/0196-6553(88)90053-3

10. Garrouste-Orgeas M, Timsit JF, Taffet M, Misset B, Zahar JR, Soufir L, et al. Excess risk of death from intensive care unit-acquired nosocomial bloodstream infections: a reappraisal. Clin Infect Dis. 2006; 42:1118-26. https://doi.org/10.1086/500318 PMid:16575729

11. Grohskopf LA, Sinkowitz-Cochran RL, Garrett DO, Sohn AH, Levine GL, Siegel JD, Stover BH, Jarvis WR; 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. https://doi.org/10.1067/mpd.2002.122499 PMid:12006957

12. Hmamouchi B, Chakkouri K, Nejmi SE, Chlilek A. Epidemiology of nosocomial infection in a paediatric intensive care unit. Ann Fr Anesth Reanim. 2005; 24:699-700. https://doi.org/10.1016/j.annfar.2005.04.011 PMid:15921880

13. Jordan Garcia I, Esteban Torné E, Bustinza Arriortua A, de Carlos Vicente JC, García Soler P, Concha Torre JA, Flores González JC, Madurga Revilla P, Palomar Martínez M; VINCIP Study Group, from Spanish Society of Pediatric Intensive Care (SECIP). Trends in nosocomial infections and multidrug-resistant microorganisms in Spanish pediatric intensive care units. Enferm Infecc Microbiol Clin. 2016; 34(5):286-92. https://doi.org/10.1016/j.eimc.2015.07.010 PMid:26364857

14. Kepenekli E, Soysal A, Yalindag-Ozturk N, Ozgur O, Ozcan I, Devrim I, Akar S, Bakir M; Turkish PICU-HCAI Study Group (2015) A national point-prevalence survey of pediatric intensive care unit-acquired, healthcare-associated infections in Turkey. Jpn J Infect Dis. 2015; 13:1-17.

15. Laupland KB, Lee H, Gregson DB, Manns BJ. Cost of intensive care unit-acquired bloodstream infections. J Hosp Infect. 2006; 63: 124-32. https://doi.org/10.1016/j.jhin.2005.12.016 PMid:16621137

16. Legras A, Robert R. Nosocomial infection: prospective survey of incidence in 5 French ICUs. Intensive Care Medicine. 1999; 24:1040-1046. https://doi.org/10.1007/s001340050713

17. Marcelo L. Abramczyk, Werther B. Carvalho, Eduardo S. Carvalho and Eduardo A. S. Medeiros. Nosocomial Infection in a Pediatric Intensive Care Unit in a Developing Country. The Brazilian Journal of Infectious Diseases. 2003; 7(6):375-380. https://doi.org/10.1590/S1413-86702003000600004

18. Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK. Diagnosis of coliform infection in acutely dysuric women. N Engl J Med. 1982; 307(8):463-8. https://doi.org/10.1056/NEJM198208193070802 PMid:7099208

19. Clarridge JE, Johnson JR, Pezzlo MT, Cumitech B: laboratory diagnosis of urinary tract infections, Washington, DC American Society for Microbiology, 1998.

20. Lennette EH, Balows A, Hausler WJ, et al. Manual of clinical microbiology. Washington: American Society for Microbiology, 1985.

21. Isenberg HD, Schoenknecht FD, von Graevenitz A. Cumulative techniques: collection and processing of bacteriologic specimens. Washington: American Society for Microbiology, 1979.

22. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: 17th informational supplement. CLSI document M100-S17. Wayne, PA: CLSI, 2007.

23. María R Becerra1, José A Tantaleán, Víctor J Suárez, Margarita C Alvarado, Jorge L Candela, Flor C Urcia. Epidemiologic surveillance of nosocomial infections in a Pediatric Intensive Care Unit of a developing country. BMC Pediatrics. 2010:10:66. https://doi.org/10.1186/1471-2431-10-66 PMid:20831797 PMCid:PMC2944329

24. Nejla Ben Jaballah, MD, Asma Bouziri, MD, Khaled Mnif, MD, Asma Hamdi, MD, Ammar Khaldi, MD, and Wassim Kchaou, MD. Epidemiology of hospital-acquired bloodstream infections in a Tunisian pediatric intensive care unit: A 2-year prospective study. Am J Infect Control. 2007; 35:613-8. https://doi.org/10.1016/j.ajic.2006.09.007 PMid:17980241

25. Raymond J, Aujard Y, European Study Group. Nosocomial infections in pediatric patients a European, multicenter prospective study. Infection Control & Hospital Epidemiology. 2000; 21(4):260-3. https://doi.org/10.1086/501755 PMid:10782588

26. Atici S, Soysal A, Kadayifci EK, Karaaslan A, Akkoç G, Yakut N, Demir SÖ, Girgin Fİ, Çulha G, Altınkanat G, Öztürk N. Healthcare-associated infections in a newly opened pediatric intensive care unit in Turkey: Results of four-year surveillance. The Journal of Infection in Developing Countries. 2016; 10(03):254-9. https://doi.org/10.3855/jidc.7517 PMid:27031457

27. Balaban İ, Tanır G, Timur ÖM, Öz FN, Teke TA, Bayhan Gİ, Sözak N, Göl N. Nosocomial infections in the general pediatric wards of a hospital in Turkey. Japanese journal of infectious diseases. 2012; 65(4):318-21. https://doi.org/10.7883/yoken.65.318 PMid:22814155

28. Aktar F, Tekin R, Güneş A, Ülgen C, Tan I, Ertugrul S, Köşker

M, Balık H, Karabel D, Yolbaş I. Determining the Independent Risk Factors and Mortality Rate of Nosocomial Infections in Pediatric Patients. BioMed Research International. 2016:1-5. https://doi.org/10.1155/2016/7240864 PMid:26981536 PMCid:PMC4770130

29. Almuneef MA, Memish ZA, Balkhy HH, Hijazi O, Cunningham G, et al. Rate, risk factors and outcomes of catheter-related bloodstream infection in a paediatric intensive care unit in Saudi Arabia. J Hosp Infect. 2006; 62:207-213. https://doi.org/10.1016/j.jhin.2005.06.032 PMid:16307822

30. Ashkenazi S, Leibovici L, Samra Z, Konisberger H, Drucker M. Risk factors for mortality due to bacteremia and fungemia in childhood. Clinical infectious diseases. 1992; 14(4):949-51. https://doi.org/10.1093/clinids/14.4.949 PMid:1576293

31. Brun-Buisson C, Meshaka P, Pinton P, Vallet B. EPISEPSIS Study Group. EPISEPSIS: a reappraisal of the epidemiology and outcome of severe sepsis in French intensive care units. Intensive Care Med. 2004; 30(4):580-588. https://doi.org/10.1007/s00134-003-2121-4 PMid:14997295

32. Engel C, Brunkhorst FM, Bone HG, et al. Epidemiology of sepsis in Germany: results from a national prospective multicenter study. Intensive Care Med. 2007; 33(4):606-618. https://doi.org/10.1007/s00134-006-0517-7 PMid:17323051

33. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Sepsis incidence and outcome: contrasting the intensive care unit with the hospital ward. Crit Care Med. 2007; 35(5):1284-1289. https://doi.org/10.1097/01.CCM.0000260960.94300.DE PMid:17414725

34. Fortaleza CM, Caldeira SM, Moreira RG, Akazawa RT, Corrente JE, Souza LR, et al. Tropical healthcare epidemiology: weather determinants of the etiology of bloodstream infections in a Brazilian hospital. Infect Control Hosp Epidemiol. 2014; 35(1):85-88. https://doi.org/10.1086/674392 PMid:24334804

35. Friedman G, Silva E, Vincent JL. Has the mortality of septic shock changed with time? Crit Care Med. 1998; 26(12):2078-2086. https://doi.org/10.1097/00003246-199812000-00045 PMid:9875924

36. Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. Crit Care. 2006; 10(2):R42.

37. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K. International study of the prevalence and outcomes of infection in intensive care units. Jama. 2009; 302(21):2323-9. https://doi.org/10.1001/jama.2009.1754 PMid:19952319

38. Karlsson S, Varpula M, Ruokonen E, et al. Incidence, treatment, and outcome of severe sepsis in ICU-treated adults in Finland: the Finnsepsis study. Intensive Care Med. 2007; 33(3):435-443. https://doi.org/10.1007/s00134-006-0504-z PMid:17225161

39. Lee CY, Chen PY, Huang FL, Lin CF. Microbiologic spectrum and susceptibility pattern of clinical isolates from the pediatric intensive care unit in a single medical center-6 years' experience. J Microbiol Immunol Infect. 2009; 42(2):160-5.

40. Lisa A. Grohskopf, Ronda L. Sinkowitz-Cochran, Denise O. Garrett, Annette H. Sohn, Gail L. Levine, Jane D. Siegel, Beth H. Stover, William R. Jarvis, and the Pediatric Prevention Network. A national point-prevalence survey of pediatric intensive care unit-acquired infections in the United States. Journal of Pediatrics. 2002; 140(4):432-438. https://doi.org/10.1067/mpd.2002.122499 PMid:12006957

41. Martin CM, Priestap F, Fisher H, et al. STAR Registry Investigators. A prospective, observational registry of patients with severe sepsis: the Canadian Sepsis Treatment and Response Registry. Crit Care Med. 2009; 37(1):81-88. https://doi.org/10.1097/CCM.0b013e31819285f0 PMid:19050636

42. Mireya UA, Marti PO, Xavier KV, Cristina LO, Miguel MM, Magda CM. Nosocomial infections in pediatric and neonatal intensive care units. Journal of infection. 2007; 54:212-220. https://doi.org/10.1016/j.jinf.2006.03.023 PMid:16678905

43. Rasslan O, Seliem ZS, Ghazi IA, El Sabour MA, El Kholy AA, Sadeq FM, Kalil M, Abdel-Aziz D, Sharaf HY, Saeed A, Agha H. Device-associated infection rates in adult and pediatric intensive care units of hospitals in Egypt. International Nosocomial Infection Control Consortium (INICC) findings. Journal of infection and public health. 2012; 5(6):394-402. https://doi.org/10.1016/j.jiph.2012.07.002 PMid:23287610

44. Richards MJ, Edwards JR, Culver DH, et al. Nosocomial Infections in Pediatric Intensive Care Units in the United States. Pediatrics. 1999; 103:804. https://doi.org/10.1542/peds.103.4.e39 PMid:10103331

45. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Guideline for isolation precautions preventing transmission of infectious agents in healthcare settings, 2007. https://doi.org/10.1016/j.ajic.2007.10.007 PMid:18068815

46. Silva E, Pedro MA, Sogayar AC, et al. Brazilian Sepsis Epidemiological Study. Brazilian Sepsis Epidemiological Study (BASES study). Crit Care. 2004; 8(4):R251-R260.

47. Caldeira SM, Cunha AR, Akazawa RT, Moreira RG, Souza LD, Fortaleza CM. Weather parameters and nosocomial bloodstream infection: a case-referent study. Revista de saude publica. 2015; 49:19. https://doi.org/10.1590/S0034-8910.2015049005438 PMid:25830871 PMCid:PMC4390072

48. Spencer RC. Predominant pathogens found in the European Prevalence of Infection in Intensive Care study. Eur J Clin Microbiol Infect Dis. 1996; 15(4):281-285. https://doi.org/10.1007/BF01695658 PMid:8781877

49. Sundararajan V, Macisaac CM, Presneill JJ, Cade JF, Visvanathan K. Epidemiology of sepsis in Victoria, Australia. Crit Care Med. 2005; 33(1):71-80. https://doi.org/10.1097/01.CCM.0000150027.98160.80 PMid:15644651

50. Urrea M, Pons M, Serra M, Latorre C, Palomeque A. Prospective incidence study of nosocomial infections in a pediatric intensive care unit. Pediatr Infect Dis J. 2003; 22:490-493. https://doi.org/10.1097/01.inf.0000069758.00079.d3 PMid:12799503

51. van Gestel A, Bakker J, Veraart CP, van Hout BA. Prevalence and incidence of severe sepsis in Dutch intensive care units. Crit Care. 2004; 8(4):R153-R162. https://doi.org/10.1186/cc2858 PMid:15312213 PMCid:PMC522831

52. Vincent JL, Sakr Y, Sprung CL, et al. Sepsis Occurrence in Acutely Ill Patients Investigators. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med. 2006; 34(2):344-353. https://doi.org/10.1097/01.CCM.0000194725.48928.3A PMid:16424713

53. Zingg W, Hopkins S, Gayet-Ageron A, Holmes A, Sharland M, Suetens C, Almeida M, Asembergiene J, Borg MA, Budimir A, Cairns S. Health-care-associated infections in neonates, children, and adolescents: an analysis of paediatric data from the European Centre for Disease Prevention and Control point-prevalence survey. The Lancet Infectious Diseases. 2017; 17(4):381-9. https://doi.org/10.1016/S1473-3099(16)30517-5

54. Yallew WW, Kumie A, Yehuala FM. Point prevalence of hospital-acquired infections in two teaching hospitals of Amhara region in Ethiopia. Drug Healthc Patient Saf. 2016; 8:71-6. https://doi.org/10.2147/DHPS.S107344 PMid:27601932 PMCid:PMC5003516

55. Záhorec R, Firment J, Straková J, et al. Epidemiology of severe sepsis in intensive care units in the Slovak Republic. Infection. 2005; 33(3):122-128. https://doi.org/10.1007/s15010-005-4019-2 PMid:15940412