Original Article

Three-year study of health care-associated infections in a Turkish pediatric ward

Canan Kuzdan[1], Ahmet Soysal[1], Gülcan Çulha[2], Gülşen Altinkanat[3], Güner Söyletir[3], Mustafa Bakir[1]

[1] *Department of Pediatric Infectious Diseases, Marmara University Medical School, Istanbul, Turkey*
[2] *Infectious Diseases Department, Marmara University Medical School, Istanbul, Turkey*
[3] *Department of Microbiology, Marmara University Medical School, Istanbul, Turkey*

Abstract

Introduction: Health care-associated infections (HCAIs) can cause an increase in morbidity, mortality and costs, especially in developing countries. As information on the epidemiology of HCAIs in pediatric patientsinTurkey is limited, we decided to study the annual incidence and antibiotic resistance patterns in our pediatric ward at Marmara University Hospital.

Methodology: All hospitalized patients in the pediatric ward were assessed with regard to HCAIs betweenJanuary 1, 2008 and December 31, 2010. Data was prospectively collected according to standard protocols of the National Nosocomial Infections Surveillance System (NosoLINE).

Results: A total of 16.5% of all hospitalized patients developed HCAIs in the three years studied. The most frequent HCAIs were urinary tract infections (UTI) (29.3%), bloodstream infections (27%) and pneumonias (21%). While the most frequent agent isolatedfrom UTI was *Escherichia coli* (26%), the most common agent in blood stream infections was *Staphylococcus epidermidis* (30.4%). Vancomycin resistance was found in 73.3% of all *Enterococcus faecium* strains. Extended-spectrum β-lactamase was detected in 58.3% of *Klebsiella pneumoniae* and *E. coli* isolates.

Conclusions: Continual HCAI surveillance is important to determineits rate. Knowledge of the HCAI incidence can influence people's use of broad-spectrum antibiotics and encourage antibiotic rotation. Moreover, the knowledge of HCAI incidence may support the infection control programmes, including education and isolation methods which ultimately may help to reducethe rate of the HCAIs.

Key words: health care–associated infections; pediatric unit; surveillance; nosocomial infections; children.

J Infect Dev Ctries 2014; 8(11):1415-1420. doi:10.3855/jidc.3931

(Received 01 July 2013 – Accepted 25 July 2014)

Introduction

Health care-associated infections (HCAIs) are important complications in both adults and children that may lead to increased morbidity and mortality, prolonged hospital stay and increased costs [1]. Incidence of HCAI varies according to age, service, underlying disease and other risk factors [2,3]. In developed countries, the rates of HCAI among children are lower than among adults. For instance, in the United States 5%-10% ofadult patients hospitalized suffer HCAI while the rate is 1.5%-4% for children of ten years of age, and 7%-9% for infants younger than 1 year of age [4]. This relationship between increased infection rate and younger age disappears in pediatric and neonatal intensive care units as the rate of HCAI reported for both is highdue to the increased severity of diseases and the need for more invasive procedures [5]. In developing countries, the incidence of HCAI has been reported to be higher than in developed nations because of the high number of patients, limited number of staff, and insufficient compliance with infection control measures [6,7].

The most frequent HCAIs are bacteremia, urinary and respiratory tract infections [3,4,8-11]. The most common causative agents of HCAIs are staphylococci and Gram-negative organisms [4]. However, information regarding the epidemiology of HCAIs in Turkish pediatric patients is limited. The aim of this study wasto assessthe epidemiology of HCAIs and species distribution as well as antimicrobial susceptibility of pathogens appearing in one of the Turkish University Hospitals.

Methodology

This study was performed in pediatric units consisting of 28 beds and 6 rooms and one pediatric intensive care unit at Marmara University Hospital (MUH). A total of 6 nurses and 5 doctors worked in this pediatric service during the day time.Continual active surveillance of HCAIswas performed by a nurse

in charge for infection control. The MUH is located in themetropolitan Istanbul's Asian side.

This study included all patients hospitalized betweenJanuary1, 2008 and December 31, 2010 at MUH pediatric units.Data was prospectively collected according to standard protocols of the National Nosocomial Infections Surveillance System (NosoLINE). Centers for Disease Control and Prevention (CDC) criteria were used as standard definitions for HCAIs [12]. HCAI was described as infection occurred 48 hours after admission or 10 days after discharge. Depending on symptoms, urine, cerebrospinal fluid (CSF), endotracheal aspirate, sputum, or wound specimens were obtained.Blood cultures were performed on all patients with suspected HCAI.

Blood cultures were performed using BACTEC peds plus/F bottles (BD Diagnostics, Sparks Glencoe, USA).Identifications were done using the VITEK2 (BioMérieux, Marcy l'Etoile, France). The Extended-spectrum β-lactamase (ESBL)was detected using the E-test, according to the manufacturer'sinstructions (AB Biodisk, Solna, Sweden). Susceptibility to non-β-lactam antibiotics was evaluated by a disk diffusion method according to the Clinical and Laboratory Standards Institute (CLSI)criteria[13].E-test strips of vancomycin and teicoplanin were used to confirm resistance to glycopeptıdes according to the manufacturer'sinstructions (AB BIODISK, Solna, Sweden). For the interpretation of susceptibility results, the breakpoints of resistance set by the CLSI were used[13].Allinformation and culture results of patients with HCAI were collected by an infection control nurse.

Results

Two thousand three hundred and fifty children were hospitalized during the 3-year study period. Of these, 389 children (16.5%) developed HCAI and were all included in this study. The HCAI are tabulated by year and infection site in Table 1.The most frequent HCAIs were urinary tract infection (UTI) (29.3%), bacteremia (27%) and pneumonia (21%). The order of the major pathogens for each year are shownin Table 2. The most common agents isolated from HCAIs were *Staphylococcus epidermidis* (10%), *Escherichia coli* (8.7%), *Enterococcus faecium* (7.8%) and *Klebsiella.pneumoniae* (6.7%).The most frequent agents isolated from UTIs were *E. coli* (26%), *K. pneumoniae* (16%), *Candida albicans* (10.8%) and *E. faecium* (10.8%) (Table 3). Whereas the most frequent agent was *S. epidermidis* (30.4%) for bacteremias (Table 4). *Pseudomonas aeruginosa*was the most frequent cause of pneumonia.

Among agents isolated from HCAIs the frequency of methicillin resistance was 84.6% for *S. epidermidis* and seven out of nine *Staphylococcus aureus* strains. Among the gram-negative species obtained only from HCAIs, the 58.3% of *K. pneumoniae* and *E.a coli* isolateshad ESBL.*C. albicans* and non-albicans *Candida* strains accounted for 56% and 44% of HCAIs, respectively.Vancomycin and ampicillin resistance was found in 73.3% and 100% of all *E. faecium* strains, respectively. Infections due to vancomycin-resistant *E. faecium* strains led to an outbreak in the pediatric service. The susceptibility profile of all *Acinetobacter baumanii* and *Pseudomonas aeruginosa* isolates are shown in table 5.

Table 1. Distribution of HCAIs with respect to yearof isolation and infection site

	No of HCAI (n)	HCAI rate (%)	No of HCAI (n)	HCAI rate (%)	No of HCAI (n)	HCAI rate (%)	No of HCAI (n)	HCAI rate (%)
Years	**2008**		**2009**		**2010**		**Total**	
No of patients hospitalized (n)	**1156**		**856**		**338**		**2350**	
UTI	43	3.72%	56	6.54%	15	4.44%	114	29.3%
BSI	47	4.07%	42	4.91%	16	4.73%	105	27%
Pneumonia	33	2.85%	33	3.86%	16	4.73%	82	21%
SSTI	4	0.35%	26	3.04%	9	2.66%	39	10%
GISI	12	1.04%	11	1.29%	3	0.89%	26	6.8%
SSI	2	0.17%	4	0.47%	3	0.89%	9	2.4%
CNSI	3	0.26%	2	0.23%	0	0%	5	1.2%
CVSI	2	0.17%	0	0%	0	0%	2	0.5%
OI	2	0.17%	4	0.47%	1	0.30%	7	1.8%
Total	148	12.8 %	178	20.79%	63	18.64%	389	100%

UTI: Urinary tract infection, BSI: Bloodstream infection, SSTI: Skin and soft tissue infection, GISI: Gastrointestinal system infection, SSI: Surgical site infection, CVSI: Cardiovascular system infection, CNSI: Central nervous system infection, OI: Other infections

Table 2. Distribution of nosocomial pathogens and resistance status with respect to year of isolation

Years	2008 n (%)	2009 n (%)	2010 n (%)	Total n (%)
Staphylococcus epidermidis	13 (8.8)	21 (11.8)	5 (7.9)	39 (10)
Methicillin sensitive	3 (23,1)	3 (14.3)	0	6 (15.4)
Methicillin resistance	10 (76.9)	18 (%85.7)	5 (100)	33 (84.6)
Escherichia coli	13 (8.9)	14 (7.9)	7(11.2)	34 (8.7)
Presence of an ESBL	9 (69.2)	9 (64.2)	2 (28.5)	20 (58.8)
Absence of an ESBL	4 (30.8)	5 (35.8)	5 (72.5)	14 (41.2)
Enterococcus faecium	15 (10.1)	12 (6.7)	3 (4.7)	30 (7.8)
Ampicillin resistance	13 (100)	12 (100)	3 (100)	28 (100)
Vancomycin resistance	12 (80)	8 (66.6)	2 (60)	22 (73.3)
Klebsiella pneumoniae	14 (9.5)	10 (5.6)	2 (3.1)	26 (6.7)
Presence of an ESBL	7 (50)	7 (70)	1 (50)	15 (57.7)
Absence of an ESBL	7 (50)	3 (30)	1 (50)	11 (42.3)
Pseudomonas aeruginosa	13 (8.7)	9 (5.1)	4(6.3)	26 (6.7)
Candida albicans	7 (4.7)	7 (3.9)	1 (1.6)	15 (3.8)
Non-albicans Candida	6(4.1)	2 (1.1)	4 (6.3)	12 (3)
Staphylococus aureus	4 (2.7)	4 (2.2)	1(1.6)	9 (2.3)
Methicillin sensitive	1(25)	1 (25)	0	2 (22.2)
Methicillin resistance	3 (%75)	3 (%75)	1	7 (77.8)
Stenotrophomonas maltophilia	3 (2)	4 (2.2)	3 (4.8)	10 (2.6)
Serratia marcescens	1 (0.7)	8 (4.5)	4(6.3)	13 (3.3)
Acinetobacter baumanii	3 (2)	5 (2.8)	2 (3.2)	10 (2.6)
Undetermined agent	33 (22.3)	42 (23.7)	13 (20.7)	88 (22.7)
Others	23 (15.5)	40 (22.5)	14 (22.3)	77 (19.8)
Total	**148 (100)**	**178 (100)**	**63 (100)**	**389 (100)**

These strains were obtained only from HCAIs

Table 3. Frequency of nosocomial pathogens causing UTI according to yearof isolation

	2008 n (%)	2009 n (%)	2010 n (%)	Total n (%)
Escherichia coli	12 (27.6)	11 (19.6)	6 (39.9)	29 (25)
Klebsiella pneumonia	10 (23.3)	7 (12.5)	1 (6.7)	18 (16)
Candida albicans	6 (14)	5 (9)	1 (6.7)	12 (10.5)
Enterococcus faecium	3 (7)	8 (14.3)	1 (6.7)	12 (10.5)
Pseudomonas aeruginosa	2 (4.7)	2 (3.6)	1 (6.7)	5 (4.4)
Enterobacter cloacae	2 (4.7)	1 (1.8)	0	3 (2.7)
Polimicrobial	2 (4.7)	7 (12.5)	0	9 (8)
Uncertain agent	3 (7)	8 (14.2)	0	11 (9.8)
Others	3 (7)	7 (12.5)	5 (33.3)	15 (13.1)
Total	**43 (100)**	**56 (100)**	**15 (100)**	**114 (100)**

Table 4. Frequency of nosocomial pathogens causing bloodstream infections according to yearof isolation

	2008 n (%)	**2009 n (%)**	**2010 n (%)**	**Total n (%)**
Staphylococcus epidermidis	11 (23.5)	16 (38.2)	5 (31.3)	32 (30.4)
Staphylococus aureus	4 (8.5)	2 (4.8)	0	6 (5.8)
Enterococcus faecium	3 (6.4)	3 (7.3)	0	6 (5.8)
Serratia marcescens	1 (2.1)	3 (7.3)	2 (12.6)	6 (5.8)
Stenotrophomonas maltophilia	3 (6.4)	0	1 (6.3)	4 (3.8)
Candida parapsilosis	2 (4.3)	1 (2.4)	1 (6.3)	4 (3.8)
Klebsiella pneumonia	2 (4.3)	1 (2.4)	0	3 (2.8)
Pseudomonas aeruginosa	2 (4.3)	0	0	2 (1.9)
Acinetobacter baumanii	1 (2.1)	1 (2.4)	0	2 (1.9)
Candida albicans	1 (2.1)	0	0	1 (0.9)
Escherichia coli	0	0	1 (6.3)	1 (0.9)
Polimicrobial	1 (2.1)	1 (2.4)	0	2 (1.9)
Uncertain agent	6 (12.7)	5 (11.3)	3 (18.6)	14 (13.3)
Others	10 (21.2)	9 (21.5)	3 (18.6)	22 (21)
Total	47 (100)	42 (100)	16 (100)	105 (100)

Table 5. Susceptibility profile of all *Acinetobacter baumanii* and *Pseudomonas aeruginosa* isolates

Organism/ Antimicrobial agents *A. baumanii* (n = 10)	**Susceptible n (%)**	**Organism/ Antimicrobial agents *P. aeruginosa* (n = 26)**	**Susceptible n (%)**
Amikacin	10 (100)	Amikacin	24 (91)
Ciprofloxacin	8 (80)	Ciprofloxacin	23 (89)
Gentamicin	8 (80)	Cefepime	20 (77)
Imipenem	7 (70)	Piperacilline Tazobactam	20 (77)
Cefepime	7 (70)	Gentamicin	19 (74)
Ceftazidime	7 (70)	Ceftazidime	19 (74)
Piperacillin Tazobactam	6 (60)	Imipenem	18 (69)

Discussion

The overall HCAI rate of 16.5%detected by this study was consistent with results of previousstudies conducted in Turkey [7,14,15] which is higher than rates reported from Canada and US [16,17]. Turkish HCAI ratesamong pediatric and adult patients in 2009, ranged from 1.3%-16% [7].In two previous studies that included children and adult patients at Pamukkale University Hospital and Marmara University Hospital,the HCAI rates were 3.5%-9.6% [14,15]. The main reasons for these high rates were considered to be prolonged hospitalizations of patients with underlying chronic diseases, patients hospitalized in pediatric intensive care unit, and insufficient compliance with infection control measures.

In the US,gastrointestinal and respiratory infections and bacteremias are the most common HCAIs in the pediatric services [3].In patients hospitalized at Marmara University Hospital, the most common HCAI was represented byUTIs, (Table 1) probably due to frequent urinary tract catheterizations.*E.coli* was the most frequent agent in UTIs, and *S. epidermidis* was the most common agent in bacteremias.This wasin agreement with two separate studies regarding nosocomial bloodstream infections in United States hospitals [18,19].

More than 50% of *E. coli* strains and of *K. pneumoniae* isolates had ESBL in this current study, (Table 2) similar to a 2004 study conducted at Marmara University Hospital. In an international study that included Turkey it was reported that the 78% of *K. pneumonia* isolates produced ESBL [20]. We considered these consistently high rates of resistance to be caused by insufficient compliance with infection control measures, stable patient profile of our hospital and unchanged physical conditions in the hospital [15].

P. aeruginosa frequently results in HCAIs and tends to develop multidrug resistance [21]. In this study *P. aeruginosa* was the most common cause of pneumonia and the fifth most common cause of allHCAIs (Table 2). The resistance patterns in *P. aeruginosa* isolates varyin different areas of the hospital and varyin time,therefore continual surveillance and a timely provision of antibiograms mayhelp guide clinicians in selecting the empirical treatment. After the publication of another study from our group in 2004 [15], which showed that *P. aeruginosa* strains were susceptible to ceftazidime while being less susceptible to other antibiotics, clinicians began using broad-spectrum cephalosporins more frequently. This current study has documented a change to a reduced susceptibility to ceftazidime and anhigher susceptibility to amikacin and ciprofloxacin.

In 2004 we reported that 6 out of 13 isolates of *E. faecium* in the pediatric ward were resistant to vancomycin [15]; as a consequence antibiotic prescription practiceschanged to a more frequent use of broad-spectrum antibiotics. The change to broad-spectrum antibiotics can be considered essential since the patients were seriously ill and may had been previously hospitalized. This current study has documented a 70% vancomycin resistance.

Although *C.albicans* was found to be the third most common agent causingurinary tract infection, *C. albicans* ranked sixth amongoverall causesof HCAIs in the present study (Table 2). This result maybe relatedto patients with hematologic or oncologic problems with a history of prior and/orlong-term hospitalization.

Conclusions

Compared to developed countries, the HCAI rate here reported was high, but it was in line with previously published reports from Turkey. As patients in our unit frequently need urinary catheterization, the most common HCAI was identified as urinary system infection. Antibiotic resistance rates are similar to other reports in Turkey. We hypothesize that thehigh rate of HCAIwith resistant bacteria reported in our study is caused by theexisting ward system, lack of infrastructure, and inability to implement infection control measures. Continual, active surveillance studies of hospital infections in developing countries, such as Turkey,is an essential component of infection control which maycontribute to improve patient care.

References

1. Haley RW, Schaberg DR, Crossley KB, Von Allmen SD, McGowan JE Jr (1981) Extracharges and prolongation of stay attributable to nosocomial infections: a prospective interhospital comparison. Am J Med 70:51-58
2. Jarvis WR, Edwards JR, Culver DH, Hughes JM, Horan T, Emori TG, Banerjee S, Tolson J, Henderson T, Gaynes RP, Jarvis WR, Edwards JR, Culver DH, Hughes JM, Horan T, Emori TG, Banerjee S, Tolson J, Henderson T, Gaynes RP, Martone WJ, National Nosocomial Infections Surveillance System (1991) Nosocomial infection rates in adult and pediatric intensive care units in the United States. Am J Med 91:185-191.
3. Richards MJ, Edwards JR, Culver DH, Gaynes RP (1999) Nosocomial infections in pediatric intensive care units in the United States. National Nosocomial Infections Surveillance System. Pediatrics 103: 39-47.

4. Raymond J, Aujard Y (2000) Nosocomial infections in pediatrics: A European, multicenter prospective study. Infect Control Hosp Epidemiol 21:260-263.
5. Cavalcante SS, Mota E, Silva LR, Teixeira LF, Cavalcante LB (2006) Risk factors for developing nosocomial infections among pediatric patients. Pediatr Infect Dis J 25:438-445
6. El-Nawawy AA, Abd El-Fattah MM, Metwally HA, Barakat SS, Hassan IA (2006) One year study of bacterial and fungal nosocomial infections among patients in pediatric intensive care unit (PICU) in Alexandria. J Trop Pediatr 52: 185-191.
7. Hacımustafaoğlu M, Çelebi S, Tuncer E, Ozkaya G, Cakır D, Bozdemir S (2009) Nosocomial infection incidence in pediatric clinic and pediatric intensive care unit. J Pediatr Inf 3:112-117.
8. Stover BH, Shulman ST, Bratcher DF, Brady MT, Levine GL, Jarvis WR (2001) Nosocomial infection rates in US children's hospitals' neonatal and pediatric intensive care units. Am J Infect Control29:152–157.
9. Singh-Naz N, Sprague BM, Patel KM, Pollack MM (1996) Risk factors for nosocomial infection in critically ill children: A prospective cohort study. Crit Care Med24:875-878.
10. Brown RB, Stechenberg B, Sands M, Hosmer D, Ryczak M (1987) Infections in a pediatric intensive care unit. Am J Dis Child 141:267-270.
11. Mühlemann K, Franzini C, Aebi C, Berger C, Nadal D, Stähelin J, Gnehm H, Posfay-Barbe K, Gervaix A, Sax H, Heininger U, Bonhoeffer J, Eich G, Kind C, Petignat C, Scalfaro P (2004) Prevalence of nosocomial infections in Swiss children's hospitals. Infect Control Hosp Epidemiol 25:765-771
12. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM (1988) CDC definitions for nosocomial infections, 1988. Am J Infect Control16:128-140
13. Clinical and Laboratory Standards Institute (2010) Performance standards for antimicrobial susceptibility testing; Twentieth informational supplement; M100-S20. June 2010 Update. Clinical and Laboratory Standards Institute, Wayne, PA.
14. Sacar S, Kavas ST, Asan A, Cevahir N, Serin S, Turgut H (2008) Surveillance of nosocomial infections in Pamukkale University Hospital: A 3-year analysis. Turkish Journal of Infection 22: 15-21.
15. Soysal A, Toprak D, Yavuz B, Türel Ö, Çulha G, Karatuna O, Söyletir G, Bakır M (2006) Nosocomial infections detected in Marmara University Hospital Pediatry Department. Turkish Journal of Hospital Infections 10: 143-148.
16. Ford-Jones EL, Mindorff CM, Langley JM, Allen U, Nàvàs L, Patrick ML, Milner R, Gold R (1989) Epidemiologic study of 4684 hospital-acquired infections in pediatric patients. Pediatr Infect Dis J8: 668-675
17. Jarvis WR (1987) Epidemiology of nosocomial infections in pediatric patients. Pediatr Infect Dis J 6: 344-351
18. Wisplinghoff H, Seifert H, Tallent SM, Bischoff T, Wenzel RP, Edmond MB (2003) Nosocomial bloodstream infections in pediatric patients an United States hospitals: epidemiology, clinical features and susceptibilities. Pediatr Infect Dis J 22: 686-691
19. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB (2004) Nosocomial bloodstream infections in US hospitals: Analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 39: 309-317
20. Paterson DL, Ko WC, Von Gottberg A, Mohapatra S, Casellas JM, Goossens H, Mulazimoglu L, Trenholme G, Klugman KP, Bonomo RA, Rice LB, Wagener MM, McCormack JG, Yu VL (2004) International prospective study of *Klebsiella pneumoniae* bacteremia: Implications of extended spectrum β-lactamase production in nosocomial infections. Ann Int Med 140: 26-32
21. Rossolini GM, Mantengoli E (2005) Treatment and control of severe infections caused by multiresistant *Pseudomonas aeruginosa.* Clin Microbiol Infect 11: 17-32.

Corresponding author

Ahmet Soysal
T.C. Sağlık Bakanlığı Marmara Üniversitesi Eğitim ve Araştırma Hastanesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Çocuk Enfeksiyon Hastalıkları Bilim Dalı, oda no: 2829
Fevzi Çakmak Mahallesi Mimar Sinan Caddesi No: 41
Üstkaynarca, Pendik
İstanbul, Turkey
Phone: + 0216-6254625
Email: asoysal@marmara.edu.tr

Conflict of interests: No conflict of interests is declared.