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Original Article

Microbiologic spectrum and susceptibility pattern of clinical isolates from the pediatric intensive care unit in a single medical center — 6 years' experience

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Background and purpose: Nosocomial infection contributes to the morbidity and mortality of patients in hospital. Timely microbiologic surveillance and assessment of antimicrobial resistance is important for dealing with nosocomial infections. This retrospective review was conducted to evaluate the microbiologic spectrum and susceptibility pattern in the pediatric intensive care unit from 2001 to 2006.

Methods: The microbiologic data and antimicrobial susceptibility of all clinical isolates in the pediatric intensive care unit between 2001 and 2006 were reviewed. The incidence and distribution of nosocomial infections and the associated pathogens were also analyzed.

Results: 1163 clinical isolates were analyzed. The frequencies of Gram-positive and Gram-negative bacteria were 30.4% and 56.2%, respectively. *Staphylococcus aureus* was the most common isolate among the Gram-positive organisms, while *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae* were the 3 leading Gram-negative isolates. The proportion of methicillin-resistant *S. aureus* (MRSA) to all *S. aureus* was 65.2%. Six vancomycin-resistant enterococci were isolated in 2003. Extended-spectrum β-lactamase (ESBL)–producing *K. pneumoniae* accounted for 20% of *K. pneumoniae* isolates since 2005. Carbapenem-resistant *P. aeruginosa* accounted for 34% of *P. aeruginosa* isolates. The nosocomial infection rate was not reduced after moving to a new hospital building in 2003. Urinary tract infection (30.2%) was the most common nosocomial infection, followed by bloodstream infection (26.5%) and lower respiratory tract infection (25.3%).

Conclusions: MRSA, carbapenem-resistant *P. aeruginosa*, and ESBL-producing *K. pneumoniae* were the major concerns in this study. Good hand hygiene and strict aseptic procedures remain the most important factors for infection control.

Key words: Cross infection; Drug resistance, bacterial; Intensive care units, pediatric

Introduction

Nosocomial infection is a major cause of morbidity and mortality for patients in hospital. Nosocomial infection results in prolonged hospital stay, increased use of antimicrobial agents, and increased medical costs [1]. A well-designed hospital infection control strategy, including good hygiene, microbiological monitoring, and nosocomial control, will greatly reduce the risk of nosocomial infection.

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Children have a relatively underdeveloped immune system. This population is at high risk for nosocomial infection, especially when they need prolonged hospital stay, major surgery, or invasive procedures [2-4]. According to the surveillance data of the pediatric prevention network of the United States, the incidence of hospital-acquired infection in pediatric intensive care units (PICUs) was 13.9 per 1000 patient days [5]. The most common nosocomial infections were bacteremia, pneumonia and urinary tract infection.

The increasing resistance rate among common nosocomial pathogens is a major problem in Taiwan. Empiric antimicrobial agents are usually given for severe infections. A clinical guideline for empiric

antimicrobial agents in this situation has been available in Taiwan for the past 10 years. However, nosocomial pathogens can vary widely between different areas, hospitals, and types of ICU; drug-resistant pathogens can also vary. Close monitoring of bacteria and their resistance patterns can lead to selection of an appropriate antimicrobial agent [6,7].

Taichung Veterans General Hospital (TCVGH), Taichung, Taiwan, is a 1515-bed referral center in mid-Taiwan. Until 2003, the PICU had a capacity of 10 beds. A new hospital building was opened in June 2003, mainly for pediatric and obstetric-gynecology patients. The capacity of the PICU increased to 13 beds, which were designed, in part, for infection control and prevention. Severely ill medical and surgical pediatric patients, except for infants younger than 4 months, were candidates for admission. The PICU has an average annual admission rate of 851 patients and an average monthly occupation rate of 70.9%. Children with neuromuscular diseases or respiratory tract infections/sepsis, and those undergoing surgery for cardiovascular diseases comprise the usual patient population. There is 1 clinician responsible for infection control, and 2 infectious disease specialists are available for consultation and monthly microbiological survey and review.

The objective of this study was to elucidate the epidemiologic trends of clinical microbiologic isolates in a PICU at a single medical center and compare these with isolates throughout the hospital. A secondary endpoint was to clarify how a new hospital building for children influenced the incidence of nosocomial infection and the microbiologic pattern of the PICU since 2003.

Methods

This retrospective study reviewed the microbiological data of all clinical isolates obtained from the PICU from 2001 to 2006. Data for drug sensitivities and nosocomial infection rates were provided by the clinical microbiology laboratory and infection control committee. Nosocomial infections were defined as hospital acquired if they occurred ≥48 h after admission to the PICU. The nosocomial infection rate was calculated as the overall infection rate per 1000 patient days. The patients' demographics, onset of infection, site of infection, use of antimicrobial agents, associated risk factors (mechanical ventilation, central catheters, or urinary catheterization), and the microbiological findings were all recorded in a predefined format.

The antimicrobial susceptibility was determined by the disk diffusion method according to the latest Clinical Laboratory Standard Institute (CLSI) recommendations. The confirmation of extended-spectrum β-lactamase (ESBL)–producing *Escherichia coli* and *Klebsiella pneumoniae*, and vancomycin-resistant enterococci (VRE) were based on the guideline of the CLSI.

Results

1163 clinical microbiologic isolates from the PICU were reviewed from 2001 to 2006. The distribution of the pathogens is shown in Table 1. The frequency of Gram-positive and Gram-negative bacteria of all isolates were 30.4% (n = 354) and 56.2% (n = 654), respectively. *Staphylococcus aureus* was the most common Gram-positive pathogen in the PICU (n = 224; 19.3%), followed by *Enterococcus* spp. and *Staphylococcus epidermidis*. Among the Gram-negative bacteria, *Pseudomonas aeruginosa* (23.9%), *E. coli* (7.6%), *Acinetobacter baumannii* (6.5%), and *K. pneumoniae* (5.7%) were the most common isolates. *A. baumannii* was more commonly isolated during 2001 to 2003 than 2004 to 2006 (63 vs 13 isolates; $p < 0.0001$). In contrast, the isolation rate of *P. aeruginosa* among the Gram-negative organisms increased significantly after 2004 (31.6% vs 50.4%; $p = 0.0002$). There was a low incidence of *Stenotrophomonas maltophilia* in the PICU, except for a peak in 2005. *Candida albicans* was the most common fungal isolate (8.7%) in the PICU. No isolates of *Candida parapsilosis* were found after 2004, while *Candida glabrata* became more frequent after 2003.

Sputum was the most common source of these isolates (57.7%), followed by urine (16.8%) and blood (10.9%). *P. aeruginosa* and *S. aureus* were the 2 most common isolates from lower respiratory tract specimens, at 35.4% and 28.3%, respectively. *E. coli*, *Enterococcus* spp. and *Candida* spp. were the most frequently isolated organisms in urine. Gram-positive and Gram-negative bacteria were isolated from blood at rates of 33.9% and 44.3%, respectively.

There was a high rate of oxacillin-resistant *S. aureus* (ORSA), with a median incidence of 65.2%. The isolation rate of methicillin-resistant *S. aureus* (MRSA) was 85.9% in 2003, decreasing to 57.8% in 2005, and increasing to 90.8% in 2006. Six VRE were isolated in 2003; 4 were *Enterococcus faecium* and 2 were *Enterococcus fecalis*. The rate of oxacillin-resistant coagulase-negative staphylococci (CoNS) was 81.8%.

Table 1. Distribution of pathogens in the pediatric intensive care unit.

Organisms	Year						Total
	2001	2002	2003	2004	2005	2006	
Staphylococcus aureus	22	34	64	23	45	56	244
Staphylococcus epidermidis	2	2	4	3	2	1	14
Other *Staphylococcus* spp.	2	5	5	1	2	2	17
Enterococcus spp.	1	4	11	1	8	11	36
Other Gram-positive bacteria	1	8	7	15	0	12	43
Acinetobacter baumannii	10	15	38	3	6	4	76
Escherichia coli	9	5	29	18	18	10	89
Enterobacter spp.	3	8	11	2	4	3	31
Klebsiella pneumoniae	10	14	19	7	5	11	66
Moraxella catarrhalis	3	2	1	2	4	3	15
Proteus spp.	2	0	0	1	1	1	5
Pseudomonas aeruginosa	22	26	60	34	80	56	278
Stenotrophomonas maltophilia	0	7	1	3	29	3	43
Other Gram-negative bacteria	6	10	6	13	0	16	51
Candida albicans	5	31	24	8	25	8	101
Other *Candida* spp.	5	8	5	1	12	8	39
Other fungus	0	1	0	2	3	9	15
Total	103	180	285	137	244	214	1163

Among the Gram-negative organisms, most *E. coli* retained good susceptibility to the fourth-generation cephalosporins, aminoglycosides, fluoroquinolones, and carbapenem. For *K. pneumoniae*, most antimicrobial agents, including amikacin, ciprofloxacin, cefepime, and carbapenem, were active against more than 80% of these isolates. There were 4 ESBL-producing *E. coli* isolates identified since 2001, and ESBL-producing *K. pneumoniae* emerged in 2005. ESBL-producing *K. pneumoniae* accounted for 20% of *K. pneumoniae* isolates during 2005 and 2006. The susceptibility rates of *P. aeruginosa* to ceftazidime and cefepime were 87.8% and 89.5%, respectively, while the susceptibility rate to carbapenem decreased from 100% in 2001 to 2002 to 66% in 2005 to 2006. Carbapenem was effective against 93.7% of *A. baumannii* isolates, but only half of these isolates were sensitive to ampicillin/sulbactam.

The annual nosocomial rate is shown in Fig. 1. 162 nosocomial infections were documented in the PICU. The frequency and type of nosocomial infections are shown in Fig. 2. Urinary tract infection (30.2%) was the most common type of nosocomial infection, followed by bacteremia (26.5%), and lower respiratory tract infection (25.3%). Gram-positive bacteria represented 28.1% of isolates, and *S. aureus* (15.7%) was the most common pathogen. Gram-negative bacteria contributed to 58.6% of the nosocomial infection isolates, and the 3 most common pathogens were *P. aeruginosa* (25.0%), *E. coli* (15.1%), and *K. pneumoniae* (5.2%). The incidence of nosocomial fungal infection was 12.2%, most of which were due to *C. albicans*.

Discussion

The prevalence of hospital-acquired infection in the PICU has been reported to be approximately 13.9 to 15.0/1000 patient days [2,3,5,8]. Bacteremia, pneumonia/lower respiratory tract infection, and urinary tract infection are the most common infections. Bacteremia is the second most common nosocomial infection in a PICU at 28% to 43% [2,3,8]. A report from the European Study Group demonstrated that pneumonia was the most frequent type of nosocomial infection

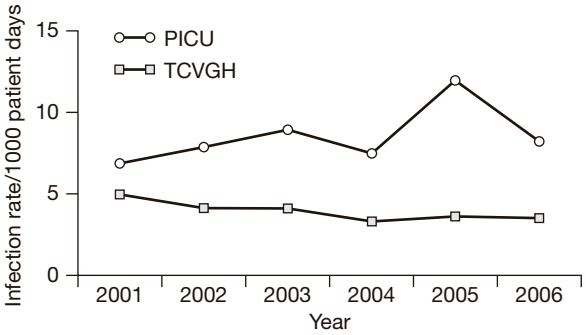

Fig. 1. Annual nosocomial infection rate in the pediatric intensive care unit (PICU) and the Taichung Veterans General Hospital (TCVGH).

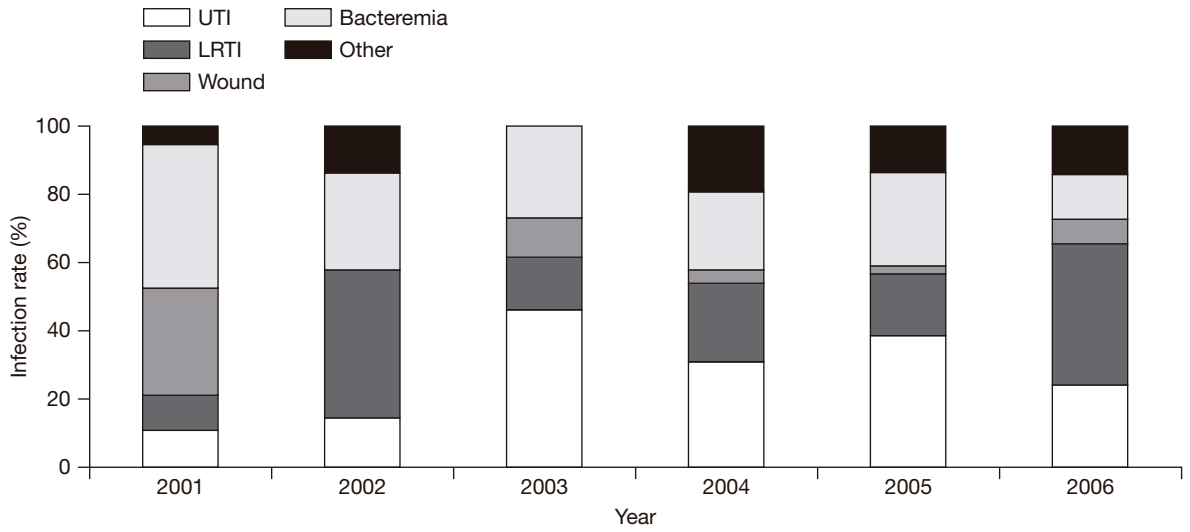

Fig. 2. Site of nosocomial infections in the pediatric intensive care unit by year.
Abbreviations: UTI = urinary tract infection; LRTI = lower respiratory tract infection.

in the PICU at 53% [5]. The average incidence of nosocomial infection at the PICU at the TCVGH was 8.23/1000 patient days, with urinary tract infection being the most common type at 30.2% since 2004. This result is similar to those from adult medical intensive care units. Prolonged use of Foley catheters in neurometabolic and post–cardiac surgery patients might be a possible reason.

The relationship of the ward environment and the rate of nosocomial infection has been well documented. Crowded wards with inadequate space between beds lead to a higher risk of contamination and an increased nosocomial infection rate [9]. However, the incidence of nosocomial infection in the PICU at TCVGH has not decreased since moving to the new building in 2003. Some possible reasons include more patients with neurodegenerative conditions who have a prolonged hospital stay, more patients with critical febrile neutropenia, and more surgical patients since 2004.

The incidence of Gram-positive cocci and Gram-negative bacilli represent 30% to 47% and 40% to 48% of nosocomial pathogens, respectively [5,10,11]. The data from the TCVGH are similar, both for type of pathogens and their resistance. This clinical evidence-based data may be used to initiate empiric antimicrobial therapy for patients suspected of having a nosocomial infection. CoNS has been documented to be a common cause of bacteremia in the PICU at 9.5% to 50.0% [3,5,8,10,12]. However, CoNS comprised only 13% of Gram-positive organisms isolated from blood in this study. The incidence of Gram-negative pathogens in blood was similar to that noted by Frank et al [12]. The methicillin resistance rate for CoNS has been reported to be 66% to 84% [5,10], compared with 81.8% in this study.

This study delineated the microbiological spectrum and antimicrobial resistance in the TCVGH PICU during the past 6 years. Gram-negative organisms contributed to more than half of the clinical isolates. *Enterobacteriaceae* and *P. aeruginosa* were the most common pathogens. *A. baumannii* was one of the major pathogens before 2003, although the incidence decreased significantly after 2004. *S. maltophilia* was not commonly isolated during 2002 to 2006 except for during an outbreak in 2005, when it caused 2 fatal nosocomial infections. A nosocomial survey and education on reinforcement of aseptic procedures, including hand washing and sterilization of medical devices, stopped the spread of the infection.

The severe acute respiratory syndrome epidemic and the opening of the new hospital in 2003 might have impacted on the true incidence of nosocomial infection. Comparison of the nosocomial infection rate focused on the incidence during 2001 to 2002 and 2004 to 2006. The nosocomial infection rate of the hospital was approximately 4.57 and 3.60/1000 patient days during 2001 to 2002 and 2004 to 2006, respectively. In the PICU, the average incidence of nosocomial infections was 7.38 and 9.26/1000 patient days in 2001 to 2002 and 2004 to 2006, respectively. The nosocomial infection rate was highest in 2005, which was related to the outbreak of *S. maltophilia*.

Multiple drug-resistant (MDR) bacteria continue to be of concern worldwide. MRSA has been reported

in 16% to 29% of pediatric nosocomial infections [5,10]. The incidence of MRSA was 65.2% in this study. According to Hsueh et al [13] and the Taiwan Surveillance of Antimicrobial Resistance [14], a rate of MRSA of 60% to 66% was found in 2000. The report of Styers et al demonstrated that the incidence of MRSA in the United States had increased to 55% in intensive care unit settings [15]. Community-associated MRSA has been reported to be one of the emerging pathogens of health care–associated infection [16,17]. However, in the TCVGH PICU, the incidence of MDR *S. aureus* remains high at 40.0% to 80.4%.

Among Gram-negative pathogens, MDR *A. baumannii*, MDR *P. aeruginosa*, MDR *S. maltophilia*, ESBL-producing *K. pneumoniae*, and ESBL-producing *E. coli* are of great concern. *Enterobacteriaceae*, mainly *E. coli* and *K. pneumoniae*, remained highly susceptible to most common third- and fourth-generation cephalosporins, aminoglycosides, fluoroquinolones, and carbapenem. However, the high rate of ESBL-producing *K. pneumoniae*, *E. coli*, and carbapenem-resistant *P. aeruginosa* steadily increased in the TCVGH (21.3%, 11.5%, and 10.0%, respectively). ESBL-producing *K. pneumoniae* has been increasing incrementally since 2005. The incidence of 20% is higher than previous reports from Taiwan (11% to 16%) [13,18-20]. The non-susceptibility rate of *P. aeruginosa* for ceftazidime in Taiwan is 10% to 22% [13,18,19,21]. The susceptibility rate of *P. aeruginosa* for carbapenem in the PICU was lower than those of previous reports in Taiwan at 66%. The correlation of increased use of carbapenem and other broad-spectrum antibiotics and the incidence of carbapenem-resistant *P. aeruginosa* strains has been described [22,23]. Possible reasons for the high rate of carbapenem-resistant *P. aeruginosa* in the PICU since 2003 include more critically ill patients admitted to the new PICU; more patients being referred from local hospitals; and the spread of resistant strains from adult wards. However, further evaluation of the reasons for the high rate of carbapenem resistance of *P. aeruginosa* in the PICU is warranted. *A. baumannii* was not a common isolate in the PICU, and there was no MDR *A. baumannii* during the surveillance period.

Candida spp. accounted for 13.3% of nosocomial infections and *C. albicans* was the most common cause. This finding is similar to other reports showing a rate of 7% to 17% [2,3,5]. *C. parapsilosis* was isolated in the PICU after 2004, although *C. glabrata* increased since 2004. In the Australian Candidemia Study from 2001 to 2004, non–*C. albicans* spp. caused 60.5% of community-acquired candidemia and 49.9% of hospital-acquired candidemia [24]. *C. glabrata* was the second commonest *Candida* spp. isolated from the bloodstream of adult patients. In contrast, *C. parapsilosis* was more frequently isolated from pediatric patients than from adults [25].

In conclusion, this study presents a general overview of the incidence and antimicrobial resistance of bacteria isolated from the TCVGH PICU from 2001 to 2006. The study also shows the emergence and rates of MDR organisms during these years, and emphasizes the importance of timely clinical and bacteriological monitoring among children in hospital, especially patients in a critical care situation. The high rate of MRSA, emergence of ESBL-producing *K. pneumoniae*, and high non-susceptibility rate of *P. aeruginosa* to carbapenems since 2004 are the major concerns for the PICU. The incidence of nosocomial infection was not reduced after moving to a new building in 2003. Therefore, environmental factors may not be a major contributing factor for hospital-acquired infection in the new PICU. Frequent hand washing and good aseptic technique should be reinforced for all health care personnel. Excellent antibiotic policy and infection control implementation are important priorities for the PICU.

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