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Original Article

Changing Epidemiology of Nosocomial Bloodstream Infections in 11 Teaching Hospitals in Taiwan Between 1993 and 2006

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BACKGROUND/PURPOSE: Healthcare-associated infections, formerly known as nosocomial infections, are one of the most important issues in current practice. Understanding trends in overall infection rates, as well as their incidence and proportion among different causative organisms, can help us to better define our infection control methods and therapy goals. To understand the changing epidemiology of nosocomial bloodstream infections (BSI) in Taiwan, we retrospectively collected nosocomial infection data from 11 hospitals and examined the trends and changing patterns of nosocomial BSI.

METHODS: Eleven major teaching hospitals in Taiwan were invited to participate in the study. The overall density of nosocomial infections and major BSI-causing organisms, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Candida* species, were collected. The distribution of the different *Candida* species was also recorded. Background parameters from the 11 hospitals, including the size of the hospital, hospital capacity, the number of blood stream infection events, and average length of stay, were also recorded.

RESULTS: The incidence of nosocomial BSI ranged 0.23–2.56 per 1,000 patient-days, which accounted for 8–43% of all nosocomial infections. The most common causative organism of nosocomial bacteremia was *S. aureus*, ranging 0.88–0.01 per 1,000 patient-days. Overall, the incidence of *S. aureus* bacteremia has decreased over the last 13 years, but this difference was not statistically significant ($p=0.053$). The rate of *Candida* fungemia ($p<0.01$) and *A. baumannii* ($p=0.03$) bacteremia increased significantly. *C. albicans* accounted for most cases of nosocomial fungemia, ranging from 40% to 80%, followed by *Candida tropicalis*, *Candida parapsilosis* and *Candida glabrata*. However, the incidence varied significantly from hospital to hospital, and the highest incidence was observed in a cancer center.

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CONCLUSION: The overall incidence rate of *S. aureus* bacteremia in the 11 major hospitals studied had decreased over the last decade, though the difference was not statistically significant. However, the rate of *Candida* fungemia and *A. baumannii* bacteremia had increased significantly.

KEYWORDS: bacteremia, *Candida albicans*, fungemia, nosocomial, Taiwan

Introduction

Healthcare-associated infections (HAI) are the most common complications in hospitalized patients and can result in increased mortality, length of stay and cost.[1] HAI, mainly comprising ventilator-associated pneumonia, catheter-related urinary tract infections, bloodstream infections (BSI) and surgical site infections, affect between 5–10% of patients admitted to acute care hospitals.[1] Thus, regular surveillance of HAI and the establishment of appropriate infection control policies should be given high priority in modern medical care. Several infection control surveillance programs had been set up around the world, e.g. the National Healthcare Safety Network (NHSN) in 2005[2–4] and the former National Nosocomial Infections Surveillance System (NNIS) in 1970 in the Unites States;[5,6] the International Nosocomial Infection Control Consortium in developing countries in Latin America, Asia, Africa and Europe;[7–9] the Infection Surveillance and Control Programs in Korea in 1991;[10,11] the German national NI Surveillance system (Krankenhaus Infektions Surveillance System) in Germany;[12] and similar programs in France and England.[13–15]

Regular surveillance of nosocomial infections can help healthcare workers to monitor the incidence of nosocomial infections and the common causative organisms, which can guide infection control measurement and the appropriate use of antimicrobial agents. In particular, nosocomial BSI, including bacteremia and fungemia, are associated with high mortality and morbidity despite antibiotic treatment. However, accurate epidemiological information regarding nosocomial BSI in Taiwan is scarce.[16,17] The only report of BSI at a single university hospital collected from 1996 to 2003 showed a predominance of aerobic Gram-negative bacilli.[17] Understanding trends in overall infection rates and the incidence and proportion of different causative organisms can help us to guide the direction of infection control. To understand the changing epidemiology of nosocomial BSI in Taiwan, we retrospectively collected the nosocomial infection data from 11 major hospitals and examined the trends and changing patterns of nosocomial BSI from 1993 to 2006.

Methods

Population and hospitals

Eleven major hospitals in Taiwan were included in the study. The number of discharged patients and hospitalization patient-days, episodes of nosocomial infection and BSI, and average length of hospital stay are shown in Table. Due to the differing availability of complete infection surveillance data from the 11 hospitals, we recorded data regarding the rate of BSI per 1,000 patient-days from 1999 to 2006 in Hospital A, from 1993 to 2006 in Hospital B, from 2000 to 2006 in Hospital C, from 2002 to 2006 in Hospital D, from 1998 to 2006 in Hospital E, from 2001 to 2006 in Hospital F, from 1997 to 2006 in Hospital G, from 1994 to 2006 in Hospital H, from 1993 to 2005 in Hospital I, from 1994 to 2006 in Hospital J, and from 2002 to 2006 in Hospital K. All 11 hospitals are teaching hospitals. Hospitals H and I are located in southern Taiwan. Hospital J is located in eastern Taiwan. The other hospitals are located in northern Taiwan. All hospitals are general hospitals except Hospital C, which is a cancer center that serves mainly hemato-oncological patients. Seven of the 11 hospitals are tertiary referral medical centers.

Definition of BSI

The HAI and BSI were defined according to the surveillance guidelines published by the Center of Disease Control (CDC) in Taiwan, which were modified from the NHSN documents from the CDC in the United States. The definition of BSI included laboratory-confirmed BSI and clinical sepsis. Laboratory-confirmed BSI should

Table. Density of incidence of healthcare-associated infections and healthcare-associated bloodstream infections in 11 hospitals

Hospital	Year	Hospital capacity	Overall HAI		Healthcare-associated BSI		Average LOS
		Patient-admission day (person-days)	Overall HAI episodes	HAI episodes/ 1,000 patient-days	Healthcare-associated BSI episodes	BSI episodes/ 1,000 patient-days	
A	1999	566,165	2,785	4.90	949	1.68	8.88
	2000	585,979	3,337	5.70	1,311	2.24	8.44
	2001	592,484	3,538	5.97	1,352	2.30	8.21
	2002	631,933	3,584	5.67	1,421	2.25	8.08
	2003	591,217	3,669	6.21	1,517	2.57	8.45
	2004	678,838	4,150	6.11	1,649	2.43	8.40
	2005	684,984	4,128	6.03	1,567	2.29	7.91
	2006	668,355	3,920	5.90	1,507	2.25	7.56
B	1993	191,895	574	2.99	139	0.72	8.74
	1994	221,998	789	3.60	232	1.05	8.03
	1995	228,453	947	4.15	246	1.08	7.30
	1996	220,273	967	4.39	304	1.40	6.98
	1997	219,253	868	3.96	280	1.28	6.61
	1998	217,404	904	4.16	252	1.16	6.75
	1999	217,478	917	4.22	258	1.19	6.78
	2000	221,435	906	4.09	264	1.19	6.86
	2001	211,055	834	3.95	247	1.17	7.06
	2002	211,725	897	4.24	276	1.30	6.96
	2003	198,643	861	4.33	284	1.43	6.63
	2004	211,553	883	4.17	273	1.29	7.16
	2005	207,639	872	4.20	282	1.36	7.37
	2006	209,232	949	4.50	289	1.38	7.22
C	2000	51,999	196	3.77	85	1.63	5.73
	2001	57,045	204	3.58	84	1.47	5.40
	2002	57,622	247	4.29	87	1.51	5.00
	2003	58,675	250	4.26	69	1.18	4.92
	2004	60,915	279	4.58	83	1.36	4.55
	2005	57,589	281	4.88	63	1.09	4.16
	2006	56,919	272	4.78	66	1.16	4.24
D	2002	184,026	609	3.31	144	0.78	7.20
	2003	246,510	987	4.00	194	0.79	8.13
	2004	281,234	1,085	3.86	219	0.78	7.93
	2005	285,011	1,046	3.67	337	1.18	7.66
	2006	282,300	917	3.25	324	1.15	7.47
E	1998	87,624	338	3.86	104	1.19	7.19
	1999	118,842	471	3.96	104	0.88	6.68
	2000	122,259	337	2.76	91	0.74	6.10
	2001	125,490	345	2.75	91	0.73	6.10
	2002	125,473	463	4.00	124	0.99	6.28
	2003	100,296	289	2.88	48	0.48	4.10
	2004	115,225	375	3.25	67	0.58	6.13
	2005	110,711	404	3.65	82	0.74	6.04
	2006	106,506	351	3.30	57	0.54	6.17

Table. *(Contd)*

Hospital	Year	Hospital capacity	Overall HAI		Healthcare-associated BSI		Average LOS
		Patient-admission day (person-days)	Overall HAI episodes	HAI episodes/ 1,000 patient-days	Healthcare-associated BSI episodes	BSI episodes/ 1,000 patient-days	
F	2001	399,956	1,417	3.54	371	0.93	8.48
	2002	430,514	1,545	3.60	418	0.97	7.64
	2003	376,682	1,423	3.80	405	1.08	7.32
	2004	440,305	1,605	3.65	433	0.98	7.06
	2005	448,583	1,617	3.60	414	0.92	7.56
	2006	455,849	1,706	3.74	505	1.11	7.55
G	1997	772,761	3,099	4.00	707	0.92	11.00
	1998	784,979	2,895	3.69	690	0.88	10.60
	1999	796,251	3,130	3.93	738	0.93	10.00
	2000	804,864	3,074	3.82	772	0.96	9.62
	2001	789,113	2,877	3.65	722	0.92	9.30
	2002	787,288	2,837	3.60	670	0.85	9.00
	2003	723,822	2,886	4.00	812	1.12	9.67
	2004	805,937	3,054	3.79	860	1.10	9.61
	2005	798,127	3,101	3.89	965	1.21	9.00
	2006	796,519	2,969	3.73	816	1.02	9.30
H	1994	269,793	1,050	3.89	263	0.98	9.10
	1995	298,444	1,136	3.81	255	0.85	8.83
	1996	320,014	1,095	3.42	265	0.83	9.81
	1997	325,258	885	2.72	207	0.64	9.53
	1998	342,324	823	2.40	198	0.58	8.58
	1999	353,131	876	2.48	236	0.67	8.40
	2000	354,378	670	1.89	212	0.60	8.29
	2001	358,734	991	2.76	280	0.78	8.03
	2002	364,431	1,505	4.13	500	1.37	7.93
	2003	316,993	1,417	4.47	464	1.46	7.32
	2004	353,715	1,382	3.91	461	1.30	7.88
	2005	352,822	1,932	5.48	494	1.40	7.52
	2006	346,245	1,590	4.59	436	1.26	8.00
I	1992	189,170	723	3.82	219	1.16	9.43
	1993	197,879	839	4.24	288	1.46	9.07
	1994	207,259	912	4.40	369	1.78	8.66
	1995	212,477	917	4.32	379	1.78	9.27
	1996	214,207	934	4.4	331	1.55	9.23
	1997	246,626	967	3.92	347	1.41	10.40
	1998	263,304	1,032	3.92	379	1.44	10.20
	1999	268,341	1,279	4.77	458	1.71	7.70
	2000	282,926	1,317	4.65	486	1.72	7.61
	2001	278,558	1,416	5.08	531	1.91	7.31
	2002	291,660	1,370	4.70	509	1.75	7.10

(Contd)

Table. *(Contd)*

Hospital	Year	Hospital capacity	Overall HAI		Healthcare-associated BSI		Average LOS
		Patient-admission day (person-days)	Overall HAI episodes	HAI episodes/ 1,000 patient-days	Healthcare-associated BSI episodes	BSI episodes/ 1,000 patient-days	
	2003	278,339	1,273	4.57	601	2.16	7.12
	2004	295,228	933	3.16	433	1.50	7.25
	2005	292,128	874	2.99	508	1.74	6.75
J	1994	265,091	878	3.31	121	0.46	11.00
	1995	241,894	945	3.91	125	0.52	9.45
	1996	252,676	1,038	4.11	181	0.72	9.06
	1997	247,662	931	3.76	153	0.62	8.57
	1998	258,754	1,001	3.87	167	0.65	8.17
	1999	270,649	951	3.51	150	0.55	8.00
	2000	263,475	947	3.59	165	0.63	8.06
	2001	246,069	890	3.62	189	0.77	7.48
	2002	271,938	971	3.57	199	0.73	7.51
	2003	254,316	946	3.72	267	1.05	7.44
	2004	304,831	971	3.19	313	1.03	8.47
	2005	267,608	888	3.32	287	1.07	7.64
	2006	271,965	964	3.54	319	1.17	7.19
K	2002	146,872	742	5.05	107	0.73	6.17
	2003	129,104	382	2.96	30	0.23	6.31
	2004	158,140	533	3.37	70	0.44	6.32
	2005	134,420	416	3.09	47	0.35	6.54
	2006	135,903	733	5.39	86	0.63	6.45

HAI=Healthcare-associated infections; BSI=bloodstream infections; LOS=length of stay.

meet at least one of the following criteria: (1) the patient has a recognized pathogen cultured from at least one set of blood cultures, which was not related to an infection at another site; (2) the patient has at least one of the following signs or symptoms: fever (>38°C), chills, or hypotension (systolic blood pressure >90 mmHg), and a common skin contaminant [e.g. diphtheroids (*Corynebacterium* spp.), *Bacillus* spp. (not *B. anthracis*), *Propionbacterium* spp., coagulase-negative *staphylococci* (including *S. epidermidis*), viridans group *Streptococci, Aerococcus* spp., or *Micrococcus* spp.)] is cultured from two or more blood cultures drawn on separate occasions; (3) a patient less than 1 year of age has at least one of the following signs or symptoms: fever (anal body temperature >38°C), hypothermia (anal temperature <36°C), apnea, and bradycardia and the signs or symptoms and positive laboratory results are not related to an infection at another site. A common skin contaminant is cultured from two or more blood cultures drawn on separate occasions.

Data collection

Data obtained from the 11 hospitals included in this study covered variable time periods. HAI were diagnosed according to the aforementioned definitions and the United States CDC guidelines. Data were collected by infection control nurses in each hospital. A structured form was sent to the hospitals to record information regarding overall patient discharge numbers, total patient-hospitalization days during the study period, the overall number of HAI and BSIs, and the number of specific pathogens (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Candida* species). For the *Candida* spp., the incidence

and relative percentages of the different species were also recorded. Data were analyzed using the χ^2 test and a p value of <0.05 indicated statistical significance.

Results

More than 20,000 patients per year were discharged from each individual hospital, except for Hospitals C and E. The other nine hospitals had one year admissions ranging from 20,061 (Hospital I, 1992) to 88,444 (Hospital A, 2006). The average number of patient discharges during the study period were as follows: 76,173.9 for Hospital A; 29,931.8 for Hospital B; 11,963 for Hospital C; 33,296.4 for Hospital D; 18,815 for Hospital E; 56,168.5 for Hospital F; 80,889.9 for Hospital G; 40,308.2 for Hospital H; 31,123.4 for Hospital I; 32,010.3 for Hospital J; and 22,185.2 for Hospital K. The average length of stay ranged from 4.1 days (Hospital E, 2003) to 11.0 days (Hospital J, 1994), with a mean value of 8.1 days. The patient-admission days ranged from 51,999 patient-days (Hospital C, 2000) to 805,937 patient-days (Hospital G, 2004). In 1992, only one hospital (Hospital I) reported its overall HAI rates and BSI rates. Thus, it was excluded from further analysis due to possible bias. During the 14-year study period, a total of 4,080,698 discharged patients were recorded, and the patient-admission days numbered 33,087,563.

As shown in Table, the overall number of healthcare-associated episodes varied between different hospitals and different time periods. The overall number of HAI was 135,525 from 1993 to 2006, and the rate of HAI per 100 discharged patients was 3.32. The average number of HAI per 1,000 patient-days was 4.10. However, the annual density of HAI (HAI per 1,000 patient-days) ranged from as low as 1.89 per 1,000 patient-days (Hospital H, 2000) to as high as 6.21 per 1,000 patient-days (Hospital A, 2003). During the 14-year study period, the density of HAI ranged from 3 to 5 per 1,000 patient-days in most of the hospitals studied (Figure 1). Data recording the incidence of HAI was available from 1997 for Hospital A, which ranked highest throughout the study period.

Among all the HAI, 40,805 episodes of BSI were recorded according the CDC criteria. The number of BSI per 100 discharged patients was 1.0, while the BSI per 1,000 patient-days was 1.23. The annual density of BSI incidence varied from 0.23 to 2.56 per 1,000 patient-days, but the incidence in most hospitals were less than 2 per 1,000 patient-days (except in Hospital A and Hospital C). BSI accounted for 8–43% of all HAI from 1993 to 2006.

Of the organisms that caused healthcare-associated BSI, *S. aureus* was the most common. The annual incidence was 0.01 BSI per 1,000 patient-days to 0.88 BSI per 1,000 patient-days (Figure 2A). The annual incidence of *S. aureus* BSI in Hospital C was the highest, ranging from 0.46 to 0.88 per 1,000 patient-days. The annual incidence of *S. aureus* BSI was less than 0.4 per 1,000 patient-days in all other hospitals (except Hospital A during 2000). Regarding *P. aeruginosa* BSI, the incidence was lower than that of *S. aureus* (<0.2 per 1,000 patient-days; except for Hospital C). The annual incidence of *P. aeruginosa* BSI in the other hospitals remained stationary in 1993–2006 (Figure 2B). The incidence of *A. baumannii* BSI ranged between 0–0.46 per 1,000 patient-days. Most hospitals, except Hospitals A and C, had an *A. baumannii* BSI incidence of less than 0.25 per 1,000 patient-days (Figure 2C).

The overall results for *S. aureus*, *P. aeruginosa*, *A. baumannii*, and *Candida* spp.-related BSI are shown in Figure 3. The trends were analyzed from 1999 to 2006. The incidence of *S. aureus* bacteremia decreased, but the p value was 0.053, which barely reached significance. The incidence of *Candida* spp.- ($p<0.001$) and *A. baumannii*-($p=0.030$) related BSI increased significantly, whereas the incidence of *P. aeruginosa* BSI was unchanged ($p=0.431$).

Of the different *Candida* species causing healthcare-associated BSI, *Candida albicans* was the most predominant (Figure 4). The incidence of *Candida*-related BSI varied widely between the hospitals, and *C. albicans* accounted for 50–80% of all *Candida* infections. The percentage of *C. albicans*-related BSI was unchanged during the study period. *Candida tropicalis*, *Candida parapsilosis*, and *C. glabrata* were the second, third, and fourth most commonly isolated *Candida* spp. in healthcare-associated BSI (Figure 4).

Discussion

The characteristics of the nosocomial infections varied from hospital to hospital and from region to region. Thus, regular surveillance is important to understand the pathogens causing nosocomial infections. National surveillance programs were initiated in many countries by the International Nosocomial Infection Control Consortium,[9]

including the Unites States,[3,5,18] Germany,[12,19] Spain,[20] England,[14] and France,[13] as well as in some developing countries in Latin America, Europe, Asia, and Africa and many other countries. The CDC in Taiwan also established guidelines for the surveillance of HAI, which were modified from the US CDC guidelines. However, few published studies regarding trends in healthcare-associated BSI in Taiwan are available.

Chang et al reported epidemiological surveillance results for nosocomial infections from a single hospital in Taiwan in 1990.[16] Surgical wound infections were the most common HAI, while BSI ranked fourth. The most frequently isolated pathogen was *Escherichia coli* in the early years but shifted to *P. aeruginosa* in later years. Gram-negative aerobic pathogens were the most frequently isolated organisms from 1981 to 1989. An increased incidence of fungal infection was also mentioned, which increased from 1.8% to 7.7% of all HAI. However, this report did not specify the relative proportion of causative organisms or the trends in healthcare-associated BSI. In 2002, Tseng et al investigated the nosocomial BSI in a single neonatal intensive care unit (ICU) in a university

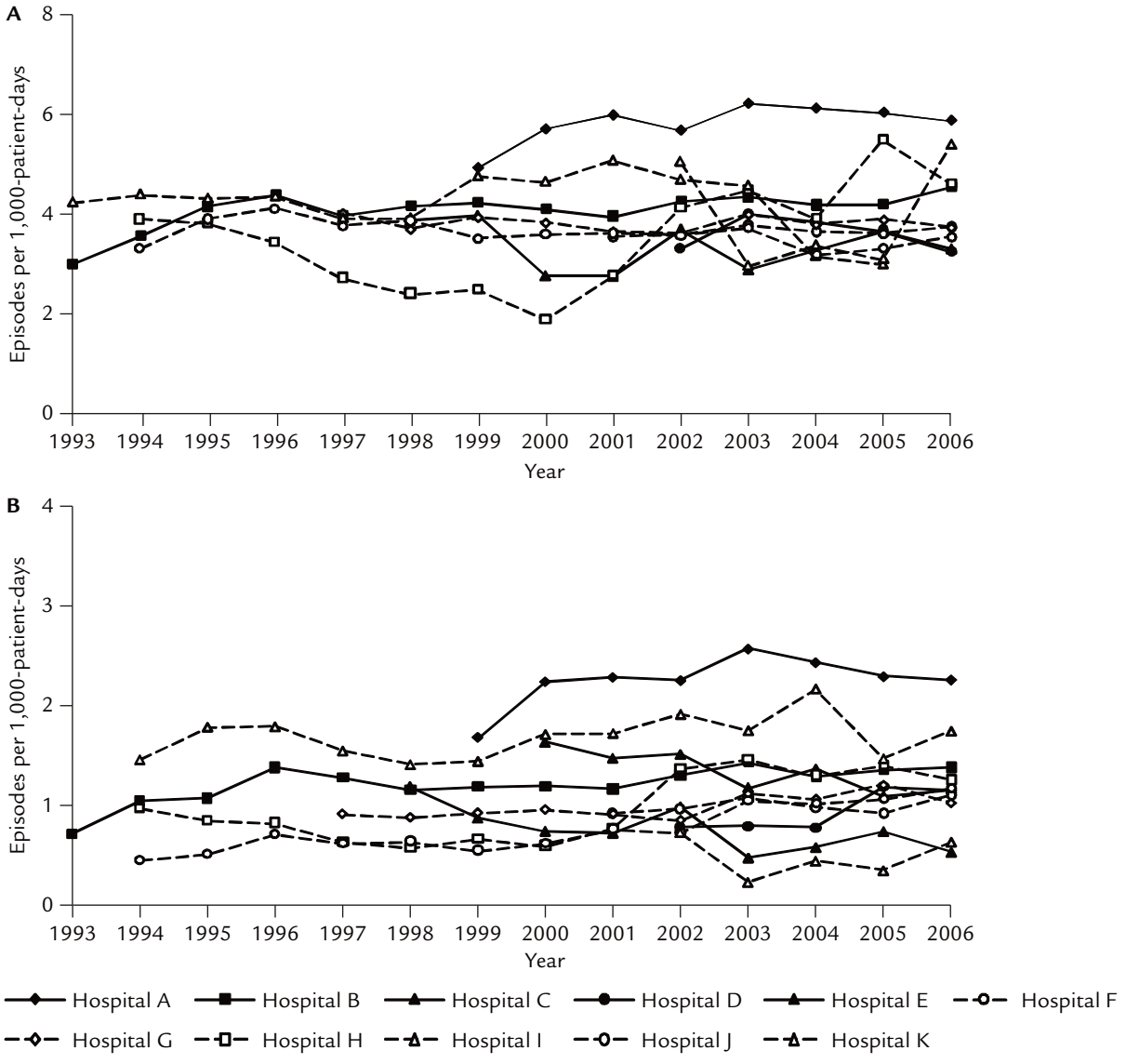

Figure 1. Density of (A) overall healthcare-associated infections and (B) bloodstream infections from 1993 to 2006.

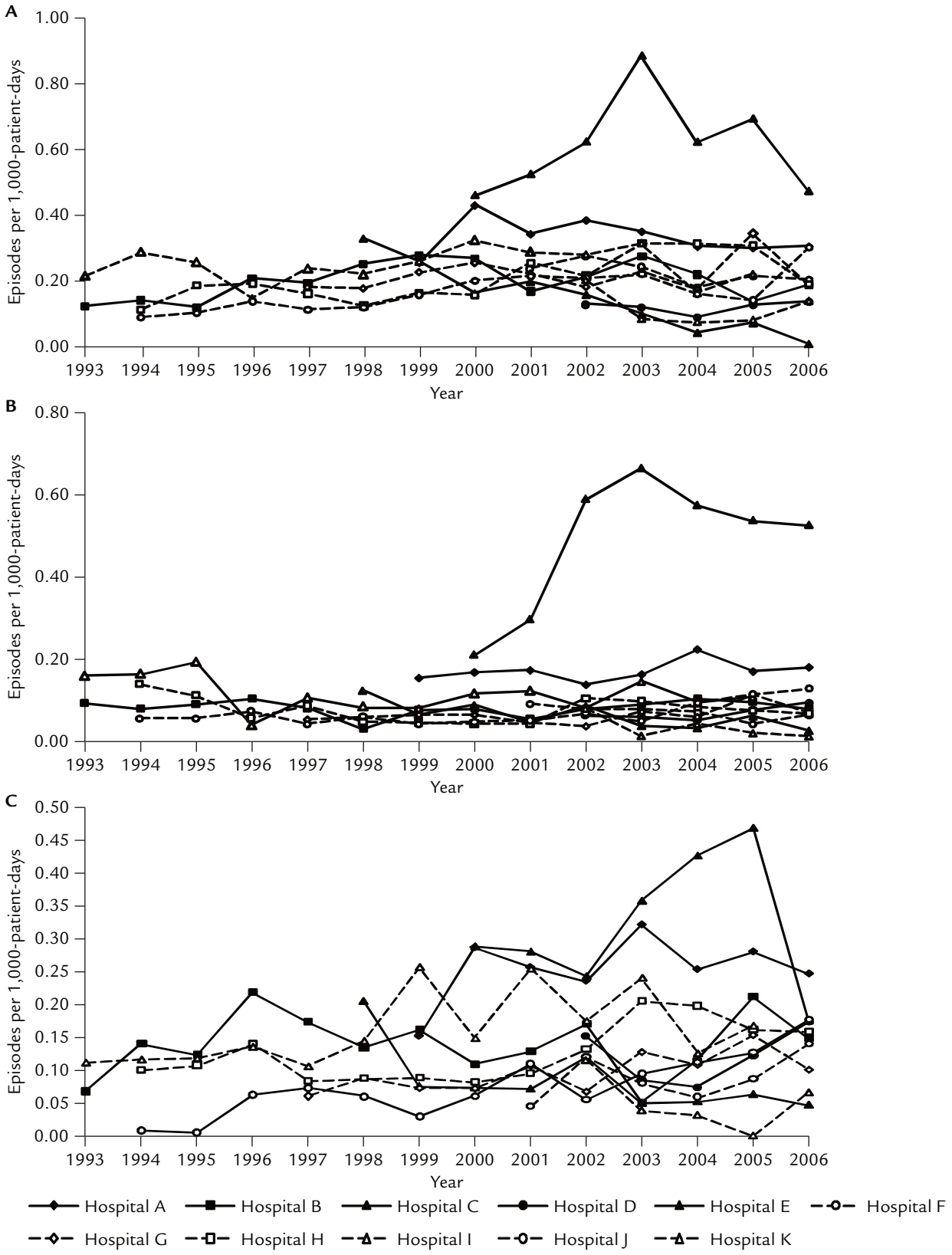

Figure 2. Trends of specific pathogens among 11 hospitals in 1993–2006. (A) *Staphylococcus aureus;* (B) *Pseudomonas aeruginosa;* and (C) *Acinetobacter baumannii*.

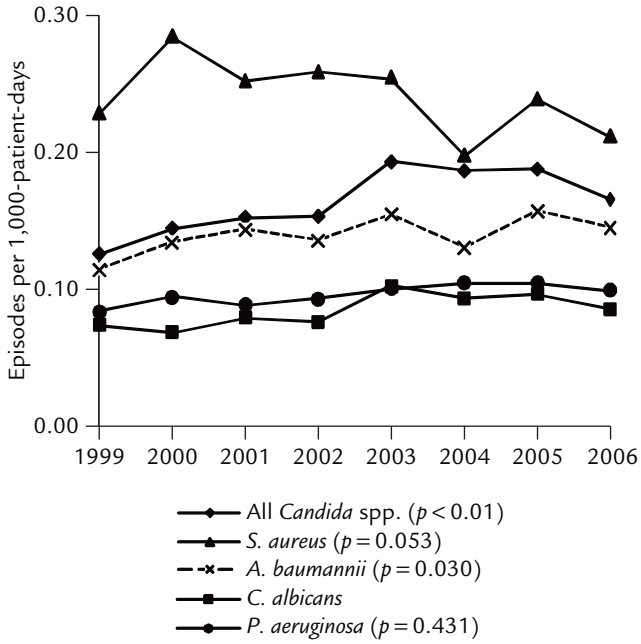

Figure 3. Cumulative results of healthcare-associated bloodstream infections with all *Candida* spp., *Candida albicans*, *S. aureus*, *P. aeruginosa*, and *A. Baumannii*.

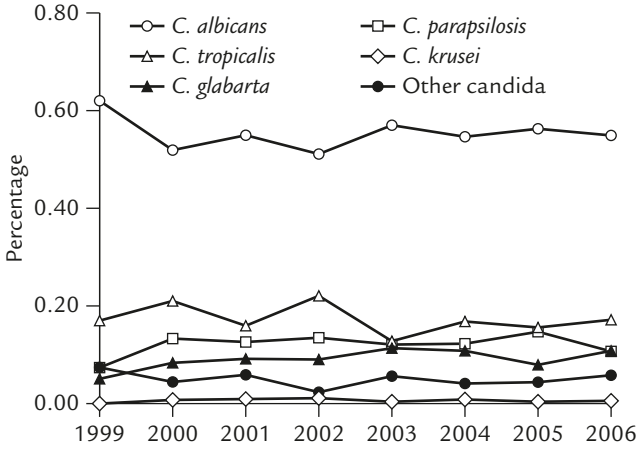

Figure 4. The relative distribution of different *Candida* species among all *Candida* associated bloodstream infections.

hospital.[21] The overall infection rate was 4.4 episodes per 1,000 patient-days. In agreement with our results, the most common causative pathogen was *S. aureus*, which accounted for 18.5% of all BSI. *E. coli* and *P. aeruginosa* accounted for only 9.6% and 8.1% of all BSIs, respectively, and ranked fourth and fifth. Different hospital settings, study periods, and target populations may explain the differences between the two studies. Another university hospital reported their experience of nosocomial BSIs between 1996–2003.[17] The overall incidence was 1.79 per 1,000 patient-days. The five leading causative organisms were coagulase-negative *Staphylococci* (16%), *S. aureus* (13%), *Candida* spp. (10%), *A. baumannii* (8%) and *E. coli* (8%). Gram-negative bacilli were the predominant pathogens related to healthcare-associated BSI during the 8-year study period. Because of the multi-center design, not all bacterial species were reported in this study. Thus, the percentage of each causative organism cannot be calculated exactly. Coagulase-negative *Staphylococci* were the most predominant strains in Hospital I during the study period, while *S. aureus* predominated in most other hospitals during the study period.

The overall incidence of BSI was 1.23 per 1,000 patient-days in our study, which was similar to the incidence of 1.79 per 1,000 patient-days reported by Wu at al[17] and lower than the 4.4 per 1,000 patient days by Tseng et al.[21] Our study subjects comprised all inpatients hospitalized in general wards and ICU, which may explain the difference. The higher rate of healthcare-associated BSI in neonatal ICUs is not surprising. Another surveillance of nosocomial infections in a neonatal ICU in Taiwan disclosed 22 BSI and 38 clinical sepsis cases over 6,448 patient-days (8.72 episodes per 1,000 patient days).[22] A Dutch neonatal ICU surveillance report showed even higher results (14.9 episodes per 1,000 patient-days).[23] Thus, our results were not limited to a single unit in a hospital but comprised a general surveillance of all inpatient wards and ICUs. Wu et al[17] also disclosed similar results to those of our study. We expanded the surveillance period and invited 11 hospitals from different regions to participate, and so our results are more representative of the current conditions in Taiwan.

All 11 hospitals in our study are teaching hospitals with different sized ICUs. Higher catheter utilization rates and HAI rates had been observed in the combined medical-surgical ICUs in teaching hospitals as compared with non-teaching hospitals.[24] Catheter utilization itself is also an important risk factor for HAI.[25] Thus, the observed incidence may be an overestimate if applied to non-teaching hospitals. The NNIS[5] and the NHSN[3,4] in the USA also differentiate medical-surgical ICUs in major teaching hospital from all other hospitals. Higher rates of catheter utilization and central line-associated BSI were observed in the medical-surgical ICUs of major teaching hospitals than in other hospitals. The NHSN surveillance

report published a summary of data obtained from June 2007 to November 2008. The surveillance data from 2006 was also included in the latter report. Summing up all the data from all ICUs and wards obtained during 2006, a total of 2,681 cases of central line-associated BSI were recorded during 1,912,392 patient-days (1.40 per 1,000 patient-days).[4] In another, 6,059 episodes were noted, while the summation of patient-days from all ICUs and wards was 6,161,064 (0.98 episodes per 1,000 patient-days).[3] This rapid decrease in the overall rates may not reflect a true trend of decreasing BSI rates, but a reflection of the different compositions of the reporting hospitals. A 3.5-fold increase in mixed medical-surgical ICUs in non-major teaching hospitals was noted, which were associated with a lower risk of HAI. In our study, we included all cases of nosocomial BSI rather than central catheter-associated BSI only. The incidence in our study was 1.23 per 1,000 patient-days, which was comparable to the incidence of 1.40 reported in the 2007 NHSN report, and slightly higher than the result of 0.98 published in the 2008 report. Since we did not record the usage of central catheters, or device-days, in our study, we cannot evaluate the rate of central line-associated BSI exactly, but it is expected to be lower than the overall rate of healthcare-associated BSI because not every inpatient requires a central line. Higher rates of BSI were reported by an NNIS surveillance report and the NICC,[5,7,8] which was conducted in 98 ICUs in 18 developing countries on four continents; though both reported catheter-associated BSI from ICUs only. The incidence in developing countries was three to five times higher than that reported by the NNIS. The lack of legal frameworks, limited national infection control guidelines, poor hand hygiene, low nurse-to-patient ratios and overcrowded units may all contribute to the high HAI rates in developing countries.[26–28] The NNIS report issued in October 2004 was based on data collected from January 1992 through June 2004, similar to our report. However, the report primarily focused on central line-associated BSI rates (events per 1,000 central line-days) in different types of ICU. Thus, we cannot compare our BSI rate with the NNIS 2004 report directly.

Wisplinghoff et al reported the result of the Surveillance and Control of Pathogens of Epidemiological Importance, a nationwide surveillance in the USA, and analyzed 24,179 cases of nosocomial BSI.[18] The incidence was 60 cases per 10,000 hospital admissions, without any significant changes between 1995–2002, and the results were not limited to patients in ICUs or central line-associated infections. In our study, a total of 81,610 BSI were noted in 8,161,396 discharged patients, which translates into 10.0 episodes per 1,000 patients, slightly higher than the results from the Surveillance and Control of Pathogens of Epidemiological Importance study. A longer period of continuous follow-up and the inclusion of non-teaching hospitals may be needed in further studies.

Of the 11 hospitals enrolled in our study, Hospital A had the highest rate of BSI (2.25 episodes per 1,000 patient-days), followed by Hospital I (1.66 episodes per 1,000 patient-days) and Hospital C (1.34 episodes per 1,000 patient-days). Hospital A and Hospital I are both major teaching hospitals according to the NHSN definition,[3] while Hospital C is a hemato-oncologic cancer center. Higher device-utilization rates and higher infection rates had been demonstrated in major teaching hospitals.[24] Also, both Hospital A and Hospital I are university hospitals, so more staff rotations, clerkships, and internship training is expected. A previous study in a Spanish surgical ICU demonstrated unusual high rates of ventilator-associated pneumonia in February and BSI in May, which may relate to staff vacations and rotations.[29] Other studies also show an increased risk of 2.75-fold when patients were cared by substitute staff during vacations.[30,31] The price of staff training and the risk of healthcare infections should be balanced when considering the issue of patient safety. Both hospitals are tertiary referral centers, so increased patient disease severity may have partially contributed to this. The average length of stay in Hospital A and Hospital I was 8.24 days and 8.36 days, respectively, while the average length of stay in our study was 8.1 days. However, both Hospital G (9.75 days) and Hospital H (8.40 days) had higher inpatient days but lower BSI rates. Further analysis of patient severity such as APACHE II scores, staff rotation rates, and catheter utilization rates should be considered in future studies to clarify this issue. The higher BSI rate in Hospital C is not surprising, since hematology/oncology wards and bone marrow transplant units are associated with a higher risk of nosocomial infections.[3] A total of 110 central line-associated BSI developed over 42,459 patient-days in bone marrow transplant units (2.59 episodes per 1,000

patient-days), while another 44 episodes during 69,487 patient-days were recorded in hematology/oncology wards (0.63 episodes per 1,000 patient-days) between 2006–2007 as reported by the NHSN.[3]

A recent report by Burton et al showed a decreasing trend in the incidence of MRSA central line-associated BSI in ICUs in the United States.[32] In all the evaluated ICUs, a significant decline was observed between 2001–2007, except in pediatric units. Both the overall proportion of *S. aureus* related central line BSI and the overall incidence of MRSA showed similar trends. Further analysis showed that the trends for MRSA central line-associated BSI increased until 2001, but declined significantly thereafter. The overall rate of MSSA central line-associated BSI steadily decreased from 1997 to 2007. In Taiwan, the incidence of *S. aureus*-related bacteremia reached a plateau in 2000 and decreased thereafter (Figure 3). Due to the dynamic nature of the NNIS/NHSN reports, less than 6% of ICUs participated during the 11-year-study by Burton et al.[33] Between 1999 and 2006, the results of our study showed a decreasing trend in *S. aureus* BSI in all inpatients, though the *p* value was not significant. No studies regarding the long-term trends in the incidence of nosocomial *S. aureus* bacteremia have been published recently. Although our observations support the notion that the incidence of healthcare-associated *S. aureus* BSI is decreasing, this should be interpreted cautiously since the disease burden of MRSA remains high.[34,35] Further analysis of data from different regions, different ICU types or wards, and the relationship between current infection control measurements is needed. Also, a longer follow-up period and a higher number of enrolled institutes may be needed to determine if the incidence of *S. aureus* bacteremia is really decreasing.

Compared with *S. aureus* BSI, the overall incidence of Candidemia is rising. However, the incidence varied from hospital to hospital. The highest incidence was observed in hemato-oncologic centers, which might reflect their patient characteristics and more prominent catheter use. A prospective surveillance conducted in 11 medical centers in Brazil from March 2003 to December 2004 reported that the overall incidence of *Candida* spp.-related and *C. albicans*-related fungemia was 0.37 and 0.15 episodes per 1,000 patient-days, respectively.[36] The incidence in our study was 0.15 and 0.10 per 1,000 patient-days, respectively. If we calculated the incidence rate per every 1,000 discharged patients, it would be 1.20 episodes per 1,000. Hospital C reported the highest rates of fungal-related BSI, reaching a peak of 0.61/1,000 patient-days in 2003 and 2006, which may be related to its patient characteristics. Previous surveillance in Taiwan disclosed a high incidence rate of 2.88 cases per 1,000 discharges at a single university hospital,[37] which was higher than other reports worldwide (e.g. 0.28–0.96 per 1,000 admissions in the United States,[18,38–40] 0.45 per 1,000 admissions in Canada,[41] 0.20–0.38 per 1,000 admissions in Europe,[42] and 0.76–0.81 per 1,000 admissions in Spain[43,44]). The relatively high incidence of nosocomial fungal BSI may be multi-factorial. First, the predominance of teaching hospitals in our survey may be an origin of bias, due to higher disease severity and longer periods of hospitalization. Second, the lack of previous general surveillance may make clinicians unaware of the high incidence in Taiwan and so they do not pay attention to the threat of rising nosocomial fungal infections. However, since our overall rates of HAI are comparable with surveillance results from the United States, the high rate of fungal BSI should demand our attention. As for the different species contributing to Candidemia, the relative proportions of *C. albicans*, *C. parapsilosis*, *C. tropicalis*, and *C. glabrata* were stationary during the study period. *C. albicans* was the most common organism isolated, accounting for about 50% of cases. Some studies report an increased incidence of other non-*albicans Candida* spp. over the past decade, but this was not observed in our study.[45–47] The irregular use of fluconazole as a prophylactic agent in our country may be the reason for this stationary trend.[48] Similar results have also been demonstrated in earlier single-center studies in Taiwan.[48]

This study has several limitations. First, since we have conducted the first inter-hospital surveillance in Taiwan, data collection in during the early years may be incomplete, and only teaching hospitals were included in this study. The lack of consensus in the recording of HAI by infection control practitioners in the different hospitals made interpretation more difficult. Some hospitals recorded the number of infection episodes per 1,000 admitted patients during earlier years, but most hospitals shifted to recording the number of episodes per 1,000 patient-days. A uniform record form may be needed to ensure the comprehensiveness and consistency of data.

Second, we only collect data on the three most common bacterial pathogens causing BSI; thus, we could not demonstrate the relative proportion of each pathogen. Instead, we reported the absolute incidence and trends for some clinically important organisms. Third, there was no verification of the inclusion of HAI in each hospital. Some hospitals may have under-reported the incidence of HAI or BSI. For example, some hospitals reported no cases of fungal BSI from 1993 to 1996, which is unusual for a general hospital with a service capacity of 21,947 to 31,542 patients per year. Further verification may be needed in follow-up surveillance programs to ensure the quality of inclusion or exclusion. Fourth, the association of current trends and the use of antimicrobial agents should also be considered, since the use of antimicrobial agents may shift the ecology of bacterial and fungal infections. Moreover, this report could not evaluate the relationship between infection control methods and trends because of the heterogeneity of our study populations.

In conclusion, this is the first inter-hospital surveillance of healthcare-associated BSI in Taiwan. The results show a higher proportion of fungal BSI compared with surveillance reports in the United States. In 11 major hospitals in Taiwan, the overall incidence of S. aureus bacteremia decreased over the last decade, although the result was not statistically significant. However, the rate of Candida fungemia and A. baumannii bacteremia increased significantly. The rate of Pseudomonas aeruginosa-related BSI remained stationary during the study period. Further follow-up surveillance is required to monitor these trends.

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