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Nosocomial bloodstream infection in a neonatal intensive care unit of a medical center: a three-year review

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Bloodstream infections are the most frequent nosocomial infections in neonatal intensive care units. This retrospective study surveyed the epidemiologic characteristics of nosocomial bloodstream infections which occurred in the neonatal intensive care unit from January 1, 1997 to December 31, 1999. The overall infection patient rate was 5.5% in the 3-year period, and the overall infection patient-day rate was 4.4 per 1000 patient-days. Low birth weight was a risk factor for bloodstream infections. The rate of infection for neonates with birth weight below 1000 g ranged from 36.6% to 45.8 % (1997: 36.6%; 1998: 45.8% and 1999: 38.9%). The most common pathogens causing nosocomial bloodstream infection were: *Staphylococcus aureus* (18.5%) (with 92% oxacillin-resistant), *Acinectobacter baumannii* (16.3%), *Klebsiella pneumoniae* (11.9%), *Escherichia coli* (9.6%), and *Pseudomonas aeruginosa* (8.1%). The mortality due to nosocomial bloodstream infection was highest among gram-negative bacteria, especially with *P. aeruginosa* (45.5%). Therefore, surveillance of nosocomial bloodstream infection and successful strategies to decrease nosocomial bloodstream infection, such as infection control and optimal antibiotic use, are warranted.

Key words: Nosocomial bacteremia, neonatal intensive care units

Nosocomial infections result in considerable morbidity and mortality among neonates, especially in neonatal intensive care units (NICUs) [1-3]. Among adult patients, urinary tract infections are the most frequent nosocomial infection, followed by surgical site infection, pneumonia, and bloodstream infections [4]. However, in a previous study of the epidemiology of nosocomial infections in NICUs, primary bloodstream infection, nosocomial pneumonia, and eye, ear, nose, and throat infections were the 3 most frequent nosocomial infections in all birth weight groups [5]. The bloodstream is the most frequent site of nosocomial infections, with rates ranging from 32% to 49% in previous reports [5-9].

Previous studies have found an incidence of nosocomial bloodstream infection (NBSI) in NICUs ranging from 5.2 to 30.4 infections per 100 patients [1-3,6-11]. While many studies dealing with nosocomial infections in the NICU have been reported, there have been only a few reports from Taiwan [12-15]. This retrospective study surveyed the epidemiologic characteristics of NBSI in the NICU.

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Patients and Methods

A 30-bed NICU was set up in China Medical College Hospital in 1983, and all premature or newborn infants younger than 1 month with severe illness in the hospital were referred to the NICU since that time.

The medical charts of patients with NBSI admitted to the NICU from January 1, 1997 to December 31, 1999 were reviewed. Clinical and demographic characteristics, isolated microorganisms, and outcomes were analyzed. Statistical methods employed included chi-square test, 2-tailed Fisher's exact test, and logistic regression model.

Case definition

Cases of NBSI was defined as one or more positive blood culture obtained over 48 h after admission to the NICU, and the presence of clinical symptoms or signs suggestive of infection. The blood cultures were processed in conventional 2-bottle broth blood-culture systems according to standard procedures [16].

Definition of infection rate

The NBSI patient rate was expressed as the number of

NBSIs per 100 intensive care unit patients, and the NBSI patient-day rate was expressed as the number of NBSIs per 1000 patient-days.

Birth weight and infection rate

Admitted babies was classified into 5 birth weight categories: (1) ≤750 g; (2) 751 to 1000 g; (3) 1001 to 1250 g; (4) 1251 to 1500 g; and (5) >1500 g. The infected patient rate was calculated in each group.

Pathogens in nosocomial bloodstream infection

Reports of positive blood cultures and the findings of susceptibility test were recorded in detail. The distribution of pathogens associated with NBSI was analyzed.

Mortality due to nosocomial pathogens

Mortality due to a nosocomial pathogen was defined as death occurring within 7 days of the onset of infection episode. Cases with mortality due to infections caused by nosocomial pathogens were recorded.

Results

During the study period, a total of 2487 patients were admitted to the NICU, including 824 in 1997, 804 in 1998, and 859 in 1999. These patients spent a total of 30 675 patient-days in the NICU in this 3-year period, including 12 190 in 1997, 9417 in 1998, and 9068 in 1999. There were a total of 137 NBSI episodes, including 53 episodes in 1997, 43 episodes in 1998, and 39 episodes in 1999.

Nosocomial bloodstream infection rate

The NBSI patient rate was 6.4% in 1997, 5.3% in 1998, and 4.5 % in 1999. The nosocomial infection patient rate over the 3-year period was 5.4 %. The nosocomial infection patient-day rate was 4.35 per 1000 patient-days in 1997, 4.57 in 1998, and 4.3 in 1999. The nosocomial infection patient-day rate in the 3-year period was 4.4 per 1000 patient-days (Table 1).

Association between birth weight and infection rates

Birth weight was the risk factor with the strongest statistical relationship to NBSI. Of neonates with birth weights of below 750 g, 32.3% to 50% had at least one episode of jargon NBSI (50% in 1997, 50% in 1998, 32.3% in 1999) as shown by positive blood culture (Table 2). The rate of infection decreased with increasing birth weight, ranging from 30.6% to 47.8 % for infants weighing 751 to 1000 g at birth, from 5.7% to 22.9% for infants weighing 1001 to 1250 g, from 2.1% to 7. 3% for infants weighing 1251 to 1500 g, and from 0. 6% to 2.2% for infants weighing above 1500 g. Two-tailed Fisher's exact test revealed significant differences in each category ($p<0.001$ in 1997, $p<0.001$ in 1998, $p<0.001$ in 1999). Logistic regression model analysis showed that the odd ratios decreased with increasing birth weight. That is, the lower the birth weight, the more likely the patient develops infection. The results of the statistical analysis are shown in Table 2.

Of the total 135 infection episodes, 7 patients with birth weight below 1000 g had more than one episode (5 patients had 2 episodes and 2 patients had 3 episodes). Two full-term babies with birth weight more than 1500 g had more than one episode. Both of them had underlying gastrointestinal illness and had received surgery. One of these babies was small for gestational age with an imperforate anus. The other had intestinal malrotation and short bowel syndrome which developed after surgery.

Distribution of pathogens in nosocomial bloodstream infections and drug resistance

The distribution of pathogens associated with NBSIs is shown in Table 3. During the study period, the most common nosocomial bloodstream pathogens in all

Table 1. Nosocomial bloodstream infection rates in the neonatal intensive care unit, 1997-1999

	Year			
	1997	1998	1999	Total
No. of admitted patients	824	804	859	2487
Duration of hospital stay (patient-day)	12190	9417	9068	30675
Infection episodes	53	43	39	135
Overall NBSI rate				
Infection patient rate[a]	6.4	5.3	4.5	5.4
Infection patient-day rate[b]	4.35	4.57	4.30	4.40

Abbreviation: NSBI = nosocomial blood stream infection

[a]Nosocomial infection patient rate = number of infections per 100 intensive care unit patients

[b]Nosocomial infection patient- day rate = number of infections per 1000 patient-days

Table 2. Birth weight-specific bloodstream infection rates, 1997-1999

Birth weight (g)	Infection episodes	No. of admissions	NI rate (%)	Odd ratio	Confidence interval
1997					
≤750	11	22	50	1.0	
751-1000	15	49	30.6	0.612	0.242, 1.546
1001-1250	10	58	17.2	0.345	0.129, 0.925
1251-1500	3	65	4.6	0.092	0.024, 0.361
>1500	14	630	2.2	0.044	0.018, 0.109
1998					
≤750	11	22	50	1.0	
751-1000	16	37	43.2	0.865	0.341, 2.195
1001-1250	11	48	22.9	0.458	0.173, 1.217
1251-1500	1	48	2.1	0.042	0.005, 0.343
	>1500	4	649	0.6	0.012 0.004,
0.042					
1999					
≤750	10	31	32.3	1.0	
751-1000	11	23	47.8	1.483	0.539, 4.079
1001-1250	2	35	5.7	0.177	0.036, 0.872
1251-1500	4	55	7.3	0.225	0.065, 0.779
>1500	12	715	1.7	0.052	0.021, 0.130

Abbreviation: NI = nosocomial infection

neonates were *Staphylococcus aureus* (25/135, 18.5%), *Acinetobacter baumannii* (22/135, 16.3%), *Klebsiella pneumoniae* (16/135, 11.9%), *Escherichia coli* (13/135, 9.6%), and *Pseudomonas aeruginosa* (11/135, 8.1%).

S. aureus was also the most common gram-positive pathogen causing NBSI. Furthermore, most of the *S. aureus* isolates (23/25, 92 %) were methicillin-resistant (Table 4). *A. baumannii* was the most common gram-negative pathogen associated with NBSI. All isolates were susceptible to imipenem.

Of the 16 *K. pneumoniae* isolates, 14 (87.5%) were resistant to cefotaxime. Other pathogens such as *E. coli* and *Enterobacter cloacae* were also resistant to cefotaxime with resistant rates of 46.2% (6/13 isolates) and 90.9% (10/11 isolates), respectively.

Among the 11 isolates of *P. aeruginosa*, 90.9% (10/11) were susceptible to ceftazidime and 81.8% (9/11) to imipenem. None of the 6 isolates of enterococci was resistant to vancomycin.

Table 3. Distribution of pathogens associated with episodes of nosocomial bloodstream infection, 1997-1999

Pathogen	No. of isolates (%)			Total no. of isolates (%)	Rank
	1997	1998	1999		
Gram-positive					
Staphylococcus aureus	14 (26.4)	5 (11.6)	6 (15.4)	25 (18.5)	1
Enterococcus	1 (1.9)	2 (4.7)	3 (7.7)	6 (4.4)	9
CONS	0	2 (4.7)	1 (2.6)	3 (2.2)	11
Gram-negative					
Acinetobacter baumannii	2 (3.7)	7 (16.3)	13 (33.3)	22 (16.3)	2
Klebsiella pneumoniae	6 (11.3)	8 (18.6)	2 (5.1)	16 (11.9)	3
Escherichia coli	4 (7.5)	8 (18.6)	1 (2.6)	13 (9.6)	4
Pseudomonas aeruginosa	3 (5.7)	3 (7.0)	5 (12.8)	11 (8.1)	5
Serratia marcescens	3 (5.7)	6 (14.0)	2 (5.1)	11 (8.1)	6
Enterobacter cloacae	8 (15.1)	0	3 (7.7)	11 (8.1)	7
Stenotrophomonas maltophilia	0	1 (2.3)	5 (12.8)	6 (4.4)	10
Fungus					
Candida albicans	6 (11.3)	2 (4.7)	0	8 (5.9)	8
Total no. of isolates	53	43	39	135	

Abbreviation: CONS= coagulase-negative staphylococci

Table 4. Drug-resistant nosocomial pathogens isolated from patients in neonatal intensive care unit, 1997-1999

Pathogen	No. of isolates (resistant/tested) (%)			
	1997	1998	1999	Total
MRSA	13/14	5/5	5/6	23/25 (92)
Penicillin-R enterococci	0/1	2/2	2/3	4/6 (66.7)
Vancomycin-R enterococci	0/1	0/2	0/3	0/6 (0)
Imipenem-R *Acinetobacter baumannii*	0/2	0/7	0/13	0/22 (0)
Cefotaxime-R *Klebsiella pneumoniae*	5/6	7/8	2/2	14/16 (87.5)
Cefotaxime-R *Escherichia coli*	0/4	6/8	0/1	6/13 (46.2)
Cefotaxime-R *Enterobacter cloacae*	8/8	0/0	2/3	10/11 (90.9)
Ceftazidime-R *Pseudomonas aeruginosa*	1/3	0/3	0/5	1/11 (9.1)
Imipenem-R *Pseudomonas aeruginosa*	0/3	0/3	2/5	2/11 (18.2)

Abbreviation: MRSA= methicillin-resistant *Staphylococcus aureus*; R = resistant

Mortality rate associated with nosocomial pathogens

Table 5 shows the mortality rate associated with infections caused by specific nosocomial pathogens. In this study, infants with *P. aeruginosa* infections had a higher mortality (45.5%) compared with infants infected by other pathogens. However, this difference was not significant on 2-tailed Fisher's exact test.

Discussion

The NBSI patient rate in the NICU of China Medical College Hospital was 5.4 per 100 patients, and the patient-day rate was 4.4 per 1000 patient-days. Previous studies have reported rates of NBSI in NICUs that ranged from 5 to 32 infections per 100 patients [6-9]. However, these findings have been criticized for a number of reasons: (1) the definitions of nosocomial infection were not standardized; (2) the mean duration of hospitalization differed from hospital to hospital; and (3) there were uncontrolled variations in exposure to known risk factors for nosocomial infection [17,18]. Gaynes *et al* [19] considered the calculation of overall nosocomial infection patient-day rates to be preferred over overall nosocomial infection patient rates. The overall nosocomial infection patient-day rate at least partially controls variations in the mean duration of hospitalization, and may allow for meaningful interhospital comparison. In this study, the rate of infection decreased from 6.4 % in 1997 to 4.5% in 1999, whereas the infection patient-day rate in each year was not significantly different from each other.

In this study, the ranges of infection rate among different birth weight groups are as follows: below 750 g, 32.3% to 50%; between 751 and 1000 g, 30.6% to 47.8%; between 1001 and 1250 g, 5.7% to 22.9%; between 1251 and 1500 g, 2.1% to 7.3%; and above 1500 g, 0.6% to 2.2% (Table 2). These results are similar to the findings of Stoll *et al* [8]. Their study revealed infection rates of 50% for infants weighting below 750 g, 33% for those between 751 and 1000 g, 21% for those between 1001 and 1250 g, and 10% for those between 1251 and 1500 g. The risk of developing NBSI decreased with higher birth weight.

The distribution of pathogens associated with NBSI in this study differed from previous studies [5,8]. In this study, *S. aureus*, 92% of which were methicillin-resistant, was the most common pathogen causing 18. 5% of NBSI cases. As for the coagulase-negative staphylococci (CONS), only a small proportion (2.2%) of cases was found in this study. However, Gaynes *et al* [5] and Stoll *et al*[8] found that CONS were the most common pathogen, presenting in 51% and 55% of cases, respectively. Freeman *et al* [21] suggested that receipt of lipid emulsions in neonates is an independent risk factor for primary bacteremia with CONS. In our NICU, lipid emulsions were seldom used because of the possibility that they may increase the infection rate, and that extravasation of the lipid emulsions may damage the soft tissue. We therefore encourage breast-feeding instead of parental nutrition. This policy may have been

Table 5. Mortality associated with nosocomial pathogens

Pathogen	Case-fatality[a] (%)
Pseudomonas aeruginosa	5/11 (45.5)
Serratia marcescens	4/11 (36.4)
Escherichia coli	4/13 (30.8)
Enterobacter cloacae	3/11 (27.3)
Candida albicans	2/8 (25.0)
Acinetobacter baumannii	5/22 (22.7)
Klebsiella pneumoniae	3/16 (18.8)
Enterococcus spp.	1/6
Staphylococcus aureus	4/25 (16.0)
Stenotrophomonas maltophilia	0/6
Coagulase-negative staphylococci	0/3
Candida parapsilosis	0/2

[a]Mortality associated with the pathogen was defined as death within 7 days after the onset of infection episode.

one of the reasons for the lower percentage of CONS.

The prevalence of antibiotic use is high in NICUs, and this has been shown to promote the development of antibiotic resistance in these units [20]. In this study, the prevalence of methicillin-resistant *S. aureus* (MRSA) in NICU was 92%. Since MRSA are spread primarily through the hands of health care workers, rates of infections are a function of infection control activities within institutions. Overcrowding, limited space, inadequate cleansing of the equipment, and initial lack of correct attitude to scrupulous hand washing techniques appear to contribute to the spread of MRSA [22]. Available data suggests the efficacy of 3 control measures: (1) identification of the entire patient reservoir (cases and carriers) for purposes of isolation; (2) strict hand washing among patients to prevent transmission; and (3) treatment of the carrier state in health care workers and patients during periods of high infection rates with safe and effective topical agents such as mupirocin [23].

The detailed mortality rates associated with nosocomial pathogens are listed in Table 5. Stoll *et al* [8] found that infants with *P. aeruginosa* sepsis had a higher mortality rate than neonates with other bloodstream infections. In this study, *P. aeruginosa* sepsis had the highest mortality rate (45.5%), although this rate was not significantly different compared with the other pathogens. This may have been due to the small sample size in each group.

In summary, this review of NBSIs in the NICU found a rate of infection of 5.4 per 100 patients and an infection patient-day rate of 4.4 per 1000 patient-days. Birth weight was the risk factor with the strongest statistical relationship to NBSI. The surveillance of NBSI and successful strategies to decrease NBSI, such as infection control and optimal antibiotic use, are warranted.

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