Healthcare-Associated Bloodstream Infections in a Neonatal Intensive Care Unit over a 20-Year Period (1992—2011): Trends in Incidence, Pathogens, and Mortality

Author(s): Evelien Verstraete, MNSc; Jerina Boelens, PhD; Kris De Coen, MD; Geert Claeys, PhD; Dirk Vogelaers, PhD; Piet Vanhaesebrouck, PhD; Stijn Blot, PhD

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ORIGINAL ARTICLE

Healthcare-Associated Bloodstream Infections in a Neonatal Intensive Care Unit over a 20-Year Period (1992–2011): Trends in Incidence, Pathogens, and Mortality

Evelien Verstraete, MNSc;[1] Jerina Boelens, PhD;[2] Kris De Coen, MD;[3] Geert Claeys, PhD;[4] Dirk Vogelaers, PhD;[1] Piet Vanhaesebrouck, PhD;[3] Stijn Blot, PhD[1]

OBJECTIVE. To analyze trends in the incidence and pathogen distribution of healthcare-associated bloodstream infections (HABSIs) over a 20-year period (1992–2011).

DESIGN. Historical cohort study.

SETTING. Thirty-two-bed neonatal intensive care unit (NICU) in a tertiary referral hospital.

PATIENTS. Neonates with HABSIs defined according to the criteria of the National Institute of Child Health and Development (NICHD).

METHODS. A hospital-based ongoing surveillance program was used to identify HABSI cases in neonates. A distinction between definite or possible HABSI was made according to the NICHD criteria. Incidence, incidence densities (HABSIs per 1,000 hospital-days and HABSIs per 1,000 total parenteral nutrition–days), and case fatality rate were calculated. Logistic regression analysis was used to find time trends. Four periods of 5 years were considered when executing variance analysis.

RESULTS. In total, 682 episodes of HABSIs occurred on 9,934 admissions (6.9%). The median total incidence density rate was 3.1 (interquartile range, 2.2–3.9). A significant increasing time trend in incidence density was observed for the period 1995–2011 ($P < .003$). A significant decrease in the case fatality rate was found in the last 5-year period ($P < .001$). No neonate died following possible HABSIs, whereas the case fatality rate among neonates with definite HABSIs was 9.7%. Most HABSIs were caused by coagulase-negative staphylococci ($n = 414$ [60.7%]). A significant increase in *Staphylococcus aureus* HABSI was observed in the last 10-year period ($P < .001$).

CONCLUSIONS. An increase in incidence density rate occurred, while the case fatality rate dropped. Better perinatal care could be responsible for the latter. A decrease in days before infection and a high incidence of coagulase-negative *Staphylococcus* HABSIs indicate the need for vigorous application of evidence-based prevention initiatives, in particular for catheter care.

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Healthcare-associated bloodstream infection (HABSI) is a frequent complication in neonatal intensive care units (NICUs). Previous studies document incidence rates ranging from 5% to 32%.[1-3] Risk factors for HABSIs include lower birth weight, lower gestational age, prolonged mechanical ventilation (MV), parenteral nutrition, and vascular access.[3-5] For neonates with very low birth weight (VLBW; 1,500 g or less), the National Institute of Child Health and Human Development (NICHD) reported an incidence of 21%.[3]

HABSIs result in longer hospitalization (plus 23 days, on average) and a rise in mortality rate, up to 24% for VLBW neonates.[3,6-10]

The past decade's further implementation of neonatal intensive care facilities has led to increasing survival rates among preterm neonates.[11,12] Neonates are of younger gestational age and lower birth weight, and because of this they might be more seriously ill. Therefore, they may be more susceptible to HABSIs.[3] Conversely, implementation of new knowledge by means of care bundles and infection control practices might stabilize or alter the possible increasing direction.[13,14]

The purpose of this study was to identify trends in the incidence densities and pathogen distribution of HABSIs over a long period (20 years, from 1992 through 2011) in a tertiary NICU setting to clearly define baseline data, allowing follow-up of prevention initiatives.

Affiliations: 1. Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium; 2. Department of Laboratory Medicine, Ghent University Hospital, Ghent, Belgium; 3. Department of Neonatal Medicine, Ghent University Hospital, Ghent, Belgium; 4. Laboratory of Clinical Biology, Ghent University Hospital, Ghent, Belgium.

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TABLE 1. Definite, Possible, and Probable Healthcare-Associated Bloodstream Infection (HABSI), according to the Criteria of the National Institute of Child Health and Human Development

HABSI	Pathogen	No. of positive blood cultures	Other criteria
Definite	Recognized (ie, *Staphylococcus aureus*, *Enterococcus* spp., *Escherichia coli*, *Pseudomonas* spp., *Klebsiella* spp., *Candida* spp., and others)	1	None
	Possible/skin contaminant (ie, *Corynebacterium* spp., *Bacillus* [not *B. anthracis*] spp., *Propionibacterium* spp., CoNS, viridans group streptococci, *Aerococcus* spp., and *Micrococcus* spp.)	2	Blood drawn within 48 h of each other (separate occasions) and having grown the same possible pathogen
Possible	Possible/skin contaminant	1	C-reactive protein >1 mg/dL, antistaphylococcal agent for ≥5 days
Probable	Possible/skin contaminant	1	Does not meet criteria for possible

NOTE. CoNS, coagulase-negative staphylococci.

METHODS

Study Design

We performed a single-center historical cohort study, considering all neonates admitted during a 20-year period (1992–2011) whose NICU stay was complicated by at least 1 HABSI. Files of all included cases were reviewed to determine the diagnostic certainty of the infection. The study was approved by the Ethics Committee of Ghent University Hospital.

Setting and Patients

Ghent University Hospital is a teaching hospital and tertiary referral center with a 32-bed NICU. Only newborn infants (ie, less than 28 days of life) are admitted to this unit. The yearly mean admission rate over the past 20 years was 492 (range, 403–593), with approximately 100 (range, 95–115) VLBW infants. Neonatal specialist services include pediatric cardiology and cardiac surgery with, on average, 70 cases per year, of whom 50 need surgery during the neonatal period. During the study period there was a progressive increase in nursing and medical staff, in accordance with the population increase.

Infection Control Practices

Besides surveillance, no official infection control program was implemented before 2006. The norm "good practice" was the standard. Hand hygiene standards did not change over time but were more visible since 2006; posters on hand hygiene were found next to all sanitary locations. Catheter dressings changed in July 1994 from nonpermeable to high-permeable polyurethane dressing. A protocol for catheter care was implemented in 2006 in accordance with the 2002 guidelines of the Centers for Disease Control and Prevention (CDC).[15]

Case Finding

Since 1992, laboratory-based surveillance of positive blood culture results has been performed by the infection control team. Clinical significance, mode of transmission (ie, congenital, vertically transmitted [mother to infant], healthcare associated, or community acquired), and source of infection were determined.

The cohort is based on this ongoing surveillance program. Since 2002, a NICAUDIT electronic database system was used to identify additional HABSI cases and to collect demographic and outcome data. For the present study, the following conditions were collected: MV, total parenteral nutrition (TPN), and major surgery.

Definitions

Healthcare-associated infection (HAI) is defined according to the CDC/National Healthcare Safety Network (NHSN) criteria published in 2008.[1] A neonatal HAI is considered healthcare associated when it is not transplacentally transmitted, occurs more than 48 hours after birth, and is not a reactivation of a latent infection caused by, for example, herpes zoster, herpes simplex, syphilis, or tuberculosis. To define the diagnostic certainty of a laboratory-confirmed bloodstream infection in patients less than or equal to 1 year of age, the following adapted CDC/NSHN criteria were considered: (1) a distinction was made between skin contaminant and recognized pathogens (Table 1) and (2) the blood-cultured pathogen could not be related to another infection site.

HABSI is defined as possible or definite according to the NICHD criteria (Table 1).[3] Blood culture results considered as probable HABSIs are not included in our cohort. A HABSI episode is defined as new if the same organism was cultured after 10 days of appropriate antibiotic therapy or if a different organism was cultured from a subsequent culture.[3]

Case fatality rate is the percentage of HABSI cases whose death is related to the HABSI, on the basis of clinical judgment. TPN is the intravenous administration of an admixture of at least 2 major nutritional components (ie, carbohydrate and amino acids or lipids).

Blood Culture Sampling and Processing

Blood cultures were obtained through an arterial central line or by peripheral puncture. There were no changes in blood culture sampling policy and no significant changes in the total number of blood cultures taken yearly during the last 10 years of the study period (mean, 492; range, 449–555). Blood cultures were assessed using the Bactec system (Becton Dickinson Microbiology Systems) until 1995 and the BacT/Alert 3D automated microbial detection system (bioMérieux) since 1996.

Occurrence Rates

Incidence is defined as the number of HABSIs per 100 neonates during the 20-year study period. Incidence density is defined as the number of HABSIs per 1,000 hospital-days, calculated for total, definite, and possible HABSIs. The HABSI rate in relation to vascular access is expressed by the number per 1,000 TPN-days (ie, total TPN-days).

Statistics

Variables are described as number (%) or median (interquartile range). Comparisons between groups were performed using the Mann-Whitney *U* test (2 groups) or the Kruskal-Wallis test (more than 2 groups) for continuous variables and the χ^2 test for categorical variables. Four consecutive periods of 5 years were considered: period 1 (1992–1996), period 2 (1997–2001), period 3 (2002–2006), and period 4 (2007–2011). Logistic regression analysis was used to evaluate the time trend in incidence densities during the 20-year study period. SPSS, version 21, was used for all tests.

RESULTS

Trends in Occurrence Rates

During the study period, 9,829 neonates were admitted to the NICU, and 682 HABSI episodes were found in 620 HABSI cases. Respectively, 444 (65%) and 238 (35%) were definite and possible HABSIs. Fifty-three (8.5%) of 620 HABSI cases developed a second episode, and 9 (1.5%) of 620 HASBI cases experienced a third episode. Characteristics, incidence, and incidence densities (total, definite, and possible) per period are tabulated in Table 2. Over the study period, the average yearly incidence was 6.9 per 100 patients and ranged from 2.2 (1994) to 13.4 (1992). Total, definite, and possible incidence densities are illustrated per year since no subtleties per quartile were observed (Figure 1). The average total incidence density rate per year was 3.1 per 1,000 hospital-days (range, 0.9–5.3).

During the study period, no overall significant trend was observed in total, definite, and possible incidence density rates ($P = .233$, .544, and .765, respectively). Because of the substantial decline observed in definite and possible incidence density rate in 1994, a secondary logistic regression analysis was performed for the period 1995–2011. This analysis revealed a significant increasing trend in total and definite incidence density rate ($P = .003$ and .020, respectively). Variance analysis showed that the distribution of the total and possible incidence density rate revealed no difference across the 4 periods (Table 2). In contrast, a difference was found in the distribution of the definite incidence density rate ($P = .040$). Furthermore, a decrease was observed in days before infection ($P = .004$). For periods 3 (2002–2006) and 4 (2007–2011), incidence per 1,000 TPN-days was respectively 7.5 (6.8–9.1) and 8.1 (7.8–9.6; $P = .222$). HABSI incidence was higher in particular subgroups (ie, VLBW, very low gestational age, TPN, and MV; Table 2).

Trends in Pathogen Distribution

The 682 HABSIs were caused by 717 pathogens, of which 80.2%, 18.7%, and 1.1% were gram-positive pathogens, gram-negative pathogens, and fungi, respectively (Table 3). Slightly more than 5% ($n = 35$) of the HABSIs were caused by 2 pathogens. In 19 polymicrobial HABSIs (54.3%) coagulase-negative staphylococci (CoNS) were involved, of which 17 occurred in the second 10-year period (2002–2011). Eleven (31.4%) blood cultures revealed mixed growth with *Enterococcus* spp., of which 6 included CoNS. In the first (1992–2001) and the second (2002–2011) 10-year period, respectively, 7 (70%) of 10 and 5 (20%) of 25 polymicrobial HABSIs involved a gram-negative pathogen. Of the 53 second-episode HABSIs, 28 were caused by the same pathogen, of which 19 (67.9%) were CoNS, and 25 episodes were caused by 2 different pathogens. Pathogen distribution, divided in two 10-year study periods, is shown in Table 3. The most common causative pathogens were CoNS, accounting for 60.7% of all HABSIs. Of these CoNS HABSIs, 183 (44%) were definite and 231 (56%) were possible HABSIs. The most common "recognized" pathogens were Enterobacteriaceae (16.0%), *Staphylococcus aureus* (11.1%), and enterococci (6.2%). *Pseudomonas* spp. (2.5%) and *Candida* (1.2%) were rare. Six *S. aureus* isolates (7.9%) were methicillin resistant.

Incidence per 1,000 hospital-days of the 4 most common pathogens are displayed in Figure 2. CoNS remained the main pathogens during the whole study period. As for enterococci, *S. aureus*, and Enterobacteriaceae, no time trend was detected. In contrast, variance analysis revealed an increase in *S. aureus* HABSI ($P < .001$) comparing the periods 1992–2001 and 2002–2011. A peak in *S. aureus* HABSI was found in 2005 ($n = 9$; 1.13 per 1,000 hospital-days), of which 4 were methicillin resistant.

Two clusters (more than or equal to 3 HABSIs of the same pathogen per week) were detected. In October 1993, 4 *Pseudomonas aeruginosa* HABSIs occurred within 3 days, and in June 2005, 3 methicillin-resistant *S. aureus* (MRSA) HABSIs occurred within 1 week.

TABLE 2. Epidemiological Features and Incidence Densities of Healthcare-Associated Bloodstream Infections (HABSIs) for the Four 5-Year Periods

Epidemiological feature	Total period (1992–2011)	Period 1 (1992–1996)	Period 2 (1997–2001)	Period 3 (2002–2006)	Period 4 (2007–2011)	*P*
Total patients, no.	9,829	2,154	2,346	2,469	2,860	
Total hospital-days, no.	131,332	52,010	52,110	56,209	55,992	.095
HABSI episodes, no. (%)	682	170 (7.9)	117 (4.9)	183 (7.4)	212 (7.4)	.042
HABSI cases, no. (%)	620	165 (7.7)	111 (4.7)	158 (6.4)	186 (6.5)	.065
Proportion of definite HABSI, %	63	56	66	74	69	.052
Incidence, cases per 1,000 hospital-days						
Total HABSI						
Median (IQR)	3.1	3.2 (0.9–5.3)	1.9 (1.8–2.8)	3.1 (2.7–3.8)	3.7 (3.4–4.1)	.091
Mean (range)	3.1	3.3 (4.4)	2.2 (1.2)	3.2 (1.7)	3.7 (1.1)	
Definite HABSI						
Median (IQR)	2	1.3 (0.9–2.5)	1.3 (1.2–1.9)	2.5 (1.8–3.0)	2.5 (2.2–3.2)	.040
Mean (range)	2	1.6 (1.9)	1.5 (1.2)	2.4 (1.9)	2.6 (1.5)	
Possible HABSI						
Median (IQR)	1.1	1.9 (0.3–2.8)	0.6 (0.5–1.1)	0.7 (0.6–1.1)	1.1 (0.8–1.4)	.327
Mean (range)	1.1	1.7 (2.5)	0.8 (0.8)	0.8 (0.7)	1.1 (1.0)	
No. per 1,000 TPN-days						
Median (IQR)				7.5 (6.8–9.1)	8.1 (7.8–9.6)	.222
Mean (range)				7.8 (4.4)	8.7 (2.5)	
Total patients with TPN, no. (days)				2,022 (24,371)	2,210 (26,124)	.249
HABSI cases with TPN, no. (days)				153 (3,779)	178 (4,569)	.585
HABSI cases per non-TPN patients, %				1	1	.868
Total TPN, days						
Median (IQR)				20 (12–31)	19 (11–33)	.914
Mean (range)				25 (194)	26 (151)	
GA, weeks						
Median (IQR)				33 (29–37)	33 (29–38)	.853
Mean (range)				33 (18)	33 (17)	
VLGA (≤31 weeks), %				42	41	.886
HABSI cases per VLGA patients, %				9	10	.614
HABSI cases per non-VLGA patients, %				5	5	.931
Birth weight, g						
Median (IQR)				1,835 (1,240–2,840)	1,755 (1,100–3,025)	.700
Mean (range)				2,004 (4,470)	1,999 (3,545)	
VLBW (≤1,500 g), %				39	43	.565
HABSI cases per VLBW patients, %				12	15	.235
HABSI cases per non-VLBW patients, %				5	5	.571
Male sex, %				60	54	.391
Length of stay, days						
Median (IQR)				41 (21–72)	37 (20–75)	.555
Mean (range)				54 (249)	52 (189)	
Total patients with MV, no. (days)				1,058 (7,035)	975 (6,339)	.181
HABSI cases with MV, no. (days)				111 (1,313)	120 (1,643)	.250
HABSI cases per non-MV patients, %				3	4	.797
Duration of MV, days						
Median (IQR)				4 (0–13)	3 (0–11)	.332
Mean (range)				9 (76)	9 (99)	
Days before infection						
Median (IQR)				10 (6–18)	8 (3–17)	.004
Mean (range)				18 (138)	11 (99)	
Inborn, % (proportion IUT, %)				46 (70)	48 (77)	.777
Major surgery, %				29	42	.055
Case fatality rate, no. (%)	38 (6.1)	12 (7.2)	10 (8.9)	12 (7.5)	4 (2.1)	<.001

NOTE. Days before infection are the days since birth until infection. GA, gestational age; IQR, interquartile range; IUT, intrauterine transfer; MV, mechanical ventilation; TPN, total parenteral nutrition; VLBW, very low birth weight; VLGA, very low gestational age.

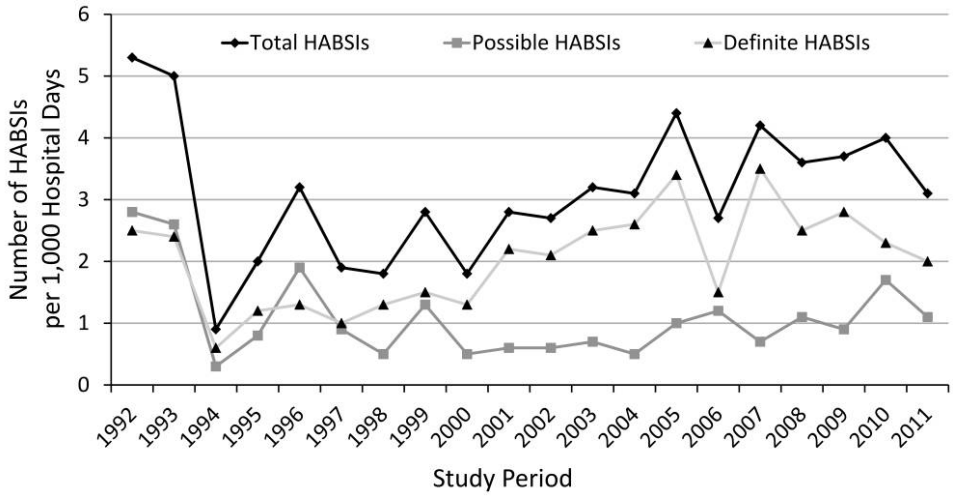

FIGURE 1. Number of total, definite, and possible healthcare-associated bloodstream infections (HABSIs) per 1,000 hospital-days (incidence densities) from 1992 through 2011.

Outcomes Associated with HABSIs

Thirty-eight of 620 HABSI cases died because of HABSI (6.1% case fatality rate). No neonates of the entire possible HABSI group ($n = 229$) died because of a HABSI, so deaths occurred in the definite HABSI group ($n = 391$; 9.7% case fatality rate). Considering the 4 periods, a significant decrease in the case fatality rate was found ($P < .001$).

No significant difference was found between 2002–2006 and 2007–2011 in case fatality rate for VLBW patients versus non-VLBW patients and for surgical patients versus non-surgical patients (data not shown). The causative pathogens and their association with mortality are tabulated in Table 3. In the group with polymicrobial HABSIs 2 neonates died (2/35 [5.7%]), which was not different from the monomicrobial HABSI group (36/647 [5.6%]; $P = .972$).

DISCUSSION

We reviewed trends in incidence density of HABSIs in a tertiary NICU setting over a 20-year period. A statistically significant increase in total and definite incidence density rate was found during the period 1995–2011. A relative increase in *S. aureus* HABSIs was observed in the last 10 years. No further changes in pathogen distribution occurred. The case fatality rate significantly decreased in the last 5 years.

Trends in Occurrence Rates

An incidence of 6.9 per 100 neonates and an incidence density rate of 3.1 per 1,000 hospital-days indicate that HABSIs remain an important issue in our NICU. Because of a large variety of case definitions, a wide range in incidence and incidence density rates was observed when reviewing literature, thereby hampering benchmarking. Future research should consider the use of a uniform case definition for the surveillance of HABSI, such as the one developed by Modi et al.[16] Additionally, NICU departments should participate in an (inter)national surveillance network to facilitate benchmarking.[16-19]

During the entire study period, fluctuations in incidence densities were observed, but no overall trend in total HABSI incidence density was found (1992–2011). In contrast, an increasing trend was found for the period 1995–2011. This secondary logistic regression analysis was made to exclude the 2 extreme incidence density values, that is, 5.3 (1992) and 0.9 (1994). In 1994, a randomized controlled trial of catheter care was conducted. During the 6 months of intervention, the overall HABSI rate dropped tremendously. The investigators assumed that a Hawthorne effect caused this favorable decline.[20] Similar effects are described when starting up surveillance of HABSIs.[13,17] Strict adherence to the study protocol might be another explanation for the observed decline. Before 1994, we may assume that no attention was paid to HABSIs, which might be responsible for the higher incidence density rates in 1992–1993.

Variance analysis revealed an increase across the 4 periods for the definite incidence density rate. Increasing survival rates of the preterm newborns during the last decades could be associated with this finding.

It is acknowledged that the criteria of the NICHD may overestimate true rates of CoNS HABSIs.[3] In this study, no distinction was made between the different CoNS (*S. epidermidis*, *S. hominis*, etc), so an overestimation of the category of definite CoNS HABSIs is likely. However, classification as definite or possible was made retrospectively, and the 2 backup systems (ie, medical files and NICAUDIT) were available only since 2002. Considering these factors, misclassification before 2002 is plausible, skewing classification toward possible CoNS HABSIs. Nevertheless, only laboratory-con-

TABLE 3. Frequencies and Associated Mortality for the Main Gram-Positive and Gram-Negative Pathogens

Pathogen	Total period (1992–2011)	Period 1 + 2 (1992–2001)	Period 3 + 4 (2002–2011)	Associated mortality
Total pathogens	717 (100)	299 (41.7)	418 (58.3)	40 (5.6)
Coagulase-negative staphylococci	414 (57.7)	186 (62.2)	228 (54.5)	3 (7.5)
Staphylococcus aureus	76 (10.6)	17 (5.7)	59 (14.1)	3 (7.5)
Enterococcus spp.	42 (5.9)	15 (5.0)	27 (6.5)	0
Other gram-positive pathogens	43 (6.0)	11 (3.7)	32 (7.7)	0
Escherichia coli	35 (4.9)	14 (4.7)	21 (5.0)	8 (20.0)
Enterobacter spp.	46 (6.4)	24 (8.0)	22 (5.3)	14 (35.0)
Klebsiella spp.	22 (3.1)	10 (3.3)	12 (2.9)	4 (10.0)
Pseudomonas spp.	17 (2.4)	14 (4.7)	3 (0.7)	4 (10.0)
Other gram-negative pathogens	14 (2.0)	7 (2.3)	7 (1.7)	3 (7.5)
Candida spp.	8 (1.1)	1 (0.3)	7 (1.7)	1 (2.5)
Total gram-positive pathogens	575 (80.2)	229 (76.6)	346 (82.8)	6 (15.0)
Total gram-negative pathogens	134 (18.7)	69 (23.1)	65 (15.6)	33 (82.5)
Polymicrobial HABSIs, no.	35	10	25	2

NOTE. Data are no. (%), unless otherwise indicated. HABSI, healthcare-associated bloodstream infection.

firmed HABSIs are included in this cohort, favoring underestimation of the true HABSI rate.

TPN-days were used to express incidence in relation to vascular access, since the number of total catheter-days was not available. Consequently, an overestimation of the HABSI rate in relation to vascular access is likely. The denominator TPN-days has already been proposed as a higher standard than catheter-days, and, although not an apt proxy, it may be more appropriate in defining days at risk.[4,18] In our cohort, we observed that almost all HABSI cases of period 3 + 4 received TPN (n = 331/344 [96.2%]) and MV (n = 231/344 [67%]). For both devices and for the 2 periods, a significant difference was found in the proportion HABSI cases per device versus HABSI cases per nondevice. This observation might confirm that TPN and MV are major risk factors. Note that MV may be instituted after HABSI, so MV statistics could be biased.

We could not discern any changes in characteristics of the HABSI cohort. It should be noted that data were missing for the period 1992–2001. However, for the period 2002–2011 there was a decrease in days before infection; in particular, the lower quartile was halved. On the basis of observations made in an adult ICU, Zingg et al[19] hypothesized that faster occurrence of infection might imply issues with catheter care, that is, adherence to or adoption of insertion bundles. This can also be valid for an NICU setting. Another NICU study of Zingg et al[21] showed that catheter indwelling time is a risk factor for HABSI and clinical sepsis, so time to infection should be placed in the context of exposure and type of catheter.

Trends in Pathogen Distribution

HABSIs caused by CoNS, *Enterococcus* spp., and Enterobacteriaceae remained stable during the study period. Only for *S. aureus* was an increase observed. In 2005 an MRSA outbreak occurred, which could be responsible for the *S. aureus* HABSI increase. Nevertheless, the incidence of *S. aureus* HABSIs remained low: 17 (0.3%) of 5,449 admissions in the first 10-year period versus 59 (1.3%) of 4,380 admissions in the last decade. The National Nosocomial Infections Surveillance System reported a 13% increase in healthcare-associated *S. aureus* infections among all birth-weight categories and a 308% increase in healthcare-associated MRSA infections (31% bloodstream infections) during 1995–2004.[22] As in our research, the *S. aureus* HABSI increase was more pronounced since 2002. However, besides the MRSA outbreak in 2005, no high incidence of MRSA HABSIs was noticed in our NICU compared with other European countries.[23]

As in other studies, CoNS are the most common causative pathogens for HABSIs in our NICU.[2,3,24-28] The relationship between CoNS HABSIs and vascular access is well known. Therefore, prevention strategies need to be directed at improving hand hygiene, skin-disinfection procedures, and so on. Every blood culture positive for CoNS should raise suspicion of contamination. It is recognized that surveillance according to the NICHD criteria tends to overestimate the HABSI rate, particularly the CoNS HABSI rate. To distinguish between contamination and true infection with a skin commensal, more criteria are needed. Such criteria are proposed by Modi et al.[16] Three of 10 predefined clinical signs could be predictive for a positive blood culture (area under the curve = 0.83). This validated model is a nonambiguous case definition, is practicable for clinicians, and may be more achievable for the neonate, because no second blood culture is required. This model will be used and tested for reliability in our future research.

An estimation of the contaminated blood cultures might be demonstrated by the number of mixed cultures with CoNS or even with *Enterococcus* spp.[16,29,30] Although enterococci are defined as recognized pathogens according to the CDC, Freeman et al[29] are attending to the possibility that enterococci in adults could be contaminants, particularly when mixed

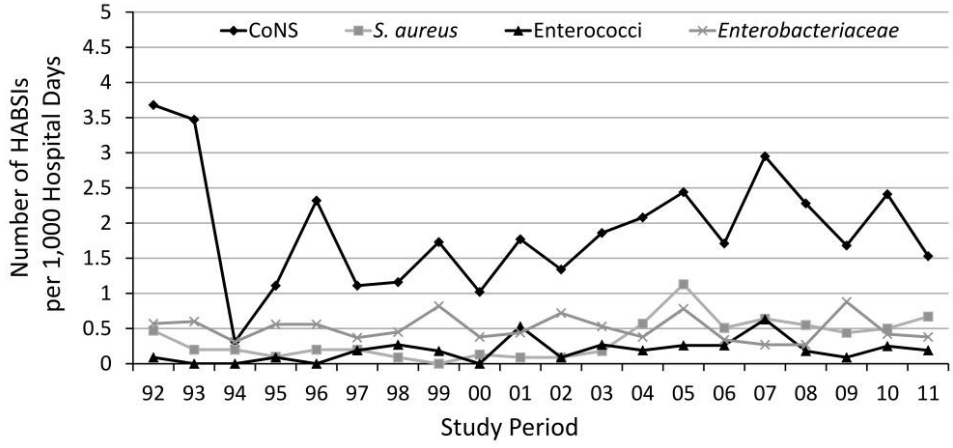

FIGURE 2. Number of healthcare-associated bloodstream infections (HABSIs) caused by coagulase-negative staphylococci (CoNS), *Staphylococcus aureus*, enterococci, and Enterobacteriaceae per 1,000 hospital-days from 1992 through 2011.

with skin organisms. In our cohort, 19 of 35 mixed cultures included CoNS and 11 included *Enterococcus* spp., of which 6 also included CoNS. Additionally, almost all mixed cultures with CoNS appeared in the second decade. These numbers might reflect a high amount of contamination and indicate the need for training programs on proper sampling techniques.[14,31]

Trends in Outcome

A mean 6% case fatality rate reflects the importance of HABSIs as a potential lethal complication in NICUs. However, case fatality remains low compared with that in other studies.[3,7,10] Similar findings were observed concerning the causative pathogens.[3,7] To our knowledge, no study separately reported definite and possible HABSI incidence densities and outcome using identical NICHD criteria. One recent study by Jean-Baptiste et al[32] of neonatal CoNS infections reported definite and possible rates but used different case definitions and did not report mortality of CoNS HABSIs separately. Because of our separate analysis, we may discern the importance of the definite and possible group: the absence of mortality in the possible group is an argument in favor of a preponderance of contamination over true infection.

Conclusion

During the period 1995–2011 an increase in incidence density rate occurred, while a decrease in case fatality was noticed during the last decade. Better perinatal care might be responsible for the latter. An incidence density of 3.1 per 1,000 hospital-days on average, a decrease in days before infection, and a high incidence of CoNS as a causative pathogen indicate that HABSIs remain an epidemiological, diagnostic, and therapeutic issue in our NICU and stress the need for vigorous application of evidence-based prevention measures, in particular for catheter care. Our research provides baseline data that allow benchmarking for the assessment of the effectiveness of future prevention strategies.

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Address correspondence to Evelien Verstraete, MNSc, Department of Internal Medicine, Ghent University Hospital, De Pintelaan 185, 9000 Ghent, Belgium (evelienh.verstraete@ugent.be).

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