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VENTILATOR-ASSOCIATED PNEUMONIA IN A MULTI-HOSPITAL SYSTEM: DIFFERENCES IN MICROBIOLOGY BY LOCATION

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ABSTRACT

OBJECTIVE: To determine whether there were differences in the microbiologic etiologies of ventilator-associated pneumonia in different clinical settings.

DESIGN: Observational retrospective cohort study of microbiologic etiologies of ventilator-associated pneumonia from 1998 to 2001 in a multi-hospital system. Microbiologic results were compared between hospitals and between different intensive care units (ICUs) within hospitals.

SETTING: Three hospitals—one pediatric teaching hospital, one adult teaching hospital, and one community hospital—in one healthcare system in the midwestern United States.

PATIENTS: Patients at the target hospitals who developed ventilator-associated pneumonia and for whom microbiologic data were available.

RESULTS: Seven hundred fifty-three episodes of ventila-

tor-associated pneumonia had culture data available for review. The most common organisms at all hospitals were *Staphylococcus aureus* (28.4%) and *Pseudomonas aeruginosa* (25.2%). The pediatric hospital had higher proportions of *Escherichia coli* (9.5% vs 2.3%; $P < .001$) and *Klebsiella pneumoniae* (13% vs 3.1%; $P < .001$) than did the adult hospitals. In the pediatric hospital, the pediatric ICU had higher *P. aeruginosa* rates than did the neonatal ICU (33.3% vs 17%; $P = .01$). In the adult hospitals, the surgical ICU had higher *Acinetobacter baumannii* rates (10.2% vs. 1.7%; $P < .001$) than did the other ICUs.

CONCLUSIONS: Microbiologic etiologies of ventilator-associated pneumonia vary between and within hospitals. Knowledge of these differences can improve selection of initial antimicrobial regimens, which may decrease mortality (*Infect Control Hosp Epidemiol* 2003;24:853-858).

Ventilator-associated pneumonia is a common hospital-acquired infection among patients requiring mechanical ventilation, resulting in excess mortality, prolonged hospitalization, and increased costs of medical care.¹⁻⁵ The estimated rate of ventilator-associated pneumonia ranges from 10% to 65% and reported mortality rates are high.^{3,8} The increase in mortality has been found in several studies to be independent of severity of illness and underlying diagnoses. An episode of ventilator-associated pneumonia can also increase the length of hospital stay by 6 to more than 30 days and add at least \$5,000 to the cost of the hospitalization.^{5,7}

Recently, the importance of adequate empiric antimicrobial therapy for nosocomial infections has been emphasized. Inadequate antibiotic therapy has been associated with increased mortality from ventilator-associated pneumonia in several studies.^{7,9-14} Risk factors for receiving inadequate antimicrobial therapy include prior antibiotic exposure, presence of invasive devices, prolonged hospital stay, and prolonged ventilatory support.¹⁴ Several studies have recommended that antibiotic choices be guid-

ed by knowledge of the common etiologic agents for ventilator-associated pneumonia in individual hospitals.¹³⁻¹⁶

There may be significant differences in the microbiologic etiologies of pneumonia in different hospitals and in different intensive care units (ICUs) within a single hospital. Little data exist about ventilator-associated pneumonia in pediatric settings. We reviewed cases of ventilator-associated pneumonia from 1998 to 2001 from three different hospitals (an urban teaching center, a suburban community hospital, and a pediatric teaching facility) in a single healthcare system to evaluate differences in common microbiologic etiologies of ventilator-associated pneumonia among different types of hospitals and among different locations within each hospital.

METHODS

Setting

This study was performed using data from three hospitals—one teaching, one community, and one pediatric—within Barnes-Jewish Christian (BJC) HealthCare, a 13-hospital integrated healthcare delivery system in

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TABLE 1
DEFINITION OF VENTILATOR-ASSOCIATED PNEUMONIA FOR ADULTS¹⁷

Pneumonia must meet only one of the following three criteria groups but may meet more:

A. Group 1: Patient has rales or dullness to percussion on physical examination of the chest AND at least one of the following:

- a. New onset of purulent sputum or change in character of sputum.
- b. Organism isolated from blood culture.
- c. Isolation of pathogen from a specimen obtained by BAL, transtracheal aspirate, bronchial brushing, or biopsy.

B. Group 2: Patient has a chest radiographic examination that shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion that *persists for greater than 48 hours* AND at least one of the following:

- a. New onset of purulent sputum or change in character of sputum.
- b. Organism isolated from blood culture.
- c. Isolation of pathogen from a specimen obtained by BAL, transtracheal aspirate, bronchial brushing, or biopsy.
- d. Isolation of virus or detection of viral antigen in respiratory secretions.
- e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen.
- f. Histopathologic evidence of pneumonia.

C. Group 3: Patient has a chest radiographic examination that shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion that persists for greater than 48 hours AND the following two criteria:

- a. Fever above 38.3°C.
- b. White blood cells greater than 10,000/mm³.

BAL = bronchoalveolar lavage.

eastern Missouri and western Illinois, which is affiliated with Washington University School of Medicine. The teaching hospital, an urban university-affiliated hospital, is a 1,000-bed primary-care and tertiary-care facility. An average of 6,400 patients are admitted annually to the six ICUs (medical, 19 beds; surgical-trauma-burns, 18 beds; cardiac care, 18 beds; medical-surgical, 12 beds; surgical cardiothoracic, 17 beds; and neurologic-neurosurgical, 20 beds).

The community hospital is a 500-bed private community hospital serving suburban St. Louis, Missouri, and the surrounding rural communities of eastern Missouri. This hospital has two 10-bed combined medical and surgical ICUs, which admit approximately 140 patients, combined, per month. There is also a 10-bed cardiothoracic ICU.

The pediatric hospital is a 235-bed academic tertiary-care center affiliated with Washington University School of Medicine. It has a 300-mile radius referral base in southeastern Missouri and southwestern Illinois. The pediatric hospital has two ICUs: a pediatric ICU (PICU) and a neonatal ICU (NICU). It is a level III NICU with 700 to 750 admissions per year with an average census of 50 patients and a 52-bed capacity. It is a combined medical-surgical PICU with 26 beds. The PICU admits approximately 1,400 patients annually.

Study Methods

The data analyzed for this study were obtained from the Infection Control and Hospital Epidemiology database of BJC HealthCare to evaluate the a priori hypothesis that differences in microbiologic etiologies of ventilator-associated pneumonia exist within and between hospitals. In each of the study hospitals, ventilator-associated pneu-

monia is a targeted nosocomial infection monitored through prospective surveillance by infection control specialists.

The infection control specialists at these three facilities are all registered nurses, and all have completed infection control certification through the Association for Professionals in Infection Control and Epidemiology, Inc. All of the BJC HealthCare hospitals participate in a coordinated Infection Control and Hospital Epidemiology Consortium, which facilitates monthly meetings of the specialists from all of the system's hospitals. Definitions and processes for surveillance are agreed on at the Consortium level, and all specialists are trained in the use of the definitions for surveillance. The definitions of ventilator-associated pneumonia used for surveillance are based on the Centers for Disease Control and Prevention National Nosocomial Infections Surveillance System definitions¹⁷ and are listed in Table 1 (adults) and Table 2 (children).

Each case of pneumonia identified by the specialists is reported, on paper or electronically, to the Consortium, where the reports from all of the hospitals are compiled into the Infection Control and Hospital Epidemiology database. The date that the patient meets the above criteria is recorded as the date of onset. Other information collected for each case includes date of intubation, date of admission, hospital and ICU location, and culture results. Demographic data were not uniformly collected. Episodes of ventilator-associated pneumonia from 1998 to 2001 from the three hospitals described above were reviewed to determine their microbiologic etiologies.

We reviewed all reported episodes of ventilator-

TABLE 2
DEFINITION OF VENTILATOR-ASSOCIATED PNEUMONIA FOR CHILDREN¹⁷

1. Patient younger than 12 months has two of the following: apnea, tachypnea, bradycardia, wheezing, rhonchi, or cough AND any of the following:
 - a. Increased production of respiratory secretions.
 - b. New onset of purulent sputum or change in character of sputum.
 - c. Organism is isolated from blood culture.
 - d. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy.
 - e. Isolation of virus or detection of viral antigen in respiratory secretions.
 - f. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen.
 - g. Histopathologic evidence of pneumonia.
2. Patient older than 12 months has chest radiologic examination that shows new or progressive infiltrate, cavitation, consolidation, or pleural effusion AND any of the following:
 - a. Increased production of respiratory secretions.
 - b. New onset of purulent sputum or change in character of sputum.
 - c. Organism isolated from blood culture.
 - d. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy.
 - e. Isolation of virus or detection of viral antigen in respiratory secretions.
 - f. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen.
 - g. Histopathologic evidence of pneumonia.

associated pneumonia for which any respiratory cultures dated from 7 days before to 7 days after the date of diagnosis were recorded by the infection control specialist. Most (82.5%) of the recorded cultures were performed within 2 days of the date of the diagnosis of pneumonia. Episodes for which negative cultures were recorded were included. Cases were excluded if no culture data were included in the pneumonia report by the infection control specialist. Only first episodes of ventilator-associated pneumonia were included in the analysis to ensure the independence of observations. Duplicate culture reports and multiple cultures with the same results from one episode of ventilator-associated pneumonia were removed. Culture results reported as "no growth" or "normal flora" were categorized as "no causative organism identified." Cases of ventilator-associated pneumonia were categorized as early, occurring within the first 4 days on the ventilator, and late, occurring after 5 or more days on the ventilator.¹⁸⁻²¹ Data were summarized for all three hospitals combined and then compared between adult and pediatric hospitals, between teaching and community adult hospitals, and between types of ICUs at all three hospitals.

Statistical Methods

Data were analyzed using SPSS software (version 10.0; SPSS, Inc., Chicago, IL). Comparisons were made using the chi-square or, when appropriate, Fisher's exact test. All tests of significance were two-tailed with a *P* value of less than .05 considered significant. Adjustment for multiple comparisons was made with the Bonferroni correction. Human Subjects Committee approval was obtained for this study from the Washington University Human Subjects Committee.

RESULTS

In the three hospitals, there were 931 episodes of ventilator-associated pneumonia among 878 patients. Most patients had one episode of ventilator-associated pneumonia (834; 94.9%); 44 patients had more than one episode (second episodes were excluded from the analysis). One hundred fifty-eight (16.9%) of the episodes were early ventilator-associated pneumonia (occurring within 96 hours of intubation). The proportion of early ventilator-associated pneumonia was lower at the pediatric hospital (11.4% vs 19.7%; *P* = .0068). Microbiologic data were included in the pneumonia report for 795 episodes. For the purposes of analysis, only first episodes of pneumonia among patients were included, leaving 753 episodes of ventilator-associated pneumonia: 200 at the pediatric hospital, 130 at the community hospital, and 423 at the teaching hospital. Only one organism was identified in most of the episodes of ventilator-associated pneumonia (589; 78.2%). Two organisms were identified in 126 (16.7%) of the episodes and 38 (5%) of the episodes had more than two organisms identified. In 128 (17%) of the cases of ventilator-associated pneumonia, no causative organism was identified (Table 3). Cases with no identified causative organism were more common in the adult hospitals (123 of 128; 96.1%).

In the three hospitals combined, *Staphylococcus aureus* was the most commonly isolated organism associated with ventilator-associated pneumonia (isolated 214 times in 753 episodes; 28.4%). Of those isolates, 78 (36.4%) were resistant to methicillin. *Pseudomonas aeruginosa* was the second most commonly identified organism (190; 25.2%). Several different gram-negative rods were found in approximately 6% of the cases (Table 3). The distribution of organisms at the three hospitals is shown in Figure

TABLE 3
MICROBIOLOGY OF VENTILATOR-ASSOCIATED PNEUMONIA AT THE THREE HOSPITALS, 1998 TO 2001 (N = 753 EPISODES)

Organism Identified	No. of Infections Associated With Organism (%)		
	Early VAP*	Late VAP*	Total
	(n = 137)	(n = 616)	
<i>Pseudomonas aeruginosa</i>	22 (16)	168 (27.3)	190 (25.2)
Methicillin-sensitive <i>Staphylococcus aureus</i>	30 (21.9)	106 (17.2)	136 (18.1)
Methicillin-resistant <i>Staphylococcus aureus</i>	11 (8)	67 (10.9)	78 (10.3)
<i>Enterobacter cloacae</i>	4 (2.9)	43 (7)	47 (6.2)
<i>Acinetobacter baumannii</i>	4 (2.9)	40 (6.5)	44 (5.8)
<i>Klebsiella pneumoniae</i>	3 (2.2)	40 (6.5)	43 (5.7)
<i>Serratia marcescens</i>	6 (4.4)	30 (4.9)	36 (4.7)
<i>Stenotrophomonas maltophilia</i>	5 (3.6)	27 (4.4)	32 (4.2)

VAP = ventilator-associated pneumonia.

*Early VAP = within 4 days of intubation; late VAP = after 5 or more days of mechanical ventilation.

1. In the adult hospitals, the proportion of infections with *P. aeruginosa* was higher in late cases of ventilator-associated pneumonia (28.8% vs 14.8%; $P = .002$) and the proportion of infections with *Haemophilus influenzae* was higher in early cases of ventilator-associated pneumonia (6% vs 0.7%; $P = .001$). In the pediatric hospital, there were no significant differences in etiologies between early and late infections.

The most common organisms associated with ventilator-associated pneumonia were similar at the adult and the pediatric hospitals (Table 4). *Staphylococcus aureus* and *P. aeruginosa* were the most frequently identified pathogens in both settings. Rates of methicillin resistance were higher at the adult hospitals (44.6% vs 14%; $P < .001$). In the pediatric setting, the proportion of infections with *Escherichia coli*, *Enterobacter cloacae*, and *Klebsiella* was higher (Table 4).

Within the pediatric hospital, the microbiology of ventilator-associated pneumonia differed between the PICU and the NICU. *Staphylococcus aureus* and *P. aeruginosa* were the most frequently identified pathogens in both ICUs; however, *P. aeruginosa* was more common in the PICU (33.3% vs 17%; $P = .01$) and *Staphylococcus aureus* was more common in the NICU (38% vs 17.6%; $P = .002$) (Fig. 2). Rates of methicillin resistance in *Staphylococcus aureus* were slightly higher in the NICU (NICU, 6 of 38 [15.8%] vs PICU, 2 of 15 [13.3%]; $P =$ not significant), although the overall numbers were small. The NICU had a higher proportion of pneumonias associated with *Escherichia coli* (14% vs 3.6%; $P = .015$) and the PICU had a higher proportion of pneumonias associated with *H. influenzae* (8.3% vs 0%; $P = .003$).

There were fewer differences between the adult teaching hospital and the adult community hospital.

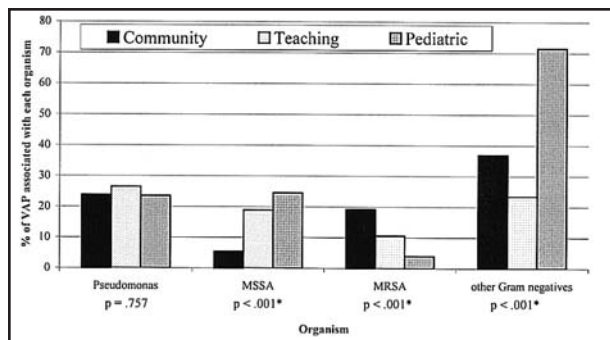


FIGURE 1. Organisms isolated from patients with ventilator-associated pneumonia by hospital. VAP = ventilator-associated pneumonia; MSSA = methicillin-susceptible *Staphylococcus aureus*; MRSA = methicillin-resistant *S. aureus*. *Statistically significant after correction for multiple comparisons.

Again, the most common organisms were *Staphylococcus aureus* and *P. aeruginosa*. The rate of methicillin resistance was higher at the community hospital than at the teaching facility (78.1% vs 36%; $P < .001$). The proportion of ventilator-associated pneumonia associated with *Enterobacter cloacae* was higher at the community hospital (7.7% vs 0.9%; $P < .001$). The proportion of ventilator-associated pneumonia with *Escherichia coli* was also higher at the community hospital (5.4% vs 1.4%; $P = .009$), although this result was not significant after correction for multiple comparisons.

Within the adult hospitals, differences were also seen by location within the hospital. The community hospital has two medical-surgical ICUs and one cardiothoracic ICU. The teaching hospital has six separate ICUs: medical, cardiac, surgical, cardiothoracic, neurologic-neurosurgical, and a combined medical-surgical ICU. The most common organisms associated with ventilator-associated pneumonia in all of the adult ICUs were *Staphylococcus aureus* and *P. aeruginosa*. *Staphylococcus aureus* was the most commonly isolated organism in the dedicated surgical ICU, in the neurologic-neurosurgical ICU, and in the combined medical-surgical ICUs. The highest level of *Staphylococcus aureus* isolation was in the neurologic-neurosurgical ICU (38% vs 25.4% in other units combined; $P = .02$), although the difference was not statistically significant after correction for multiple comparisons. *P. aeruginosa* was the most commonly isolated organism in the dedicated medical ICU, the dedicated cardiac care unit, and the cardiothoracic units. *Acinetobacter baumannii* occurred with increased frequency in the dedicated surgical ICU (10.2% vs 1.7%; $P < .001$). *H. influenzae* occurred with increased frequency in the cardiothoracic ICUs (8% vs 1%; $P = .005$), as did *Escherichia coli* (8% vs 1.8%; $P = .022$), although that difference was not significant after correction for multiple comparisons.

DISCUSSION

Nosocomial infections are common causes of excess morbidity and hospital costs among patients

TABLE 4
MICROBIOLOGY OF VENTILATOR-ASSOCIATED PNEUMONIA AT THE PEDIATRIC AND ADULT HOSPITALS

Organism Identified	No. of Cultures With Organism (% of VAP)		P
	Pediatric Hospital (n = 200 VAP)	Adult Hospitals (n = 553 VAP)	
<i>Staphylococcus aureus</i>	57 (28.5)	157 (28.4)	.7151
Methicillin-resistant <i>Staphylococcus aureus</i>	8 of 57 (14)	70 of 157 (44.6)	.0001*
<i>Pseudomonas aeruginosa</i>	47 (23.5)	143 (25.9)	.9462
<i>Escherichia coli</i>	19 (9.5)	13 (2.3)	.0001*
<i>Enterobacter cloacae</i>	33 (16.5)	14 (2.5)	.0001*
<i>Acinetobacter baumannii</i>	16 (8)	28 (5.1)	.1291
<i>Klebsiella pneumoniae</i>	26 (13)	17 (3.1)	.0001*
<i>Klebsiella oxytoca</i>	7 (3.5)	3 (0.5)	.0022*
<i>Serratia marcescens</i>	13 (6.5)	23 (4.2)	.0225

VAP = ventilator-associated pneumonia.

*Statistically significant after Bonferroni correction for multiple comparisons.

requiring intensive care. We evaluated microbial etiologies of ventilator-associated pneumonia in three hospitals in a single healthcare system. The organisms associated with ventilator-associated pneumonia that we identified are similar to those reported in the literature.^{12,13,15,16,18} The most common causes overall are *P. aeruginosa* and *Staphylococcus aureus*. Early cases of ventilator-associated pneumonia are more commonly associated with methicillin-sensitive *Staphylococcus aureus* and late cases with methicillin-resistant *Staphylococcus aureus*.¹⁹ Although there are fewer reports of causative organisms in the pediatric literature, our findings were similar to their findings,^{22,23} with aerobic gram-negative bacteria and *Staphylococcus aureus* being the most commonly identified.

We identified significant differences among the three different hospitals and the different ICUs within each hospital. Methicillin resistance in *Staphylococcus aureus* was more frequent at the adult hospitals than at the pediatric hospital and, specifically, was higher at the community hospital than at the teaching hospital. The increased resistance among adults may be due to a higher rate of chronic illness and more extensive contact with the healthcare system. The lower proportion at the teaching hospital may be attributable to more aggressive infection control efforts. The elevated level of resistance at the community hospital may be due to several outbreaks of methicillin-resistant *Staphylococcus aureus* in the ICUs there. This amount of methicillin resistance at the community hospital is instructive, reinforcing that antibiotic resistance is not limited to large urban teaching hospitals.

We also found significant differences between ICUs within individual hospitals. Within the pediatric hospital,

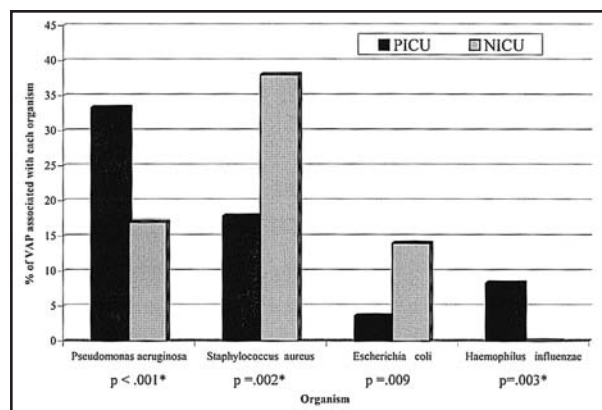


FIGURE 2. Microbiology of ventilator-associated pneumonia at the pediatric hospital: pediatric intensive care unit (PICU) versus neonatal intensive care unit (NICU). VAP = ventilator-associated pneumonia. *Statistically significant after correction for multiple comparisons.

methicillin-resistant *Staphylococcus aureus* rates were higher in the NICU than in the PICU (Fig. 2). *A. baumannii* occurred with increased frequency in the adult surgical ICU and *Staphylococcus aureus* occurred with increased frequency in the neurologic-neurosurgical ICU.

There are few data available about microbial etiologies of ventilator-associated pneumonia in different settings. In 1999, Rello et al.²⁴ found significant variation in the etiologies of ventilator-associated pneumonia among four different hospitals, three in Spain and one in France. Their study used quantitative bronchoscopic techniques for diagnosis and also included antibiotic use as a variable. However, their study was performed only in teaching facilities and only in adult hospitals. They suggested the possibility that, in large hospitals, the etiology of ventilator-associated pneumonia may vary significantly between ICUs, which we found to be true. Namias et al.¹⁵ found significant variability in antibiotic susceptibility between ICUs in a large teaching hospital. However, their study was confined to one hospital during a short (3-month) time period. They recommended the use of ICU-specific antibiograms to improve empiric antibiotic selection.

The importance of making appropriate antibiotic choices initially in the treatment of nosocomial infections is being increasingly appreciated. We found the organisms frequently associated with inadequate antimicrobial therapy in ventilator-associated pneumonia, specifically *P. aeruginosa*, *Staphylococcus aureus*, and *Acinetobacter* species,¹⁴ to be common and to fluctuate in frequency between different hospitals and ICUs. Awareness of local patterns of microbiologic etiologies of nosocomial infections can improve the selection of appropriate therapy.²⁴⁻²⁶ This information may also be helpful in developing targeted interventions to prevent contamination and infection.

This study has several limitations. This was a retrospective study, relying on data collected by infection con-

trol specialists, although the specialists in this health system are highly trained. Patients who had multiple cultures performed, if more than one organism was identified, will be overrepresented in the database. However, these results reflect the microbiologic data available to the treating physicians and their culturing practices. Although we had a fairly large sample size, 753 episodes of ventilator-associated pneumonia with culture data, the data came from only three hospitals and may not be generalizable to other institutions. Also, we did not collect information on antibiotic use in each setting.

As increased attention is turned to the role of adequate initial antibiotic therapy in treating nosocomial infections such as ventilator-associated pneumonia, the importance of local microbiologic data in making antibiotic selections is being recognized. This article demonstrates that the expected pathogens that empiric regimens should cover may vary significantly between individual hospitals and even between individual ICUs within one hospital. Knowledge of these local differences could improve selection of initial antimicrobial regimens and may improve outcomes from nosocomial infections.

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