

# Investigation of pulmonary infection pathogens in neurological intensive care unit

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**Purpose:** The purpose of this study is to investigate the distribution and antimicrobial susceptibility of pathogenic bacteria in inpatients with pulmonary infection in the neurological intensive care unit (NICU).

**Methods:** A total of 947 sputum specimens of 428 inpatients from May 2007 to May 2008 in the NICU were enrolled in the study, and bacterial identification and antibiotic susceptibility tests were analyzed using a VITEK 2 system.

**Results:** A total of 400 positive bacterial strains were separated from 947 sputum specimens, with Gram-negative bacteria accounting for 69.0% of the total strains collected. The most common strain of Gram-negative bacteria was *Klebsiella pneumoniae* (20.5%). Gram-positive bacteria accounted for 10.0% of the total strains, with the most common strain being *Staphylococcus aureus* (2.5%). Fungal species accounted for 21.0% of the total strains, and the most common strain collected was *Candida albicans* (12.25%). Imipenem was the most effective antibiotic against Gram-positive and Gram-negative bacteria. The drug resistance rate of Gram-positive bacteria to penicillin G was 100%, and the Gram-positive bacteria were 100% sensitive to teicoplanin, vancomycin, and linezolid.

**Conclusions:** Gram-negative bacterial infections account for the majority of pulmonary infections in the NICU, with fungal infections being the second most common infection type observed. In addition, fungal infections seem to be related to mortality in the NICU.

**Keywords:** nosocomial infection, pulmonary infection, drug resistance, neurological intensive care unit

## Introduction

The neurological intensive care unit (NICU) is the main place where neurocritical patients are admitted. The chance of infection in the NICU is higher than in the general wards because operations such as endotracheal intubation, incision, sputum suction, and catheterization are performed. Pulmonary infection is a major form of nosocomial infection, and it is associated with increased length of stay and mortality in intensive care units (ICUs).<sup>1,2</sup> With the new types of antibiotics widely used in the clinic, the emergence of pathogenic bacteria have increased, and multidrug resistant and high drug-resistant strains are having a negative impact on the prognosis of inpatients.<sup>3</sup> To understand the distribution and changes in trends of pathogenic bacteria in NICU, we carried out bacterial culture and antimicrobial susceptibility tests on sputum specimens of inpatients from May 2007 to May 2008 in the NICU of our hospital.

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# Methods

This research was approved as a clinical prospective observational cohort study by the ethics committee of the First Affiliated Hospital of Chongqing Medical University in Chongqing, China. Informed consents were obtained from all subjects prior to the study. Our NICU comprises 18 beds with an average of 1500 admissions/year.

A total of 947 sputum specimens were collected from 428 patients with pulmonary infection after admission in our NICU from May 1, 2007 to May 31, 2008. All patients were admitted to the NICU for more than 48 h. The standardized criteria for respiratory infections include fever, cough, increased leukocyte count ( $>10 \times 10^9/L$ ), increased neutrophil percentages ( $>80\%$ ), and harsh breath sounds with dry and medium rales or wheezy phlegm. Signs of pulmonary infection were observed by chest X-ray. Routine sputum specimens were submitted for tests, and bronchoalveolar lavage fluid was collected if the patient underwent tracheal intubation or tracheotomy. Bacterial identification and antibiotic susceptibility tests were performed on all specimens with a VITEK 2 system (bioMérieux, Marcy l'Etoile, France) in the Department of Microbiology in our hospital,<sup>4,5</sup> and the following standard quality control strains were obtained from the National Committee for Clinical Laboratory Standards of China: *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 25923, and *Escherichia coli* ATCC 25922.

The  $\mu$  test, description of measurement, and enumeration of data were performed using SPSS 11.0 (SPSS Inc, Chicago, IL). The central tendency was described by arithmetic mean, and the relative number was demonstrated with the ratio and frequency. Statistical significance was defined as  $P < 0.05$ .

# Results

A total of 428 neurocritical patients were enrolled in this study: 225 were females and 203 were males. The demographics, underlying diseases, and outcomes of these patients are shown in Table 1. The median age was 61.2 years, and the median length of the hospital stay was 7.4 days. Thirty patients (7%) died during the period of admission.

A total of 400 pathogenic strains were detected in 947 sputum specimens with a 42.2% positive rate. Of these strains, 276 were Gram-negative bacteria, accounting for 69.0% of total species, and included *Klebsiella pneumoniae*, *P. aeruginosa*, and *Acinetobacter baumannii*. Among the strains collected, forty were Gram-positive bacteria, accounting for 10.0%, and included *S. aureus*, *Staphylococcus epidermidis*, and

**Table 1** The demographics, underlying diseases, and outcomes of inpatients

Variable	Values
Median age	61.2 years (16–89)
Gender	
Male	225 (52.6%)
Female	203 (47.4%)
Admission diagnosis	
Cerebral infarction	140 (32.7%)
Intracerebral hemorrhage	69 (16.1%)
Subarachnoid hemorrhage	38 (8.9%)
Encephalitis	48 (11.2%)
Tuberculous meningitis	15 (3.5%)
Multiple sclerosis	27 (6.3%)
Guillain–Barre syndrome	20 (4.7%)
Acute myelitis	12 (2.8%)
Status epilepticus	35 (8.2%)
Encephalopathy	24 (5.6%)
Median length of NICU stay	7.4 days (2–30)
Outcome	
Discharged	398 (93.0%)
Mortality	30 (7.0%)

*Hemolytic staphylococcus*. A total of 84 strains were fungi, including *Candida albicans* (Table 2).

Imipenem was the most effective antibiotic for the treatment of Gram-positive and Gram-negative bacteria. The drug resistance rate of Gram-positive bacteria was 100% to penicillin G and above 80% to erythromycin, azithromycin, and clarithromycin. Gram-positive bacteria were 100% sensitive to teicoplanin, vancomycin, and linezolid. The antibiotic

**Table 2** The distribution and ratio of pulmonary infection pathogens in NICU

Bacterium	Numbers (strain)	Percentage
Gram-negative bacteria	276	69.0
<i>Klebsiella pneumoniae</i>	82	20.5
<i>Pseudomonas aeruginosa</i>	62	15.5
<i>Acinetobacter baumannii</i>	48	12.0
<i>Pseudomonas maltophilia</i>	14	3.5
<i>Enterobacter cloacae</i>	10	2.5
<i>Flu hemophilic bacteria</i>	6	1.5
<i>Acinetobacter junii</i>	4	1.0
<i>Enterobacter aerogenes</i>	4	1.0
Others	46	11.5
Gram-positive bacteria	40	10.0
<i>Staphylococcus aureus</i>	10	2.5
<i>Staphylococcus epidermidis</i>	10	2.5
<i>Hemolytic staphylococcus</i>	7	1.75
Others	13	3.25
Fungus	84	21.0
<i>Candida albicans</i>	49	12.25
<i>Candida tropicalis</i>	15	3.75
Others	20	5.0

**Table 3** Resistance rates of common Gram-negative bacilli to antibiotics (%)

Antibiotics	<i>Klebsiella pneumoniae</i> (N = 82)	<i>Pseudomonas aeruginosa</i> (N = 62)	<i>Acinetobacter baumannii</i> (N = 48)
Ampicillin	100	100	100
Co-trimoxazole	100	100	100
Amoxicillin	100	–	100
Cephalothin	100	–	100
Cefotaxime	100	–	100
Netilmicin	100	–	100
Cefuroxime	100	–	100
Ticarcillin	100	95.16	100
Piperacillin	100	61.29	100
Cefazolin	90	100	100
Ampicillin/ sulbactam	90	100	87.50
Gentamicin	82.72	75.38	72.92
Nitrofurantoin	80	100	100
Ceftriaxone	76.25	100	100
Cefepime	72.84	55.38	55.32
Trimethoprim/ sulfamethoxazole	72.5	100	86.96
Aztreonam	72.5	67.21	78.26
Tetracycline	72	100	100
Ceftazidime	71.6	66.15	77.08
Ceftizoxime	62	96.55	76.67
Ticarcillin/ clavulanic acid	60.78	95.08	68.97
Tobramycin	60.49	73.85	60.42
Amikacin	56.25	37.70	34.78
Ciprofloxacin	54.34	76.92	75
Levofloxacin	51.25	59.02	17.02
Piperacillin/ tazobactam	16.25	28.13	20
Cefotetan	10	100	100
Ertapenem	10	–	–
Imipenem	1.23	35.38	2.08
Cefoxitin	0	–	100
Meropenem	0	43.10	0

resistance rates of common Gram-negative bacilli and Gram-positive cocci are shown in Tables 3 and 4.

A total of 36 strains were detected from 30 deceased inpatients; 14 of these were fungal strains, with a 38.9% positive rate. A total of 364 strains were detected in 398 discharged inpatients, with 70 fungal strains with a 19.2% positive rate. When the positive rates of fungal infection in the mortality and discharged groups were compared, a statistical difference was found ( $P < 0.05$ ).

## Discussion

Patients in the NICU are always dangerously ill, and most of them display limited activity and consciousness disturbances.

Pulmonary infection is the most common complication for these patients. In this study, we investigated the distribution and antimicrobial susceptibility of pathogenic bacteria associated with pulmonary infection in inpatients in NICU. Pathogenic bacteria were defined when bacterial identification determined that the same pathogenic bacteria two successive or predominant bacteria growth was observed 3 times. Thus, only 400 strains of pathogens were detected with a 42.2% positive rate. Finally, we analyzed the positive strains and found that a low positive rate did not affect the level of bacteria distribution or the resistance rate.

In our NICU, the most common pathogens associated with pulmonary infection were Gram-negative bacilli, accounting for 69.0%; this finding is in accordance with reports that Gram-negative bacteria are the most common pathogens associated with nosocomial infections.<sup>6</sup> In the general population, the majority of pulmonary infections are caused by *S. pneumoniae*, but in our NICU, the three most common pathogens associated with pulmonary infection were *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii*. Our data show that *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii* have high resistance rates to penicillins, with the exception of piperacillin/tazobactam. Studies have shown that drug-resistant mechanism for penicillins may be mainly due to the fact that the bacterium produces  $\beta$ -lactamase, which breaks open the  $\beta$ -lactam ring of the antibiotic, rendering the penicillins ineffective.<sup>7</sup> *K. pneumoniae* and *A. baumannii* are relatively efficient to carbapenems, and resistance rates for imipenem are 1.23% and 2.08%, respectively; both are efficient to meropenem. Carbapenem antibiotics gain access to the cytoplasm and combine with penicillin-binding protein (PBP) through the proteins with permeability on bacterial outer membrane, by interfering with cell wall synthesis and thus sterilize, because the majority of  $\beta$ -lactamase have with a high degree of stability, so the treatment can achieve a better efficacy.<sup>8</sup> Clinicians can use carbapenem antibiotics as empiric antibiotics to treat infections caused by *K. pneumoniae* and *A. baumannii*.<sup>9</sup> After obtaining drug susceptibility data, we can rationally adjust the concentrations of effective antibiotics.

*P. aeruginosa* showed a resistance rate of more than 30% to imipenem and meropenem. This rate is higher than that reported in literature.<sup>6</sup> Piperacillin/tazobactam as combination therapy against *P. aeruginosa* showed the lowest resistance rate.<sup>10</sup> Prevalence of *P. aeruginosa* has gradually increased and has become one of the major pathogenic

**Table 4** Resistance rates of common Gram-positive cocci to antibiotics (%)

Antibiotics	<i>Staphylococcus aureus</i> (N = 10)	<i>Staphylococcus epidermidis</i> (N = 10)	<i>Hemolytic staphylococcus</i> (N = 7)
Penicillin G	100	100	100
Erythromycin	100	80	100
Azithromycin	100	80	100
Clarithromycin	100	80	100
Ciprofloxacin	100	70	100
Tetracycline	100	20	14.29
Amoxicillin	90	90	100
Ampicillin/sulbactam	90	90	100
Cefaclor	90	90	100
Oxacillin	90	90	85.71
Gentamicin	90	50	100
Imipenem	88.89	90	100
Ceftriaxone	88.89	90	100
Cefuroxime	88.89	90	100
Cefotaxime	88.89	90	100
Rifampicin	70	40	14.29
Fosfomycin	44.44	10	100
Trimethoprim/sulfamethoxazole	42.86	90	60
Moxifloxacin	33.33	10	0
Fusidate	22.22	10	0
Dalfopristin	0	0	0
Linezolid	0	0	0
Teicoplanin	0	0	0
Vancomycin	0	0	0

bacteria in the ICU.<sup>11,12</sup> Some researchers have found that carbapenem-resistant *P. aeruginosa* is a risk factor for patient mortality.<sup>13</sup> The resistance mechanisms include the production of  $\beta$ -lactamses, efflux pumps, and target-site or outer membrane modifications.<sup>14</sup>

Gram-positive bacteria were the least prevalent group of pathogens found in the NICU and include *S. aureus*, *S. epidermidis*, and *Hemolytic staphylococcus*. These strains are sensitive to teicoplanin and vancomycin, show high sensitivity to rifampicin, and are resistant to penicillin antibiotics. These findings are in accordance with the literature.<sup>15,16</sup>

In our study, we found that fungus was the second largest group of pathogens associated with pulmonary infection in our NICU. This proportion (21%) is higher than that reported in literature.<sup>17</sup> *C. albicans* is the most common fungal pathogen and is effective to fluconazole. One study showed that invasive fungal infections have become a major cause of morbidity and mortality in ICU, and invasive candidiasis accounts for up to 15%–30% of all nosocomial infections in critically ill patients.<sup>18</sup> We also found that fungal infection seemed to be related to mortality in our NICU. There are some reasons to explain the high proportions of fungal infections in the NICU. First, using

broad-spectrum antibiotics might inhibit the normal flora in the body and cause malignant growth of fungi. Second, patients in the NICU are severely ill with low immunity and high vulnerability to fungal infection. Finally, some medications commonly used to treat nervous system diseases, such as glucocorticoids, could cause disorder to the balance of the microecology in the body, causing dysbacteriosis and inducing increased fungal infection.

Currently, antibacterial resistance has become a serious problem in the NICU. This study was carried out at a single center, and our goal was to understand the changes in the distribution of bacterial strains and bacterial resistance in the NICU. We found that Gram-negative bacteria are still the most common pathogens associated with nosocomial pulmonary infections, whereas the percentages of fungal infection are higher than those reported in the literature and more related to mortality in our NICU. Bacteria are highly resistant to commonly used antibiotics, so bacterial culture and drug susceptibility tests are necessary for rationalizing the use of antibiotics and for correctly taking standard preventive measures and care.

## Disclosure

The authors have no conflict of interest to declare.

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