Nosocomial infections due to *Acinetobacter baumannii* in a pediatric intensive care unit in Turkey

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SUMMARY: Özdemir H, Kendirli T, Ergün H, Çiftçi E, Tapısız A, Güriz H, Aysev D, İnce E, Doğru Ü. Nosocomial infections due to *Acinetobacter baumannii* in a pediatric intensive care unit in Turkey. Turk J Pediatr 2011; 53: 255-260.

The aim of this study is to document the clinical characteristics and outcomes of *Acinetobacter baumannii* infections in pediatric patients in a pediatric intensive care unit (PICU) in Turkey. The ages ranged from 1 month to 16 years with a mean age of 55.5 months, and the male-to-female ratio was 1:1.5. Ventilator-associated pneumonia (10 patients) was the leading diagnosis, followed by catheter-related blood stream infection (4 patients), and bacteremia and ventilator-associated pneumonia associated with meningitis (1 patient) due to *A. baumannii*. Mechanical ventilation (93.3%), central venous catheter (73.3%), urinary catheter (93.3%), and broad spectrum antibiotic usage (80%) were the frequently seen risk factors. Neuromuscular (40%) and malignant (26.7%) disorders were the most common underlying diseases. Nosocomial *A. baumannii* is commonly multidrug-resistant, prolongs the length of stay in the PICU and increases the mortality rates in pediatric critical care.

Key words: Acinetobacter baumannii, nosocomial infection, pediatric intensive care unit.

Acinetobacter baumannii is an aerobic, Gram-negative coccobacillus. It is an important nosocomial pathogen and causes clinical infections, such as lower respiratory infections, urinary tract infections and bacteremia[1,2]. It is among the agents most commonly isolated from patients with severe nosocomial infections, especially those diagnosed in intensive care units (ICUs)[3,4]. In the literature, there is limited information regarding patients in pediatric ICUs (PICUs).

Risk factors for acquisition of *A. baumannii* include hospitalization, poor general medical status of patients, mechanical ventilation, cardiovascular or respiratory failure, previous infection or antimicrobial therapy, and the presence of central venous or urinary catheters[5]. Treatment of *A. baumannii* infections has become difficult because of the emerging resistance to multiple antibiotics in organisms[6]. The aim of this report was to document the clinical characteristics and outcomes of *A. baumannii* infections in pediatric patients in a PICU in Turkey.

Material and Methods

We reviewed the medical and laboratory records of 15 critically ill children who were determined to have *A. baumannii* infections between January 2008 and December 2008 in the Department of Pediatrics Intensive Care Unit of Ankara University Medical School, Turkey. The Department of Pediatrics has a 120-bed capacity, and the PICU has 6 beds for critically ill pediatric patients. A pediatric intensivist studies full-time in our PICU, and nosocomial infections are followed jointly by pediatric infectious diseases experts and the intensivist. Two-hundred and three pediatric patients were admitted to our PICU in this study period. In 2008, mechanical ventilation, central venous catheter and urinary catheter utilization rates were 0.78, 0.41 and 0.45, respectively. Hospital infection rate was 17.34/1000 bed days and device-associated infection rates were as follows: ventilator-associated pneumonia rate 15.68/1000 ventilator days, central venous catheter-related blood stream infection rate 10.56/1000 central venous

catheter days, and urinary catheter-related urinary system infection rate 1.6/1000 urinary catheter days.

Demographic data, clinical and laboratory features, antibiotic susceptibility of isolates, and treatment along with outcome were collected. Nosocomial infections (ventilator-associated pneumonia, catheter-related blood stream infection and urinary catheter-related infection) were defined by the standard Centers for Diseases Control and Prevention (CDC) definitions[7]. The Microbiology Laboratory of Ankara University Medical School processed all clinical samples for bacterial cultures with conventional methods. Blood cultures were processed using the Bactec 9240 blood culture system (Becton Dickinson, Cockeysville, MD, USA). Susceptibilities to antimicrobial agents were determined by the disc diffusion method in accordance with the guidelines of the Clinical Laboratory and Standards Institute[8].

Results

During a 12-month period, 15 critically ill children were infected by *A. baumannii*. Totally, 203 pediatric patients were admitted to the PICU during the study period. The mean ICU length of stay (LOS) of patients without *A. baumannii* infection was 7.6±7.5 days, while in children with *A. baumannii* infection, the mean LOS was 65.5±48.7 days ($p<0.001$). The mortality rate of infected patients was 33.3% and of the non-infected patients was 13.3% ($p>0.05$) during this study period. On the other hand, the mortality rate among non-infected patients decreased to 7.9% by excluding the end-stage patients with malignancy and those who died within the first 24 hours.

The ages ranged from 1 month to 16 years, with a mean age of 55.5±63.6 months, and the male-to-female ratio was 1:1.5. Ventilator-associated pneumonia was determined in 10 patients, catheter-related blood stream infection in 4 patients, and bacteremia, ventilator-

Table I. The Clinical and Laboratory Features of the Patients

Characteristic	n (%)
[a]Age (months)	55.5±63.6
Gender	
Male	6 (40)
Female	9 (60)
[a]Laboratory findings	
White blood count (/mm^3)	10 066±6938
Hemoglobin (g/dl)	9.5±1.6
Platelet count (/mm^3)	234 333±187 219
C-reactive protein (mg/dl)	10.0±12.9
Risk factors	
Mechanical ventilation	14 (93.3)
Central venous catheter	11 (73.3)
Urinary catheter	14 (93.3)
Broad spectrum antibiotic usage	12 (80)
Underlying diseases	
Neuromuscular disorder	6 (40)
Malignancy	4 (26.7)
Metabolic disorder	2 (13.3)
Cardiac disorder	2 (13.3)
Immunodeficiency syndrome	1 (6.7)
Infection types	
Ventilator-associated pneumonia	11 (64.7)
Catheter-related infection	5 (29.4)
Meningitis	1 (5.9)
[a]ICU length of stay before A. baumannii infection (day)	32.1±47.8
[a]ICU length of stay (day)	65.5±48.7
Mortality	5 (33.3)

[a]mean±SD

Table II. Antibiotic Susceptibility of the Isolates

Antibiotics	Susceptibility rate %
Colistin	100
Cefoperazone-sulbactam	73.3
Tobramycin	66.7
Ampicillin-sulbactam	60
Imipenem	53.3
Meropenem	46.7
Ciprofloxacin	46.7
Gentamicin	20
Amikacin	13.3
Ceftazidime	13.3
Piperacillin-tazobactam	6.7
Trimethoprim-sulfamethoxazole	6.7
Amoxicillin-clavulanate	0
Ampicillin	0
Ceftriaxone	0
Cephalothin	0
Piperacillin	0
Tetracycline	0

associated pneumonia and meningitis in 1 patient due to *A. baumannii*. Mechanical ventilation (93.3%), central venous catheter (73.3%), urinary catheter (93.3%), and broad spectrum antibiotic usage (80%) were the frequently observed risk factors in critically ill patients due to *A. baumannii*. Neuromuscular (40%) and malignant (26.7%) disorders were the most common underlying diseases. The clinical and laboratory features of the patients infected by *A. baumannii* are summarized in Table I. Most of the isolates were multidrug-resistant. According to the antibiogram of the isolates, the antibiotics with the highest *in vitro* susceptibility were colistin, cefoperazone-sulbactam and ampicillin-sulbactam, at 100%, 73.3% and 60%, respectively (Table II).

One-third of the patients did not respond to the antibiotics, including colistin, and died. One of them had a neuromuscular disorder as the underlying disease and the others had malignancy. The infection types were ventilator-associated pneumonia in 3/5, and bacteremia in the others. The treatment choice for the patients who were infected with *A. baumannii* and the clinical results of these treatments are shown in Table III.

Discussion

A. baumannii has become a formidable pathogen and has been responsible for a number of nosocomial infection outbreaks[1,9]. It has a remarkable capacity to develop resistance to all currently available antimicrobial agents, which complicates treatment, often contributes to prolonged hospital stays, and leads to substantial economic burden[10]. It is now increasingly reported as an important nosocomial pathogen implicated in outbreaks of respiratory, blood, central nervous system, and wound infections[11].

In addition to an ICU stay, risk factors for *A. baumannii* colonization and infection are recent surgery, central vascular catheterization, tracheostomy, mechanical ventilation, enteral feedings, APACHE II score, underlying malignancy, prior infection, organ system failure, prolonged hospitalization, and prior antibiotic use[12,13]. In a study with large numbers of pediatric patients, Chang et al.[6] reported that their patients' mean age was 6 years, and nearly half of them had an underlying disease, as malignancy and neurological disorder. Additionally, 92.3% of those patients had been mechanically ventilated, and 88.5% of them had been treated with multiple classes of antibiotics before the onset of infection[6]. Katragkou et al.[14] showed that use of carbapenems and other beta lactams, aminoglycosides, ranitidine, mechanical ventilation, central venous or urinary catheters, and LOS in PICU were among the factors significantly

Table III. The Treatment Choices and Clinical Results of the Patients

Patient no	Underlying disease	Type of infection	Treatment	Clinical result
1	Neuromuscular disorder	VAP	CS, colistin	Recovery
2	Malignancy	VAP	CS, colistin	Exitus
3	Metabolic disorder	VAP	CS, colistin	Recovery
4	Immunodeficiency syndrome	Bacteremia	Meropenem, CS, amikacin	Recovery
5	Neuromuscular disorder	VAP	CS, SAM, colistin	Recovery
6	Metabolic disorder	VAP	Colistin	Recovery
7	Malignancy	VAP	Meropenem, SAM, colistin	Exitus
8	Malignancy	Bacteremia	CS, colistin	Exitus
9	Neuromuscular disorder	VAP	Meropenem, SAM, colistin	Exitus
10	Cardiac disorder	Bacteremia	CS, colistin	Recovery
11	Neuromuscular disorder	VAP-bacteremia-meningitis	CS, SAM, colistin	Recovery
12	Neuromuscular disorder	VAP	Colistin	Recovery
13	Malignancy	Bacteremia	Colistin	Exitus
14	Cardiac disorder	VAP	CS, Colistin	Recovery
15	Neuromuscular disorder	VAP	Colistin	Recovery

VAP: Ventilator-associated pneumonia. CS: Cefoperazone-sulbactam. SAM: Ampicillin-sulbactam.

associated with imipenem-resistant *A. baumannii* acquisition. By multivariate analysis, however, only aminoglycoside use and LOS in the PICU were identified as independent risk factors. In our study, we determined that most of our patients had a history of central vascular and urinary catheterization, mechanical ventilation, underlying neuromuscular disorder and malignancy, and prior antibiotic use. Additionally, the mean ICU LOS of the patients infected with *A. baumannii* was 11 times longer than for the patients without *A. baumannii* infection.

In most institutions, the majority of *A. baumannii* isolates are from the respiratory tracts of hospitalized patients. In large surveillance studies from the United States, 5-10% of cases of ICU-acquired pneumonia were due to *A. baumannii*[15]. In this study, we detected that nearly two-thirds of our patients presented with pneumonia, and all of those patients were mechanically ventilated. In recent years, this pathogen has become increasingly resistant to antimicrobial agents, and serious outbreaks are most commonly caused by multidrug-resistant strains; nearly half of the isolates in our patients were multidrug-resistant. *A. baumannii* outbreaks are also difficult to control because this microorganism spreads easily and persists in hospital settings, thus favoring the transmission between patients, either via human reservoirs or via inanimate materials[16]. Understanding the epidemiology of nosocomial *A. baumannii* infections and distinguishing the outbreak strain from epidemiologically unrelated Acinetobacters are essential to develop effective strategies to control their spread. The use of modern molecular techniques, such as pulsed-field gel electrophoresis (PFGE) and polymerase chain reaction-based typing, has shown to be suitable for the investigation of hospital outbreaks[17]. In this report, we could not determine the genetic relatedness of the Acinetobacter strains, because of the retrospective design of the study. However, by considering the differences in the antibiotic susceptibilities of the isolates, we can say that the infections were caused by the multiple clones.

The evidence suggests that hospital-acquired *A. baumannii* infections prolong the lengths of hospital stays and subsequent health care costs. However, the direct effects of *A. baumannii* on mortality appear less well defined[15]. In a cardiac surgical ICU, the mortality rate of the patients infected with multidrug-resistant *A. baumannii* was reported as 80%, and the general mortality rate of this ICU was reported as 2.9%[18]. In another study, the overall mortality rate of *A. baumannii* infection was 43.9% and the mortality rate among the patients infected with other organisms was 26.3%[19]. However, in a recent study performed by the CDC, which involved thorough adjustment of important

confounding variables and used clear definitions for comparison groups, there was no significant increase in mortality between those infected with multidrug-resistant *A. baumannii* and those with no infection[15]. In our study, we revealed that the mortality rate of the patients infected with *A. baumannii* was higher than of the patients without *A. baumannii* infection. Furthermore, those patients with *A. baumannii* infection had a longer stay in our PICU than the others. On the other hand, 80% of our patients who died had a malignancy as an underlying disease. Thus, the underlying disease of the patients may be related with death as much as the infection sites and antibiotic susceptibility of *A. baumannii*. However, the most important factor in the empirical treatment of *A. baumannii* infections in ICUs is to address the ICU's floras and the antibiotic susceptibility of these floras. The tendency of fast-developing resistance to multiple antimicrobials of the Acinetobacter genus complicates the treatment of Acinetobacter infections, requiring the search for new agents and return of old drugs. Until the appearance of resistance, carbapenems alone or combined with amikacin were the main therapeutic options in the treatment of these infections. However, resistance to carbapenems in the last few years has led to the use of ampicillin-sulbactam or colistin[20]. Eventually, cefoperazone-sulbactam could be selected as an empirical treatment, and then the treatment options could be regulated according to the antibiograms, as cefoperazone-sulbactam (80 mg/kg/day), ampicillin-sulbactam (300-400 mg/kg/day) or colistin (50 000-75 000 IU/kg/day).

In conclusion, the LOS in the ICU was long and the mortality rate was high in pediatric patients with nosocomial *A. baumannii* infections. Exposure to invasive approaches such as central vascular and urinary catheterization and mechanical ventilation, presence of an underlying disease and prior antibiotic usage are the risk factors for *A. baumannii* infection.

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