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Epidemiology of *Acinetobacter baumannii* Isolates in an Intensive Care Unit in Kazakhstan

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ABSTRACT

Objective: Objectives: *Acinetobacter baumannii* is an important pathogen of infections in many hospitals, especially in intensive care unit patients, conditioned difficulty to control spread and treatment. The objective of the present study is to report the prevalence and antibiotic resistance rates of *A. baumannii* strains in ICU patients during a five-year period in a tertiary care hospital in Kazakhstan.

Methods: Consecutive, non – duplicate isolates of *A. baumannii* were collected and processed during the course of routine diagnostic work up from adult patients hospitalized in ICU. Identification of isolates and antibiotic susceptibility testing were performed by Vitek 2 automated system.

Results: In total 325 *A. baumannii* strains were evaluated. The most frequent of strains were from tracheostomy tubes (67 isolates, 22.1%), followed by tracheal aspirates (58 isolates, 19.1%) and urinary tract (47, 15.5%). The prevalence of *A. baumannii* strains in ICU was significantly increased from 6.9% in 2011 to 34.1% to 2015 (p=0.002). Most of testing isolates were 96.7% and higher resistant to cephalosporins, carbapenems, quinolones. Lower resistance 50% and highest was obtained to aminoglycosides.

Conclusion: we report for the first time in Central Kazakhstan the prevalence and resistance rates of *A. baumannii* in ICU in a single tertiary hospital. The present report is alarming because the increasing resistance can lead to no alternative situation on the choice of drugs for the casual treatment of infections caused by extremely resistant *A. baumannii* strains. *J Microbiol Infect Dis 2018; 8(3):83-88.*

Keywords: *Acinetobacter baumannii*, carbapenems, increasing resistance, intensive care, prevalence

INTRODUCTION

Acinetobacter baumannii is an important pathogen of infections in many hospitals, especially in intensive care unit patients, conditioned difficulty to control spread and treatment.

The incidence of *A. baumannii* infections has continuously increased, due to the increasing proportion of seriously ill patients who require advanced medical support [1-5,10]. *A. baumannii* associated infection in ICU characterized rapidly developing resistance to multiply antimicrobial agents, prolong hospital stay and increasing morbidity and mortality [6-7].

Currently, *A. baumannii* is an important agent of infection in ICU patients for which effective therapy is limited [8]. Given inappropriate initial antimicrobial therapy of multidrug resistant *A. baumannii* infection is a strong predictor for mortality [9].

Antibiotic resistance of *A. baumannii* strains is considerably different among countries, hospitals and even departments. These differences condition different patterns of antimicrobial usage and different antimicrobial control measures and policies [10].

All these findings support the need of strict adherence to monitoring antibiotic resistance of *A. baumannii* strains in intensive care unit, together with the control measures to prevent the spread of multi-drug resistant strains. The objective of the present study is to report the prevalence and antibiotic resistance rates of *A.*

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baumannii strains in ICU patients during a five-year period in a tertiary hospital of Kazakhstan.

METHODS

Study design

This prospective study was carried out over a period from January 2011 to December 2015 in the Department of Microbiology, of JSC National Scientific Medical Research Center located in Astana, Kazakhstan.

Data collection

Consecutive, non-duplicate (325) isolates of *A. baumannii* were collected and processed during the course of routine diagnostic work up from adult patients hospitalized in ICU after cardiac surgery (surgery on the heart and major blood vessels). All patients in the ICU were monitored for bacterial infection at body sites for a period at least one month. Strains were analyzed by infection site and pathogen type.

Respiratory tract specimens included sputum, tracheal aspirate, tracheostomy tube, bronchoalveolar lavage. Urethral tract included urine samples, collected through the urinary catheter. Other types of specimens obtained from the patients were: blood specimens, wound samples and drainage. All specimens were collected at the bed site, transported to the Laboratory of Microbiology and were inoculated on proper culture media within two hours according to the guidelines [11].

Samples cultivation

Clinical specimens were inoculated onto 5% sheep blood agar, Mannitol salt agar, Endo agar, Sabouraund dextrose agar (Himedia, India). Plates were incubated at 37 ^{0}C for 18-24 hours.

Identification of isolates

Methods used for confirmation of identification included test of colonial morphology, hemolytic activity on appropriate agar media, Gram strain, rapid tests (coagulase, oxidase, catalase, indole) and use of automated identification system Vitek 2 – Compact (bioMerieux, Marcy l'Etoile, France).

Antibiotic susceptibility testing

Susceptibility tests were performed with broth microdilution method (Vitek 2-Compact, bioMerieux, Marcy l'Etoile, France) for following antibiotics: meropenem, imipenem, amikacin, gentamicin, tobramycin, ciprofloxacin, levofloxacin and colistin. Colonies from 18-24 hours culture were used to inoculate the microdilution cards. Disk diffusion method was used to netilmicin. The diameter of inhibition zones was measured according to the standards of the EUCAST (version 5.0) and data were reported as susceptible and resistant.

All data were analyzed using Microsoft Access and Excel. Trends over time of antibiotic resistance rates were determined by linear regression with the yearly data. A p value of <0.05 was considered to be statistically significant.

Data were entirely anonymised throughout the entire study and thus ethical approval was not needed.

RESULTS

During the study period from January 2011 to December 2015 of the total cultures processed, the number of pathogenic bacterial isolates was 1515, of them 869 constituted (57.3%) gram negatives, 564 (37.2%) gram positive and 82 (5.4%) fungi. Overall, *A. baumannii* isolated constituted 34.8% of the total gram negative load (303 out of 869). The prevalence of A. baumanni strains was 20% of the total isolates.

The maximum number of *A. baumannii* strains were isolated from tracheostomy tube 67 (22.1%), followed by 58 (19.1%) in tracheal aspirate and 47 (15.5%) in urinary tract (Table 1).

During study period from blood specimens were isolated 6.7% (22) strains of *A. baumannii*. The prevalence of *A. baumannii* strains in ICU was significantly increased from 6.9% in 2011 to 34.1% to 2015 (p=0.002). The resistance distributions of *A. baumannii* strains and changes in their distributions by year are shown in (Table 2). All strains were resistant to piperazillin-tazobactam. Resistance to ceftazidime, meropenem, imipenem, tobtamycin, gentamicin, ciprofloxacin, and norfloxacin gradually and dramatically increased over time. Most of testing isolates were 96.7% and higher resistant to carbaphenems and quinolones. Lower resistance 50% and highest was obtained to aminoglycosides.

Table 1. The changes in detection rate of isolates by years (2011-2015) reported from intensive care unit.

Microorganism, (n (%))	**2011**	**2012**	**2013**	**2014**	**2015**	**Total**	**p-value[3]**
Sputum	0	6 (16.7)	8 (22.2)	11 (30.6)	11 (30.6)	36 (11.9)	0.018
Tracheal aspirate	5 (8.6)	4 (6.9)	15 (25.9)	17 (29.3)	17 (29.3)	58 (19.1)	0.040
Tracheostomy tube	1 (1.5)	9 (13.4)	15 (22.4)	13 (19.4)	29 (43.3)	67 (22.1)	0.023
BAL[1]	4 (10.5)	4 (10.5)	8 (21.1)	10 (23.6)	12 (31.6)	38 (12.5)	0.005
Urinary tract	5 (10.6)	6 (12.8)	12 (25.5)	11 (23.4)	13 (27.7)	47 (15.5)	0.031
Wound samples	5 (11.4)	7 (15.9)	10 (22.7)	8 (18.2)	14 (31.8)	44 (14.5)	0.049
Drainage	0	1 (7.7)	2 (15.4)	3 (23.1)	7 (53.8)	13 (4.2)	0.019
BSI[2]	3 (13.6)	3 (13.6)	4 (18.1)	5 (22.7)	6 (27.2)	22 (6.7)	0.006
Total	24 (7.3)	41 (12.6)	73 (23.4)	78 (24)	109 (33.5)	325	0.002

Table 2. Antibiotic resistance rates of *A. baumannii* isolated from patients in ICU

Antibiotic (n (%))	2011 n=24	2012 n=41	2013 n=73	2014 n=78	2015 n=109	p-value*
Meropenem	18 (75)	30 (73.1)	60 (80.8)	74 (94.8)	100	0.016
Imipenem	12 (50)	32 (78.0)	67 (91.7)	74 (94.8)	100	0.027
Amikacin	13 (54.1)	21 (51.2)	45 (61.6)	66 (84.6)	88 (80.7)	0.041
Tobramycin	4 (16.6)	8 (19.5)	17 (23.2)	41 (52.5)	80 (73.3)	0.021
Gentamicin	7 (29.1)	26 (63.4)	51 (69.8)	56 (71.7)	91 (83.4)	0.037
Netilmicin	0	0	4 (5.4)	26 (33.3)	55 (50.4)	0.223
Ciprofloxacin	22 (91.6)	39 (95.1)	69 (94,5)	75 (96.1)	100	0.024
Levofloxacin	21 (87.5)	36 (87.8)	69 (94.5)	101 (92.6)	100	0.032

* Linear regression

DISCUSSION

As is known, antibiotic resistance keeps increasing among gram-negative pathogens from ICU patients. Particularly, *A. baumannii* display pun drug and extremely drug resistances that it making therapy selection difficult and impossible. *A. baumannii* has become a major hospital-acquired strain in many hospitals around the world. *A. baumannii* associated infections are characterized considerable mortality, and using empirical therapy will not satisfactory results due to rapidly increasing resistance to antibiotics.

In this study, *A. baumannii* was isolated in 20% of all bacteriological specimens; this corresponds to similar study carried out by Pathwardhan et al [12]. *A. baumannii* strains were isolated in 23% cases and by Brkicet al [13] in 17.2% of the total isolates. However, in our study the prevalence *A. baumannii* was isolated in 303 samples forming 34.8% of the total gram-negatives. In similar studies same authors reported figures much less 10% [14-16]. Moreover, the prevalence of *A. baumannii* strains in our ICU was significantly increased from 6.9% in 2011 to 34.1% to 2015 (p=0.002).

The respiratory system is the most common site for Acinetobacter infection because of its transient pharyngeal colonization of healthy persons and a high rate of tracheostomy colonization. Among the source of the isolates, most of *A. baumannii* was isolated from tracheostomy tube – 22.1%, followed by 19.1% in tracheal aspirate, 12.5% from bronchealveolar lavage and 11.9% from sputum. Other studies similar to this, were carried out by Villers et al. [17] where prevalence in tracheal aspirate were 24.8% and Jaggi et al [15] as 18% in their studies. Acinetobacter associated infections often develop into bacteremia and septicemia, and lower respiratory tract involvement with these strains progresses to bacteremia and septicemia. In our study, the maximum isolates of *Acinetobacter baumannii* were obtained from the respiratory tract, and this finding is consistent with the findings of other similar studies [18-19].

In the period our study the prevalence of *A. baumannii* in the causation of surgical site infection was caused about 14.5%, moreover, during the study period this was increased from 11.4% to 31.8% (p=0.049). Other studies, similar to this, were carried by Jaggi et al [15] reported about 12.5% and Jones et al [20] have shown similar results (11.7%). The risk of urinary tract infections in ICU is connected with the duration of catheterization and increases by 5% each day. In our hospital prevalence of *A. baumannii* associated urinary tract infections were 15.5% (increased from 10.6% to 27.7% p=0.031). Other studies by Duszyńska et al have shown similar results (20%) [21].

Bloodstream infections - the leading infectious complications in patients in intensive care unit (ICU), found in 15% of patients with nosocomial infections and in 1% of all hospitalized patients. In our study the prevalence of *A. baumannii* from bloodstream infection were increased from 13.6% in 2011 to 27.2% in 2015 (p=0.006).

Antibiotic resistance of *A. baumannii* is a major and leading problem in the ICU. Microbiological clinical studies around the world report high level and increasing resistance rates to antibiotics of *A. baumannii* isolates – are a factor in nosocomial infections [22-24].Many studies were shown highly resistant rates to all classes of antibiotics. In a study conducted by Yuce et al. [25] reported resistance rates of 98% to ceftazidime, 95% to cefepime, 84% to meropenem, 90% to ciprofloxacin, and 100% to piperacillin-tazobactam. Eser et al. reported same level of resistance rates of 65%, 80%, 98%, 92%, 100%, and 86% for imipenem, amikacin, piperacillin-tazobactam, cefepime, ceftriaxone, tetracycline and trimetoprim-sulfametoxazole, respectively [26].

Resistance rates obtained in our study are also high and gradually increasing to 100% (to quinolones p=0.003). The high resistance rates reported in study may be associated with antimicrobial agent usage policies and consumption as well as specific infection programs.

As is known, carbapenems have been the first line treatment for gram-negative infection in ICU patients. In our study, a review of the distributions by year revealed developed that carbapenem resistance rates alarming increased. In 2011 the *A. baumannii* resistant to meropenem and imipenem was found to 76.1% and 50% respectively, while these resistance rates had increased to 100% both of carbaphenems (p=0.021 and p=0.029, respectively) in 2015.

Actually, Acinetobacter strains are resistant to major classes of antibiotics and retain activity just to colistin and same old toxic antibiotics. In our study all isolates of *A. baumannii* were susceptibility to colistin. In this study, examining the five-year average antimicrobial resistance of *A. baumannii* strains, the lowest resistance was found to aminoglycosids. No significant resistance increased in netilmicin (from 0 to 50% p=0.222), but this encourages further monitoring of the development of resistance.

Currently, aminoglycoside agents, such as tobramycin and amikacin, are therapeutic options for infection with multidrug-resistant Acinetobacter isolates that retain susceptibility. In our study lower increasing resistant rates were found to gentamicin and tobramycin from 27.3% to 83.3% (p=0.026) and from 14.3% to 73.7% (p=0.016) respectively. Other studies reported the similar results [27-28].

However, as the resistance against to netilmicin and tobramycin is not very high in our hospital, it can still be used as the drug of choice against multidrug resistant strains of *A. baumannii* but preparations mentioned above are not registered in Kazakhstan.

In conclusion, we report for the first time in Central Kazakhstan the prevalence and resistance rates of *A. baumannii* in ICU in a single tertiary hospital. The present report is alarming because the increasing resistance can lead to no alternative situation on the choice of drugs for the casual treatment of infections caused by extremely resistant *A. baumannii* strains.

In order to reduce the emergence and spread of extremely drug resistant *A. baumannii* strains in the ICU, it is strongly recommended to carry out monitoring (including rapid microbiological diagnostics with the results of antibiotic resistance), comprehensive infection control measures, and optimization of the use of antibiotics in each hospital. Therefore local resistance surveillance programs have the greatest value in the development of appropriate therapeutic recommendations for specific types of patients and infections.

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