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Epidemiological Monitoring of Nosocomial Infections Caused by *Acinetobacter Baumannii*

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ABSTRACT

Introduction: *Acinetobacter baumannii* is a frequent cause of infections in hospitals around the world, which is very difficult to control and treat. It is particularly prevalent in intensive care wards. **Aim:** The main objective of the research was to establish the application of epidemiological monitoring of nosocomial infections (NIs) caused by *A. baumannii* in order to determine: the type and distribution of NIs, and to investigate antimicrobial drug resistance of *A. baumannii*. **Material and Methods:** 855 patients treated at the Clinic of Anesthesiology and Reanimation, University Clinical Center Tuzla during 2013 were followed prospectively for the development of NIs. Infections caused by *A. baumannii* were characterized by the anatomical site and antibiotics resistance profile. **Results:** NIs were registered in 105 patients (12.3%; 855/105). The predominant cause of infection was *A. baumannii* with an incidence of 51.4% (54/105), followed by ESBL-producing *Klebsiella pneumoniae* with 15.2% (16/105) of cases, methicillin-resistant *Staphylococcus aureus* with 8.6% (9/105), and ESBL-producing *Proteus mirabilis* with 7.6% (8/105). According to the anatomical site, and type of NIs caused by *A. baumannii*, the most frequent were respiratory infections (74.1%; 40/54). Infections of surgical sites were registered in 11.1% (6/54) of cases, while bloodstream infections in 9.2% (5/54). *A. baumannii* isolates tested resistant against most antibiotics examined, but showed a high degree of susceptibility to tobramycin (87%; 47/54) and colistin (100%; 54/54). **Conclusion:** The increasing incidence of multi- and extensively drug-resistant *Acinetobacter* spp. emphasizes the importance of administration of an adequate antibiotic strategy and the implementation of strict monitoring of the measures for controlling nosocomial infections.

Key words: nosocomial infections, intensive care unit, *Acinetobacter baumannii*, multidrug resistance.

1. INTRODUCTION

The problem of nosocomial infections is as old as the hospitalization. Yet it is an ongoing problem of modern medicine, and represents a permanent danger even to patients hospitalized in the most modern and well equipped hospitals. Medical, legal and economic consequences of nosocomial infections have begun to emphasize the importance of their control. The causative agents of nosocomial infections can be almost all organisms, but most often they involve bacteria. The types of bacteria that cause hospital infections can change over time depending on the use of antibiotics and introduction of new diagnostic and therapeutic procedures (1).

Acinetobacter is a bacterium that is widespread in nature, water and soil. It can be found on the skin, in the throat and nose of healthy people. There are more than 20 different types that do not create problems, but *Acinetobacter baumannii* (*A. baumannii)*, *A. calcoaceticus* and *A. lwoffii* have the greatest clinical significance and represent one of the leading causes of nosocomial infections in all countries of the world, especially in intensive care units. (2). One of the major risk factors for nosocomial infections is the emergence of resistance to antimicrobial drugs. The development and spread of resistance is usually considered to be due to an excessive and inappropriate use of antibiotics. Sources of infection of these microorganisms should always be sought within the hospital environment, where there are typically present multi-resistant isolates of *A. baumannii* (MRAB) (3). MRAB isolates exhibit resistance to three or more groups of antibiotics that can be used to treat infections caused by this microorganism (aminoglycosides, carbapenems, cephalosporins and quinolones) (2).

Given the distinct survival ability, *Acinetobacter baumannii* is easily spread in the hospital environment causing nosocomial infections. Numerous studies have noted the presence of *Acinetobacter baumannii* in the hospital environment (working surfaces, medical equipment, hands of hospital staff, fixtures, etc.) (4,5). Hands are one of the most important vectors of infection spread in

health care facilities. They are constantly in direct contact with the environment, colonized with microorganisms which are transmitted to the critical places (6). Patients being treated in intensive care units and those with weakened immune systems are at the highest risk of developing infections.

Acinetobacter baumannii can cause various types of infections, mostly related to intensive care and invasive treatments (ventilator-associated pneumonia, bloodstream infections, surgical site infections, urinary tract infections, skin and soft tissue infections, meningitis) (7,8,9). However, every positive test on *Acinetobacter baumannii* does not always mean the infection and does not necessarily require treatment with antibiotics, but it requires the implementation of measures to prevent and combat the spread of a causing pathogen to other patients. Given the prevalence of these organisms, diseases caused by *Acinetobacter baumannii* must be distinguished from mere colonization. The real infection is sometimes difficult to treat because it often occurs in severe patients, because these bacteria are often resistant to most conventional antimicrobials, which represent a serious therapeutic problem (10).

Based on epidemiological specificities prevailing in hospitals it is quite understandable that the epidemiological monitoring is required, particularly focused in areas where there are extremely high-risk groups of patients, such as intensive care units. Two basic principles are the essence of epidemiological monitoring of nosocomial infections. One of them consists of the fact that monitoring should be the basis for timely implementation of measures to combat hospital infections, and the other should focus monitoring on certain research and testing in the hospital as well as the introduction of specific measures based on the obtained data.

The main goal of this research was to establish the active epidemiological monitoring of nosocomial infections caused by *Acinetobacter baumannii* in order to determine: the type and distribution of nosocomial infections related to modern epidemiological nomenclature that groups this monitoring into urinary tract infections, surgical site infections, respiratory infections, bloodstream and other infections, and to investigate the antimicrobial resistance profile of *Acinetobacter baumannii* as one of the most important risk factors for infection.

2. MATERIAL AND METHODS

The study was conducted on a sample of 855 patients who had been treated at the Clinic of Anesthesiology and Reanimation, University Clinical Center (UCC) Tuzla during 2013. All patients were prospectively studied since the day they were admitted until the end of the episode by the Infection Control Team. Any infection in these patients during the studied period was registered.

This study used multiple tests conducted through several surveys, which have features of the research instrument and are adapted to this type of testing. Monitoring method to track and collect data was used, which contains segments of monitoring daily, weekly and monthly reports. Criteria for diagnosis and classification of nosocomial infections was used according to internationally recognized definitions established by the Centers for Disease Control and Prevention (CDC) in the United States.

All samples were tested at the Polyclinic for Laboratory Diagnostics, Institute of Microbiology, UCC Tuzla. Cultivation, isolation and identification of *Acinetobacter baumannii* (as well as other causative agents of nosocomial infections) from patient samples were performed using standard microbiological methods. Production of extended spectrum β-lactamases (ESBL) was assessed using the microdilution method in VITEK2/AES (AST-GN27card, (bioMérieux, Marcy l'Étoile, France) and each isolate confirmed by the double disk synergy test for detection of ESBL (BD BBL™ Sensi-Disc™ Antimicrobial susceptibility Test Discs; Mueller Hinton agar, Liofilchem s.r.l. Bacteriology products). Identification of multi-resistant *Acinetobacter baumannii* was performed similarly to identification of ESBL-producers, using the microdilution method in VITEK2/AES (AST-N222 card), according to the procedure contained in the manufacturer's instructions.

3. RESULTS

At the Clinic of Anesthesiology and Reanimation of UCC Tuzla from January to December 2013, a total of 855 patients were treated. Nosocomial infections were registered in 105 patients, or 12.3%. The predominant causative agents of these infections were *Acinetobacter baumannii* (54/105) with a frequency of 51.4%, followed by ESBL-producing *Klebsiella pneumoniae* (16/105) with 15.2% of cases, then methicillin resistant *Staphylococcus aureus* (MRSA) with a frequency of 8.6 % (9/105), ESBL-producing *Proteus mirabilis* with a frequency of 7.6% (8/105), *Pseudomonas aeruginosa* with 6.7% (7/105), and *Clostridium difficile* in 3.8% (4/105) of cases. Other causative agents of nosocomial infections identified in this study were ESBL-producing *Escherichia coli* in 2.9% (3/105) of cases, ESBL-producing *Enterobacter cloacae* in 1.9% (2/105), and also *Citrobacter* species and *Enterococcus* species with the frequency of 0.95% (1/105), each.

Based on the anatomical site, or types of hospital infections caused by *Acinetobacter baumannii* at the Clinic of Anesthesiology and Reanimation during 2013, it was observed the most frequently registered were respiratory infections, in 40/54 of patients or 74.1%. Surgical site

	LIST OF ANTIBIOTICS										
	amikacin	cefepime	ceftazidime	ciprofloxacin	colistin	gentamicin	imipenem	meropenem	piperacillin/tazobactam	tobramycin	sulfamethox./trimethop.
TOTAL	50	54	54	53	54	53	54	54	54	54	54
R (%)	92	92.6	94.4	96.2	0	60.4	88.9	88.9	98.1	13	94.4
S (%)	4	7.4	5.6	3.8	54	13.2	11.1	9.3	1.9	87	5.6
I (%)	4	-	-	-	-	26.4	-	1.8	-		-

Table 1. Antimicrobial susceptibility profile of Acinetobacter baumannii, causative agent of nosocomial infections at the Clinic of Anesthesiology and Reanimatology, UCC Tuzla in 2013. Abbreviations: R, resistant; S, sensitive; I, intermediate sensitive.

infections were registered in 6/54 of cases, or 11.1%, while bloodstream infections were recorded in 5/54 of patients, or 9.2%. Urinary tract infections were registered in 2/54 of cases or 3.7%, while other infections were recorded in only one case, or 1.9%.

Nosocomial infection control is sometimes performed by microbiological examination of swab samples taken from common hospital surfaces (walls, tables, handles etc.), medical equipment and hands of medical staff (4, 5). Swabs are taken according to the rules that are determined and defined for control of nosocomial infections, and in accordance with the degree of risk of infection. Swabs of patients' surrounding were taken during handling of patients with isolated multi-resistant bacterial strains and a confirmed nosocomial infection, and are used to assess contamination of their imminent environment and possible transmission of infection by hands of health care workers.

During 2013 at the Clinic of Anesthesiology and Reanimation a total of 175 swabs were taken from hospital surfaces, medical equipment and hands of medical staff of which 31/175 or 17.7% were positive for some nosocomial infection. By the analysis of positive swabs, it was shown that *Acinetobacter baumannii* was isolated and identified from 16 of them (16/31 or 51.6%). Further analysis revealed antibiograms similar to antibiograms of strains from samples taken from patients with registered nosocomial infections.

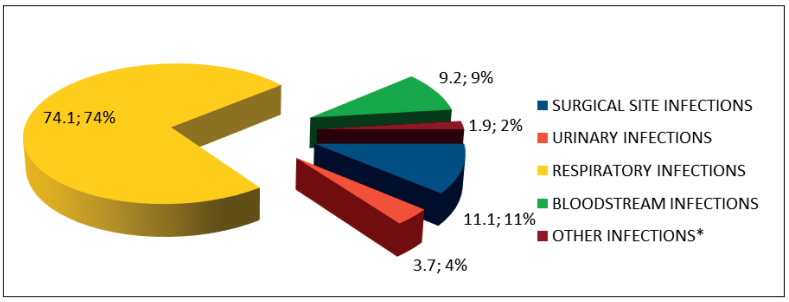

Figure 1. Distribution of bacterial pathogens of nosocomial infections at the Clinic of Anesthesiology and Reanimatology, UCC Tuzla during 2013.

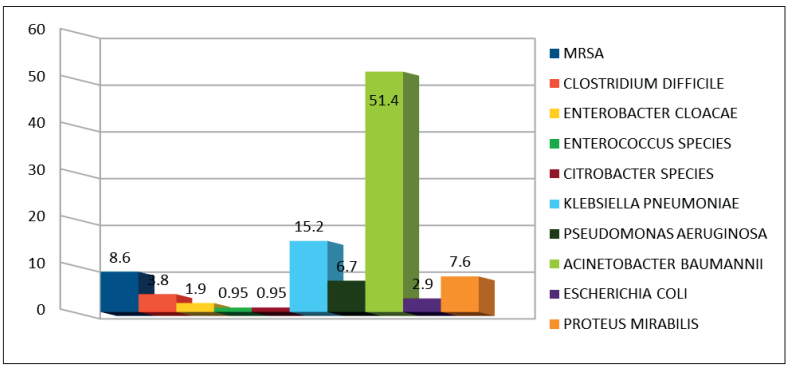

Figure 2. Frequency of different types of nosocomial infections caused by Acinetobacter baumannii at the Clinic of Anesthesiology and Reanimatology, UCC Tuzla during 2013. Abbreviations: MRSA; methicillin-resistant Staphylococcus aureus.

Antimicrobial susceptibility of *Acinetobacter baumannii* isolated from patient samples with nosocomial infections was examined on the standard range of antibiotics (Table 1). Results in Table 1. show that the strains of *Acinetobacter baumannii* isolated in our study exhibited the highest degree of susceptibility to colistin (100%; 54/54) and tobramycin (87%; 47/54), while they were highly resistant to other antibiotics tested. Thus, our *Acinetobacter* isolates showed more than 90% resistance towards amikacin (92%; 46/50), sulfamethoxazole/trimethoprim (94.4%; 51/54), ciprofloxacin (96.2%; 51/53), piperacillin/tazobactam (98.1%; 53/54), cefepime (92.6%; 50/54) and ceftazidime (94.4%; 51/54). Somewhat lower rate of resistance was noted for gentamicin (60.4%; 32/53), although only 13.2% of isolates were noted to be susceptible to this antibiotic (7/53), while the rest of them (13.2%; 14/53) exhibited intermediate resistance. Furthermore, most of our isolates were also mostly resistant towards carbapenems, with the resistance rate of 88.9% for each imipenem (48/54) and meropenem (48/54).

4. DISCUSSION

Acinetobacter baumannii is an increasingly common cause of nosocomial infections in hospitals around the world, which is very difficult to control and treat therapeutically. It is particularly prevalent in intensive care units. It can be isolated from the body of a patient, hands of medical staff, medical equipment and work surfaces. It can survive for months on hospital surfaces (2.11).

Isolation and identification of *Acinetobacter baumannii* in the laboratory is a key step in the series of procedures used in fighting against the spread of intrahospital infections. Tracking the types of pathogens and their prevalence in certain departments, as well as sensitivity to antibiotics, makes it possible to already in the microbiological laboratory register a nosocomial infection. Typical patterns of antibiotic sensitivity could point to a common source or route of transmission of these infections. Literature data show that the incidence of *Acinetobacter baumannii* as a cause of nosocomial infections has increased significantly (12). Thus, the report of the National Nosocomial Infections Surveillance (NNIS) from the United States shows a significant increase in the period from1986 to 2003 (7).

The results of our study showed that *Acinetobacter baumannii* is the predominant cause of respiratory infections, the most frequent clinical manifestations of *Acinetobacter* infections are ventilator-associated pneumonia. Dima and colleagues also report that the *Acinetobacter* species are predominant cause of ventilator-associated pneumonia (13). Moreover, researchers from Poland showed the results similar to our study, reporting a high percentage of *Acinetobacter* species as a cause of nosocomial infections in the ICU (14). Exogenous transmission of *Acinetobacter* should be considered when infections are endemic and when case rates increase (15).

Targeted microbiological research of hospital environment is carried out when an outbreak of nosocomial infection is confirmed, in order to detect the cause and mode

of transmission of infection. The vector for the spread of infection may be healthcare workers with poor hand hygiene, but since the organism can persist for a prolonged period of time in the hospital environment, contamination from the hospital equipment is also quite possible (3, 4, 5). Thus, the study of El Shafie and associates stated that during an outbreak of hospital infection, microbiological analysis confirmed isolation and identification of multi-resistant *Acinetobacter baumannii* (MRAB) as a causative agent, from patients samples and from samples taken from the hospital environment, medical equipment and hands of medical staff (16). Also our study recorded similar antibiogram of *Acinetobater baumannii* from samples taken from the patients and the hospital environment. Generally, over the past decade, the strategies controlling outbreaks of *A. baumannii* infection have been different in every hospital, but effective measures usually entail identification of contaminated objects, implementation of contact isolation measures and modification of cleaning protocols (17).

The main danger associated with *A. baumannii* is its capability to acquire antimicrobial resistance genes extremeles rapidly, leading to multidrug resistance (3). The antibiotic resistance is especially common in ICUs, an environment with a high antibiotic pressure and severly ill patients (17). Antimicrobial resistance among *Acinetobacter* spp. has increased substantially in the past decade and has created a major public health dilemma. The data from our study also show the alarming capacity of *A. baumannii* to develop antibiotic resistance to a wide range of antibiotic classes examined, from aminoclycosides, quinolones, 3rd and 4th generation cepahalosporins, to carbapenems. Only one isolate was sensitive to all antibiotics examined, while the rest of them shared more than 90% resistance towards amikacin, sulfamethoxazole/trimethoprim, ciprofloxacin, cefepime, ceftazidime and piperacillin/tazobactam. Extremely high rates of resistance were also observed to carbapenems, 88.9% for both imipenem i meropenem. While some European studies recorded much lower resistance to carbapenems, researcher from Turkey and Korea also report high resistance rate of *Acinetobacter* to imipenem, 65.3% and more than 80%, respectively (18). Thus, the high rate of carbapenem resistance among *Acinetobacter* isolates in our hospital should be surveyed cautiously.

The emergence of multidrug resistant gram-negative bacilli and no new development of antibiotics has brought polymixins, back to use during the past few years, as the last resort for the treatment of infections caused by multi-resistant gram-negative bacteria (11, 18). *Acinetobacter baumannii* resistance to multiple antibiotics has left colistin (polymixin E), the drug abandoned in 1980s due to its unacceptable rates of nephrotoxicity, often as the only effective therapeutic option (18). As shown above, while all of our *Acinetobacter* isolates were susceptible to colistin, for seven of them out of tested antibiotics colistin represented the only treatment option. Unfortunately, resistance to colistin in *A. baumannii* (extensively drug-resistant *A. baumannii*) has been reported recently all over the world, with resistance rates ranging from <7% in most reports to 30.6% and 40.7% in reports from Korea and Spain, respectively (18). The increasing incidence of multi- and extensively drug-resistant *Acinetobacter* spp. emphasizes the importance of administration of an adequate antibiotic strategy and the need for new and effective treatment options, as well as the implementation of strict monitoring of the measures for controlling nosocomial infections.

5. CONCLUSION

A. baumannii is a predominant cause of nosocomial infections at the Clinic of Anesthesiology and Reanimation, UCC Tuzla, responsible for approximately half of nosocomial infections recorded in this department during 2013. Respiratory tract infections accounted for almost three-fourths of infections caused by *A. baumannii*, which were highly resistant to a broad panel of antibiotics, and in most cases exhibiting sensitivity to only tobramycin and colistin. Cross-transmission of bacterial strains among patients and staff results in genetic transmission among bacteria, which further results in emergence and propagation of resistant strains, which are especially difficult to treat in patients with serious underlying diseases (ICUs). The increasing incidence of multidrug resistant pathogens emphasizes the importance of an active epidemiological monitoring as a critical part of the program for preventing and controlling hospital infections. Moreover, hospital environments and patients are a suitable medium for the emergence and spread of nosocomial infections, which require prolonged hospitalization and treatment and significantly increase the cost of hospital days and burden the health funds. Understandably, all this in addition to the economic impact of the outbreak, has social, psychological and emotional implications.

CONFLICTS OF INTEREST: NON DECLARED.

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