FREQUENCY AND ANTIBIOTIC RESISTANCE IN CLINICAL ISOLATES *ACINETOBACTER BAUMANNII*

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ABSTRACT

Multidrug resistant Gram-negative bacteria represent a global problem due to their global spread and growing distribution. They lead to major difficulties in therapy and to increased lethality and much more expensive treatment. *Acinetobacter baumannii* is a typical agent of this group of microorganisms.

The purpose of this study is to determine the frequency of distribution of *A. baumannii* in a variety of clinical materials of hospital patients and their antibiotic resistance to different groups of antibiotics used in medical practice.

Methods: A total of 371 strains *A. baumannii* were tested. They were isolated from clinical materials of patients of "St. Kirkovich Hospital" Medical University, Stara Zagora for a five-year period (2010-2014). The identification of the isolates was done by: routine methods, semi-automated Crystal system and automated API system. The disc diffusion method of Bauer Kirby was used to determine the antibiotic resistance.

Results: Among the 371 isolated strains of *A. baumannii* dominate those of surgical wounds /40.2%/, followed by isolates of the respiratory system (27.2%). Antibiotic resistance to different antibiotic classes shows: Piperacillin - 92.3% R, Ampicillin / Sulbactam - 69% R, Ceftazidime - 91.6% R, Cefepime - 91% R, Imipenem - 32.7% R, Meropenem - 48.9% R, Amikacin - 76.2% R, Ciprofloxacin -86.6% R.

Key words: *Acinetobacter baumannii*, antimicrobial resistance

One of the main challenges of therapy of infections is the increasingly growing number of multidrug-resistant bacteria. Multiple antibiotic resistance occurs in both Gram-positive and in Gram-negative bacteria. A significant problem are Gram-negative glucose-nonfermenting bacteria, to which the *Acinetobacter baumannii* belongs. The microorganism is characterized by a number of features that support its topicality: a high percentage of the isolates with multiple resistance to antimicrobials; the resistance is determined by several mechanisms simultaneously; tends to a constant increase of the resistance; permanent opening and quick spread of new mechanisms of resistance, incl. to carbapenems. This severely limits the therapeutic options (1, 2). *A. baumannii* is among the most common causes of serious infections - bacteraemia, pneumonia, soft tissue infections, urinary tract infections (3-7); in most cases these are hospital-acquired

infections caused by isolates with the same types of resistance (8, 9); it requires constant monitoring, study of strains and summarizing the results in order to optimize antibiotic policy in hospitals.

The aim of this study is to determine the prevalence of *A. baumannii* in various clinical specimens from hospital patients, their antibiotic resistance to other classes of antibiotics used in medical practice and included in the Hospital antibiotic policy.

Materials and Methods: In the period 2010-2014 a total of 371 strains of *A. baumannii* were tested. The strains were isolated from materials of patients University Hospital "St. Kirkovich" Stara Zagora. Routine methods, semiautomated system Crystal (BBL) and automated API were used for the identification of the isolates. Disc method of Bauer Kirby was applied to determine the antibiotic resistance; interpretation of results was based on CLSI 2012.

Results and discussion: For the described 5-year period a total of 371 *A. baumannii* strains

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from different clinical materials, (6.4% of the total clinically significant isolates) were analyzed. The study included only the first isolate of each patient.

The distribution of bacteria according to types of materials is described in **Figure 1**.

Figure 1. Distribution of *A. baumannii* in the types of examined materials

The results show that 40.2% of *A. baumannii* strains were isolated from surgical wounds, 27.2% - from the respiratory system and 22.1% - from urine cultures. *A. baumannii* is a typical nosocomial pathogen discovered both in materials from patients and the hospital environment objects (10). This explains the much higher isolation from surgical wounds versus other clinical specimens and especially wound isolates obtained from non-surgical clinics - 8.4%. *A. baumannii* causes wound colonization and infection in patients with operative wounds, severe burns or trauma, especially associated with low hospital hygiene (11-13).

A. baumannii uroisolates are more common in men (70%); they are equally spread in both surgical and non-surgical patients. The high percentage of *A. baumannii* in patients from

internal clinics is due to their complex chronic urological history (patients who have undergone prior surgery or invasive procedures, mainly catheterization) (6).

In 7 patients (1.9%) *A. baumannii* were isolated from blood culture. Those are patients in intensive care, where the microorganism is detected in other tested materials (tracheobronchial secretions or wound infection), excluded from the study. One strain *A. baumannii* was isolated from CSF. This is a Neurosurgery's patient with postoperative infection. There are references about cases of cerebrospinal shunt associated *A. baumannii* meningitis in neurosurgical patients (14).

The relative frequency of *A. baumannii* compared to other clinically significant microorganisms is shown in **Figure 2**.

Figure 2. Proportion of *A. baumannii* against all clinically significant isolates by type materials

The frequency analysis of *A. baumannii* compared to other clinically significant microorganisms species from tested materials showed that *A. baumannii* was isolated most commonly from materials of the respiratory system (9.2%). These are mainly isolates from

the tracheo-bronchial secretions in patients in intensive care (85.1% of cases). Ventilator associated pneumonia is the most common clinical manifestation of *A. baumannii* nosocomial infection (5-10% in the US). Often nosocomial pneumonia is accompanied by

bacteremia, which aggravates the prognosis (15).

The antibiotic resistance of the isolates is summarized below. The data is presented by type of clinical materials in **Table 1**.

Table 1. Antibiotic resistance of *A. baumannii* in %

Antimicrobial agents Clinical specimen	SAM	PIP	TZP	CAZ	FEP	MEM	IPM	AN	NN	CIP
Total number of isolates	69	92,3	81,5	91,6	91	48,9	32,7	76,2	13,6	86,6
Surgical wounds	67	91.4	79.5	87.2	90.3	52.2	33.3	83.6	13	88.1
Respiratory system	66.7	93.5	93.3	94.6	89.4	60	49.4	58.8	17.5	89.3
Urocultures	71.6	89	75	92.1	92	29.2	7	81.3	12.5	85.7
Hemocultures	20	100	100	100	100		20	100		100
Nons-surgical wounds	80	88,5	71,4	92	84,2	31,3	22,2	73	0	72

The high percentage of *A. baumannii* isolates show resistance (69-92.3%) to the most frequently used antibiotics in practice - penicillins, cephalosporins and fluoroquinolones. Such high values of resistance are not common in other Gram-negative bacteria, but are cited in other similar studies about *A. baumannii* (16), because it is typical for these species. (17-19). Multiple resistance of our *A. baumannii* isolates often make effective therapy difficult. A careful selection of antibiotic therapy is needed, if possible according to an antibiogram.

The resistance of *A. baumannii* to limited antibiotics, such as carbapenems, is relatively higher (MEM-48.9%, IPM-32.7%). In concern with the carbapenems, our isolates have the same or lower resistance than other Bulgarian studies (40% -82-85%) (4, 16). The rapid appearance of strains of *A. baumannii*, resistant to all β -lactam antibiotics, including carbapenems, illustrates the potential of this organism to respond quickly to the selective pressure of the environment (17). Research through molecular genetic methods show even forming a Bulgarian branch of *A. baumannii*, isolated from various hospitals in the country, which produce different types of carbapenemases (8). Resistance to carbapenems shows that they can not be a good choice for empirical therapy or alternative therapy by multidrug resistant isolates. This requires continuous improvement of antibiotic policy in hospitals to limit the use of third-generation cephalosporins and carbapenems as inducers of ESBL_s and carbapenemases.

The resistance of *A. baumannii* is lowest the to Tobramycin - 13.6%. In our hospital circulates a nosocomial strain, resistant to all other antibiotics and sensitive only to Tobramycin. The relatively low frequency of resistance to Tobramycin is reported in other similar studies

too (16). Tobramycin is an opportunity for therapy and appropriate option for empirical therapy in patients at risk, especially in clinics with high isolation of *A. baumannii*.

Some of the isolates were tested to Colistin - 56 strains (15.6%), and to Tigecyclin - 97 strains (27.1%). All these strains showed no resistance. Our results confirm the data of other authors for low /1.3% for Colistin/ (16) to missing resistance of *A. baumannii* to these drugs. These antibiotics are a viable therapeutic alternative in multidrug resistant isolates. However, there are reports of in vitro increasing levels of resistance of *A. baumannii* to polymyxins and Tigecyclin (20-22).

Highest resistance showed isolates from the blood stream, followed by those of the respiratory system; the lowest is the resistance of the isolates from urine and wound infections.

Strains from blood cultures and respiratory system in all patients are an expression of hospital infections. The interpretation/generalization of the results shows that regardless of the type of research material, the treatment of *A. baumannii* isolates should be the same as the treatment of multidrug resistant microorganisms. In the development of therapeutic schemes hospitals should avoid selective pressure of 3-generation cephalosporins and carbapenems, to slow down the increase of the resistance.

CONCLUSION

➤ *A. baumannii* isolates showed a high frequency of resistance to penicillins, cephalosporins, fluoroquinolones and Amikacin, which requires an individual approach to therapy, after the result of the antibiograms.

- Resistance to carbapenems is high enough, which makes their use uncertain as empirical therapy.
- The lower frequency of resistance to Tobramycin allows discussion as a treatment option and possibly empirical therapy.
- Lack of resistance to Colistin u Tigecyclin of *A. baumannii* isolates suggests a safe alternative therapy.
- A constant update of hospital antibiotic policy is needed to reduce the growth of antibiotic resistance.

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