

## Epidemiological profile of carbapenem-resistant *Acinetobacter baumannii* in a hospital in the countryside of Minas Gerais

### Perfil epidemiológico do *Acinetobacter baumannii* resistente a carbapenens num hospital do interior mineiro

### Perfil epidemiológico del *Acinetobacter baumannii* resistente al carbapenem en un hospital en el interior del estado de Minas Gerais

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The aim of this study was to analyze the prevalence of *Acinetobacter baumannii* resistant to carbapenems in biological samples and in sectors of the General Hospital in the Federal University in the Triângulo Mineiro. Data were collected through the analysis of the results of a bacterial culture, which were in the files of the Department of Microbiology of the Clinical Pathology Service in the period from 2008 to 2014. Among the 420 samples of *Acinetobacter baumannii* resistant to carbapenems, the highest prevalences were found in the Adult Emergency Unit (26.4%) and in the Adult Intensive Care Unit (22.8%). The prevalence of carbapenem-resistant *Acinetobacter baumannii* was higher in samples of wound secretions (25%), followed by samples of the lower respiratory tract (21.4%). Knowledge of the prevalence of carbapenem-resistant *Acinetobacter baumannii* is paramount for the establishment of measures to prevent and control hospital infections.

**Descriptors:** *Acinetobacter baumannii*; Carbapenems, Drug resistance.

O objetivo desse estudo foi analisar a prevalência de *Acinetobacter baumannii* resistente a carbapenens nas amostras biológicas e nos setores do Hospital de Clínicas da Universidade Federal do Triângulo Mineiro. A coleta de dados foi realizada através da análise dos resultados dos exames de cultura presentes nos arquivos do setor de microbiologia do Serviço de Patologia Clínica no período de 2008 a 2014. Dentre as 420 amostras de *Acinetobacter baumannii* resistentes a carbapenens, as maiores prevalências foram encontradas nos setores de: Pronto Socorro Adulto (26,4%) e Centro de Terapia Intensiva Adulto (22,8%). A prevalência de *Acinetobacter baumannii* resistente a carbapenem foi maior nas amostras de secreções de ferida (25%), seguidas por amostras do trato respiratório inferior (21,4%). O conhecimento da prevalência do *Acinetobacter baumannii* resistente a carbapenens é de fundamental importância para que medidas de prevenção e controle das infecções hospitalares sejam implantadas.

**Descritores:** *Acinetobacter baumannii*; Carbapenêmicos, Resistência a medicamentos.

El objetivo de este estudio fue analizar la prevalencia de *Acinetobacter baumannii* resistente a los carbapenémicos en muestras biológicas y en los sectores del Hospital de Clínicas de la Universidad Federal del Triângulo Mineiro, MG-Brasil. La recolección de datos se realizó mediante el análisis de los resultados de las actuales pruebas de cultivo en el Servicio de Patología Clínica y en los archivos del departamento de microbiología de 2008 a 2014. Entre las 420 muestras de *Acinetobacter baumannii* resistente a los carbapenémicos, las prevalencias más altas se encontraron en los siguientes sectores: Unidad de Cuidados Intensivos de Adultos (22,8%) y de Emergencia Adulto (26,4%). La prevalencia de *Acinetobacter baumannii* carbapenem-resistentes fue mayor en las muestras de las secreciones de heridas (25%), seguidas de las muestras del tracto respiratorio inferior (21,4%). El conocimiento de la prevalencia de *Acinetobacter baumannii* resistente a los carbapenémicos es de fundamental importancia para la prevención y control de las infecciones hospitalarias.

**Descriptores:** *Acinetobacter baumannii*; Carbapenémicos; Resistencia a medicamentos.

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## INTRODUCTION

The number of infections caused by microorganisms of the genus *Acinetobacter* has increased in recent years<sup>1</sup>. The species *Acinetobacter baumannii* is the most important representative of them, and is capable of causing infections in the community, especially in hospitals<sup>2</sup>. The fast and global emergence of *a. baumannii* as an important nosocomial pathogen is remarkable, and demonstrates its successful adaptation to the environment of XXI century hospitals<sup>3</sup>.

The *A. baumannii* causes primarily infections in the lungs, urinary tract, surgical wounds and blood, and the main risk factors for infection are invasive procedures, such as the use of mechanical ventilation, and of central venous or urinary catheters<sup>4</sup>. Other factors which can indicate a predisposition to *A. baumannii* infections include previous antibiotic therapy, major surgeries, burns and immunosuppression<sup>2</sup>.

Uma das principais razões para o aumento do interesse atual no *A. baumannii* é sua notável capacidade de adquirir genes de resistência rápida levando ao surgimento de cepas multirresistente<sup>2</sup>. The widespread use of antimicrobials in hospitals has also contributed to the increase of its resistance<sup>4</sup>. In addition, multidrug-resistant *A. baumannii* infections have been linked to increased morbidity and longer periods of hospitalization<sup>5</sup>. The *A. baumannii* is able to survive for extended periods of time in the environment of a hospital, which further increases its ability to cause nosocomial outbreaks<sup>2</sup>.

Carbapenems are the drugs of choice for the treatment of infections caused by gram-negative multiresistant bacilli<sup>6</sup>, but the *A. baumannii* resistance to these antimicrobials has increased throughout the world in the last decade<sup>7</sup>. The first carbapenem resistant *A. baumannii* was described at the beginning of 1990, and is now increasingly considered, around the world, to be a signaling event to the emergence of antimicrobial resistance. *A. baumannii's* resistance to carbapenem is

considered a significant health problem because of the limited options of antibiotic treatment. In these antibiotic Multiresistant strains, the colistin, also known as polymyxin, is often the last resort for treatment, because it has a high incidence of nephrotoxicity.

Not to mention that colistin-resistant bacterial cultures have already been related<sup>2</sup>.

The acquisition of multidrug resistance by *A. baumannii* is mediated by a variety of mechanisms, including the acquisition of movable genetic elements, such as plasmids, transposons and integrons, and natural transformation. Other resistance mechanisms involve the degradation of enzymes, efflux pumps, modification of the target, and poring deficiency<sup>4</sup>. The enzyme-mediated resistance is the ability of the bacteria to produce enzymes that transform the antibiotics in non-toxic or inactive forms<sup>8</sup>. Efflux pumps are responsible for actively pumping the drug out of the cell. That diminishes its concentration, and prevents it from achieving its desired effect<sup>9</sup>. The poring deficiency and the changes in penicillin-binding proteins (PBP), which constitute the targets of  $\beta$ -lactam antibiotics, prevent the drugs from penetrating into cells and reaching their intended destinations<sup>10</sup>.

One of the main concerns about antimicrobial resistance in *A. baumannii* has been its acquisition of resistance to carbapenem<sup>4</sup>. The main reason for *A. baumannii* to acquire wide spectrum  $\beta$ -lactam resistance is in the  $\beta$ -lactamases which hydrolyze the  $\beta$ -lactam ring of the antibiotic by breaking the amide bond, since they end up losing the ability to inhibit the synthesis of the bacterial wall<sup>2</sup>. The carbapenemases represent the most versatile family of  $\beta$ -lactamases, with a range of unparalleled spectrum.

The classification of  $\beta$ -lactamases depends on two properties, both molecular and functional. According to their functional classification,  $\beta$ -lactamases are gathered in groups from 1 to 4. Group 2 has multiple subgroups, which are different according to a specific substrate or inhibitor. According to this classification, the carbapenemases are

found mainly in the groups 2f and 3<sup>11</sup>. A classification based on amino acid homology divides the  $\beta$ -lactamases in four main classes, from A to D. Molecular classes A, C, and D include the  $\beta$ -lactamases with serine in their active site, and the  $\beta$ -lactamases of class B are all metalloenzymes, with zinc in their active site<sup>12</sup>.

Several studies have linked the presence of metallo- $\beta$ -lactamase enzymes (class B) with *A. baumannii* resistant to carbapenems, but the most prevalent carbapenemases in this species are the class D  $\beta$ -lactamases<sup>13</sup>. In recent years, the incidence of nosocomial infections associated with resistant microorganisms has increased worldwide and the *A. baumannii*, responsible for these infections, has emerged as an important multidrug-resistant pathogen.

It is paramount to acquire information regarding the epidemiology of isolated samples of the *Acinetobacter baumannii* variety which is resistant to carbapenems. Only doing that will we be able to implant and update measures to prevent and control hospital infections, not to mention antimicrobial treatment strategies. That would contribute to diminish the number of hospital infections, and consequently, to reduce the mortality of the patients. The aim of this study was to analyze the prevalence of *Acinetobacter baumannii* resistant to carbapenems in biological samples and in sectors of the General Hospital in the Federal University in the Triângulo Mineiro - GH/UFTM.

## METHOD

This is a descriptive, observational and retrospective research which examined the prevalence of *Acinetobacter baumannii* resistant to carbapenems in biological samples and in the sectors of the General Hospital at the UFTM.

Data were collected through the analysis of the results of bacterial cultures of urine, liquids, secretions and hemoculture, which were in the files of the Department of

Microbiology of the Clinical Pathology Service in the period from 2008 to 2014.

Data relating to cultures which were positive for the presence of *Acinetobacter baumannii* were classified according to the biological sample, the sector in which the patient was admitted, and the resistance or sensitivity to carbapenems presented by the sample.

These data were placed in a worksheet in the software Excel XP®, from Microsoft®. Then, the processing and analysis were conducted with the use of the software Statistical Package for the Social Sciences (SPSS), version 20.0 for Windows XP®.

Only one sample per patient was included in the study and only data from the first admission was considered. The results are presented in graphs, in descending order of frequency in each sample type and each sector. Statistical analyses were performed using the classic Chi-square test, with a fixed significance level of  $p < 0.05$ .

This project was approved by the Research Ethics Committee (CEP), under the Protocol 38592414.7.0000.5154.

## RESULTS

In the analysis of the cultures made with urine, secretions and blood of patients, found in the files of the Department of Microbiology of the Clinical Pathology Service of the General Hospital at the UFTM, in the period 2008 to 2014, there were 694 cultures which were positive for *Acinetobacter baumannii*. From these, 60.5% were resistant to carbapenems, representing 420 samples. 39.5% (274 samples) of them were not resistant to those antibiotics.

The annual frequency of the 694 samples of *Acinetobacter baumannii*, both resistant and susceptible to carbapenems, and their respective percentage, are represented in Table 1. In 2008, only 10 among the 66 samples of *A. baumannii* were resistant to carbapenems, to a total of 15.6%. In 2009, there was a significant increase ( $p < 0.05$ ) of resistant samples of *A. baumannii*: the total

was of 53, corresponding to 48.1%. In 2010, there was also a significant increase ( $p < 0.05$ ) compared to the previous year, with 84 (66.1%) resistant samples. The diminishing of samples of *A. baumannii* resistant to carbapenems between 2010 and 2011 was not significant. In 2011 and 2012 were found 51 (56%) and 71 (80.6%) resistant samples,

respectively: a significant increase ( $p < 0.05$ ). There was no significant difference between 2012 and 2013. In turn, the number of samples of *A. baumannii* resistant to carbapenems decreased significantly ( $p < 0.05$ ) between 2013, with 85 (84.1%) samples and 2014 with 66 (59.4%) samples.

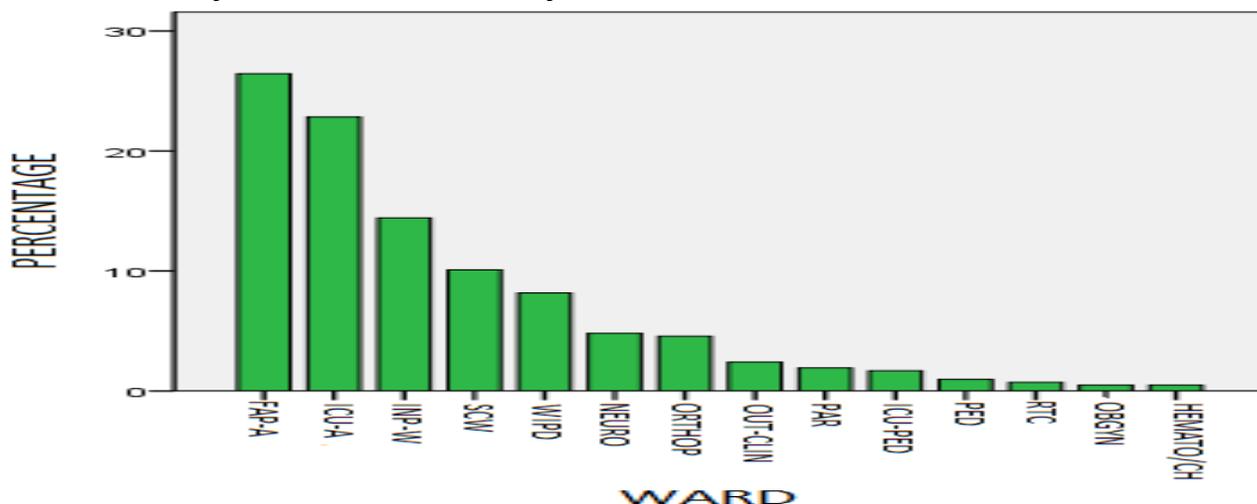
**Table 1** - Annual Distribution of *Acinetobacter baumannii* resistant and susceptible to carbapenems from 2008 to 2014 in the General Hospital of the General Hospital at the UFTM.

	RESISTANT		SUSCEPTIBLE		TOTAL		p
	N	%	N	%	N	%	
2008	10	15.2	56	84.8	66		
2009	53	48.1	57	51.8	110	<0.01	
2010	84	66.1	43	33.8	127	<0.01	
2011	51	56.0	40	43.9	91		
2012	71	80.6	17	19.3	88	<0.01	
2013	85	84.1	16	15.8	101		
2014	66	59.4	45	40.5	111	<0.01	
<b>TOTAL</b>	420	60.5	274	39.5			

Among the 420 samples of *Acinetobacter baumannii* resistant to carbapenems, the highest prevalences were found in: Adult Emergency Units, with 110 cases (26.4%) and Adult Intensive Care Unit, with 95 cases (22.8%). The inpatient ward was the department with the third highest prevalence, with 14.4%; followed by the Surgical Clinic Ward (10.1%);

Ward for Infections and Parasitic Diseases (8.2%); Neurology (4.8%); Orthopedics (4.6%); Outpatient Clinic (2.4%); Post Anesthesia Recovery (1.9%); Intensive Care Unit (Pediatric) (1.7%); Pediatrics (1%); Renal Therapy Unit (0.7%); Gynecology and obstetrics (0.5%); and, Hematology/Chemotherapy Central (0.5%) (Chart 1).

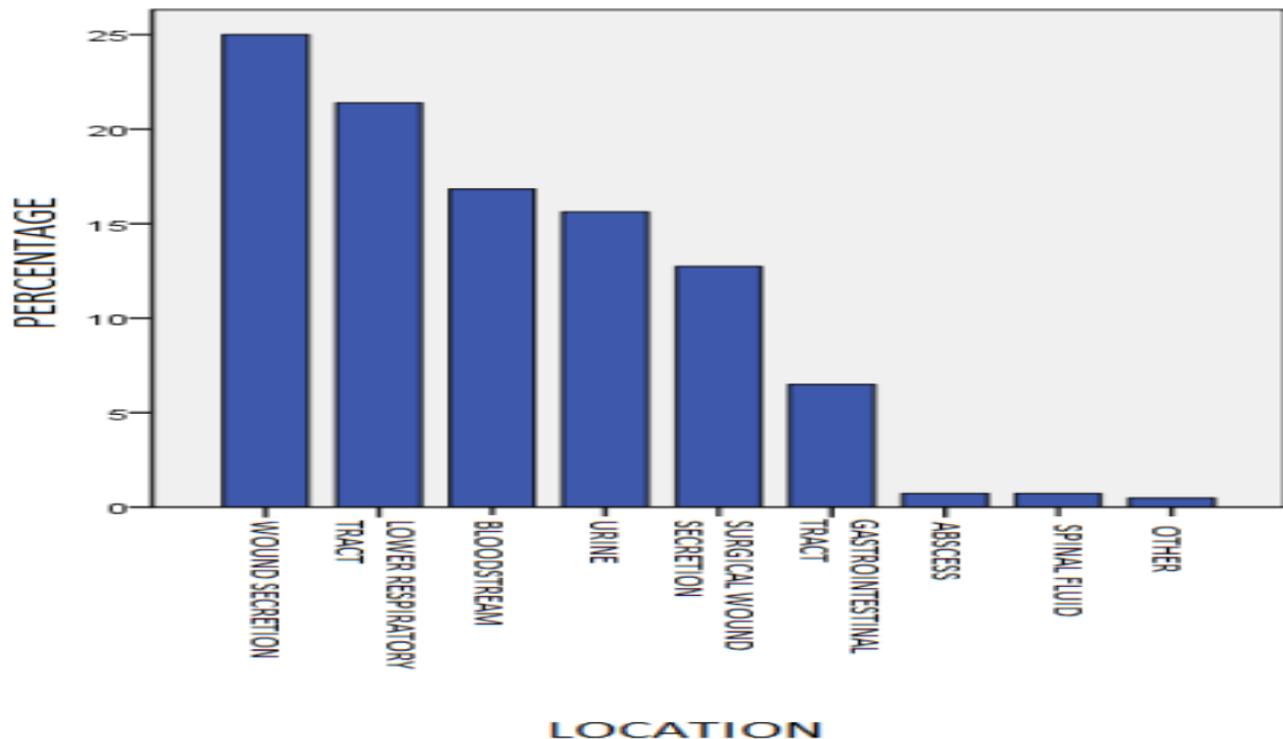
**Chart 1** - Prevalence of *Acinetobacter baumannii* resistant to carbapenems in the various wards of the General Hospital at the UFTM, in the period 2008 to 2014.



The prevalence of carbapenem-resistant *Acinetobacter baumannii* was higher in samples of wound secretions (25%), followed by samples of the lower respiratory tract (21.4%), which include bronchoalveolar lavage, tracheal aspirate, pleural fluid and sputum. The third highest prevalence was in

the sample of the blood culture (16.8%), followed by urine (15.6%), surgical wound secretion (12.7%), gastrointestinal tract (6.5%), abscess (0.7%), spinal fluid (0.7%) and others (0.4%), which include aortofemoral prosthesis (0.2%) and intracavitary electrodes (0.2%) (Chart 2).

**Graph 2** - Prevalence of *Acinetobacter baumannii* resistant to carbapenems in different clinical samples in the General Hospital at the UFTM in the period 2008 to 2014.



## DISCUSSION

This study found that 60.5% of the *Acinetobacter baumannii* in the sample cultures was resistant to carbapenems. The result of a study by Gomides *et al.*<sup>14</sup> corroborated these results. It indicates that 61.7% of the *Acinetobacter baumannii* in a hospital, in 2014, was resistant to carbapenems.

In a research conducted in Porto Alegre in the period from 2006 to 2008, Dauda *et al.*<sup>15</sup> found only 37.1% of isolate cultures of *A. baumannii* which were resistant to imipenem and meropenem. Leiser *et al.*<sup>16</sup> showed an average rate of 31% *A. baumannii* resistant to carbapenems in a hospital in the State of Paraná, between 2003 and 2004. Another study by Heinek<sup>17</sup> in Porto Alegre, in 2011,

found 67.4% of carbapenem-resistant *A. baumannii*. Nóbrega<sup>18</sup> found, among the isolate cultures of *A. baumannii* in Goiânia, from 2007 to 2010, that 87.1% of them were resistant to imipenem.

These differences in the prevalence of resistance to carbapenems may reflect the variability of the mechanisms by which the infections of *Acinetobacter baumannii* are transmitted at different hospitals, or the different actions taken by the Committee for the Control of Hospital Infections in each hospital, which are measures for the prevention and control of the infections.

The results found here showed a significant increase in the rate of isolation of *Acinetobacter baumannii* resistant to carbapenems in the period from 2008 to 2010.

Gales *et al.*<sup>19</sup> conducted a study in which they updated the information regarding the resistance rates of isolate gram-negative bacilli from Latin American medical centers enrolled in the SENTRY Antimicrobial Surveillance Program, during the period from 2008 to 2010. Results have shown that, when compared to a study with the same objective conducted between 1997 and 1999, there was an increase in the rate of imipenem-resistant *Acinetobacter baumannii*, in Brazil, from 12.6% to 71.4%.

According to Zarrili *et al.*<sup>20</sup> it is likely that the increased resistance to carbapenems in Brazilian hospitals is connected with the increase in the use of broad spectrum antimicrobials for the treatment of hospital-acquired infections caused by multidrug-resistant gram-negative organism.

The highest prevalence of *Acinetobacter baumannii* resistant to carbapenems in this study was found in Adult Emergency Units (AEU), followed by Adult Intensive Care Unit (ICU) with 26.4% and 22.8%. There are few data on the prevalence of resistant *Acinetobacter* spp. in the different wards of hospitals, since most studies who investigate multidrug-resistant bacteria are restricted to the ICU. Santos *et al.*<sup>21</sup> studied 32 samples of *Acinetobacter baumannii* resistant to carbapenems and found a higher prevalence of those in the ICU (59.3%), followed by the inpatient clinic (15.6%) (which in this study was the third highest prevalence), and in the Emergency Room (9.4%).

It was verified that the prevalence of carbapenem-resistant *Acinetobacter baumannii* was higher in samples of wound secretions (25%), followed by samples of the lower respiratory tract (21.4%) and blood cultures (16.8%). In the study by Nóbrega *et al.*<sup>18</sup>, it was found that the main sites of isolation of imipenem resistant *A. baumannii* were the respiratory tract (47.5%), followed by infections in the bloodstream (21.3%) and surgical wound infections (13.4%). Similarly, Gomides *et al.*<sup>14</sup> showed a higher frequency of *Acinetobacter baumannii* resistant to

carbapenems in tracheal secretions (27.7%) and in blood (7.6%), while Santos *et al.*<sup>21</sup> showed that the isolate cultures of *Acinetobacter baumannii* resistant to carbapenems had come from 23 respiratory secretions (71.8%), six wound secretions (18.8%), two samples of urine (6.2%) and one blood sample (3.1%).

## CONCLUSION

This study showed a high occurrence rate (60.5%) of isolated cultures of carbapenem-resistant *Acinetobacter* spp. among inpatients in the General Hospital at the UFTM. It is necessary to conduct future genetic studies in order to elucidate the mechanisms of carbapenem resistance, and to know better the prevalence of the carbapenem-resistant *Acinetobacter* spp. in clinical samples, and its distribution in the different wards in the General Hospital at the UFTM. That is an essential step for the planning and implementing of measures for the prevention and the control of hospital infections, as also are the treatment strategies with antimicrobials.

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## CONTRIBUTION

**Giani Del Ciello** was responsible for data collection, analysis, and interpretation, and for the writing of the article. **Marcelo Costa Araújo** conceived, designed and critically reviewed the research.

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