

# Antimicrobial resistance patterns among *Acinetobacter baumannii* isolated from burn intensive care unit in Tripoli, Libya



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## Summary

**Background:** *Acinetobacter baumannii* is a troublesome and increasingly problematic healthcare-associated pathogen, especially in critical care unit. These organisms have a capacity for long-term survival in the hospital environment.

**Aim:** This study aimed to investigate the drug resistance patterns of *Acinetobacter baumannii* strains isolated from burn ICU (BICU).

**Method:** The antibiotic susceptibility of 167 *Acinetobacter baumannii* isolates to imipenem, meropenem, gentamicin, ciprofloxacin, fusidic acid, amikacin, trimethoprim, cefepime, ceftazidime, ceftriaxone, cefotaxime, and amoxicillin-clavulanic acid was determined by disk agar diffusion test.

**Findings:** A total 167 *A. baumannii* strains out of 4286 isolates were collected from various specimens during study period. The overall proportion of *A. baumannii* isolates among all clinical isolates has increased slightly throughout the study from 3.5% to 4.2%. Carbapenem remained the antimicrobial most active antibiotic against *A. baumannii* isolates compared with other antibiotics. However, during the two years there was an increase in resistance from 50.6% to 71.3% to imipenem ( $P < 0.01$ ), and meropenem from 50.6% to 74.5% ( $P < 0.01$ ). ICU isolates exhibited significantly higher level of resistance to imipenem (71.6%) and meropenem (73.4%) compared with non-ICU strains (42.6% and 44.6% respectively) ( $P < 0.01$ ).  
**Conclusion:** Due to the high antimicrobial resistance in the ICU, we must focus on both a wiser use of antimicrobials and the prevention of infection. Continuous monitoring of antimicrobial susceptibility and strict adherence to infection prevention guidelines are essential to eliminate major outbreaks in the future.

## Introduction

The emergence of resistance among gram-negative bacilli has been a growing problem during the past two decades. Among the problem microorganisms is *Acinetobacter baumannii*, which emerged as one of the leading nosocomial pathogen, particularly in Intensive Care Units (ICUs), where several outbreaks have been described<sup>1-3</sup>. It is probably now accounts for 2-10% of Gram-negative bacterial infections in ICUs in Europe and the United States<sup>4</sup>. The epidemic potential and the clinical severity of *A. baumannii*

infections are primarily related to the ability to survive and spread within hospital environment and to develop resistance to a variety of antimicrobial agents, including broad-spectrum beta-lactams, fluoroquinolones, aminoglycosides, and carbapenems<sup>5</sup>. Multidrug resistant *A. baumannii* (MDR) usually retained in vitro susceptibility to carbapenems<sup>6</sup>. Imipenem remain drugs of choice, but their efficacy can be compromised by the increasingly spread of resistance in several countries<sup>7-9</sup>. The aim of the study was to determine the drug resistance patterns of *A. baumannii* strains isolated from different units at burn and plastic surgery centre (BPSC) include burn ICU (BICU) patients during 2008-2009.

## Materials and Methods

### Bacterial isolates

All *A. baumannii* clinical isolates identified in the BPSC (Tripoli, Libya) between 2008 and 2009 were selected. Initially conventional biochemical tests such as Gram stain, catalase, and oxidase tests were used<sup>10</sup>. Then, *Acinetobacter* were characterized by phenotypic method by using API 20NE (bio-Mérieux, France) for the identification at the species level. Hundred and sixty seven non-duplicate *A. baumannii* isolates recovered from routine cultures performed in the microbiology laboratory from wounds and abscesses swabs, urine, blood culture, and others, derived from different wards (burn units, paediatric burn, plastic units) and BICU patients.

### Antimicrobial susceptibility testing

Minimal inhibitory concentrations (MICs) were performed by agar dilution method and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines against all isolates to determine the susceptibility of these isolates to such antibiotics<sup>11</sup>. The antibiotic classes tested included: imipenem (10µg), meropenem (10µg), gentamicin (10µg), ciprofloxacin (5µg), fusidic acid (10µg), amikacin (30µg), trimethoprim (25µg), cefepime (30µg), ceftazidime (30 µg), ceftriaxone (30 µg), cefotaxime (10 µg), and amoxicillin-clavulanic acid (30µg). Isolates showing intermediate level of susceptibility classified as resistant. MDR *A. bauman-*

*nii* defined as resistance to more than three classes of antibiotics. *Escherichia coli* ATCC 25922 and ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853 were used as quality controls in each susceptibility determination. All *P* values were two-tailed. *P* value <.05 was considered as significant. Open Epi software (Epi Info™ 7, Atlanta, GA, USA) was used for all statistical analyses.

## Results

During the study, 167 *A. baumannii* strains were isolated from patients, representing 73/2070 (3.5%) and 94/2216 (4.2%) of total samples received during the years 2008 and 2009 respectively. There were 72 females (43.1%) and 95 males (56.9%). The median age was 35 (7months- 80years). The body sites and fluids from which the organism was recovered included urine (10 [6.0%] of the isolates), wound and abscess swabs (119 [71.2%]), bronchial lavage (16 [9.6%]) and blood (12 [7.2%]); the remaining isolates were recovered from other sites. *A. baumannii* ranked the fifth most frequently isolated microorganism isolated from patients in BICU, preceded by *Staphylococci*, *Pseudomonas*, *Klebsiella* and *Candida*.

The majority of strains were derived from BICU (n=113, 67.7%) compared with wards (n=54, 32.3%). The antimicrobial resistance pattern is shown in **Table 1**, during two years of the study, all *A. baumannii* isolates were highly resistant to third generation cephalosporins (ceftazidime, ceftriaxone,

**Table 1.** Distributions of antibiotic resistance for isolates of the *A. baumannii* complex.

Antimicrobial agents	ICU (n=113)		Non-ICU (n=54)		Total 167	
	n*	%*	n*	%*	n*	%*
Amoxicillin/clavulanic acid	113	100	52	96.2	165	98.8
Cefotaxime	113	100	52	96.2	165	98.8
Ceftazidime	113	100	51	94.4	164	98.2
Ceftriaxone	113	100	52	96.2	165	98.8
Cefepime	108	95.5	46	85.2	154	92.2
Imipenem	81	71.6	23	42.6	104	62.3
Meropenem	83	73.4	24	44.4	107	64.1
Amikacin	109	96.4	47	87	156	93.4
Gentamicin	112	99.1	48	88.8	160	95.8
Ciprofloxacin	103	91.1	47	87	150	89.2
Trimethoprim	112	99.1	48	88.8	160	95.8
Fusidic acid	112	99.1	52	96.2	164	98.2

\*= number of isolate which are resistant to tested antibiotic.

°= total percent of isolates resistant to tested antibiotic

and cefotaxime), and fusidic acid. High rates of resistance also demonstrated to cefepime (92.2%), amikacin (93.4%) and ciprofloxacin (89.2%). About 97.7% of the isolates defined as MDR. Of 167 *Acinetobacter* isolates, 62.3% and 64.1% were resistant to imipenem and meropenem, respectively. However, there was significant increase in the proportion of resistance to imipenem (from 37/73 [50.6%] in 2008 to 67/94 [71.3%] in 2009) ( $P < 0.01$ ), and to meropenem (from 37/73 [50.6%] in 2008 to 70/94 [74.5%] in 2009) ( $P < 0.01$ ). ICU isolates exhibited significantly higher level of resistance to imipenem (71.6%) and meropenem (73.4%) compared with non-ICU strains (42.6% and 44.6% respectively) ( $P < 0.01$ ). In addition, this study revealed that all ICU isolates were (100%) resistant to third generation cephalosporins compared with non-ICU strains.

## Discussion

Within a few decades ago *A. baumannii* rapidly developed resistance to a wide variety of antibiotics that emerged in many parts of the world, mostly by acquisition of gene clusters carried by plasmids, transposons, integrons, and resistance islands within the genome<sup>12-17</sup>. This phenomenon led to the emergence of increasingly multidrug resistance in this species<sup>18</sup>. To date, some strains of *A. baumannii* have become resistant to almost all currently available antibacterial agents, including carbapenems<sup>19-20</sup>. In the present study, the overall proportion of *A. baumannii* isolates among all clinical isolates has increased slightly throughout the study from 3.5% to 4.2%. *A. baumannii* was the fifth most frequently isolated bloodstream microorganism obtained from patients in BICU preceded by *Staphylococci*, *Pseudomonas*, *Klebsiella* and *Candida*.

Carbapenem remained the antimicrobial most active antibiotic against *A. baumannii* isolates compared with other antibiotics, and there was striking variation during the two years of the study, there was significant increase in resistance from 50.6% to 71.3% to imipenem, while meropenem showed significantly increased level of resistance from 50.6% to 74.5%. Lower rates of resistance was demonstrated in some parts of the world such as Taiwan, the carbapenem resistance of the *Acinetobacter* species was 10%<sup>21</sup>, (3.2%) was reported in Japan<sup>22</sup> and in Saudi Arabia (3.0%)<sup>23</sup>. Regional variation in imipenem resistance was also noted when North America (4.5% of isolates) and Latin America (11% of isolates) were compared<sup>24</sup>. Antimicrobial susceptibility of 490 *A. baumannii* strains collected in 37 centres in 11 European countries from 1997 to 2000, imipenem and meropenem were the most active agents with resistance rates of 16% and 18% respectively. Turkey showed the highest

resistance rates for almost all of the tested antimicrobials, followed by Italy and the UK<sup>25</sup>. The most recent data for 2006 from 40 centres in 12 European countries participating in the monitoring program revealed a considerable increase in resistance rates for meropenem (43.4%) and imipenem (42.5%)<sup>26</sup>. In another study, rate of resistance to imipenem has increased from 0% to 42% during the study period<sup>27</sup>. In Greece, the proportion of imipenem-resistant *A. baumannii* isolates from patients hospitalised between 1996 and 2007 in tertiary care hospitals in several regions of the country rose from 0% to 85.1% (ICUs), 60.4% (medical wards) and 59% (surgical wards). Meanwhile, bloodstream isolates from the same dataset exhibited even higher resistance rate<sup>28</sup>. The latest results were relatively similar to our rates of resistance.

ICU isolates exhibited significantly higher level of resistance to imipenem (71.6%) and meropenem (73.4%) compared with non-ICU strains (42.6% and 44.6% respectively). *A. baumannii* and could disseminate in the ICU, probably after contamination of the hospital environment and by nosocomial transmission<sup>8, 14, 29-32</sup>. A high resistance rate to imipenem and meropenem in *Acinetobacter* spp. isolates may lead to extensive use of polymyxins. Our results was lower than a report from the ICUs in Turkey that revealed resistance rates of 80.3% and 71.2% for imipenem and meropenem, respectively<sup>33</sup>. In a recent report from a single ICU in Bulgaria found that carbapenem-resistance was 75%<sup>34</sup> while in a UK, a retrospective study on 399 *Acinetobacter* bacteraemias over an eight-year period identified a tremendous increase in carbapenem resistance from 0% in 1998 to 55% in 2006<sup>35</sup>. While in Spain, the rate of resistance to imipenem in *Acinetobacter* species is 43%<sup>36</sup>. Recently 58% of *A. baumannii* were resistant to imipenem<sup>37</sup>.

An outbreak of carbapenem-resistant *A. baumannii* was described in a burn unit of a Norwegian hospital from a transferred Spanish patient who was identified as the source<sup>38</sup>. A similar outbreaks were also described in Belgium, UK and US<sup>39-40</sup>. Peleg et al. demonstrated the emergence of carbapenem resistance among Australian *A. baumannii* isolates, it was significantly linked to an increased used of meropenem<sup>41</sup>. Similarly in Taiwan, Ye et al found that the only independent risk factor for appearance of imipenem-resistant isolates in patients formerly with imipenem-sensitive isolates is the use of carbapenem<sup>17</sup>. In conclusion, due to the high possibility of transmission of the antibiotic resistance through a variety of transmissible elements include plasmid and presence of many asymptomatic colonizers has raised the importance of active surveillance to identify potential colonizers and reservoirs of the microorganism combined with implementation of infection control measures, including strict hand hygiene, appear to be effective in controlling such outbreaks of multi-

drug resistant bacteria in clinics and hospitals. Furthermore, such measures may reduce infection, mortality rates, length of hospitalization and associated costs.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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