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ORIGINAL ARTICLE

Antibiotic Resistance of *Acinetobacter baumannii* in Iran: A Systemic Review of the Published Literature

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Abstract
Objectives: *Acinetobacter baumannii* is a bacterium responsible for health care-associated infections, and it frequently develops multiple drug resistance (MDR). The prevalence of antibiotic-resistant *A. baumannii* in Iran has increased, and this may cause significant clinical problems. Therefore, in order to elucidate the development of antibiotic resistance, we performed a systematic review of the literature published on antibiotic-resistant *A. baumannii* reported in Iran.
Methods: Thirty-six publications that met the criteria for inclusion were reviewed from an initial 87 papers. Selected papers published between 2008 and September 2014, were categorized on the basis of the sample collecting year been between 2001 and 2013.
Results: Analysis of data revealed that, in general, there was an increase in antimicrobial resistance. During the initial time point of these studies (2001—2007) there was a high rate of resistance to all antibiotics, with the exception of carbapenems, lipopeptides, and aminoglycosides that had a low resistance rate in comparison with the others. Also, the resistance rate was increased in one group of these three antimicrobial groups from 2010 to 2013. In particular, there was an increase in resistance to carbapenems (imipenem and meropenem) from 2010—2011 and 2012—2013, whereas no significant change in the resistance rate of the other two antimicrobial groups (lipopeptides and aminoglycosides) during the study time was observed, although we did observe certain trends in amikacin (aminoglycoside group antibiotic) between 2011—2012 and 2012—2013.
Conclusion: These findings indicate that antimicrobial resistance of *A. baumannii* in Iran has increased, which may very well affect the antimicrobial resistance of this organism worldwide. Based on these results, novel prevention and treatment strategies against *A. baumannii* infections are warranted. Furthermore, these data may assist in revising treatment guidelines and regional policies in care units to slow the emergence of antimicrobial resistance.

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1. Introduction

Acinetobacter baumannii is a gram-negative, strictly aerobic, nonfermenting coccobacillus belonging to the Moraxellaceae family [1]. Species belonging to this genus are opportunistic pathogens with increasing relevance in both community-acquired and nosocomial infections, particularly among patients in intensive care units (ICUs) and high-dependency units (HDUs) [2−5]. These organisms have been implicated in various infections, including ventilator-associated pneumonia, endocarditis, meningitis, and infections of the skin, soft tissues, urinary tract, and those originating from prosthetic devices [4,6]. *A. baumannii* has been isolated from numerous sources such as soil, water, animals, and humans, while its presence in health care institutions and on environmental surfaces has been extremely difficult to control [6].

Three decades ago, *A. baumannii* infections were effectively treated with traditional antibiotics [7,8]. By contrast, it currently exerts resistance to nearly all major classes of antibiotics, including broad-spectrum penicillins, cephalosporins, carbapenems, most aminoglycosides, fluoroquinolones, chloramphenicol, and tetracyclines. In the past decade, multidrug resistant (MDR) clinical isolates have shown global distribution [3]. Therefore, this pathogen has become a "red-alert" for the following reasons: rapid emergence of resistance, increased incidence, and the worldwide spread of MDR isolates [7]. The rapid spread of MDR strains in nosocomial infections that exhibit resistance to most or all common antibiotics is a troubling evolution [3]. Thus, a study of the antibiotic resistance patterns both in individual hospitals and on countrywide levels may help to clarify the mode of *A. baumannii* antibiotic resistance spread and epidemiology worldwide [9]. The current review was performed to elucidate the mode of antibiotic resistance of *A. baumannii* in Iran.

2. Materials and methods

2.1. Database searches

Biomedical databases (Scopus, Medline, Web of Science, EBSCO, IranMedex) were searched in order to retrieve all related manuscripts published in English and Persian. The search identified publications of epidemiological studies in order to compile adequate information on *A. baumannii* antimicrobial resistance in Iran. The following key words were used: "*Acinetobacter baumannii* and Iran", "antimicrobial resistance and *Acinetobacter baumannii* and Iran", "antimicrobial resistance and either gram negative bacilli and Iran or Iran", "nosocomial or hospital acquired and Iran" . Study publications were obtained through PubMed, MEDLINE, and IranMedex database searches. Also, references cited within these articles were used to find additional relevant articles. In this review, *A. baumannii* susceptibility breakpoints based on Clinical Laboratory Standards Institute (CLSI)-relevant antibiotics were primarily those listed by the World Health Organization Recommended Surveillance Standards.

2.2. Study settings

From the first 87 papers, we identified a total of 36 that were written in English and considered to be eligible for inclusion in this review. The selected papers were published between 2008 and September 2014. We categorized studies on the basis of sample collection year, between 2001 and 2013; some papers collect samples during different years (Table 1). Two studies were performed in three regions of Iran, including central, north, and south. Twenty-two studies were performed north of Iran, with 18 in Tehran (capital of Iran). Two studies occurred in the south of Iran, three in the west, and three in the east. Although the studies used various methods, they were all approved by the CLSI and the National Committee for Clinical Laboratory Standards (NCCLS) and, therefore, suitable for trend analysis.

2.3. Microbiological methods

Clinical specimens in studies were collected from hospitalized patients with different disease and various sampling. Twenty of the studies obtained data from various clinical specimens, including blood, cerebrospinal fluid, urine, sputum, and respiratory tract samples. Data from eight studies were obtained from patients with burn wounds and seven from hospitalized patients in ICUs. Antibiotic susceptibility testing methodologies were declared in all studies, all of which were performed according to the CLSI breakpoints. Twenty-six studies used the Kirby-Bauer disk diffusion method, nine used the E-test, and two used broth microdilution. To identify resistance genes, 25 of the studies used one or more polymerase chain reaction-based molecular methods.

3. Results

3.1. Phenotypic resistance rates for different antibiotics

The susceptibility data for 3049 *A. baumannii* isolates are shown in Table 2. These data reflect the 12-year period from 2001 to 2013 of sampling time in the studies identified. The data demonstrate that, with the exception of carbapenems, lipopeptides, and aminoglycosides, there was a high rate of resistance to antimicrobial groups during the initial time point of this study (2001−2007). Also, the resistance rate was increased in one group of these three antimicrobial groups from 2010 to 2013. In particular, there was an increase in resistance to carbapenems (imipenem and meropenem) from 2010−2011 and 2012−2013, whereas no significant