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Three-Year Trend of Antimicrobial Resistance of *A. baumannii*: A Retrospective Study from Ardabil, Northwestern Iran

Jafar Mohammadshahi[1], Mohsen Arzanlou[2], Shahram Habibzadeh[1], Hadi Peeri Doghaheh[2], Roghayeh Teimourpour[2]*

[1] *Department of Infectious Diseases and Tropical Medicine, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran*

[2] *Department of Microbiology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran*

***Corresponding authors:** Roghayeh Teimourpour, **Address**: Department of Microbiology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran. **E-mail:** r.teymourpour@gmail.com

Tel: +984555333776

Abstract

***Background & Aims*:** *Acinetobacter baumannii* is one of the most important pathogenic bacteria causing nosocomial and opportunistic infection with the high rate of antibiotic resistance. The aim of the present work was to study the antimicrobial resistance pattern of *Acinetobacter* isolates recovered from patients admitted to Imam Khomeini Hospital and identifying the related risk factors. Also, in this study, the efficacy of different combined antimicrobial therapy against *A. baumannii* was evaluated.

Materials & Methods: In this retrospective study, a total of 108 medical records related to patients admitted to Imam Khomeini Hospital in Ardabil province from 2011 to 2013 was entered into the study. For each patient, demographic, bacterial culture, and antibiogram data were obtained and analyzed.

***Results*:** Results indicated that pulmonary infections were the most common clinical source of *Acinetobacter* infection. The highest rate of resistance (100%) was related to ceftizoxime, chloramphenicol, furazolidone, nitrofurantoin, cephalothin, cephalexin, ticarcillin, piperacillin, amoxicillin, and aztreonam followed by ceftazidime, imipenem, co-trimoxazole, ceftriaxone, cefotaxime, and cefixime (80%). The lowest rate of resistance was seen against polymyxin B, ampicillin/sulbactam and meropenem. Our results indicated that 86.9 % and 91.7% of isolates were resistant to ceftriaxone and imipenem, respectively. Since carbapenems are the drug of choice and the last-resort agent for the treatment of MDR strain of *A. baumannii* , this high resistance level would be a serious concern.

***Conclusion*:** The epidemiological survey will be helpful in controlling infections in hospital environment and prescribing proper antimicrobial agents.

Keywords: *Acinetobacter baumannii*, antibiotic resistance, antibiogram, nosocomial infection

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Introduction

Acinetobacter spp. are gram-negative, aerobic, and ubiquities bacteria belonging to the Moraxellaceae family. Up to now, more than 38 species have been identified in the *Acinetobacter* genus. Among them, *A. baumannii* is the most common cause of nosocomial infection. It is generally harmless in immunocompetent individuals but it can cause severe infections in immunocompromised patients or people who have underlying diseases. The weakened immune system, Diabetes, use of contaminated hospital ventilator, extended hospital stays, severe skin burns, etc. are important risk factors that increase the risk of infection by *Acinetobacter* spp(1, 2).

One of the most important characteristics of *Acinetobacter* species is resistance to several antibiotics which makes it difficult to treat Acinetobacter related infections. In different parts of the world, there is a great difference in the rate of resistance to different antibiotics due to environmental factors and use of different types of disinfectants for cleaning the surfaces(3-5).

Many studies indicated that *Acinetobacter* spp. especially *A. baumannii* are innately resistant to many available antibiotics including broad-spectrum cephalosporins, β-lactam antibiotics, aminoglycosides, and quinolones. However, carbapenems are the gold-standard and the last treatment option, but resistance to these agents is also being increasingly reported. Therefore, identification of antibiotic resistance pattern of indigenous strain along with determination of source of infection will be critical in the management of infection and will help reduce the rate of infection(6-8). The aim of this study was to determine the antimicrobial resistance pattern of *A. baumannii* strain isolated from patients referred to Imam Khomeini Hospital and to identify associated risk factors and appropriate empirical therapy.

Patients and methods

Data collection:

In this retrospective study, information of 108 patients with *A. baumannii* infection admitted to Imam Hospital in Ardabil province between 2011-2013 was evaluated. In this study, several variables including age, genus, presence of underlying disease, patient-days of hospitalization, and antimicrobial susceptibility test results were recorded.

Statistical analysis:

The data were analyzed using SPSS 22.0 software package (SPSS Inc., Chicago, IL, USA). Statistical analysis were performed by employing chi-square, Fisher's exact test. The p-value less than 0.05 was considered statistically significant.

Ethical approval:

In this retrospective study, the personal information of patients was kept confidential.

Results

In this study, 108 patients with the mean age of 60.41±10.01 years were studied. The majority of cases (39.1%) were between the ages of 51 and 60 years. The minimum and the maximum age was 35 and 81 years, respectively. Of 108 patients, 58 cases (53.7%) and 50 (46.3%) cases were male and female, respectively. In this study, the average length of stay in hospital was 28.01 ± 10.97 days. The minimum and maximum length of hospital stay was 8 days and 49 days, respectively. The highest rate of hospitalization was observed in group 4(31-40 days, 41.7%).

ICU ward with 80 (74.1) cases, internal ward with 21 cases (19.4), and infectious disease ward with 7.5 cases (6.5) had the highest rate of hospitalization (Figure1).

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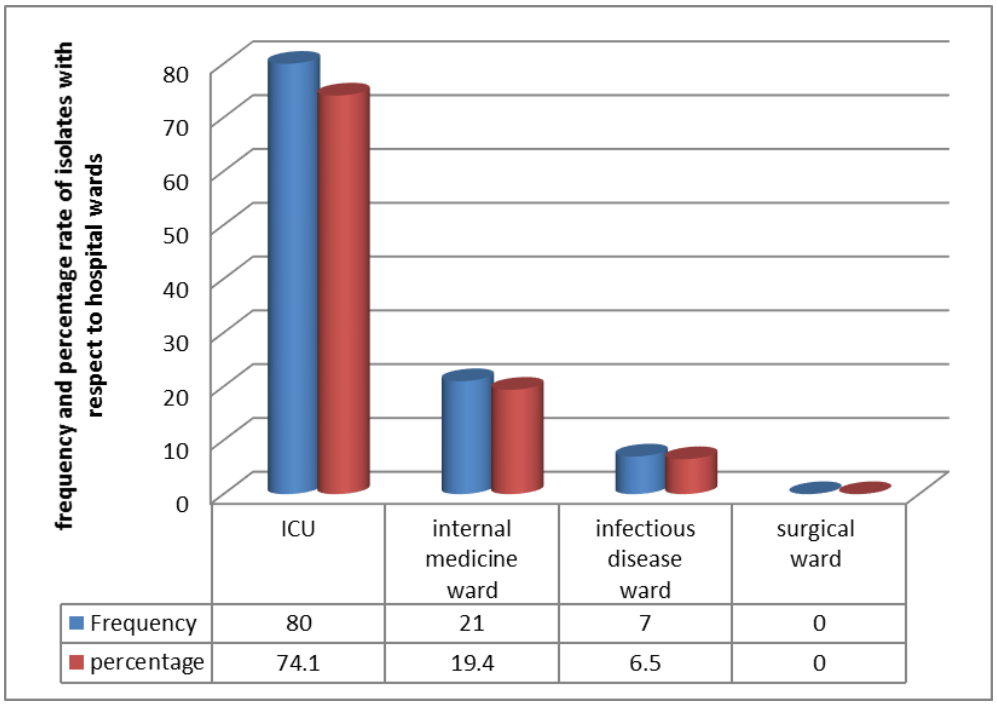

Fig1: Frequency and percentage distribution of the patients with respect to wards

The results of this study showed that 11 (10.2%) out of the total number of patients died during hospitalization. The history of diabetes, high blood pressure, cardiac disease, renal disease, and malignancy were observed in 50, 50, 25, 15 and 15 cases, respectively (Figure2).

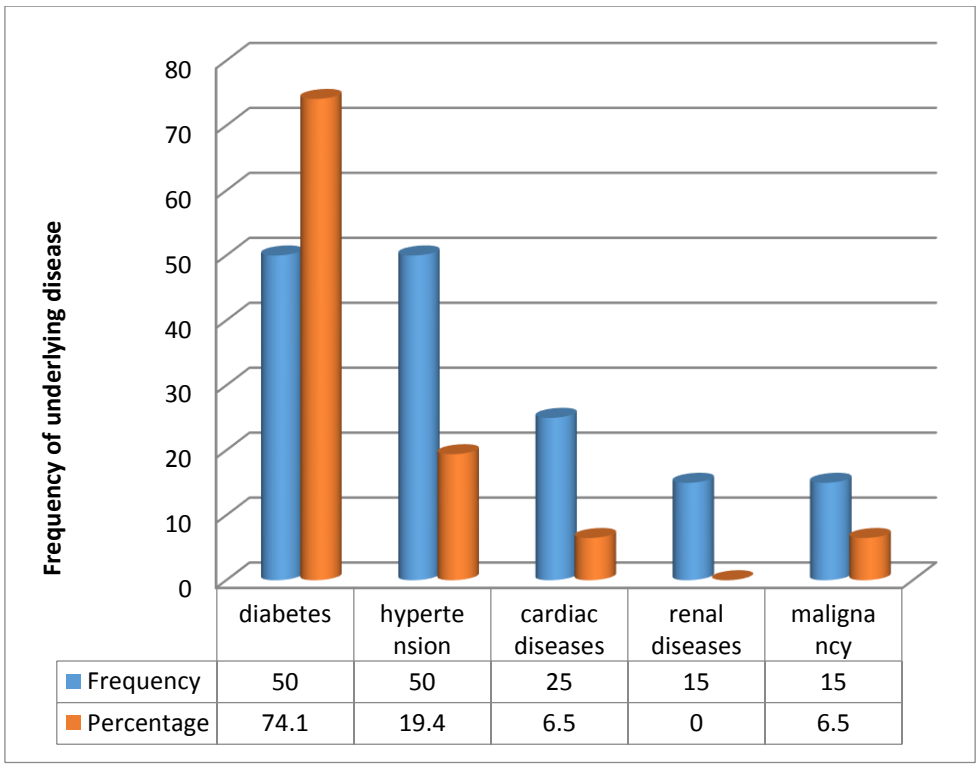

Fig2: Frequency of underlying diseases in the studied patients

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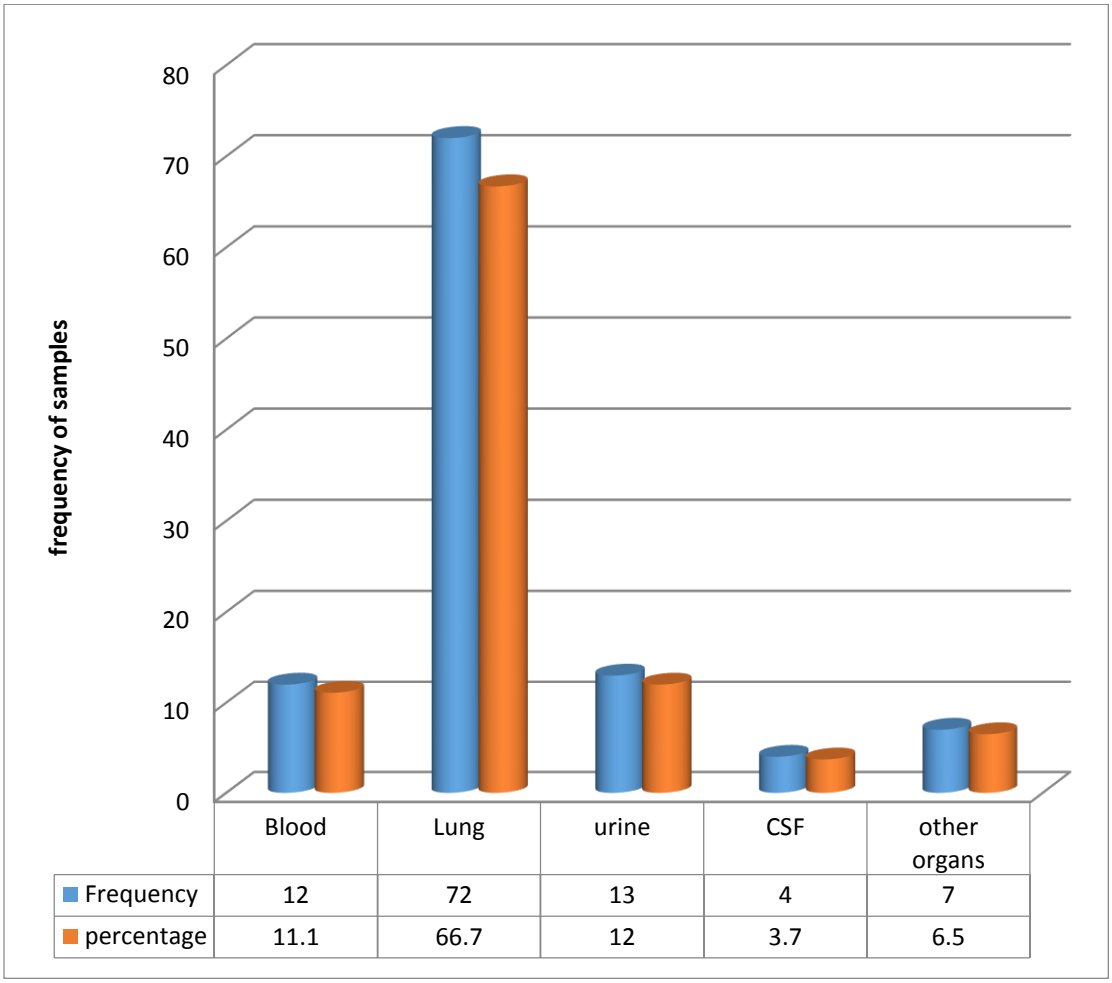
Blood (n=12,11.1%), sputum (n-72,66.7%), urine (n=13,12%), CSF (n=4,3.7%), and other organs (n=7,6.5%) were the most frequently samples for A. baumannii isolation (Figure3).



	Blood	Lung	urine	CSF	other organs
Frequency	12	72	13	4	7
percentage	11.1	66.7	12	3.7	6.5

Fig3: Frequency and percentage distribution of sample type

The results of antimicrobial susceptibility test with selected antibiotics are presented in Table 1. As shown in Table 1, the highest drug resistance was observed in ceftizoxime, chloramphenicol, furazolidone, nitrofurantoin, cephalothin, cephalexin, ticarsalin, piperacillin, amoxicillin, and aztreenam(100%). The antibiotic resistance to ceftazidime, imipenem, co-trimoxazole, ceftriaxone, ceftizoxime, and cefexime was also reported to be over 80%. However, the lowest antibiotic resistance was observed for polymyxin B, ampicillin / sulbactam, and meropenem. Among the beta- lactam antibiotics/ beta-lactamase inhibitors (cephalosporins and Aminoglycosides group), the lowest resistance rate was observed in ampicillin-sulbactam antibiotic (5.3%), cefepime (6.1%), and Tobramycin(0%) (Figure4,6).

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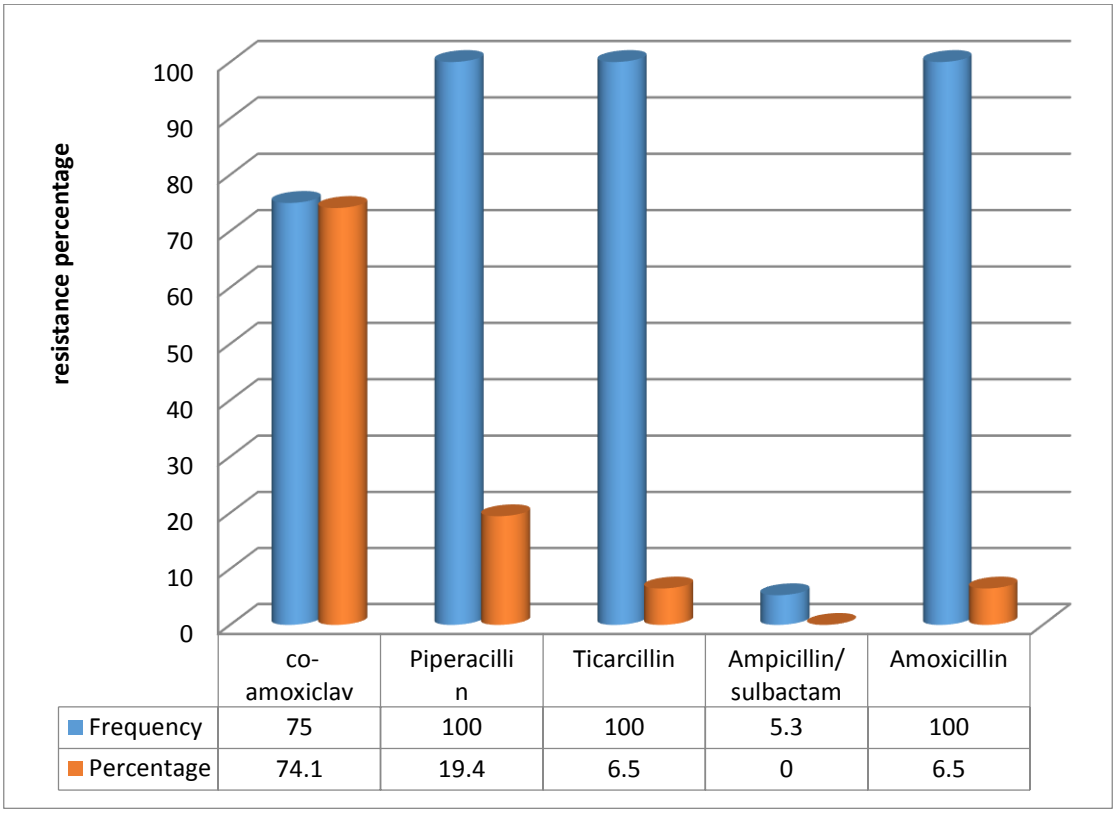
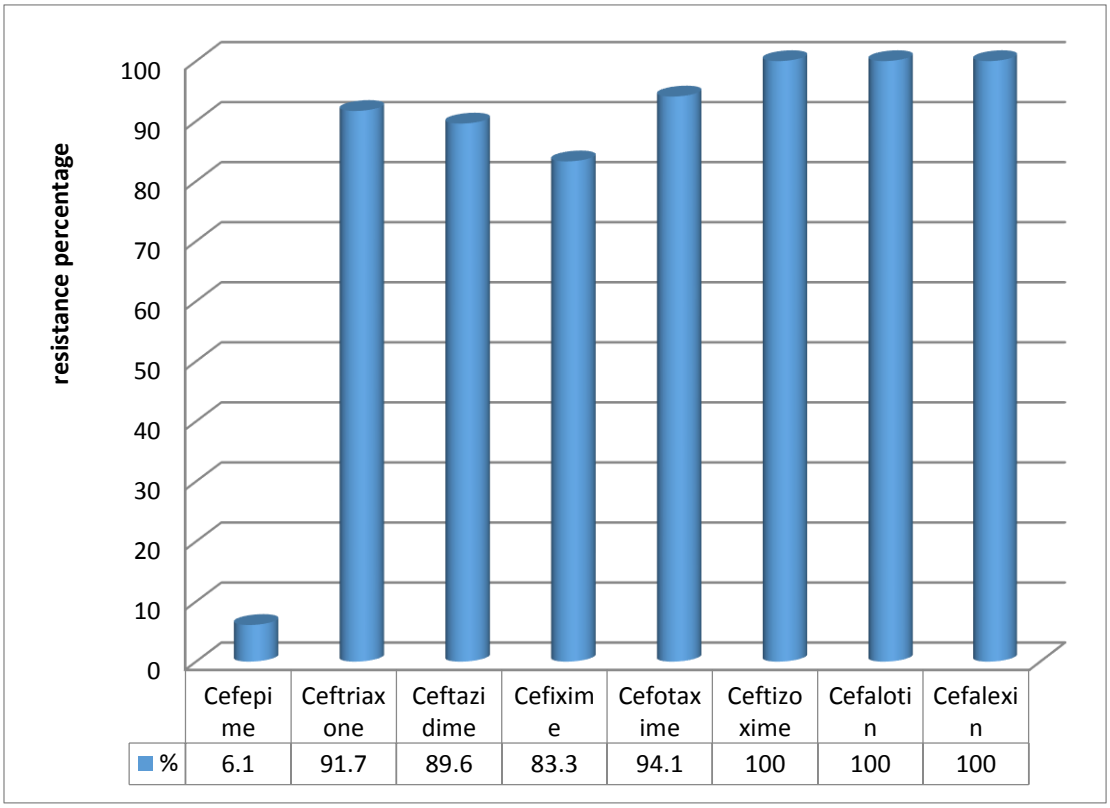


	co-amoxiclav	Piperacillin	Ticarcillin	Ampicillin/sulbactam	Amoxicillin
Frequency	75	100	100	5.3	100
Percentage	74.1	19.4	6.5	0	6.5

Fig4: Resistance percentage in beta- lactam / *beta-lactamase inhibitor*



	Cefepime	Ceftriaxone	Ceftazidime	Cefixime	Cefotaxime	Ceftizoxime	Cefaloti n	Cefalexin
%	6.1	91.7	89.6	83.3	94.1	100	100	100

Fig5: *Resistance percentage in cephalosporins*

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Table1: the results antibiotic susceptibility test

Total	resistance		intermediate		sensitive		name	drug	
	%	frequency	%	frequency	%	frequency			
12	75	9	8.3	1	16.7	2	Co-amoxiclav	Penicillin	β-Lactam antibiotic
15	100	15	-	-	-	-	Piperacillin		
3	100	3	-	-	-	-	Ticarcillin		
19	5.3	1	15.8	3	78.9	15	Ampicillin / Sulbactam		
4	100	4	-	-	-	-	Amoxicillin		
33	6.1	2	87.87	29	6.1	2	Cefepime	cephalosporins	
24	91.7	22	4.2	1	4.2	1	Ceftriaxone		
42	89.6	43	2.4	1	8.3	4	Ceftazidime		
6	83.3	5	16.7	1	-	-	Cefixime		
17	94.1	16	-	-	5.9	1	Cefotaxime		
15	100	15	-	-	-	-	Ceftizoxime		
6	100	6	-	-	-	-	Cefalotin		
2	100	2	-	-	-	-	Cefalexin		
28	22.2	4	-	-	77.8	14	Meropenem	carbapenems	
61	86.9	53	1.6	1	11.5	7	Imipenem		
3	100	3	-	-	-	-	Aztreonam	Monobactam	
64	50	32	20.3	13	29.7	19	Amikacin	Aminoglycoside	
21	71.4	15	9.5	2	19	4	Gentamicin		
3	-	-	-	-	100	3	Tobramycin		
6	100	6	-	-	-	-	Nitrofurantoin	Nitrofurantoin	
5	100	5	-	-	-	-	Furazolidone		
65	6.2	4	89.2	58	4.6	3	Ciprofloxacin	Fluoroquinolone	
1	-	-	-	-	100	1	Norfloxacin		
1	-	-	-	-	100	1	Ofloxacin		
3	-	-	100	3	-	-	Rifampicin	others	
15	100	15	-	-	-	-	Chloramphenicol		
4	75	3	-	-	25	1	Tetracycline		
54	87	47	3.7	2	9.3	5	co-trimoxazole		
42	-	-	2.4	1	97.6	41	Polymyxin		

Discussion

A. baumannii is the major cause of opportunistic infections such as bacteremia, urinary tract infections (UTIs), secondary meningitis, and infective endocarditis, and wound and burn infections especially in hospitalized patients and who are admitted to the intensive care units. Long-term intubation, continuous catheterization, use of contaminated equipment, intensive surgery and trauma are the major risk factor for *Acinetobacter* related infections.

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Increasing antibiotic resistance and development of MDR strain make it a great threat and problem to human public health(9, 10). Different types of antibiotic resistance mechanisms have been documented about *A. baumanii* such as pathogenicity islands, efflux pumps, beta-lactamase, and small RNAs. By using these mechanisms, carbapenem-resistant and multidrug-resistant *A. baumannii* have become the leading cause of ventilator-associated pneumonia and hospital-acquired infections among intensive care unit patients in different parts of world (11-13). In the case of acinetobacter treatment, carbapenem resistance is a substantial problem that contributed to extensive use of third-generation cephalosporins, aztreonam, and imipenem. The surveillance data from different centers worldwide indicated that susceptibility to carbapenem and tobramycin as an effective treatment choice for MDR stain has decreased remarkably. Thus, it was put on priority list for effective drug development by WHO(14) . A study in Europe in 2007 showed that *Acinetobacter* alone accounts for about 19% of ventilator-associated pneumonia cases(15). A study in 2013 showed that hard surfaces and hands of medical staff were the source of premature infant infection by *A. baumanii*(16).

According to our results, the rate of infection among patients aged 51to 60 is substantially higher than other ones. Also, males are more prone to bacterial infections than females. Consistent with previous studies long term hospitalization significantly increases the likelihood of infection and ICU is the most common site for acquisition of infection.

The results of the present work revealed that diabetes is a major underlying disease and predisposing factor of *Acinetobacter* related infection and the lungs are the most common site of infection.

Finally, according to previous studies hand hygiene, isolation of infected patients, environmental cleaning and use of aseptic technique for inserting and removing vascular catheters and endotracheal tubes are important strategies in successful control of infection(17, 18).

Conclusion

Resistance to various disinfectants and dry surfaces making it especially easy to spread in a hospital setting. Hence, monitoring this bacterium in hospitals especially in the ICU ward is discretely needed. In this regard, many hospitals in the world use air ionizer for air purification and *Acinetobacter* elimination in the wards.

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Disclosure

The authors state that there is no conflict of interest to disclose.

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