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journal homepage: <http://ees.elsevier.com/apjtm>Original research <http://dx.doi.org/10.1016/j.apjtm.2016.07.016>Multidrug resistance *Acinetobacter* species at the intensive care unit, Aseer Central Hospital, Saudi Arabia: A one year analysisAli Al Bshabshe¹, Martin R.P. Joseph², Ali Al Hussein³, Waleed Haimour⁴, Mohamed E. Hamid^{2*}¹Department of Medicine, College of Medicine, King Khalid University, Abha, Saudi Arabia²Department of Microbiology, College of Medicine, King Khalid University, Abha, Saudi Arabia³Intensive Care Unit, Aseer Central Hospital, Abha, Saudi Arabia⁴Microbiology Laboratories, Aseer Central Hospital, Abha, Saudi Arabia

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ABSTRACT

Objective: To identify and to determine the antimicrobial susceptibility of *Acinetobacter baumannii* (*A. baumannii*) clinical isolates from ICU at Aseer Central Hospital.**Methods:** The study was conducted in the Intensive Care Unit, Aseer Central Hospital, Saudi Arabia over 13 months period (2014–2015). *Acinetobacter* species ($n = 105$) were isolated from various clinical samples. Isolates were identified using selected phenotypic criteria and confirmed using the Vitek 2 automated system. This system was used to determine the susceptibilities of 21 antimicrobial agents. Patients, isolates and drug data were analyzed using the SPSS statistical software package to determine some epidemiological and microbiological patterns.**Results:** Of the 105 stains, *A. baumannii* accounted for 49 (46.67%), *A. baumannii* complex, 19 (18.09%), *A. baumannii*haemolyticus 32 (30.47%), *Acinetobacter haemolyticus* 4 (3.81%), *Acinetobacter lwoffii* 1 (0.95%) and unidentified *Acinetobacter* species 2 (1.3%). Of the 105 *Acinetobacter* strains, 103 (98.1%) were found multidrug resistant (MDR). *A. baumannii* strain were 100% sensitive to colistin and 74.5% to trimethoprim + sulfamethoxazole. The remaining 19 antimicrobial agents revealed low or no sensitivities: amikacin 16.3%; ampicillin 7.7%; ceftazidime, 7.3%. Distribution of similar sensitivities was shown by other *Acinetobacter* species. Mean number of isolates from males and females indicates no statistical variation ($P = 0.867$) whereas age groups showed significant differences ($P = 0.008$) as it is clear from the high percentage of infected individuals more than 60 years followed by those aged 20–29 years old (19.05%). Upper respiratory tract (30.48%), lower respiratory tract (47.65%) and subcutaneous tissue (9.5%) were the main sources of *Acinetobacter* spp. but mean numbers of isolates from these specimens indicate no discrepancy between specimens ($P = 0.731$).**Conclusions:** *Acinetobacter* species including *A. baumannii* were found MDR (98.1%) according to the current *Acinetobacter* spp. antimicrobial categorization. Approximately half of these strains were *A. baumannii*. All *Acinetobacter* species were 100% sensitive to colistin and to some extent to trimethoprim + sulfamethoxazole (74.5%). ICU-acquired pneumonia among patients over 60 years of age who spend prolonged times at artificial ventilations made up the majority of the cases.

1. Introduction

Acinetobacter species especially *Acinetobacter baumannii* (*A. baumannii*) are emerging as a serious cause of health care-

associated infections especially in intensive care units (ICU). The rising numbers of multi-drug resistant (MDR) *Acinetobacter* species have limited the therapeutic choices for infections control [1]. Infections in crucially sick cancer patients have augmented mortality and added to the ICU stay [2].

Acinetobacter associated infections represent a tough challenge to control in seriously sick patients especially those in ICU. *Acinetobacter* species have the capacity to acquire resistance to almost all presently existing antimicrobial agents [3]. Also, ICU admission

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and hospitalization of patients infected by *A. baumannii* increases the risk of ventilator-associated pneumonia [4]. *A. baumannii* was found the most common and increasingly important pathogen associated with ventilator-associated pneumonia particularly the late-onset and recurrent ventilator-associated pneumonia in a tertiary care hospital in Riyadh, Saudi Arabia [5]. A retrospective study conducted between 2005 and December 2010 in Riyadh region indicated that there was a significant increase in antimicrobial resistance *A. baumannii* [6].

A. baumannii is ubiquitous which may be found in food, water and soils as well as on the skin of healthy human. Strains of *A. baumannii* endure adverse environmental condition such as dryness for long time [7]. Such characteristics help *A. baumannii* to spread easily by all potential routes. Clinical health workers in all hospital sections stated the danger of *A. baumannii* but the problems is much worse in internal medicine or ICU. Variations in recording *A. baumannii* among wards could be a result of selective pressure induced on organisms generated by the random unsupervised use of broad-spectrum antibiotics [8].

In recent years, *A. baumannii* showed a radical decrease in susceptibility to carbapenems. The main carbapenem resistance mechanism was found due to class D-OXA-type enzymes (oxa-23 and oxa-24/40) with carbapenemase activity. The authors concluded that this is a key epidemiological worry as medicinal choices turn out to be narrow. Doctors will rely on polymyxin in combinations with other antibiotics [9]. Recent study reported the appearance of ST236 in Saudi Arabia and Egypt, and the spread of carbapenem resistant *A. baumannii* clones belonging to ST884, ST945 and ST1096 in Saudi Arabia [10].

Our current understanding of the *Acinetobacter* associated illness as emerging problem is lacking. Prevalence, risk factors and antimicrobial sensitivity patterns in Saudi Arabia and Aseer region in particular are still need to be determined. One study which was conducted during 2011/2012 at Aseer Central Hospital indicated that all isolates were sensitive to imipramine, meropenem and colistin and showed high resistant to nitrofurantoin and cefoxitin but least resistant to imipenem and ticarcillin. These authors express worry on the rising resistant to antibiotics [11]. The purpose of the work was to establish the magnitude of *A. baumannii* associated with infections in Aseer region and their antimicrobial profile in the southern Saudi Arabia. Publishing such information will establish database and will assist authorities to establish policies towards controlling the infections.

This study aimed to identify and to determine the antimicrobial susceptibility of *A. baumannii* clinical isolates from ICU at Aseer Central Hospital.

2. Materials and methods

2.1. Ethical approval

The present research was approved by the College of Medicine Ethical Committee. Individual consent from each patient was overlooked by the committee because of the retrospective nature of the study.

2.2. Study design and subjects

In this observational study, adult patients ($n = 105$) were admitted to the intensive care unit (ICU), Aseer Central Hospital during 2014 and 2015 and were retrospectively evaluated.

2.3. Bacterial isolates

Acinetobacter species were isolated from 105 ICU hospitalized infected patients over a 13 month period, Feb. 2014 to Feb. 2015. Isolates were identified using selected phenotypic criteria and confirmed using the Vitek 2 automated system. Samples were processed for culture by standard conventional methods and preliminary identification was performed by gram staining, culturing on MacConkey's agar. Non-lactose fermenting bacteria were sub-cultured and incubated for additional overnights. Genus *Acinetobacter* was identified by gram staining, cell and colony morphology, positive catalase test, negative oxidase test and absence of motility [7].

2.4. Antibiotic sensitivity

Identified species were tested (*in vitro*) against 21 antibacterial drugs using the Vitek 2 automated system. Antibiotics and their strength used were according to the Clinical and Laboratory Standards Institute guidelines [7]. The tested antimicrobial agents were: amikacin, ampicillin, aztreonam, cefepime, cefotaxime, ceftazidime, ciprofloxacin, colistin, fosfomycin, gentamicin, imipenem, levofloxacin, meropenem, mezlocillin, moxifloxacin, piperacillin, rifampicin, tetracycline, tobramycin, trimethoprim and trimethoprim + sulfamethoxazole.

2.5. Statistical analysis

Data were examined using SPSS software version 16.0. Univariate analysis of variance was used to compare variation among means of different variables. P value < 0.05 was considered as the level of significance.

3. Results

3.1. Identification of *Acinetobacter* species

Of the 105 stains, *A. baumannii* accounted for 49 (46.67%), *A. baumannii* complex, 19 (18.09%), *A. baumannii/haemolyticus* 32 (30.47%), *Acinetobacter haemolyticus* 4 (3.81%), *Acinetobacter lwoffii* 1 (0.95%) and unidentified *Acinetobacter* species 2 (1.3%) (Figure 1).

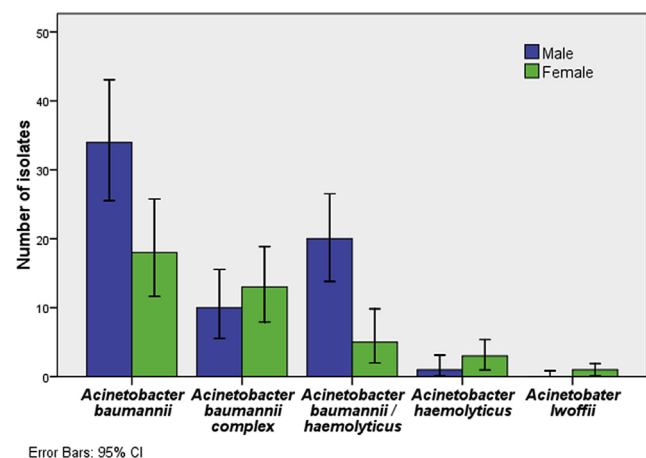


Figure 1. Identities of *Acinetobacter* species recovered from 105 patients at the ICU, Aseer Central Hospital (2014–2015).

Table 1

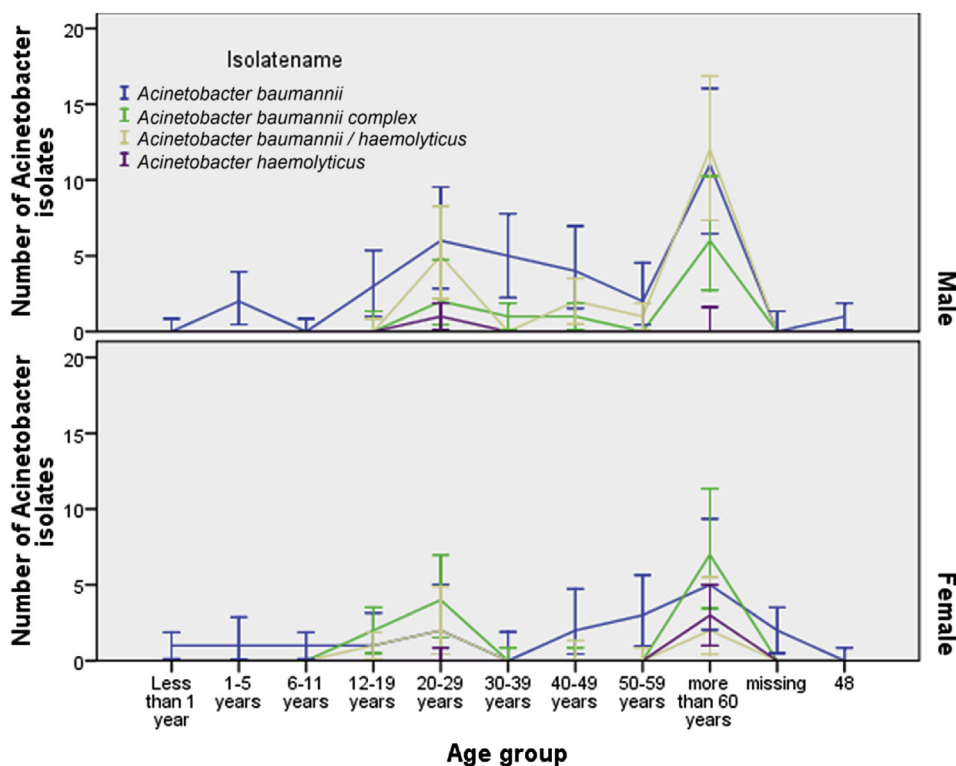
Sensitivity and resistance results of *Acinetobacter* species of 21 various antimicrobial agents [n (%)].

Antimicrobial agent	<i>Acinetobacter baumannii</i>		<i>Acinetobacter baumannii</i> complex		<i>Acinetobacter baumannii</i> / <i>haemolyticus</i>		<i>Acinetobacter haemolyticus</i>		<i>Acinetobacter lwoffii</i>	
	S	R	S	R	S	R	S	R	S	R
Amikacin	8 (16.3)	41 (83.7)	0 (0.0)	3 (100.0)	6 (18.8)	26 (81.3)	3 (75.0)	1 (25.0)	1 (100.0)	0 (0.0)
Ampicillin	1 (7.7)	12 (92.3)	0 (0.0)	16 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
Aztreonam	2 (8.0)	23 (92.0)	0 (0.0)	18 (100.0)	0 (0.0)	24 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cefepime	1 (3.4)	28 (96.6)	0 (0.0)	18 (100.0)	3 (11.5)	23 (88.5)	1 (25.0)	3 (75.0)	1 (100.0)	0 (0.0)
Cefotaxime	1 (2.2)	45 (97.8)	0 (0.0)	15 (100.0)	2 (6.5)	29 (93.5)	0 (0.0)	3 (100.0)	0 (0.0)	0 (0.0)
Ceftazidime	3 (7.3)	38 (92.7)	0 (0.0)	19 (100.0)	2 (6.9)	27 (93.1)	1 (50.0)	1 (50.0)	1 (100.0)	0 (0.0)
Ciprofloxacin	3 (6.1)	46 (93.9)	0 (0.0)	19 (100.0)	3 (9.4)	29 (90.6)	1 (33.3)	3 (66.7)	1 (100.0)	0 (0.0)
Colistin	46 (100.0)	0 (0.0)	13 (100.0)	0 (0.0)	28 (100.0)	0 (0.0)	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fosfomycin	0 (0.0)	23 (100.0)	0 (0.0)	15 (100.0)	0 (0.0)	24 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
Gentamicin	2 (5.4)	35 (94.5)	3 (25.0)	9 (75.0)	2 (6.7)	28 (93.3)	1 (33.3)	2 (66.7)	1 (100.0)	0 (0.0)
Imipenem	2 (4.5)	42 (95.5)	0 (0.0)	16 (100.0)	0 (0.0)	24 (100.0)	2 (50.0)	2 (50.0)	0 (0.0)	0 (0.0)
Levofloxacin	2 (4.8)	40 (95.2)	0 (0.0)	12 (100.0)	5 (16.1)	26 (83.9)	0 (0.0)	2 (100.0)	1 (100.0)	0 (0.0)
Meropenem	0 (0.0)	46 (100.0)	0 (0.0)	14 (100.0)	0 (0.0)	31 (100.0)	0 (0.0)	2 (100.0)	1 (100.0)	0 (0.0)
Mezlocillin	1 (2.3)	43 (97.7)	0 (0.0)	0 (0.0)	0 (0.0)	28 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)
Moxifloxacin	0 (0.0)	39 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	30 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Piperacillin	1 (2.9)	33 (97.1)	0 (0.0)	18 (100.0)	1 (4.5)	21 (95.5)	1 (33.3)	2 (66.7)	1 (100.0)	0 (0.0)
Rifampicin	0 (0.0)	22 (100.0)	9 (100.0)	0 (0.0)	0 (0.0)	24 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tetracycline	1 (2.3)	43 (97.7)	0 (0.0)	0 (0.0)	1 (3.4)	28 (96.6)	0 (0.0)	2 (100.0)	1 (100.0)	0 (0.0)
Tobramycin	3 (6.8)	41 (93.2)	8 (72.7)	3 (27.3)	4 (12.5)	28 (87.5)	2 (66.7)	1 (33.3)	1 (100.0)	0 (0.0)
Trimethoprim	0 (0.0)	23 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Trimethoprim + sulfamethoxazole	35 (74.5)	12 (25.5)	15 (78.9)	4 (21.1)	22 (68.8)	10 (31.3)	2 (50.0)	2 (50.0)	0 (0.0)	1 (100.0)

3.2. Antimicrobial assays

Sensitivity and resistance results of *Acinetobacter* species to the 21 antimicrobial agents are shown in Table 1. Of the 105 *Acinetobacter* strains, 103 (98.1%) were found MDR since all

MDR were resistant to more than two antimicrobial classes (Table 1). Results indicated that *A. baumannii* strains were sensitive to colistin and 74.5% to trimethoprim + sulfamethoxazole. The remaining 19 antimicrobial agents revealed low or no sensitivities: amikacin 16.3%; ampicillin 7.7%; ceftazidime,



Error Bars: 95% CI

Figure 2. Distribution of *Acinetobacter* species according to sex and age among 105 patients attended the ICU, Aseer Central Hospital (2014–2015).

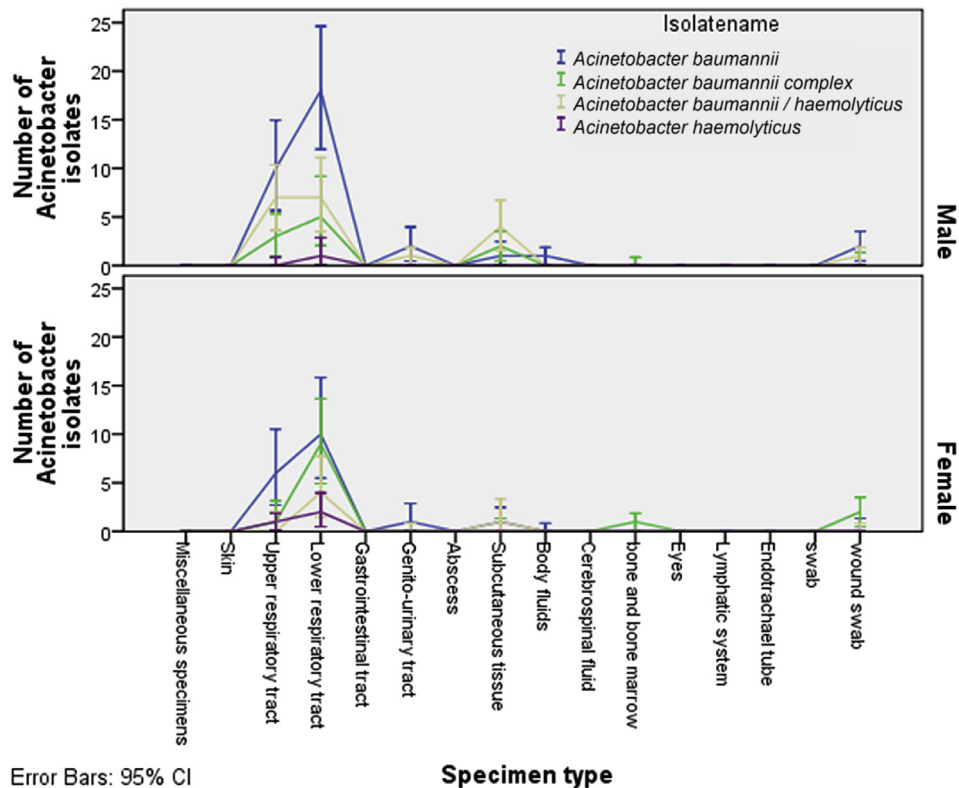


Figure 3. Numbers of *Acinetobacter* species according specimens types and sex of 105 patients attended the ICU, Aseer Central Hospital (2014–2015).

7.3%. Similar sensitivities were shown by other *Acinetobacter* species.

Resistance pattern of *Acinetobacter* species recovered from 105 patients at the ICU, Aseer Central Hospital (2014–2015) is shown in Table 1. Note all species show high sensitivities to colistin and to some extent to trimethoprim + sulfamethoxazole.

3.3. Distribution of *Acinetobacter* species according to sex and age group

The majority of the patients were males (63.81%) compared to females (36.19%) ($P = 0.867$). Age group more than 60 years was the major affected groups in the ICU with *Acinetobacter* spp. (47.62%) followed by those aged 20–29 years old (19.05%). These two groups vary significantly than other age groups ($P = 0.008$) (Figure 2).

3.4. Distribution of *Acinetobacter* species according to specimen type

Upper respiratory tract (30.48%), lower respiratory tract (47.65%) and subcutaneous tissue (9.50%) were the main sources of *Acinetobacter* spp. (Figure 3).

4. Discussion

The growing numbers of multi-drug resistant (MDR) *Acinetobacter* species have reduced the medicinal selections for managing *Acinetobacter* infections. *Acinetobacter* species including the leading species, *A. baumannii*, are developing as real infectious threat mainly in intensive care units (ICU). This study aimed to identify and to establish the antimicrobial profile

of *A. baumannii* isolates from ICU at Aseer Central Hospital. Hospital units have been the focus of repeated concerns regarding the rising number of nosocomial infections.

A. baumannii, a gram-negative, non-fermentative and a noted opportunistic nosocomial pathogenic bacterium which is able to live for long time in varied environmental conditions including hospital environment and human body surface [12]. It causes different nosocomial infections particularly nosocomial pneumonia, blood infection, urinary tract infection, surgical wound infection, especially in patients in ICU [13]. Our present findings do not differ from the global data. We noticed the respiratory specimens (upper and lower) from which we have isolated *Acinetobacter* species comprised 80.95% of all specimens.

Antibiotic policies and infection control measures are considered of immense value in fighting the mounting trends of nosocomial incidents. Genuine efforts are needed to develop new antimicrobial agents against these pathogens and to monitor the efficacy of the presently accessible drugs. For instance, hand hygiene has been found to have impact in controlling infection in Aseer Central Hospital [14]. Infections due to drug-resistant gram-negative rods are an emerging risk factor for increased mortality in ICU. A number of studies have indicated the rising trends of pathogens from other body systems and hospital wards [15,16].

Numerous definitions have been introduced in medical literature to describe distinctive patterns of resistance among pathogen encountered in healthcare settings. Multidrug-resistant (MDR), extensively-drug resistant (XDR) and pandrug-resistant (PDR) bacteria are now in use in the medical literature. In this regard MDR in *Acinetobacter* spp. is defined as strain which is found non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial structural categories [17]. MDR *A. baumannii* is recognized globally as an emerging significant health care risk. This bacterium is normally

resistant to all β -lactams and fluoroquinolones and has to be treated with colistin, amikacin, or tigecycline [18].

According to the *Acinetobacter* spp. antimicrobial categories and agents used to define MDR, XDR and PDR [17], the number of MDR identified in this paper is large (98.1%). One of the most serious and common risks of infections in ICU is the use of medical devices and procedures. ICU-acquired pneumonia (ventilator-associated pneumonia) represents a chief cause of morbidity and mortality in patients in the ICU worldwide [19]. Our findings go in line with this fact, we have isolated *Acinetobacter* spp. from more than 80% of the specimens of the ICU patient. Among those the mostly affected with significant ratio ($P < 0.05$) were those aged above 60 years (Figure 2). But gender was not significant in this distribution. This age with such risk may be because of the prolong stay under ventilation.

A. calcoaceticus baumannii complex which had been isolated from patients at Aseer region [11] have shown 100% sensitivity to imipramine, meropenem and colistin. Contrary to the present finding, all our *A. baumannii* isolates ($n = 49$) were found 100% resistant to meropenem (Table 1) but as expected colistin sensitivity is in full agreement with the previous work [11]. *A. baumannii* was found to have reduced susceptibility to carbapenems at the Security Forces Hospital in Saudi Arabia [9]. Studies unveiled that *A. baumannii* had the uppermost rate of resistance to carbapenem and sulbactam [20,21]. Two predominant genotypes related to European clone II were found among isolates of *A. baumannii* contained bla (OXA-23), and bla (OXA-24/40) [20].

Rising levels of carbapenem-resistant *Acinetobacter* spp. are noticed in many countries. Warning of infections due to carbapenem-resistant *Acinetobacter* spp. is required especially when patients are relocated between hospitals. This will help efforts to control the spread of carbapenem resistance [21]. The synergistic effect of sulbactam/tazobactam in combination with either meropenem or colistin to combat MDR *A. baumannii* isolates has been implemented [22]. Colistin and meropenem combination was also used to control extensively drug-resistant and pandrug-resistant *A. baumannii* isolates [23,24]. The use of colistin in addition to vancomycin as a medicinal choice against MDR *A. baumannii* infections particularly in pediatric wards has been recommended [25].

The main limitation of this study is that it no molecular analysis was done to trace the mode of transmission and identify any outbreak linkage. Also, the sample size may be considered comparatively small. This may result in a lack of authority to establish the present of XDR or any other phenomena related to the epidemiology of *Acinetobacter* spp. in ICU and the hospital at large.

The present study concluded that all *Acinetobacter* spp. were MDR. Virtually half of these strains were *A. baumannii*. These were found 100% sensitive to colistin and to some extent to trimethoprim + sulfamethoxazole (74.5%). *A. baumannii* complex and *A. baumannii/haemolyticus* accounted for a substantial ratio (48.6%) with sensitivities to the tested antimicrobials similar to those given by members of the *A. baumannii*. Respiratory specimens in ICU represented a source for the majority of the *Acinetobacter* spp. as it indicated ICU-acquired pneumonias. This predominates among patients over 60 years of age who spend prolong times at artificial ventilation made up the majority of the cases.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

- [1] Jung JY, Park MS, Kim SE, Park BH, Son JY, Kim EY, et al. Risk factors for multi-drug resistant *Acinetobacter baumannii* bacteremia in patients with colonization in the intensive care unit. *BMC Infect Dis* 2010; **10**: 228.
- [2] Nazer LH, Kharabsheh A, Rimawi D, Mubarak S, Hawari F. Characteristics and outcomes of *Acinetobacter baumannii* infections in critically ill patients with cancer: a matched case-control study. *Microb Drug Resist* 2015; **21**: 556-561.
- [3] Murray CK, Hospenthal DR. *Acinetobacter* infection in the ICU. *Crit Care Clin* 2008; **24**: 237-248, vii.
- [4] Tsakiridou E, Makris D, Daniil Z, Manoulakas E, Chatzipantazi V, Vlachos O, et al. *Acinetobacter baumannii* infection in prior ICU bed occupants is an independent risk factor for subsequent cases of ventilator-associated pneumonia. *BioMed Res Int* 2014; **2014**:193516.
- [5] El-Saed A, Balkhy HH, Al-Dorzi HM, Khan R, Rishu AH, Arabi YM. *Acinetobacter* is the most common pathogen associated with late-onset and recurrent ventilator-associated pneumonia in an adult intensive care unit in Saudi Arabia. *Int J Infect Dis* 2013; **17**: e696-701.
- [6] Lakshmana Gowda K, Marie MA, Al-Sheikh YA, John J, Gopalkrishnan S, Chikkabidare Shashidhar P, et al. A 6-year surveillance of antimicrobial resistance patterns of *Acinetobacter baumannii* bacteremia isolates from a tertiary care hospital in Saudi Arabia during 2005–2010. *Libyan J Med* 2014; **9**: 24039.
- [7] Guo-Xin M, Dan-Yang S, Xi-Zhou G, Jun-Chang C, Rui W, Zhi-Gang C, et al. Laboratory to clinical investigation of carbapenem resistant *Acinetobacter baumannii* outbreak in a general hospital. *Jundishapur J Microbiol* 2014; **7**: e13120.
- [8] Qian Y, Dong X, Wang Z, Yang G, Liu Q. Distributions and types of multidrug-resistant *Acinetobacter baumannii* in different departments of a general hospital. *Jundishapur J Microbiol* 2015; **8**: e22935.
- [9] Al-Obeid S, Jabri L, Al-Agamy M, Al-Omari A, Shibl A. Epidemiology of extensive drug resistant *Acinetobacter baumannii* (XDRAB) at Security Forces Hospital (SFH) in Kingdom of Saudi Arabia (KSA). *J Chemother* 2015; **27**: 156-162.
- [10] Lopes BS, Al-Agamy MH, Ismail MA, Shibl AM, Al-Qahtani AA, Al-Ahdal MN, et al. The transferability of blaOXA-23 gene in multidrug-resistant *Acinetobacter baumannii* isolates from Saudi Arabia and Egypt. *Int J Med Microbiol* 2015; **305**: 581-588.
- [11] Abdalla NM, Osman AA, Haimour WO, Sarhan MA, Mohammed MN, Zyad EM, et al. Antimicrobial susceptibility pattern in nosocomial infections caused by *Acinetobacter* species in Asir Region, Saudi Arabia. *Pak J Biol Sci* 2013; **16**: 275-280.
- [12] Maragakis LL, Perl TM. *Acinetobacter baumannii*: epidemiology, antimicrobial resistance, and treatment options. *Clin Infect Dis* 2008; **46**(8): 1254-1263.
- [13] Dijkshoorn L, Nemec A, Seifert H. An increasing threat in hospitals: multidrug-resistant *Acinetobacter baumannii*. *Nat Rev Microbiol* 2007; **5**: 939-951.
- [14] Mahfouz AA, El Gamal MN, Al-Azraqi TA. Hand hygiene non-compliance among intensive care unit health care workers in Aseer Central Hospital, south-western Saudi Arabia. *Int J Infect Dis* 2013; **17**: e729-732.

- [15] Ibrahim ME, Bilal NE, Hamid ME. Comparison of phenotypic characteristics and antimicrobial resistance patterns of clinical *Escherichia coli* collected from two unrelated geographical areas. *Glob J Health Sci* 2014; **6**: 126-135.
- [16] Al-Harhi AA, Al-Fifi SH. Antibiotic resistance pattern and empirical therapy for urinary tract infections in children. *Saudi Med J* 2008; **29**: 854-858.
- [17] Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012; **18**: 268-281.
- [18] Perez F, Hujer AM, Hujer KM, Decker BK, Rather PN, Bonomo RA. Global challenge of multidrug-resistant *Acinetobacter baumannii*. *Antimicrob Agents Chemother* 2007; **51**: 3471-3484.
- [19] Zhang Y, Yao Z, Zhan S, Yang Z, Wei D, Zhang J, et al. Disease burden of intensive care unit-acquired pneumonia in China: a systematic review and meta-analysis. *Int J Infect Dis* 2014; **29**: 84-90.
- [20] Perez F, Endimiani A, Ray AJ, Decker BK, Wallace CJ, Hujer KM, et al. Carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* across a hospital system: impact of post-acute care facilities on dissemination. *J Antimicrob Chemother* 2010; **65**: 1807-1818.
- [21] Lu PL, Huang LY, Lian ST, Chang K, Lin CL, Hwang IJ, et al. How carbapenem-resistant *Acinetobacter* spp. established in a newly constructed hospital. *Int J Antimicrob Ag* 2008; **31**: 463-466.
- [22] Marie MA, Krishnappa LG, Alzahrani AJ, Mubarak MA, Alyousef AA. A prospective evaluation of synergistic effect of sulbactam and tazobactam combination with meropenem or colistin against multidrug resistant *Acinetobacter baumannii*. *Assoc Basic Med Sci* 2015; **15**: 24-29.
- [23] Vourli S, Frantzeskaki F, Meletiadis J, Stournara L, Armaganidis A, Zerva L, et al. Synergistic interactions between colistin and meropenem against extensively drug-resistant and pandrug-resistant *Acinetobacter baumannii* isolated from ICU patients. *Int J Antimicrob Ag* 2015; **45**: 670-671.
- [24] van Belkum A, Halimi D, Bonetti EJ, Renzi G, Cherkaoui A, Sauvonnnet V, et al. Meropenem/colistin synergy testing for multidrug-resistant *Acinetobacter baumannii* strains by a two-dimensional gradient technique applicable in routine microbiology. *J Antimicrob Chemother* 2015; **70**: 167-172.
- [25] Ceccarelli G, Oliva A, d'Ettorre G, D'Abramo A, Caresta E, Barbara CS, et al. The role of vancomycin in addition with colistin and meropenem against colistin-sensitive multidrug resistant *Acinetobacter baumannii* causing severe infections in a paediatric intensive care unit. *BMC Infect Dis* 2015; **15**: 393.