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Multiple Drug-Resistant Bacterial Infections among Intensive Care Units – a Nationwide Study

Mohammad Al-Tamimi[1*], Ahmad Jaber[2], Dania Aldajeh[3], Deema Al-Namora[2], Abdelrahman Altarazi[2], Iman Aolymat[4], Khalil Altamimi[5], Hamza Othman[2], Toqa Abu-Muhaisin[2], Walaa Isied[2], Eyad Fehmi[2], Mohammad Al shalabi[2], and Yazeed Abukhait[2]

[1] Department of Microbiology, Pathology and Forensic Medicine, Faculty of Medicine, The Hashemite University, P.O. Box 330127, Zarqa 13133, Jordan

[2] Faculty of Medicine, The Hashemite University, P.O. Box 330127, Zarqa 13133, Jordan

[3] Faculty of Medicine, University of Jordan, P.O. Box 11942, Amman, Jordan

[4] Department of Anatomy, Physiology and Biochemistry, Faculty of Medicine, The Hashemite University, P.O. Box 330127, Zarqa 13133, Jordan

[5] Department of Obstetrics and Gynecology, Royal medical services, Amman, Jordan

*Corresponding author:

Mohammad.altamimi@hu.edu.jo

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Abstract

Background: There is an alarming increase in multi-drug resistant (MDR) bacterial infections worldwide. The Mediterranean region, including Jordan, reports a particularly high prevalence of hospital-acquired MDR infections, especially in Intensive Care Units (ICUs).

Aim: To investigate the prevalence, antibiotic susceptibility, risk factors, and resistance genes associated with bacterial infections in ICUs across Jordan.

Methodology: A total of 177 bacterial isolates were collected from 12 ICUs across Jordan between September 2019 and April 2022. Patient demographics, isolate characterization, antibiotic susceptibility, and resistance genes were recorded and analyzed.

Results: The isolates included *Klebsiella* (22.6%), *Staphylococcus* (18.0%), *Escherichia* (17.5%), *Acinetobacter* (16.4%), *Enterococcus* (6.2%), *Pseudomonas* (6.2%), and others (13.0%). Of all isolates, 41.2% were MDR, 17.5% were extensive drug-resistant (XDR), and 6.8% were pandrug-resistant (PDR). MDR rates were highest in *Klebsiella* (82%), followed by *Acinetobacter* (79%), *Pseudomonas* (63%), *Staphylococcus* (56%), and *Escherichia* (51%). High resistance rates were observed for all antibiotics except vancomycin, colistin, linezolid, and teicoplanin (<10%). Significant associations were found between MDR infections and Gram-negative bacteria, central lines, mechanical ventilation, nasogastric tubes, a history of recurrent infections, previous surgeries, bedridden patients, prophylactic antibiotic use, recent antibiotic exposure in the last two weeks, and elevated white blood cell counts ($P<0.05$). MDR infections were also significantly linked to higher rates of complications and death ($P<0.05$). The most common resistance genes identified were *KPC* in *K. pneumoniae* (28.6%), *mecA* for *Staphylococci* (62.5%), *CTX-M* among *E. coli* (48.4%), *OXA-51* and *OXA-23* genes in *A. baumannii/spp* (100%) and *vanA* gene for *E. faecalis/spp* (45.5%).

Conclusion: ICUs serve as critical reservoirs for MDR bacterial infections. Implementation of nationwide, evidence-based antibiotic stewardship programs is strongly recommended.

Keywords: Multiple drug resistance (MDR); Intensive care unit (ICU); Klebsiella; Staphylococcus; Escherichia; Acinetobacter; Jordan

INTRODUCTION

Multi-drug resistance (MDR) bacterial infections are usually associated with high morbidity and mortality, as conventional antibiotics are of no value. Furthermore, some bacterial strains have developed resistance to last-resort antibiotics or even to every known antibiotic. Antibiotic resistance has been increasing at an alarming rate, especially in the last decade [1]. The antibiotic resistance challenge is represented by the World Health Organization (WHO) report, which states that antibiotic resistance is the most serious public health issue of our time [2,3]. Bacterial resistance has multiple effects on social, economic, biological, clinical, political, ethical, public health, and medical aspects [3-5]. Nowadays, multiple organisms are known to be resistant to multiple antibiotics, including *Staphylococcus aureus*, *Clostridium difficile*, vancomycin-resistant *Enterococci*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter*, *Escherichia coli*, *Streptococcus pneumonia*, *Neisseria gonorrhoeae*, and *Mycobacterium tuberculosis* [1,3,4].

Antibiotic resistance patterns vary significantly depending on geographic location, socio-economic conditions, healthcare infrastructure, and political commitment [3,5,6]. These differences are influenced by factors such as, the prevalence of specific bacterial pathogens, the genetic background of bacterial strains, environmental exposures, including animals and food sources, as well as policies on antibiotics use and the implementation of strategies to combat antibiotic resistance [3,5,6]. While some countries have successfully contained the spread of resistance, the prevalence of antibiotic-resistant bacteria continues to rise in many others [2,5]. Most action plans to tackle antibiotic resistance have been developed and implemented in the United States and Europe. In contrast, some countries are still in the early stages of developing such plans, and others lack effective measures or clear strategies to control the growing threat of antibiotic resistance [5,6].

Multiple studies conducted in the Mediterranean region have reported a high prevalence of antibiotic resistance, especially in the eastern and southern regions [5,7]. In fact, the Mediterranean region was considered hyperendemic for MDR hospital-associated pathogens [8,9]. Political instability and the high number of refugees in the Middle East further contribute to the unregulated use of antibiotics, exacerbating the burden of drug-resistant infections [10]. Notably, the Mediterranean area witnessed a surge in methicillin-resistant *S. aureus* (MRSA) infections, with Jordan reporting the highest recorded MRSA rate [11]. Additionally, high resistance levels have been documented for *E. coli*, *S. pneumoniae*, *Enterobacteriaceae*, *P. aeruginosa,* and *A. baumannii* [8,11-13]. Recent studies in Jordan specifically highlight a widespread pattern of antimicrobial resistance among MRSA, *S. pneumoniae*, *A. baumannii*, *E. coli*, *P. aeruginosa*, and *K. pneumoniae* [14-18].

Of particular concern is hospital-acquired (HA) antimicrobial resistance, especially in Intensive Care Units (ICUs). HA infections are associated with prolonged hospital stays, increased healthcare costs, greater government healthcare expenditure, and higher mortality rates [19,20]. There are significant international variations in infection prevalence, pathogen types, resistance rates, resistance genes, mortality,

and clinical outcomes. These data are essential for understanding global and regional differences and for optimizing infection control strategies [19,20]. The absence of organized antibiotic resistance surveillance programs, along with inadequate strategies to combat resistance and the continuous rise in national resistance rates, poses a global threat [9]. Therefore, the main aims of this study were to investigate the frequency and types of microorganisms, antibiotic resistance patterns, resistance genes, associated risk factors, and clinical outcomes of ICU-acquired infections in referral hospitals across Jordan.

MATERIALS AND METHODS

Study population

A total of 133 confirmed cases of bacterial infection were systemically recruited from ICU patients admitted to 12 referral hospitals across all governorates and major cities of Jordan between September 2019 and April 2022, following the obtaining of formal voluntary consent. Specimens were collected from university, private, and military hospitals.

Inclusion criteria were: (1) clinical and para-clinical evidence of bacterial infection, including at least one positive bacterial culture; (2) age over one year; and (3) ability to give informed consent. For each patient, a comprehensive survey was completed using data from the patients, their families, and medical records.

The survey collected demographic details such as age, gender, occupation, residence, hospital name, and mode of admission. Clinical information included signs and symptoms, past medical and surgical history, medication history, smoking status, and social and family history. Risk factors assessed included the presence of central line, mechanical ventilation, immobility, length of hospital stay, history of wound or admission in the last year, history of recurrent infections and prophylactic antibiotics use.

Laboratory data collected included bacterial strain/s and antibiotics susceptibility, along with hemoglobin level (Hb), white blood cell (WBCs) count, platelets count, red cell distribution width (RDW), C-Reactive Protein (CRP), kidney function test (KFT), liver function test (LFT), glycated hemoglobin (HbA1c), ABO, and RhD blood groups were collected.

Finally, clinical and laboratory outcome measures were recorded, including symptoms improvement, normalization of temperature and WBCs count, negative culture results, and any complications such as sepsis, renal failure, disseminated intravascular coagulation (DIC), or death.

Bacterial isolates

A total of 177 bacterial isolates were identified among 133 participants. Isolates were identified using Gram stain, culture and colony morphology, biochemical tests, Vitek 2 compact system, and other methods according to standard bacterial identification protocols of the clinical microbiology laboratory at each hospital. Pure cultures were transferred under strict sterile conditions to the microbiology laboratory at The Hashemite University and were stored appropriately for further analysis of antibiotic susceptibility testing and molecular analysis of resistance genes.

Antibiotics susceptibility testing:

Antibiotics susceptibility for isolates was tested using Kirby-Bauer disc diffusion test with amikacin, gentamicin, tobramycin, ceftriaxone, ampicillin,

amoxicillin/clavulanate (Augmentin), ampicillin/sulbactam, cefazolin, cefoxitin, cefuroxime, aztreonam, trimethoprim/sulfamethoxazole, cefotaxime, cefpodoxime, ceftazidime, cefepime, piperacillin/tazobactam, ciprofloxacin, levofloxacin, imipenem, meropenem, and ertapenem, according to procedure outlined by Clinical and Laboratory Standards Institute (CSLI) [21]. Furthermore, antibiotic susceptibility was confirmed using an automatic Vitek 2 compact system with Gram-negative and Gram-positive antibiotic susceptibility cards. Colistin, vancomycin, linezolid, and teicoplanin E-test or microdilution test were performed for confirmation [21]. The definition of MDR, pandrug resistance (PDR), and extensive drug resistance (XDR) followed the international expert proposal for standard definitions of acquired resistance. MDR was defined as resistance to at least one agent among three or more antimicrobial categories, XDR was defined as resistance to at least one agent in all but two or fewer antimicrobial categories, and PDR was defined as resistance to all agents in all antimicrobial categories [22].

Molecular analysis of resistance genes

Bacterial DNA was extracted using a DNeasy Blood and Tissue kit (Qiagen, Germany) according to the manufacturer's instructions. To analyze molecular genes associated with antibiotic resistance, multiple primers, and protocols were applied according to the gene of interest. Carbapenemase resistance genes (*KPC*, *OXA*, *VIM*, and *IMP*) were detected by uniplex PCR and specific primers as described previously [14]. ESBL genes (*CTX-M*, *TEM*, and *SHV*) were investigated by uniplex PCR and protocols described previously [15]. *MecA*, *vanA,* and *vanB* genes were analyzed as previously described [23].

All primers were obtained from the University of Science and Technology, Jordan. PCR products were electrophoresed in a 1.5% agarose gel stained with ethidium bromide and visualized using UV transillumination. Positive and negative controls for different antibiotics resistance genes including *A. baumannii* NCTC 13305, *E. coli* NCTC 13451, *E. coli* NCTCC 13476, *E. coli* ATCC 25922, *K. pneumonia* NCTCC 13439, *K. pneumoniae* ATCC 700603, *Enterococcus faecalis* ATCC 51299, *E. faecium* ATCC 700221 were used as described previously [14,15,23].

Statistical analysis

Descriptive statistical analysis was used for the determination of demographic, clinical, risk factors, laboratory, and outcome frequencies. Percentages were calculated to describe the frequency of categorical variables. Chi-square and Fisher's exact tests were used to assess the association between multiple drug resistance in relation to their demographic, clinical, risk factors, laboratory, and outcome data. The level of statistical significance was set at ≤ 0.05. Data was analyzed using Microsoft Excel 2010 and SPSS version 24.0.

RESULTS

Characteristics of study participants and bacterial isolates

A total of 133 ICU patients with confirmed bacterial infection were enrolled from 12 hospitals across Jordan. Just over half (54%) were older than 40 years old, and the gender distribution was approximately equal, (48.9% males and 48.1% females). Notably, 82% of patients were non-smokers. However, 75% had documented comorbidities, and

50% had a BMI in the overweight or obese range. Most participants (70%) were admitted from the emergency department and more than 84% had catheters placement during their hospital stay (Table 1). Additional clinical and laboratory characteristics of the study population, including risk factors and outcomes, have been described in detail previously [24].

A total of 177 bacterial isolates were obtained from the study participants. The majority were collected from the lungs (33.3%), blood (26%), and the urinary tract (24.3%). The most commonly identified pathogen was *Klebsiella* (22.6%), followed by *Staphylococcus* (18%) and *Escherichia* (17.5%) (Table 2). A detailed characterization of bacterial isolates has been reported previously [24].

Table 1. Demographic and clinical data of ICU patients (n = 133). BMI: body mass index, ND: not determined.

Category	Variable	Range	Number	Percentage (%)
Demographic	Age (years)	0-20	7	5.3
		21-40	29	21.8
		41-60	25	18.8
		61-80	48	36.1
		>80	24	18.0
	Gender	Male	65	48.9
		Female	64	48.1
		ND	4	3.0
	BMI	Underweight <18.5	13	9.8
		Normal 18.5-24.9	40	30.1
		Overweight 25-29.9	31	23.3
		Obese >30	36	27.1
		ND	13	9.8
Hospital and admission	Hospital	Jordan	29	21.8
		Specialty	25	18.8
		Al basheer	23	17.3
		Jordan University Hospital	23	17.3
		Others	33	23.5
	Mode of Admission	Inpatient	40	30.1
		Emergency	93	69.9
Clinical history	Past Medical History		101	75.9
	Past Surgical History		58	43.6
	Allergic History		13	9.8
	Smoking		24	18.0
	Medications		75	56.4
Infection risk factors	Central Line		46	34.6
	Ventilator		74	55.6
	Catheter		112	84.2
	Nasogastric tube		74	55.6

Table 2. Antibiotic resistance among bacterial infections of ICU patients (n = 177 isolates). MDR: Multiple drug resistance, PDR: Pandrug resistance, XDR: Extensive drug resistance, ND: not determined.

Bacteria	Total n (%)	None MDR n (%)	MDR n (%)	PDR n (%)	XDR n (%)	ND n (%)
Klebsiella	40 (22.6)	2 (5.0)	15 (37.5)	7 (17.5)	11 (27.5)	5 (12.5)
Staphylococcus	32 (18.0)	13 (40.6)	16 (50.0)	0 (0)	2 (6.3)	1 (3.1)
Escherichia	31 (17.5)	13 (41.9)	14 (45.2)	0 (0)	2 (6.5)	2 (6.5)
Acinetobacter	29 (16.4)	0 (0)	5 (17.2)	4 (13.8)	14 (48.3)	6 (20.7)
Enterococcus	11 (6.2)	4 (36.4)	6 (54.5)	0 (0)	1 (9.0)	0 (0)
Pseudomonas	11 (6.2)	7 (63.6)	3 (27.3)	1 (9.0)	0 (0)	0 (0)
Others	23 (13.0)	4 (17.4)	14 (60.9)	0 (0)	1 (4.3)	4 (17.4)
Total	**177 (100)**	**43 (24.3)**	**73 (41.2)**	**12 (6.8)**	**31 (17.5)**	**18 (10.2)**

Antibiotic resistance patterns of ICU bacterial isolates

Out of the 177 total bacterial isolates, 116 (65.5%) were classified as either MDR, XDR, or PDR. This included 73 MDR isolates (41.2%), 31 XDR isolates (17.5%), and 12 PDR isolates (6.8%). Among specific pathogens, 82% of *Klebsiella* isolates, 79% of *Acinetobacter* isolates, 56% of *Staphylococcus* isolates, and 51% of *Escherichia* isolates were MDR. In contrast, the majority of Pseudomonas isolates (63%) were not MDR (Table 2). Alarmingly, high resistance rates (70–80%) were observed against commonly used antibiotics like ampicillin, amoxicillin, cefoxitin, ceftriaxone, trimethoprim, levofloxacin, and ciprofloxacin. Moderate resistance was noted for meropenem and amikacin (~50%), while resistance to last-line antibiotics—vancomycin, colistin, linezolid, and teicoplanin—remained low (below 10%) (Figure 1).

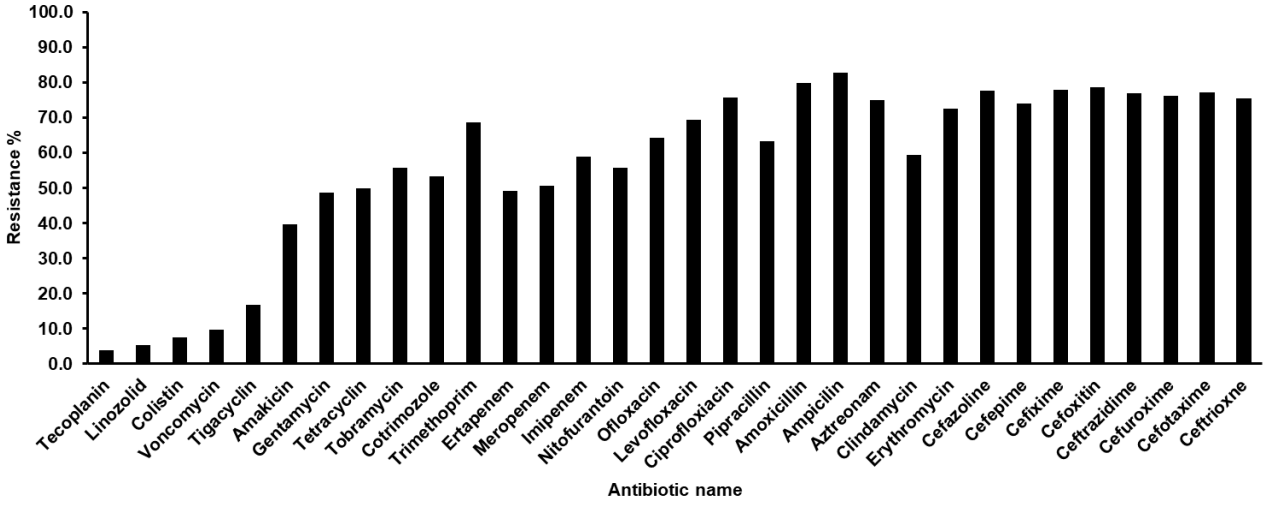

Figure 1. Antibiotics resistance pattern of all isolates (n = 177).

Association between MDR and other variables

A significantly lower frequency of MDR cases was observed in patients from Al-Salt Governorate, while a higher frequency was found among overseas patients (Odds Ratio (OR) = 0.12 vs 2.08, P = 000). MDR prevalence was also significantly higher among housewives compared to retired and unemployed patients (OR = 5.2, 0.23, and 0.23 respectively, P = 000). In addition, MDR cases were more common in Jordan hospital compared to Specialty hospital (OR = 2.8 vs 0.25, P = 000). A significant negative association was noted between MDR and a history of chronic obstructive pulmonary disease (COPD), with a lower risk of MDR among COPD patients compared to those without COPD patients (OR = 0.1 vs 1.43, P = 0.000). Conversely, a significant positive association was noted between MDR and a history of surgery (OR = 1.8 vs 0.76, P = 0.019)

The type of bacterial isolate was significantly associated with MDR status, with a higher frequency of MDR found in Gram-negative bacteria (GNB) (P = 0.040), particularly *Acinetobacter* and *Klebsiella* (OR = 19.1 and 6.2, respectively, P = 0.000). Several clinical factors were significantly associated with increased MDR risk, including the use of central line, ventilator, nasogastric tube, history of recurrent infection, bedridden patients, using prophylactic antibiotics, and antibiotics use in the last 2 weeks (P < 0.05). MDR was also significantly associated with elevated white blood cell counts.

Finally, MDR was strongly associated with higher rates of complications and death (P < 0.05). While MDR was negatively associated with the improvement of symptoms and normalization of WBC count (P < 0.05) (Table 3).

Table 3. Association between MDR infections and other variables (*Significant associations, P ≤ 0.05). Hemoglobin level (Hb), White Blood Cells (WBCs) count, Platelets count, Red Cell Distribution Width (RDW), C-Reactive Protein (CRP), Kidney Function Test (KFT), Liver Function Test (LFT), Glycated hemoglobin (HbA1c).

Variable		MDR infections
Demographics	Age	0.136
	Gender	0.935
	Residency	0.000*
	BMI	0.181
	Job	0.000*
	Hospital	0.000*
	Mode of Admission	0.56
History	Past medical history	0.385
	Hypertension	0.444
	Diabetes	0.088
	Ischemic heart disease	0.190
	Chronic obstructive pulmonary disease	0.000*
	Past surgical history	0.025*
	Allergy	0.058
	Smoking	0.220
	Medication	0.604

Variable		MDR infections
Infection Risk Factors	Isolate type	0.000
	Primary Infection site	0.276
	Temperature	0.375
	Duration of infection	0.094
	Central Line	0.001*
	Ventilator	0.025*
	Catheter	0.993
	Nasogastric tube	0.030*
	History of a wound in the last year	0.228
	Hospitalization in the last year	0.661
	History of recurrent infection	0.026*
	Patient is bedridden	0.001*
	Antibiotics use last 2 weeks	0.001*
	Prophylactic antibiotics	0.036*
Laboratory investigations	Hb g⁄dL	0.235
	WBC⁄μL	0.005*
	Platelets count⁄μL	0.461
	RDW	0.325
	CRP mg/L	0.394
	KFT	0.220
	LFT	0.535
	HbA1c	0.579
	Blood group (ABO)	0.494
	Blood group (RhD)	0.670
Outcome	Fever disappeared	0.097
	Improvement of symptoms	0.000*
	Normalization of WBCs	0.012*
	Negative culture after treatment	0.289
	Complications	0.009*
	Death	0.047*

Molecular analysis of resistance genes

Among *K. pneumoniae* isolates, the most common resistance gene was *KPC* (10/35; 28.6%), followed by *IMP* (5/35; 14.7%), and one isolate had a *VIM* gene (1/35; 2.9%). For *Staphylococci* species (20/32; 62.5%) harbor the *mecA* gene. *CTX-M* gene was the most common among *E. coli* isolates (15/31; 48.4%), followed by *TEM* (7; 22.6%). All *A. baumannii/spp* isolates had *OXA-51* and *OXA-23* genes (29/29; 100%). For *E. faecalis/spp* (5/11; 45.5%) had the *vanA* gene while (1/11; 9.1%) had the *vanB* gene (Table 4)

Table 4. Molecular analysis of resistance genes among ICU bacterial isolates.

Bacteria	Species	Isolates Number (%)	Resistance genes Number (%)
Klebsiella	*Klebsiella pneumoniae*	35 (19.8)	*KPC* 10 (28.6) *IMP* 5 (14.7) *VIM* 1 (2.9)
Staphylococcus	*Staphylococcus aureus*	18 (10.2)	*mecA* 12 (66.7)
	Coagulase negative Staphylococci	14 (7.8)	*mecA* 8 (57.1)
Escherichia	*Escherichia coli*	31 (17.5)	*CTX-M* 15 (48.4) *TEM* 7 (22.6) *SHV* 1 (3.2)
Acinetobacter	*Acinetobacter baumannii/spp*	29 (16.4)	*OXA-51* 29 (100.0) *OXA-23* 29 (100.0) *IMP* 9 (31.0) *KPC* 0 (0.0) *VIM* 0 (0.0)
Enterococcus	*Enterococcus faecalis/spp*	11 (6.2)	*vanA* 5 (45.5) *vanB* 1 (9.1)

DISCUSSION

MDR bacteria cause around 700 000 deaths worldwide every year and it is estimated they will cause 10 million deaths by 2050, with a severe loss of economic resources [25]. The Middle East region is considered hyperendemic for MDR [7,8,11,12]. Within the Middle East, Jordan had experienced a surge of MDR infections [14,15,17,18]. ICU departments, especially in lower-middle-income countries constitute a special risk for acquiring infections due to MDR organisms [19,26]. A national comprehensive study on MDR infections among ICUs in Jordan has not been conducted before. Accordingly, this study aimed to investigate the frequency and extent of MDR among ICUs, common infection sites, risk factors, antibiotics susceptibility patterns, resistance genes, and outcomes across different referral hospitals all over Jordan to have an up-to-date, nationwide view.

In this study, the infection rate among ICU patients due to Multidrug-resistant bacteria was 65.5%, classified as MDR (41.2%), PDR (6.8%), and XDR (17.5%). It is much higher than rates documented in the United States, Europe, China, Malaysia, and other Mediterranean countries [27-32], while a higher rate of MDR among ICU has been reported in Pakistan [33]. Most ICU isolates reported by this study were GNB (123/177; 72.4%) compared to Gram-positive bacteria (47/177; 27.6%). The MDR/PDR/XDR rate was much higher with GNB (96/123; 78.1%) compared to Gram-positive bacteria (20/47; 42.6%). *A. baumannii* had the highest MDR/PDR/XDR rate among all microorganism types (23/23; 100%), followed by *K. pneumonia* (33/35; 94.3%). Furthermore, there was a significant association between MDR and GNP (P = 0.040) with the highest levels of resistance reported for *Acinetobacter* spp., followed by *Klebsiella* (OR 19.1 and 6.2, P = 0.000). Several previous studies in the United States and Europe have shown similar results. The U.S. National Healthcare Safety Network reported increasing occurrence of MDR-

GNB among which more than 60% were *Acinetobacter spp.* [28]. Similarly, the European Antimicrobial Resistance Surveillance Network reported recognizable resistance trends for GNP, with the highest levels of resistance reported for *Acinetobacter* spp., followed by *E. coli* and *K. pneumoniae* [29]. Other national and international studies also reported a higher frequency of MDR- *A. baumannii* among ICU with rates reaching 100% [14, 26, 27, 33-36].

Previous studies related to MDR among ICU patients in Jordan investigated colonization rate, device-related infections, and environmental surfaces inside the ICU [37-39], single-centered [34,39], single infection (bloodstream infections) [39], or single organism either *A. baumannii* or *K. pneumonia* [34,35,40]. The most common antibiotic resistance genes reported in this study were *KPC* in *K. pneumoniae* (28.6%), *mecA* for *Staphylococci* (62.5%), *CTX-M* among *E. coli* (48.4%), *OXA-51* and *OXA-23* genes in *A. baumannii/spp* (100%) and *vanA* gene for *E. faecalis/spp* (45.5%). A single study among ICU patients in Jordan reported *OXA-51* at 100% and *OXA-23* at 87.5% among ESBL-positive *A. baumannii* [35]. Other studies reported similar rates of resistance genes among hospitalized patients in Jordan [14,15,17,41,42].

This study's most common infection site was in the lung followed by blood and urinary tract. Similarly, respiratory and blood isolates were the most common among ICU patients [34,40]. Higher MDR rate was associated with many risk factors including a history of recurrent infection, history of a previous operation, prophylactic antibiotics, bedridden patients, using antibiotics in the last two weeks, and invasive devices use including central lines, nasogastric tubes, and ventilators. A meta-analysis of risk factors for MDR GNB in ICUs concluded a significant role for previous operative procedures, central venous catheter, mechanical ventilation, and antibiotic use [43]. Prophylactic antibiotics are commonly overused with operative procedures [44], while devices and environmental surfaces in ICUs are contaminated with MDR bacteria [38,39]. Accordingly, proper antibiotic use, early removal of devices, proper sterilization of instruments and surfaces in the ICU, and application of infection control policies would decrease the risk of the development of MDR infection in ICU [28].

Significantly higher frequency of MDR bacteria was noted among overseas patients, housewives, and certain hospitals. Another study also noted a significant increase of MDR *A. baumannii* among overseas patients in Jordan mostly because Jordan is a hub for medical tourism from nearby countries with political instabilities, wars, and poor health systems [14]. Inappropriate overuse of antibiotics by housewives have been suggested [45]. Patients with MDR infections had significantly higher rates of complications and death similar to other studies [19,30,34] and negatively associated with improvement of symptoms and normalization of WBCs.

Antibiotic susceptibility testing indicated a 70-80% resistance rate to frequently used antibiotics including penicillins, cephalosporines, and quinolones, about 50% resistance to carbapenems, and less than 15%, resistance to tigecycline, vancomycin, colistin, linezolid and teicoplanin. Resistance rates are generally similar to or higher than previous local studies among ICU [35,36,40]. Other studies have concluded the higher frequency of extended-spectrum beta-lactamases and carbapenem-resistant isolates

among Jordanian hospitals [14,15]. The increased resistance rates to last-resort antibiotics like vancomycin and colistin are of particular concern. Colistin resistance was as high as 28% to 49.7% with *K. pneumonia* and vancomycin resistance was 33.3% with *E. faecium* among clinical isolates from Jordan [17,36].

Multiple factors can contribute to increased MDR infections in Jordan including antibiotic abuse, poor application of infection control strategies, overseas patients from war zones, genetic and environmental factors, and local health policies [19,26,28,36]. For example, 86.6% of community pharmacists thought it was legal to dispense antibiotics without a prescription, 22.9% of physicians prescribe antibiotics over the phone and more than 50.0% routinely prescribe antibiotics to treat common cold symptoms [45].

CONCLUSIONS

According to this study, ICUs in Jordan are reservoirs for MDR bacterial infections, especially *Acinetobacter* and *Klebsiella* species. Sixty-five percent prevalence is an alarming indicator that could be a leading cause of morbidity and mortality. Addressing this problem requires both infection prevention and appropriate treatment. We recommend initiating nationwide evidence-based antibiotic stewardship programs, which will ensure better faculty and house staff education, appropriate diagnosis and treatment of disease, and ultimately, the reduction in the acquisition and spread of MDR bacteria. Knowledge of local patterns of resistance and individual risk factors for resistance will lead to better care of critically ill patients at the national and international levels.

Conflict of interest statement

All authors declare no conflicts of interest.

Ethical approval

The study protocol was approved by the IRB at the Hashemite University and the Jordanian Ministry of Health／Prince Hamza Hospital IRB (No: 1/ 1631), and all other referral hospitals included in this study.

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الالتهابات البكتيرية المقاومة للعديد من المضادات الحيوية في وحدات العناية المركزة – دراسة وطنية

محمد التميمي[1]، أحمد جابر[2]، دانيا الدعجه[3]، ديما النمورة[2]، عبد الرحمن الطرزي[2]، إيمان عليمات[4]، خليل التميمي[5]، حمزة عثمان[2]، تقى أبو محيسن[2]، ولاء سيّد[2]، إياد فهمي[2]، محمد الشلبي[2]، ويزيد أبو خيط[2]

[1] قسم الأحياء الدقيقة، والأنسجة، والطب الشرعي، كلية الطب، الجامعة الهاشمية، صندوق البريد 330127، الزرقاء 13133، الأردن

[2]كلية الطب، الجامعة الهاشمية، صندوق البريد 330127، الزرقاء 13133، الأردن

[3]كلية الطب، الجامعة الأردنية، صندوق البريد 11942، عمّان، الأردن

[4]قسم التشريح، ووظائف الأعضاء، والكيمياء الحيوية، كلية الطب، الجامعة الهاشمية، صندوق البريد 330127، الزرقاء 13133، الأردن

[5]قسم النسائية والتوليد، الخدمات الطبية الملكية، عمّان، الأردن

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الملخص

الخلفيه: هناك زيادة مقلقة في الالتهابات البكتيرية المقاومة للعديد من المضادات الحيوية (MDR) على مستوى العالم. تشهد منطقة البحر الأبيض المتوسط، بما في ذلك الأردن، انتشارًا مرتفعًا للعدوى المكتسبة في المستشفيات، خاصة في وحدات العناية المركزة (ICUs).

الهدف: البحث في معدل انتشار الالتهابات البكتيرية في وحدات العناية المركزة عبر الأردن، وحساسيتها للمضادات الحيوية، وعوامل الخطر المرتبطة بها، والجينات المقاومة للمضادات الحيويه.

المنهجية: تم جمع 177 عزلة بكتيرية من 12 وحدة عناية مركزة في مختلف أنحاء الأردن بين سبتمبر 2019 وأبريل 2022. تم تسجيل بيانات المرضى، وتوصيف العزلات، وحساسيتها للمضادات الحيوية، والجينات المقاومة.

النتائج: شملت العزلات البكتيرية كلبسيلا (22.6%)، ستافيلوكوكاس (18.0%)، إشريشيا (17.5%)، أسينتوباكتر (16.4%)، إنتيروكوكاس (6.2%)، بسودوموناس (6.2%)، وأخرى (13.0%). من إجمالي العزلات، كان 41.2% منها مقاوم لعدة مضادات حيويه (MDR)، و17.5% مقاومة على نطاق واسع للأدوية (XDR) ، و6.8% مقاومة لجميع الأدوية (PDR). كانت معدلات MDR على النحو التالي: كلبسيلا (82%)، أسينتوباكتر (79%)، بسودوموناس (63%)، ستافيلوكوكاس (56%)، وإشريشيا (51%). لوحظت معدلات مقاومة عالية لجميع المضادات الحيوية باستثناء فانكوميسين، كوليستين، لينزوليد، وتيكوبلانين (10%>). كان هناك ارتباط كبير بين عدوى MDR والبكتيريا سالبة الجرام، والقسطرة الوريدية المركزية، وأجهزة التنفس الصناعي، والأنابيب الأنفية المعدية، والعدوى المتكررة، والعمليات الجراحية السابقة، وحالات المرضى طريحي الفراش، واستخدام المضادات الحيوية الوقائية، واستخدام المضادات الحيوية خلال الأسبوعين الأخيرين، وارتفاع عدد كريات الدم البيضاء (P<0.05). كما ارتبطت عدوى MDR بشكل ملحوظ بزيادة المضاعفات ومعدلات الوفيات (P<0.05). كانت أكثر الجينات المقاومة شيوعًا KPC في K. pneumoniae (28.6%) ، mecA في (62.5%) Staphylococcus spp، CTX-M في E. coli (48.4%) ، جينات OXA-51 و OXA-23 في A. baumannii (100%) ، وجين vanA في E. faecalis spp. (45.5%) .

الاستنتاج: تُعد وحدات العناية المركزة مستودعات للالتهابات البكتيرية المقاومة للمضادات الحيوية. يوصى بشدة بتنفيذ برامج ترشيد استخدام المضادات الحيوية على المستوى الوطني، استنادًا إلى الأدلة العلمية.

الكلمات الدالة: مقاومة متعددة للأدوية (MDR)، وحدة العناية المركزة (ICU)، كليبسيلا، العنقودية، إشريشيا، أسينيتوباكتور، الأردن.