Journal of Infection and Public Health 13 (2020) 637–643

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

The clinical and epidemiological risk factors of infections due to multi-drug resistant bacteria in an adult intensive care unit of University Hospital Center in Marrakesh-Morocco

Adel El mekes[a,b], Kawtar Zahlane[a], Loubna Ait said[a], Ahmed Tadlaoui Ouafi[c], Mustapha Barakate[b,*]

[a] Laboratory of Medical Analysis, Ibn Tofail Hospital, University Hospital Center-Mohammed VI, Marrakesh, Morocco
[b] Laboratory of Biology and Biotechnology of Microorganisms, Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco
[c] Laboratory of Biotechnology and Molecular Bioengineering, Faculty of Science and Technology Gueliz, Cadi Ayyad University, Marrakesh, Morocco

ARTICLE INFO

Article history:
Received 31 December 2018
Received in revised form 5 August 2019
Accepted 25 August 2019

Keywords:
Epidemiology
Risk factor
Antibiotic resistance
Nosocomial infection
Morocco

ABSTRACT

Background: Intensive care units (ICUs) are considered epicenters of antibiotic resistance. The aim of this study is to determine clinical risk factors, epidemiology and the causative agents of multi-drug resistant bacteria in the ICU of the University Hospital in Marrakesh-Morocco.
Methods: A one year case control study was carried out in our 10-bed clinical and surgical ICU from March 2015 to March 2016. The epidemiological surveillance was done by collecting data in the medical records with the help of a questionnaire. The antibiotic susceptibility testing was used following the recommendations of the Antibiogram Committee of the French Society of Microbiology and the European Committee for Antimicrobial Susceptibility Testing, 2015.
Results: Among the 479 admitted patients, 305 bacteria were isolated and identified as *Acinetobacter baumannii* (31%), *Enterobactereacae* species (30%), and *Staphylococcus* (24%), *P. aeruginosa* (10%) and other bacterial strains (5%). The rate of MDR bacteria acquisition was 41% (124/305) with domination of *A. baumannii* resistant to imipenem (70%) and followed by Extended Spectrum β-lactamases producing *Enterobacteriaceae*, *P. aeruginosa* resistant to Ceftazidime, and Methicillin-resistant *S. aureus* (18%, 7%, and 5% respectively). The distribution of the common nosocomial infections were dominated by pneumonia, bacteremia, and catheter-related blood stream infections (39%, 29%, and 17%) respectively. Multivariate analysis identified lack of patient isolation precautions (OR: 7.500), use of quadri or triple therapy (OR: 5.596; OR: 5.175), and mechanical ventilation (OR: 4.926), as the most significant clinical and epidemiological factors associated with acquisition of MDR bacteria. The attributable mortality, in this ICU, of patients with MDR bacteria, is about 12%.
Conclusions: The incidence of MDR was higher compared with that of developed countries. The implementation of standard infection control protocols, active surveillance of MDR and generation of data on etiological agents and their antimicrobial susceptibility patterns are urgently needed in our hospital.

Introduction

The multidrug resistant (MDR) bacterial infections have played an important role worldwide in public health in the last decades. These infections increase morbidity, mortality and health care costs [1,2]. In fact, the Center for Disease Control and Prevention (CDC) has evaluated the high increase in antibacterial resistance as one of the most important reasons threatening human health over the world. The rate of Healthcare Acquired Infections (HAI) was two to three fold higher in developing countries compared to Europe or United States of America [3]. In addition, the prevalence of infections acquired in Intensive Care Units (ICU) was higher than it was in other hospital units. This might be due to the severity of disease and prolonged stay in the ICU [4]. Furthermore, immunosuppression of ICU patients and a higher number of invasive devices like central venous catheterization, mechanical ventilation, urinary

* Corresponding author at: Laboratory of Biology and Biotechnology of Microorganisms, Department of Biology, Faculty of Sciences Semlalia, P. Box. 2390 Marrakesh, 40000, Morocco.
E-mail addresses: mbarakate@uca.ma, mbarakate@uca.ac.ma (M. Barakate).

https://doi.org/10.1016/j.jiph.2019.08.012

tract catheters were among the main risk factors for MDR bacterial infections [4,5].

This study presents the clinical and epidemiological risk factors of MDR bacterial infections as well as evaluation of bacterial resistance level in the ICU of Ibn Tofail Hospital, University Hospital Center (UHC) Mohammed VI in Marrakesh-Morocco.

Methodology

Definitions

Multi-resistance to antibiotics

In literature, to characterize the different patterns of antimicrobial resistance to antibiotics, a group of international experts came together through a joint initiative by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC), to create a standardized international terminology [6]. The definition most frequently used for MDR bacteria was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories [6].

Definiton of muti-drug resistant bacteria

In this study, we isolated many resistant bacteria. In order to choose the most resistant ones, we followed the recommendations of the antibiogram committee of the french microbiology society (2015). The four MDR bacteria we studied are : *Acinetobacter baumannii* resistant to imipenem, *Pseudomonas aeruginosa* resistant to ceftazidime, *Staphylococcus aureus* resistant to methicillin and extended-spectrum beta-lactamase producing *Enterobacteriaceae* (CA-SFM, 2015).

Participants and setting

Patients and definitions

This case-control study was conducted in a 10-bed adult ICU from March 2015 to March 2016. A total of 479 patients from the clinical and surgical ICU were enrolled with a first clinical episode of HAI. A case subject was defined as any patient who had infection with MDR bacteria at least 48 h after the ICU admission during the study period. Meanwhile, a control subject was defined as patients admitted in the ICU without being infected by MDR bacteria.

- MDR ICU-acquired infections were defined as those acquired no less than 48 h after ICU admission;
- For each patient clinical and microbiological date were collected. Each day medical staff discussed positive bacteriological examinations and decided whether there was colonization or infection according to clinical signs presented by the patients (fever, white blood cell count, C-reactive protein level, chest X-ray infiltrates).
- The decision of MDR healthcare infection, and need for starting an antimicrobial therapy was taken with both laboratory and clinical findings. The infection should not be present at the time of admission.

Sampling methods

- The first sample(urine, blood, tracheal aspirate, and others) collected from every patient admitted to the ICU was sent for bacteriologic culture to exclude infection at the time of admission to ICU and to get the true picture of infection rate;
- Microbiology samples were taken from areas such as peripheral venous blood, central venous catheter, urine endotracheal secretions, bronchoalveolar lavage, pus, and other any suspected during the ICU stay. Only the initial isolates were considered in the study and repeat isolates from the same sites were excluded;

Inclusion and exclusion criteria

Inclusion criteria

- Patients aged 18 years or more, admitted to participing ICU, remaining there at the survey time were included regardless after that time patient was discharged or remain in the ICU.
- Patients whose ICU-length of stay was longer than 48 h were considered eligible for our study.

Exclusion criteria

- Patients stayed less than 48 h in the ICU, testing positive for infections within 48 h, and showing evidence of existing infections on admission were excluded;
- All patients who were infected at the time of admission or before 48 h after hospitalization at the ICU.
- Duplicate isolates defined as the same bacteria isolated from the same patient and sample were excluded from our study.

Data collection

In order to evaluate the clinical and epidemiological risk factor for acquisition of MDR bacteria the data collection was carried out with an epidemiological monitoring questionnaire. Several clinical and epidemiological variables were studied: age, gender, previous medical history of hospitalization and the hospital unit of hospitalization, underlying diseases, nutritional state, invasive procedures, biological and clinical signs of infection, date and site of the infection, origin of the sample taken to analyze and the isolation of MDR bacteria infected patients. Additionally, we investigated the period of stay in the ICU, the outcome of patients after the stay in ICU and the rate of mortality caused by infections with MDR bacteria.

Laboratory methods

Bacterial isolation and identification

The bacterial isolates were obtained from clinical samples sent to the medical microbiological laboratory for diagnostic purposes. The specimens were urine, bronchoalveolar lavage, blood, catheters, pus, and cerebrospinal fluid samples. The clinical samples were processed according to the routine laboratory diagnostic protocol, which included identifications by morphological, biochemical and culture characteristics. The identification of purified isolates was carried out with API gallery (Biomerieux). When a sample was infected with MDR bacteria, this bacteria was conserved at the minus 80 ° using Brain Heart Infusion liquid culture with 20% of glycerol for future experiments.

The identification of antibiotic resistance level of isolated bacteria was performed with the disc diffusion method in Muller Hinton agar (MH) as recommended by the antibiogram committee of the French Microbiology Society and The European Committee on Antimicrobial Susceptibility Testing, 2015. The determination of phenotypic characteristics of MDR bacteria was also used.

Statistical analysis

The data was collected in Microsoft Office Excel 2013 and the results were analyzed with the statistical package for social sciences (SPSS v 23, Chicago, USA). The Chi-square or Fisher's exact test was used to compare discrete variables. Fisher's exact test was preferred when one or more expected values were equal or less than five. All p-values < 0.05 were considered statistically significant. In addition, multivariate analyses were performed to evaluate the most important associations between risk factors and the infection acquisition. For this, we chose the logistic regression model and calculated the odd's ratio (OR) to prove the strength of the associ-

ation between the important factors. The odds ratio (OR) and their corresponding 95% confidence intervals (CIs) for each variable were calculated to prove the level of association between the important risk factors and the acquisition of MDR resistant bacteria.

Results

Clinical and epidemiological results

From a total of 479 admitted patients, 366 were male patients showing a male-female ratio of 2.3. Regarding the age distribution, 344 (71%) patients were between 20 and 60 years old. Statistically, the mortality rate was higher in male patients 133 (68%) than among female patients. This rate was also higher between the ages of 20–40 years old.

As shown in Fig. 1, 91% of the ICU patients had no medical comorbidities at the admission; 53% of the patients were admitted due to polytrauma in the ICU; 61% were transferred from the emergency unit to the ICU and 41% were between 20–39 years old. The stay in ICU longer than 15 days was determined in 21% of the cases. The urinary catheters were used in 99% of the patients; peripheral venous catheters were used in 98% of the cases whereas the central venous catheters were only used in 70% of the patients. Almost half of the patients (52%) needed assisted mechanical ventilation and 51% had nasogastric intubation. In addition, 44% of patients were treated with antibiotics for more than 8 days.

Among the totality of hospitalized patients, 66% of the patients acquired MDR bacteria. Fig. 2 shows the distribution of infections caused by MDR bacteria. The main infections were the nosocomial respiratory tract infections (39%) while the lowest percentages were the postoperative infection (7%), nosocomial meningitis (4%) and urinary tract infection (3%). Moreover, the crude mortality rate was 39% (189/479) for infections caused by both of susceptible and resistant bacteria. The mortality rate caused by MDR bacteria was 12% (58/479) also shown in Fig. 2.

According to univariate logistic regression analysis with ($p \leq 0.05$) the following data was obtained: age (p = 0,036), polytrauma as admission diagnosis (p = 0), lack of patient isolation precautions (p = 0), antibiotic therapy treatment (p = 0), curative antibiotic (p = 0), monotherapy (p = 0,003), bitherapy (p = 0,085), triple antibiotic therapy (p = 0), quadri antibiotic therapy (p = 0), stay period in ICU (p = 0). In addition, the invasive devices, such as artificial mechanical ventilation (p = 0.001), nasogastric intubation (p = 0), artificial patients feeding (p = 0.001), antibiotic treatment duration (p = 0,018), were significant risk factors for acquiring MDR bacteria (Table 1).

Bacteriological results

A total of 305 bacterial strains were isolated from 213 pathological samples. According to the identification using API 20E gallery, *A. baumannii* (31%), *Enterobactereacae* (30%), *Staphylococcus* spp. (24%), *P. aeruginosa* (10%) and other bacterial strains (5%) were the common bacterial pathogens. Among the most important isolated Enterobacteraecae strains were *Klebiella pneumonae* (40%), *Proteus mirabilis* (32%), *Escherichia coli* (15%), *Enterobacter* spp. (8%), *Serratia marcescens* (2%), *Morganilla morgannii* (2%) and *Proteus regret* (1%). Clearly, our results show a higher percentage of Gram-negative bacteria (76%) than Gram-positive bacteria (24%) isolated strains.

Antibiotic resistance profile

The antibiotic resistance tests revealed that 40% (124/305) of the isolated strains were MDR bacteria. The most common was *A. baumannii* resistant to imipenem (ABRI) 70%, followed by multiresistant Enterobactereacae species (18%), *P. aeruginosa* resistant to ceftazidime (PARC) 7%, and *S. aureus* resistant to methicillin (SARM) 5%. The analysis of MDR bacteria distribution among pathological samples demonstrated that ABRI strains were mainly isolated from bronchial samples (48%). PARC strains were mainly isolated from pus samples (50%) and MRSA were isolated from catheters (50%). Finally, ESBL producing Enterobacteriaceae were isolated from blood samples (48%), Fig. 3.

All *A. baumanni* tested were resistant to β-lactams, while the resistance rate among Enterobacteriaece species was only 56%, *P. aeruginosa* 54% and *S. aureus* 44%. Table 2 shows the resistance rate of MDR bacteria to other antibiotics. ABRI showed significant resistance to gentamicin (94%), tobramycin (93%) and ciprofloxacin (94%). Similarly, ESBL-Extended-spectrum β-lactamase– producing *Enterobactereacae* were resistant to ciprofloxacin (81%), and tobramycin (86%). SARM were resistant to gentamicin, amikacin, tobramycin and ciprofloxacin all with the same value (86%). All PARC isolates were resistant to imipenem, sulphametoxazole (97%), and ceftazidime (75%).

Risk factors and outbreaks of acquiring MDR bacteria

However, to measure and classify factors related to acquisition of MDR bacteria in ICU, only the lack of patient isolation precautions (OR: 7.5, p = 0.000), inappropriate antibiotic therapy treatment (OR: 5.175, p = 0.001) and longer stay period (15 days) in ICU (OR: 0.378, p = 0.000) were the most significant clinical and epidemiological factors (Table3). This is according to the multivariate analysis based on binary logistic regression model including the Wald test.

Table 4 shows the ICU outbreak characteristics. ABRI was the highest cause of mortality among the MDR bacteria in ICU infections.

Discussion

MDR bacterial infections are becoming one of the most cause of public healthcare threat worldwide. They have been related to the most damageable outbreaks mainly in ICU patients. This is the first study searching for clinical and epidemiological risk factors for MDR bacteria at the ICUs of Marrakesh University Hospital Center. This work could be considered as a pilot study to find possible answers to significant risk factors and variables responsible for acquiring infections with most virulent and damageable MDR bacteria. The multivariate analysis had identified as well as many other studies that patients isolation, stay period in ICU, and inappropriate therapy were the most significant factors associated to the infections with MDR bacteria [4,7,14,19,25].

In our study, the age, nasogastric intubation and the curative antibiotic with its duration does not seem to contribute in the acquisition of MDR bacteria. Other studies have demonstrated that male gender, previous hospitalization, an immunocompromised state, catheterization, surgery, and the admission to ICU from the same hospital did not have a significant statistically relationship to acquire MDR bacteria in ICU [4,14,25].

The distribution of HAI and MDR bacteria in our ICU was mainly represented by pneumonia and bacteremia and could be explained by the high rates of isolated ABRI and ESBL-producing *Enterobacteriaceae* species, followed by PARC and SARM. In fact, recent studies showed that *A. baumannii* was found to be the most frequent cause of healthcare-associated infections including pneumonia, bloodstream infections, and catheter-associated infections [3,16,18,21,23,24]. Another multicenter study that was done in 14 hospitals in Europe, North America, and South America concerning bloodstream infections showed that *P. aeruginosa* has been incriminated in these infections with a rate of 5.3% [19]. The authors concluded that new mutations, selection of resistant strains, and

Table 1
Comparision of clinical and epidemiological characteristics between cases and controls based on univariate analysis.

Risk factor	Case patients N = 49	Control patients N = 430	Total N = 479	P value
Socio-demographic factors				
Sex				0.314
Male	34(69 %)	302 (63.3 %)	336	
Female	15(31 %)	128 (26.7 %)	128	
Age (20–39 years)	36 (54,5%)	163 (39,6%)	199	0,036
Comorbidities	11 (16,7%)	31(7,5%)	42	0,020
Admission diagnosis with polytrauma	48 (26,2%)	204 (49,6%)	252	<0.0001
ICU factors				
Lack of patients isolation precautions	39 (59,1%)	370 (91,6%)	409	<0.0001
Directed curative antibiotic therapy	36 (59,0%)	37(2,9%)	43	<0.0001
Probabilistic curative antibiotic	14 (23,0%)	13(5,4%)	27	<0.0001
Preventive antibiotic of prophylaxis	18 (29,5%)	31 (15,6%)	104	0,371
Monotherapy	18 (35,3%)	34 (8,3%)	49	0,003
Bitherapy	11 (16, 7%)	15 (3,6%)	45	0.085
Triple therapy	16 (24,2%)	3 (0,7%)	31	0,085
Quadritherapy	9 (13, 6%)	67 (16,5%)	12	<0.0001
Stay period in ICU (≤ 15 days)	33 (50,0%)	408 (99,3%)	100	<0.0001
Urinary catheter	65 (98,5%)	405 (98,5%)	473	0.450
Peripheral venous catheter	52 (78,8%)	281 (68,4%)	469	0.306
Central venous catheter	52 (78,8%)	281 (68,4%)	333	0.111
Mechanical ventilation	47 (71,2%)	202 (49,1%)	249	0.001
Nasogastric intubation	44 (66,7%)	178 (43,3%)	222	<0.0001
Artificial patients feeding	45 (71,4%)	194 (41,7%)	239	0.942
Antibiotic treatment duration (>8 days)	13 (68,4%)	22(36,1%)	35	0.018

NOTE. MDR, multidrug resistant; ICU, intensive care unit.

Table 2
Antibiotic co-resistance profile of ICU isolated MDR bacteria.

	Antibiotics	ABRI (N = 85) (%)	ESBL *Enterobactereacae* (N = 25) (%)
Carbapenems	Ertapenem	NR	41%
	Imipenem	NR	31%
Aminoglycosides	Gentamicin	94 %	71%
	Amikacin	74%	16%
	Tobramycin	93%	86%
Fluoroquinolones	Ciprofloxacin	94%	81%
Trimethoprim-sulphamethoxazole	Trimethoprim-sulphamethoxazole	48%	81%
Polypeptides	Colistin	0%	0%

NOTE: ABRI, *Acinetobacter baumannii* resistant to imipenem; ESBL, Extended-spectrum β-lactamase– producing *Enterobactereacae*; NR, not recommended.

Table 3
Risk factors associated with MDR bacterial infections in ICU based on multivariate analysis.

Variables	OR	95% CI	Wald test	P value
Lack of patients isolation precautions	7.500	3.931–14.309	37.362	0.000
Longer stay period (until 15 days)	0.378	0.256–0.558	23.844	0.000
Triple therapy	5.175	1.941–13.798	10.794	0.001
Quadritherapy	5.596	1.276–24.545	5.212	0.022
Admission diagnosis with polytrauma	2.271	1.409–5.256	8.888	0.003
Age (years)	0.266	0.066–1.067	3.490	0.062
Bitherapy	1.810	0.695–4.715	1.475	0.22
Monotherapy	1.922	0.827–4.464	2.308	0.129
Probabilistic curative antibiotic	2.566	1.015–6.487	3.967	0.46
Nasogastric intubation	0.619	0.054–7.064	0.149	0.70
Antibiotic treatment duration	0.564	0.019–16.667	0.110	0.740
Artificial patients feeding	1.097	0.091–13.207	0.005	0.942

NOTE. MDR, multidrug resistant; OR, odds ratio; CI, confidence interval; ICU, intensive care unit.

Table 4
MDR bacteria outbreaks in ICU.

ICU outbreak characteristics	ABRI	Enterobacteriaceae ESBL	PARC	SARM
Survived patients	24 (40 %)	0	1 (14,2%)	2 (20%)
Deceased patients due to hospitalization reasons	4 (6.7%)	1 (20%)	6 (85,8%)	0
Deceased patients due to infection	31(52,3%)	4 (80%)	6 (85,8%)	8 (80 %)
Total	59 (100%)	5 (100 %)	7 (100 %)	10(100 %)

NOTE: ABRI, *Acinetobacter baumannii* resistant to imipenem; PARC, *Pseudomonas aeruginosa* resistant to ceftazidime; ESBL, Extended-spectrum β-lactamase– producing *Enterobactereacae*; MRSA, *Staphylococcus aureus* resistant to methicillin; ICU, intensive care unit.

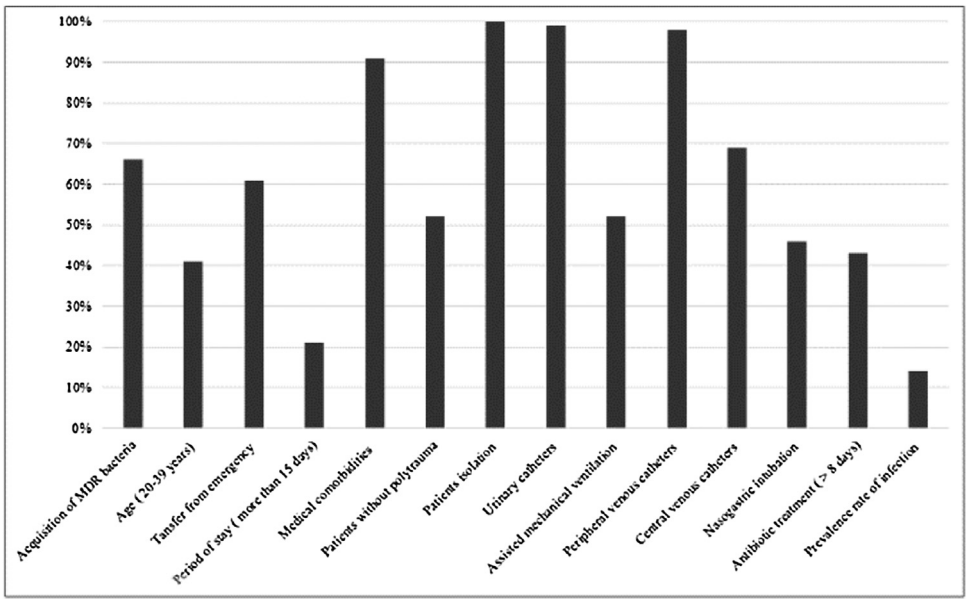

Fig. 1. Distribution of the most important clinical and epidemiological factors among patients.

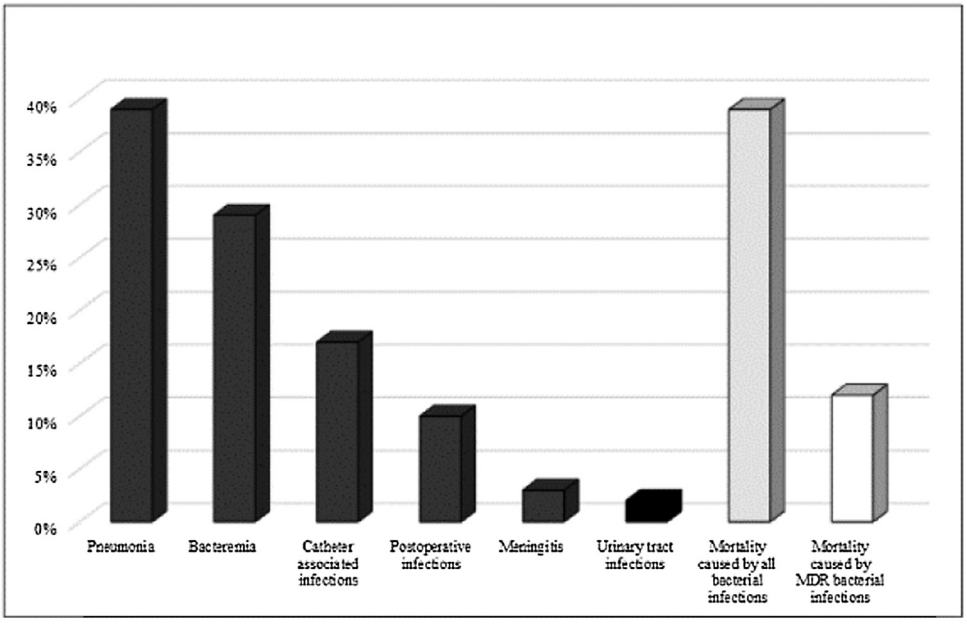

Fig. 2. Mortality and healthcare acquired infections caused by MDR bacteria.

suboptimal infection control were the main factors influencing the rapid spread of multidrug-resistant pathogens in the ICU.

The obtained data showed that 76% of the bacterial infections were due to Gram-negative bacteria. *A. baumannii*, *Enterobactereacae* species and *P. aeruginosa* strains were the main isolated bacteria. This result is similar to what is known from other studies that Gram-negative bacteria are the most common cause of HAIs in low and middle-income countries [7,8]. In this respect, the most common isolated MDR bacteria in India and Nepal were *K. pneumoniae* and *E. coli* [9,10]. However, a surveillance of antimicrobial studies conducted in Europe, found that the main Enterobacteriaceae was *E. coli* [11], one of the main concerns of this European surveillance was to draw attention to the high resistance level of isolated bacteria to the beta-lactam and to the last generation of antibiotics. The results reported in another investigation [7], which supports the findings of our surveillance and shows the high resistance to beta-lactam and last generation antibiotics. Furthermore, the most important findings in the same study, have demonstrated that the high use of imipenem is a major responsible factor for the alarming increase of MDR *A. baumannii* to imipenem [7].

In contrast, an epidemiological survey conducted in France showed a low incidence of resistance to imipenem in *A. baumannnii* estimated to 11% in 2011 [11]. Some authors found lower cases of *A. baumannii* highly resistant to amikacin, gentamicin, and piperacillin-tazobactam. In addition, other scientists found a low rate of resistance for meropenem and imipenem [8,12,13]. Recent researches showed similar results to our findings of the high percentage of sensitivity of *A. baumannii* to colistin (all the *A. baumannii* strains) and its high resistance level to imipenem [4,8,12,14,15].

In the last years, the interest is growing to monitor and evaluate the ESBL producing Enterobacteriaceae among ICUs patients. Researches have documented and agreed on the high sensitivity

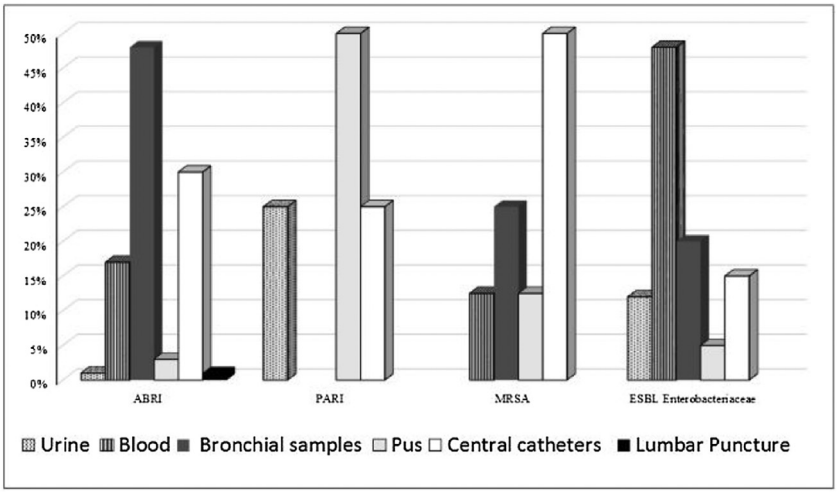

Fig. 3. Distribution of MDR bacteria depending on the nature of pathological samples.

of this bacteria to imipenem [16,17]. In addition, other results suggested that ESBL producing *Enterobacteriaceae* isolates were also resistant to cotrimoxazole and ciprofloxacin. This might be explained by the rapid increase resistance of *K. pneumonia*, *E. coli*, and Proteus sp [18,19]. Recently, a research study conducted in several German ICUs showed that ESBL producing Enterobacteriaceae was mainly caused by *E. coli* and *K. pneumoniae* [16]. Scientists from USA have isolated a MDR *E. coli* strain resistant to both colistin and carbapenems [18]. Besides, a report found that the resistance level of *Enterobacteriaceae* species to carbapenem antibiotics is about 57% [21]. In contrast to these results, the isolated ESBL producing Enterobacteriaceae strains in our context showed a lower percentage of resistance to carbapenems (31%).

The alarming resistance level of PARC isolated in our hospital to cephalosporins, sulfonamide-trimethoprim, and carbapenems was also described by the CDC's national healthcare safety network and other researchers [1,3,8]. The ICUs in United States and European countries showed high rate of resistance to aminoglycosides, fluoroquinolones, carbapenems and cephalosporins. This pathogen was sensible only to amikacin and colistin [18]. In our investigation, *Pseudomonas* was completely susceptible to colistin. However, we found that (42%) of *Pseudomonas* was resistant to amikacin.

Recently, clinicians and scientists all over the world paid a particular attention to nosocomial infections, caused by MRSA which has resistance to other associated antibiotics [20,21]. However, our investigation showed lower percentages of MRSA than the results obtained in the UHC of Casablanca. In other Arabian countries, the rate of this pathogen was between 10–18% [20,21]. In an Italian ICU, the isolation rate of this resistant bacteria was higher [22]. Usually in the literature, the high MRSA rate was associated with resistance to cotrimoxazole, ciprofloxacin followed by amoxicillin-clavulanic acid and linezolid [17,18,20,21]. We reported in our study the high co-resistance level of MRSA to aminoglycosides, fluoroquinolones and sulfonamide-trimethoprim, which is different to some reports in the literature. Correspondingly, the data obtained in other studies are consistent with our results regarding the high susceptibility of MRSA to vancomycin [8,20]. Thus, our data confirm that only glycopeptides (vancomycin and teicoplanin) are constantly active against MRSA. These findings could be explained by the absence of regulations in the use of antibiotics at the ICUs. This leads to an easy development of bacteria resistance to new antibiotics. A better application of hospital hygiene measures can minimize the spread of this pathogen. This should be responsibility of the hospital committee of nosocomial infections.

This is the first study to investigate the relation between clinical and epidemiological risk factors of infections related to the acquisition of resistance to MDR bacteria in an ICU of a Moroccan University Hospital. From the obtained data, the main conclusion is that the ICU of Marrakesh UHC showed a high prevalence of MDR bacteria caused mainly by non-fermenting MDR Gram-negative bacteria, such as *A. baumannii* with high resistance to carbapenems.

These findings provide enough information to take urgent actions to reduce MRD bacteria in the ICU. To improve patients outcomes a combination of infection control measures and rational antimicrobial use in hospitals specifically in ICUs level is needed. All these actions will play a role in limiting outbreaks and eradicating the MDR bacteria from our ICU.

Conclusion

Our results urge the implementation of obligatory and practical actions to reduce MRD bacteria in the ICU. Among these actions are the rational antimicrobial use in the hospital, specifically in the ICU and the application of infection control measures. These changes may play a role in limiting the outbreaks as well as reducing and eradicating the MDR bacteria from our ICU. As a consequence, the patients outcomes can be improved.

Based on the promising findings presented in this paper, and as reported by other studies, it will be interesting and important to study the local patterns of resistance to antibiotics in a molecular level. This will highlight the genes responsible for antibiotic resistance of MDR bacteria isolates.

Funding

This work was supported by the Cadi Ayyad University, Marrakesh, Morocco.

Competing interests

None declared.

Acknowledgments

The authors appreciate the efforts and assistance of the healthcare workers in ICU and all the staff in the hospital medical bacteriological laboratory. We also gratefully acknowledge Dr. Yarden Bustamante for her help and assistance in reading and cor-

recting this manuscript. The source of funding for our study is based on the annual research budget allocated by the university.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jiph.2019.08.012.

References

[1] Aranaz-Andrés JM, Aibar-Remón C, Vitaller-Murillo J, Ruiz-López P, Limón-Ramírez R, Terol-García E. Incidence of adverse events related to health care in Spain: results of the Spanish National Study of Adverse Events. J Epidemiol Community Health 2008;62(12):1022–9.
[2] Ak O, Batırel A, Ozer S, Colakoglu S. Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: a prospecive cohort study. Med Sci Monit 2011;17(5). PH29-34.
[3] 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(5):268–81.
[4] Vu DP, Heiman FL, Mattias L, Behzad N, Quynh DD, Lennart E, et al. Burden of hospital acquired infections and antimicrobial use in vietnamese adult intensive care units. PLoS One 2016;11(1):e0147544.
[5] Routsi C, Pratikaki M, Platsouka E, Sotiropoulou C, Nanas S, Markaki V, et al. Carbapenem-resistant versus carbapenem-susceptible *Acinetobacter baumannii* bacteremia in a Greek intensive care unit: risk factors, clinical features and outcomes. Infection 2010;38(12):173–80.
[6] 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;18:268–81.
[7] Kaye KS, Pogue JM. Infections caused by resistant Gram-negative bacteria: epidemiology and management. Pharmacotherapy 2015;35(10):949–62.
[8] Zahlane K, Soraa N, Idmoussa A, Labaali A, Aitsaid L. Beta-Lactam resistance profile in bacterial isolates at IbnTofail hospital. CHU Mohammed VI, Marrakech (Morocco). Revue Tunisienne d'Infectiologie 2014;8(1):57–64.
[9] Khan ID, Basu A, Kiran S, Trivedi S, Priyanka P, Anupam C. Device Associated Healthcare-Associated Infections (DA-HAI) and the caveat of multiresistance in a multidisciplinary intensive care unit. Med J Armed Forces India 2017;73(3):222–31.
[10] Narayan PP, Subhash PA, Santosh D, Jaya PS, Shyam KM, Hari PK, et al. Epidemiology of device-associated infections in an intensive care unit of a teaching hospital in Nepal: a prospective surveillance study from a developing country. Am J Infect Control 2017;45(9):1024–9.
[11] Núñez-Núñez M, Navarro MD, Palomo V, Rajendran NB, del Toro MD, Voss A, et al. The methodology of surveillance for antimicrobial resistance and healthcare-associated infections in Europe (SUSPIRE): a systematic review of publicly available information. Clin Microbiol Infect 2018;24(2):171–4.
[12] Arsalane L, Qamouss Y, Chafik A, Boughalem LL. Epidémiologie des bactéries multi résistantes dans un service de réanimation polyvalente d'un hôpital universitaire de Marrakech entre octobre 2006 et septembre 2009. Les Technol Lab 2010;21(5):11–9.
[13] Kumburu HH, Sonda T, Mmbaga BT, Alifrangis M, Lund O, Kibiki G, et al. Patterns of infections, aetiological agents and antimicrobial resistance at a tertiary care hospital in northern Tanzania. Trop Med Int Health 2017;22(4):454–64.
[14] Chelazzi C, Pettini E, Villa G, De Gaudio AR. Epidemiology, associated factors and outcomes of ICU-acquired infections caused by Gram-negative bacteria in critically ill patients: an observational, retrospective study. BMC Anesthesiol 2015;15(1):125.
[15] Ait el kadi M, Aghrouch M, Seffar M, El harti J, Bouklouze A, Cherrah Y, et al. Prévalence des souches *d'Acinetobacterbaumannii* et de *Pseudomonasaeruginosa* résistantes à l'imipénème par production de métallo-β-lactamases. Med Mal Infect 2006;13(36):386–9.
[16] Brahmi N, Beji O, Abidi N, Kouraichi N, Blel Y, El Ghord H, et al. Epidemiology and risk factors for colonization and infection by *Acinetobacter baumannii* in an ICU in Tunisia, where this pathogen is endemic. J Infect Chemother 2007;13(6):400–4.
[17] Kohlenberg A, Schwab F, Meyer E, Behnke M, Geffers C, Gastmeier P. Regional trends in multidrug-resistant infections in German intensive care units: a real-time model for epidemiological monitoring and analysis. J Hosp Infect 2009;73(3):239–45.
[18] Kuehnert MJ, Hill HA, Kupronis BA, Tokars JI, Solomon SL, Steven LJ, et al. Methicillin-resistant–Staphylococcus aureus Hospitalizations, United States. Emerging Infect Dis 2005;11(6):868–72.
[19] Tripathi P, Agrawal G, Gajbhiye S. Clinical and antimicrobial profile of *Acinetobacter* spp.: an emerging nosocomial superbug. Adv Biomed Res 2014;3(1):13.
[20] Benouda A, Elhamzani S. *Staphylococcus aureus:* epidémiologie et prévalence des souches résistantes à la méthicilline (SARM) au Maroc. Rev Tunisienne Infect 2009;3(1):15–20.
[21] Bouhali Zriouil S, Bekkali M, Zerouali K. Epidemiology of *Staphylococcus aureus* infections and nasal carriage at the Ibn Rochd university hospital center, Casablanca, Morocco. Braz J Infect Dis 2012;16(3):279–83.
[22] Mediavilla JR, Patrawalla A, Chen L, Chavda KD, Mathema B, Christopher V, et al. Colistin and carbapenem-resistant Escherichia coli harboring mcr-1 and blaNDM-5, causing a complicated urinary tract infection in a patient from the United States. MBio 2016;7(4):5–8.
[23] Baranzelli A, Wallyn F, Nseir S. Infections bronchopulmonaires à *Stenotrophomonas maltophilia* et à *Acinetobacter baumannii*. Rev Pneumol Clin 2013;69(3):250–9.
[24] Brki DV, Prese A, Stanko KI, Ple S, Tripkovi V, Branka B. *Acinetobacter baumannii* microbiological and phenotypic characteristics of isolates from Intensive Care Unit of the Department of Internal Medicine at the University Hospital Centre in Zagreb over a four- year period. Signa Vitae 2015;10(Suppl. 1):13–5.
[25] Agarwal R, Gupta D, Ray P, Aggarwal AN, Jindal SK. Epidemiology, risk factors and outcome of nosocomial infections in a Respiratory Intensive Care Unit in North India. J Infect 2006;53(December (2)):98–105.