



Comparative study of multidrug-resistant bacterial infections in hospitals and community settings in the region of Monastir – Tunisia

Étude comparative des infections bactériennes multi-résistantes en milieu hospitalier et communautaire dans la région de Monastir – Tunisie

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ABSTRACT

Introduction and aim : Multidrug resistance in bacteria has become a widespread scourge. The objective of this study is to investigate the epidemiology of multidrug-resistant bacteria (MDR) at Fattouma Bourguiba University Hospital of Monastir - Tunisia compared to the community and to define their antibiotic resistance profiles.

Methods: It was a retrospective and descriptive study over a period of 5 years (2016-2020) conducted at the microbiology department of Fattouma-Bourguiba University Hospital of Monastir - Tunisia. All MDR strains isolated from diagnostic microbiological samples collected from patients hospitalized in high-risk infectious departments and from outpatients were included in our study.

Results : A total of 4324 MDR among 16353 bacteria were isolated during the study period, i.e. a resistance rate of 26.4% with a predominance of hospital strains (80.3% versus 19.7% in the city). Third generation cephalosporin-resistant *Enterobacteriaceae* were the most prevalent and were mainly represented by extended-spectrum beta- lactamases (67.1% versus 83.4% in the community). *Escherichia coli* was the most frequent species (40.9%). It was frequently associated with resistance to fluoroquinolones (in more than 73% of cases). Imipenem-resistant *Acinetobacter baumannii* was mostly responsible for hospital acquired infections (77%). Co- resistances concerned most of the antibiotics but spared colistin. Methicillin-resistant *Staphylococcus aureus* infections were more frequent in the city (20.5% versus 19.3% in hospitals). Resistance associated was mainly to fusidic acid (49.6%). Glycopeptides have maintained their activity and only 2% were of decreased sensitivity to vancomycin.

Conclusion : The emergence of MDR always represents a public health challenge. Thus, hygiene measures associated with an optimization of antibiotic therapy are necessary for a better control of their diffusion.

Key Words: Community, Extended-spectrum beta-lactamases, Hospital infections, Multidrug-Resistant Bacteria, Tunisia.

RÉSUMÉ

Introduction et objectif : La multirésistance des bactéries aux antibiotiques est devenue un fléau généralisé. L'objectif de cette étude est d'étudier l'épidémiologie des bactéries multirésistantes (BMR) au CHU Fattouma Bourguiba de Monastir – Tunisie par rapport à la communauté et de définir leurs profils de résistance aux antibiotiques.

Méthodes: C'était une étude rétrospective et descriptive sur une période de 5 ans (2016-2020) menée au service de microbiologie du CHU Fattouma-Bourguiba de Monastir – Tunisie. Toutes les souches BMR isolées à partir d'échantillons microbiologiques à visée diagnostique collectés chez des patients hospitalisés dans des services infectieux à haut risque et chez des patients externes ont été incluses dans notre étude.

Résultats: Un total de 4324 BMR parmi 16353 bactéries ont été isolées durant la période d'étude, soit un taux de résistance de 26,4% avec une prédominance des souches hospitalières (80,3% contre 19,7% en ville). Les *entérobactéries* résistantes aux céphalosporines de troisième génération (EBRC3G) ont été les plus répandues, principalement représentées par des bêta-lactamases à spectre étendu (67,1% contre 83,4% dans la communauté). *Escherichia coli* a été l'espèce la plus fréquente parmi ces EBRC3G (40,9%). Elle a été fréquemment associée à une résistance aux fluoroquinolones (dans plus de 73% des cas). *Acinetobacter baumannii* résistant à l'imipénème a été surtout responsable d'infections nosocomiales (77%). Les co- résistances ont concerné la plupart des antibiotiques mais ont épargné la colistine. Les infections à *Staphylococcus aureus* résistant à la méticilline ont été plus fréquentes en ville (20,5% contre 19,3% à l'hôpital). La résistance associée a concerné principalement l'acide fusidique (49,6%). Les glycopeptides ont maintenu leur activité et seulement 2% ont présenté une sensibilité diminuée à la vancomycine.

Conclusion: L'émergence de BMR représente toujours un défi de santé publique. Ainsi, des mesures d'hygiène associées à une optimisation de l'antibiothérapie sont nécessaires pour un meilleur contrôle de leur diffusion.

Mots clés: Bactéries Multi-Résistantes, Bêta-lactamases à spectre étendu, Communauté, Infections hospitalières, Tunisie.

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INTRODUCTION

Multidrug resistance in bacteria has become a widespread scourge and a major public health concern in the 21st century. In fact, the number of healthcare-associated infections caused by antimicrobial-resistant microorganisms has been estimated at 426.277 per year in Europe [1]. By 2050, the population will be heavily affected: about 444 million people will be infected [2]; effective antibiotics may be no longer available, developed or discovered as antibiotic resistance will continue to develop and spread more rapidly than new treating agents [3]. As a result, 10 million deaths are expected unless effective measures are implemented [4]. This multidrug resistance to antimicrobial agents continues to increase and the spread of these germs in the community environment is becoming a major issue.

Faced with the emergence of these bacteria, it is essential to assess the situation in Tunisian hospitals and communities both at the national and regional level and act accordingly, therefore the need to provide recent data on antibiotic resistance by focusing on some emerging resistances, which represent a daily challenge for the medical profession in the region of Monastir - Tunisia.

The objectives of this study is to investigate the epidemiology of multidrug-resistant bacteria (MDR) in Fattouma Bourguiba University Hospital of Monastir – Tunisia compared to the community and to specify their antibiotic resistance profiles.

METHODS

Study design

It was a retrospective and descriptive study, over a period of 5 years (from January 1, 2016 to December 31, 2020) performed in the department of Microbiology at Fattouma Bourguiba University Hospital in Monastir - Tunisia.

Population

It was focused on all MDR strains isolated from bacteriological samples for diagnostic purposes from patients admitted in the same university hospital, particularly in high infectious risk departments (intensive care units (ICU) (anesthesia and medical reanimation (AN-REA/MED-REA)), surgery, pediatrics, infectious diseases) and those consulting in regional hospitals and emergency department. Community-acquired infections were infections that were contracted outside the hospital or diagnosed within 48 hours of admission without prior healthcare contact. Nosocomial infections were healthcare acquired infections that were not present or incubating at the time of hospital admission.

The selected MDR were: third generation cephalosporin-resistant *Enterobacteriaceae* (3GCREB), carbapenem-resistant *Enterobacteriaceae* (CRE), methicillin-resistant *Staphylococcus aureus* (MRSA), imipenem- and/or ceftazidime-resistant *Pseudomonas aeruginosa* (IRPA/CAZ-RPA) and imipenem-resistant *Acinetobacter baumannii* (IRAB).

Applied protocols

Bacterial identification was carried out by conventional methods and antibiotic susceptibility testing by agar diffusion method according to EUCAST recommendations. For the interpretative reading of the antibiogram, some tests were performed such as the synergy test (ST) between a 3rd generation cephalosporin disc and a disc associating a beta-lactamase inhibitor and the test with cloxacillin at a concentration of 250mg/l as a cephalosporinase inhibitor. The determination of the minimum inhibitory concentrations (MIC) of carbapenems was done by the VITEK2® (bioMérieux, France) and that of colistin and glycopeptides using the UMIC® kit (biocentric, France). Data on antibiotic resistance were collected from the expert system of microreader for antibiograms « SIRscan Micro® » (I2A, France). Basic data on the supply of health care in the city of Monastir were summarized in Table 1.

Table 1. Basic data on the supply of health care in the region of Monastir - Tunisia

Healthcare Facility Level	2016	2017	2018	2019	2020
University Hospital ⁽¹⁾	74 778	75 171	74 074	65 351	46 109
Regional Hospital ⁽²⁾	122 395	115 604	125 364	112 060	88 266
District Hospital ⁽³⁾	305 816	307 064	321 491	318 259	223 783
TOTAL	502 989	497 839	520 929	495 670	359158

(1) THIRD LINE PUBLIC CHANNEL: University Hospital of Monastir

(2) SECOND LINE PUBLIC CHANNEL: Regional Hospital of Ksar Hellal and Moknine

(3) FRONTLINE PUBLIC CHANNEL: District Hospital of Bekalta, Bembla, Béni Hassen, Jammel, Ksibet Mediouni, Ouardanine, Sahline, Sayada, Teboulba and Zeramdine.

Statistical analysis

The statistical indicators that have been calculated were the incidence density (ID) of MDR per 1000 days of hospitalization (HD), the prevalence of MDR strains per 100 population and frequency of specified MDR strains per 100 MDR bacteria.

RESULTS

During the reporting period, 4324 MDR were isolated from 16353 bacteria, representing a prevalence of 26.4% of germs with high pathogenic potential. There was a predominance of hospital strains compared to community strains (80.3% versus 19.7%) (Table 2).

3GCREB were the most common (63.1%). Their prevalence was higher in hospital setting (27.8% versus 13.3%) (Table 2). Seventy-one percent of all 3GCREB were extended-spectrum beta-lactamases (ESBL) producers: in fact, in hospital settings, out of a total of 2066 3GCREB collected, 1386 were ESBL producers (ST positive), about 67.1% versus 83.4% in the community. Among 3GCREB, *Escherichia coli* was the predominant species (40.9%), followed by *Klebsiella pneumoniae* (39.4%). However, in terms of prevalence, 3GCR *K. pneumoniae* was the highest (39.9%) followed by *Enterobacter sp.* (22.7%) (Table 3). ESBL production was highest for *E. coli* (92.2%) followed by *K. pneumoniae* (58.8%) and *Enterobacter sp.* (38.9%).

Table 2. Frequency and Prevalence of Multidrug Resistant Bacteria by Isolation Environment over a period of 5 years (2016 - 2020) in the region of Monastir -Tunisia.

	IN HOSPITAL SETTINGS			IN COMMUNITY		
	N(1)	n, F (%) ⁽²⁾	P (%) ⁽³⁾	N(1)	n, F (%) ⁽²⁾	P (%) ⁽³⁾
3GCREB⁽⁴⁾	7441	2066 (59.5)	27.8	4986	662 (77.7)	13.3
CRE⁽⁴⁾	7441	369 (10.6)	5	4986	58 (6.8)	1.2
IRAB⁽⁴⁾	570	439 (12.6)	77	48	33 (3.9)	68.7
IRPA⁽⁴⁾	1375	244 (7)	17.7	194	27 (3.2)	13.7
CAZ-RPA⁽⁴⁾	1375	78 (2.3)	5.7	194	8 (0.9)	4
MRSA⁽⁴⁾	1427	76 (8)	19.3	312	64 (7.5)	20.5
TOTAL	10813	3472 (100)	26.1	5540	852 (100)	13.6

(1) N: Number of total population

(2) n, F (%) : Number and frequency of multi-Drug-Resistant Bacteria

(3) P (%) : Prevalence of multi-Drug-Resistant Bacteria

(4) CAZ-RPA: Ceftazidime-resistant *Pseudomonas aeruginosa*, CRE: carbapenem-resistant *Enterobacteriaceae*, 3GCREB: third generation cephalosporin-resistant *Enterobacteriaceae*, IRAB: imipenem-resistant *Acinetobacter baumannii*, IRPA: imipenem resistant *Pseudomonas aeruginosa*, MRSA: methicillin-resistant *Staphylococcus aureus*.

Table 3: Distribution of *Enterobacteriaceae* resistant to third generation cephalosporins by species over a period of 5 years (2016 - 2020) in the region of Monastir - Tunisia

Species of <i>Enterobacteriaceae</i>	N(1)	n, F (%) ⁽²⁾	P (%) ⁽³⁾
<i>Escherichia coli</i>	6706	1117 (40.9)	16.6
<i>Klebsiella pneumoniae</i>	2692	1074 (39.4)	39.9
<i>Enterobacter sp</i>	969	220 (8.1)	22.7
Others⁽⁴⁾	2060	317 (11.6)	15.4
TOTAL	12 427	2728 (100)	21.9

N: Number of total population

(1) n, F (%) : Number and frequency of third generation cephalosporin-resistant *Enterobacteriaceae*

(2) P (%) : Prevalence of multi-Drug-Resistant Bacteria

(3) Others: *Citrobacter freundii*, *Citrobacter koseri*, *Morganella sp*, *Proteus mirabilis*, *Providencia sp*, *Serratia marcescens*...

Imipenem resistant *Acinetobacter baumannii* was mainly responsible for hospital infections (12.6% versus 3.9%)

and the proportion of IRAB among the 618 *Acinetobacter* strains was very high (77% versus 68.7%) (Table 2). However, the prevalence of MRSA infections was more frequent in urban areas (20.5% versus 19.3% in hospitals) (Table 2).

The evolution of the overall ID shows an important increase in 5 years. For 3GCREB, the incidence has increased since 2017: ID increased from 1.4 per 1000 HD in 2017 to 2.5‰ in 2018. Similarly for CRE, there has been an increase in ID from 0.2 per 1000 HD in 2018 to 0.7‰ in 2020. In contrast, there is a trend toward a decrease in MRSA infections. The MRSA ID, which remained stable since 2016, has continued to decline until 0.2‰ HD in 2020. The rate of ABRI has peaked in 2018 (0.6‰ HD) vs.0.4‰ and 0.3‰ in 2017 and 2019 respectively (Figure 1).

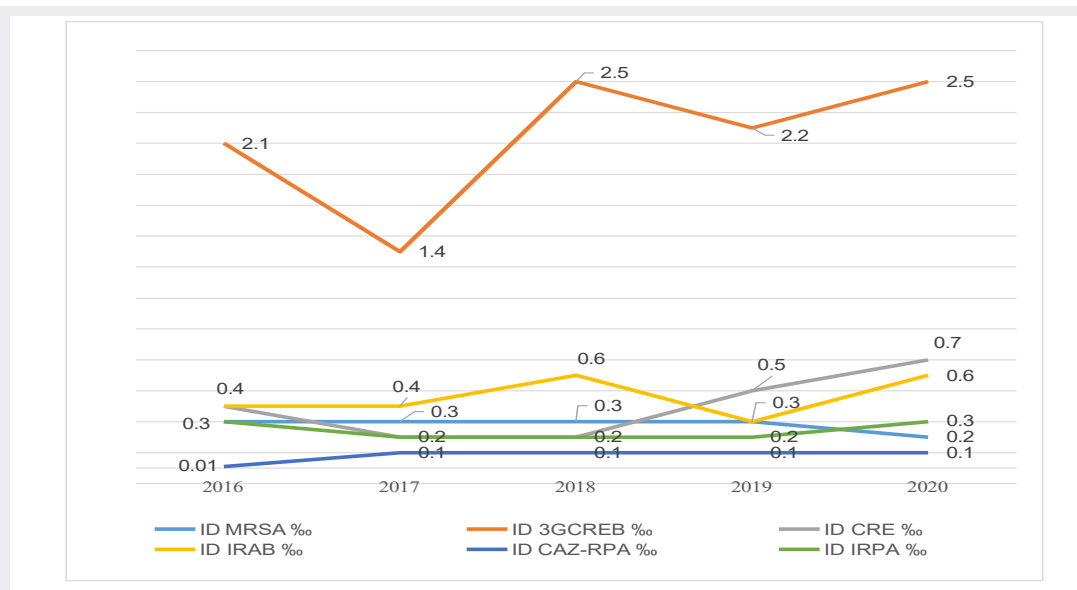


Figure 1. Evolution of the incidence density per 1000 days of hospitalization according to the type of Multi-Drug Resistant Bacteria in the university hospital of Monastir – Tunisia.

* CAZ-RPA: ceftazidime-resistant *Pseudomonas aeruginosa*, CRE: carbapenem-resistant *Enterobacteriaceae*, 3GCREB: third generation cephalosporin-resistant *Enterobacteriaceae*, ID: Incidence density, IRAB: imipenem-resistant *Acinetobacter baumannii*, IRPA: imipenem-resistant *Pseudomonas aeruginosa*, MRSA: methicillin-resistant *Staphylococcus aureus*.

The distribution of MDR by department showed predominance in the ICU: the ID in AN-REA and MED-REA were respectively of 38.6‰ HD and 27‰ HD (Table 4). Among these MDR, the 3GCREB were almost present in all departments. In AN-REA,

the ID of 3GCREB was 16.2‰ HD, about 2 times higher than the total of the departments of pediatrics, surgery and infectious diseases. The multiresistant non-fermenting Gram-negative bacilli and CRE were acquired during the stay in the ICU.

Table 4. Incidence density of Multidrug Resistant Bacteria per 1000 days of hospitalization in high infectious risk departments of the university hospital of Monastir – Tunisia over a period of 5 years (2016 - 2020).

	Anesthesia-Reanimation	Medical Reanimation	Pediatrics	Surgery	Infectious diseases
Number of HD ⁽¹⁾	20128	16417	61690	386971	39576
3GCREB ⁽²⁾ (n, ID (‰)) ⁽³⁾	326 (16.2)	194 (11.8)	238 (3.9)	831 (2.1)	85 (2.1)
CRE ⁽²⁾ (n, ID (‰)) ⁽³⁾	91 (4.5)	62 (3.8)	15 (0.2)	129 (0.3)	13 (0.3)
IRAB ⁽²⁾ (n, ID (‰)) ⁽³⁾	225 (11.2)	110 (6.7)	21 (0.3)	42 (0.1)	4 (0.1)
CAZ-RPA ⁽²⁾ (n, ID (‰)) ⁽³⁾	14 (0.7)	22 (1.3)	1 (0.01)	27 (0.1)	1 (0.01)
IRPA ⁽²⁾ (n, ID (‰)) ⁽³⁾	89 (4.4)	45 (2.7)	21 (0.3)	55 (0.1)	2 (0.1)
MRSA ⁽²⁾ (n, ID (‰)) ⁽³⁾	31 (1.5)	16 (1)	8 (0.1)	142 (0.4)	15 (0.4)
TOTAL (n, ID (‰))⁽³⁾	776 (38.6)	449 (27)	304 (4.9)	1226 (3.2)	120 (3)

(1) HD: Hospitalization days

(2) CAZ-RPA: Ceftazidime-resistant *Pseudomonas aeruginosa*, CRE: carbapenem-resistant *Enterobacteriaceae*, 3GCREB: third generation cephalosporin-resistant *Enterobacteriaceae*, IRAB: imipenem-resistant *Acinetobacter baumannii*, IRPA: imipenem resistant *Pseudomonas aeruginosa*, MRSA: methicillin-resistant *Staphylococcus aureus*.

(3) n, ID (‰): Number and Incidence density of Multi-Drug-Resistant Bacteria per 1000 days of hospitalization.

For enterobacterial species, resistance to third generation cephalosporin is frequently associated with resistance to fluoroquinolones (73.1% in hospitals versus 68.3% in the community) and to gentamicin in over 60% of cases.

For multidrug-resistant *A. baumannii*, co-resistances concerned most antibiotics. However, none of these strains were resistant to colistin. Similarly, IRPA had a high rate of resistance to other families of antibiotics including colistin: 6.7% of strains were resistant to colistin. Resistance profiles associated with methicillin resistance in *Staphylococcus aureus* involved mainly fusidic acid, norfloxacin and gentamicin. In the community, no resistance to glycopeptides or quinupristin-dalfopristin was observed.

DISCUSSION

Multidrug resistance to antibiotics is a major public health concern. The emergence of multi-resistant strains is of concern because of their involvement in hospital and community-acquired infections and their significant association with high rates of morbidity and mortality [5, 6]. These concerns affect all bacterial species but with different degrees depending on the department. The frequency of these strains is a consequence of hygiene policies in health care institutions and the degree of application of the isolation precautions used for patients who are either known or suspected to carry MDR.

According to our data, the overall prevalence of MDR isolation was 26.4%. This rate is lower than that reported by the University of Gondar study where the MDR rate was 40.5% [7] and close to that recorded by a Chinese study (33.4%) between January 2012 and December 2013 [8].

Analysis of our isolates showed that 3GCREB was the most important class of MDR. Moreover, 27.8% of the total of *Enterobacteriaceae* involved in hospital infections were 3GCREB. Our results are similar to

those of Algeria where the rate of 3GCREB was 25.7% but significantly higher than previously reported values of 3GCREB from the region of Mahdia which were 10.3% during the period 2002-2014 [9]. However, these pathogens are less frequently encountered in France (22.5%) [10]. The existing literature on MDR has shown that there is a significant geographical variation in the occurrence of these pathogens within and between countries. This geographical variation can be related with the variability of epidemiological factors, antibiotic prescription and consumption policy, compliance with hospital hygiene measures and the degree of commitment of hospitals to MDR control programs.

Most of these 3GCREB were ESBLs (73.5% in hospital versus 85.9% in community). In Algeria, 92% of the 3GCREB isolates were ESBLs, whereas this proportion was only 26% in France [11]. Eleven point one percent of the *Enterobacteriaceae* isolated from outpatients were ESBLs. This rate is close to that revealed by the study of Birgand G. where the overall prevalence of ESBL in the community was estimated at 14%, with a significant upward trend of 5.4% per year [12]. Indeed, the epidemiology of ESBL-producing *Enterobacteriaceae* has changed and since 2002 we have witnessed a community diffusion of these ESBL due to an abusive empirical prescription of antibiotics particularly fluoroquinolones and cephalosporins and to the high incidence of previous hospitalizations [13].

In terms of frequency of isolation of species, *E. coli*, *K. pneumoniae* and *Enterobacter spp* were the most frequently isolated species with frequencies of 40.9%, 39.4% and 8.1% respectively, i.e. 88.4% of the total number of 3GCREB.

Several authors share the dominance in favor of *E. coli*: In Germany, *E. coli* was the main bacterium isolated among 3GCREB [14]. In London and South-East England, among 3GCREB, *E. coli* was first with a rate of 51.2% followed by *K. pneumoniae* (21.7%) and *Enterobacter sp* (17.9%) [15].

The emergence of CRE, with a prevalence of 5% in hospitals, has been favored by the use of carbapenems as therapeutic alternatives for 3GCREB infections. This frequency of isolation was 2.8% in Algeria [16].

The emergence of CRE, with a prevalence of 5% in hospitals, has been favored by the use of carbapenems as therapeutic alternatives for 3GCREB infections. This frequency of isolation was 2.8% in Algeria [16].

Non-fermentative Gram-negative bacilli (*P. aeruginosa* and *A. baumannii*) are mainly responsible for healthcare-associated infections. These bacteria are at risk of therapeutic impasse because of their multi-resistance, their need for very broad-spectrum molecules and their capacity to generate epidemics.

A. baumannii is a widespread pathogen, resistant to desiccation, responsible for strong contamination of the environment of patients' carriers. The frequency of isolation and antibiotic resistance of *A. baumannii* varies considerably between countries, institutions and even departments within the same hospital. In fact, the percentage of IRAB was 77% among all of clinical isolates of *Acinetobacter*. This is comparable with the rate recorded at the Military Hospital Mohammed V in Rabat (77.5%) during 2 years (2012-2014) and close to that of a study in Iran (74.6%) and China (71%) but higher than that found in Europe (66.4%) and North America (44%) [17]. However, lower IRAB proportions were observed in hospitals in Germany where incidence of IRAB in 2018 did not exceed 5% (4.4%) [18].

Similarly for *P. aeruginosa*, the frequency of isolation of multi-resistant strains is variable. These proportions were 17.7% and 5.6% for IRPA and CAZ-RPA respectively, similar to those reported in France (17.8% and 8.1%) [19], but lower than those reported by the bacteriology laboratory of the military hospital in Rabat (26.2% for IRPA) [20]. Multidrug resistance in *P. aeruginosa* has a poor prognosis: most surveys have shown excess hospital mortality in patients infected or colonized by multidrug-resistant strains of *P. aeruginosa* [21].

Furthermore, Gram-positive cocci, and more particularly MRSA, were more frequent in community settings than other MDR. The frequency of MRSA isolation was 20.5% in the city versus 19.3% in hospitalized patients. Resistance to meticillin can be determined clinically by detection of the *mecA* gene through PCR as well as resistance to ceftioxin (FOX 30µg). The *mecA* gene primarily encodes the penicillin-binding protein (PLP2a) which is responsible for this type of antimicrobial resistance. Community-acquired MRSA is genetically distinct from hospital-acquired MRSA by the presence of a small type of SCCmec and the frequent production of Panton- Valentine leukocidin. The emergence of community-acquired MRSA is related to the inappropriate use of antibiotics and domestic animals as a permanent reservoir [22]. In Egypt, MRSA has been characterized in 76.6% and 11.5% of hospital and community *S. aureus* strains, respectively [22]. A decrease in MRSA prevalence was observed in various European countries between 2011 and 2015 with a European average of 17% among *S. aureus*. In Switzerland, MRSA represents 7.5% of *S. aureus* [23].

The study of antibiotic resistance of 3GCREB isolated in our laboratory has shown high rates of co-resistance to fluoroquinolones (73.1% in hospital and 68.3% in the community) and gentamicin (more than 60% of cases). Resistance to imipenem among these strains was recorded in both hospital (14.5%) and community settings (6.6%). These levels of resistance have become alarming because resistance to carbapenems in these strains can lead to therapeutic impasses as these molecules are often a last resort.

Non-fermentative Gram-negative bacilli are known to have natural resistance to several families of antibiotics. Co-resistance rates to other antibiotic families are very high among our *A. baumannii* and *P. aeruginosa* strains. However, colistin retains its activity on these strains and is therefore the drug of choice for the treatment of multi-resistant *A. baumannii* and *P. aeruginosa* infections, despite its side effects, particularly tubular toxicity, which is the main potential complication, mainly in intensive care patients who frequently have a combination of renal stress factors [21].

Regarding MRSA, the rates of associated resistance concern mainly fusidic acid (49.6%) followed by norfloxacin (39.1%) and gentamicin (34.4%). Glycopeptides still have a good activity on our MRSA strains: only 2% of our strains were of decreased sensitivity to vancomycin. Therefore, they are molecules of choice in the treatment of MRSA infections thus continuous monitoring of the sensitivity of these strains to glycopeptides is compulsory.

Apart from MRSA, whose frequency has been decreasing in recent years, the frequency of MDR infections is increasing. Over the five years of the study, we noticed that the overall trend for MDR is rising. For MRSA, their isolation remains low and steady around 0.3 per 1000 HD since 2016 unlike 3GCREB where incidence density rates were higher in 2020 compared with 2016 (2.1 versus 2.5 per 1000 HD).

Moreover, the frequency of hospital-acquired multidrug-resistant infections in ICUs is the highest (38.6% in the AN-REA department and 27% in the MED-REA department) and this is related to the presence in the patients of immunosuppression, underlying comorbidities, long duration of hospitalization before the infection, recent surgery. But the main risk factor remains the exposure of resuscitated patients to broad spectrum antibiotic therapy.

Multi-Drug Resistant Bacteria are not easily transmissible unless certain factors concur: usually a combination of host susceptibility and virulence of the microorganism involved. Means of controlling the spread of these germs must be established in order to keep the prevalence below the epidemic threshold, and the spread can only be prevented if all institutions carry out joint interventions. The control of MDR infections requires a comprehensive approach, including strategies for the identification of risk factors, early detection and identification of resistant organisms, as well as the implementation of infection prevention strategies. The fight against multi-resistance to antibiotics needs not only a rationalization of antibiotic use in humans but also a drastic reduction in the use of antibiotics in veterinary medicine. This

fight also requires the allocation of sufficient resources for research into new therapeutic means, namely nanomedicines and phagotherapy.

The emergence of MDR in hospital as well as in community settings is alarming and thus is particularly due to deficiency in infection control practices and prevention policies. The main objective of prevention is to prevent infections, to maintain an optimal antimicrobial treatment and thus preserve the quality of care. This prevention is based on simple but essential actions, essentially on the reinforcement of hygiene measures as hands play a central role in the transmission of potential pathogens, the screening of patients carrying MDR and their isolation in order to avoid cross transmission between patients. However, any prescription of antibiotics must be rational and must take into account the local epidemiology.

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