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Original Research Article

Bacteriological Profile of Urinary Tract Infections at the Avicenne Military Hospital in Marrakech

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Abstract

Urinary tract infection is the attack of a tissue of the urinary tract by one or more micro-organisms. It is a major public health problem. The objective of this work is to propose, based on updated data, the microbial ecology of urinary tract infection at the Avicenne Military Hospital in Marrakech, and to follow the antibiotic sensitivity profile of uropathogenic bacteria. This is a retrospective descriptive study over 4 years from January 2014 to December 2018, which was conducted on urinary cytobacteriological examinations from hospitalized patients and outpatients, treated at the microbiology laboratory of the Military Hospital Avicenne of Marrakech. Of the 17607 ECBUs that were examined, the diagnosis of urinary tract infection was retained in 2349 (13%). 75% of the ECBUs came from hospitalized patients and 25% from outpatients, with a sex ratio of 1.1. The analysis of the ECBU showed that Enterobacteriaceae constituted 80% of the positive urine isolates, with a predominance of *Escherichia coli* (62%), followed by *Klebsiella pneumoniae* (13%). The reading and interpretation of the antibiograms showed that *Escherichia coli* was resistant to aminopenicillin associated with clavulanic acid in 51% of the cases against 55% for *Klebsiella pneumoniae*. The resistance of enterobacteriaceae to fluoroquinolones is about 33% for *Escherichia coli*, 30% for *Klebsiella spp*, while for the Trimmethoprim+Sulfamethoxazole combination more than half of the strains were resistant. On the other hand, aminoglycosides still have a good activity profile on enterobacteriaceae. The prevalence of BMR is 6.5%, represented by enterobacteriaceae producing extended spectrum betalactamases (ESBL) isolated in 89% of cases, with a predominance of *Escherichia coli* (52%) followed by *klebsiella pneumoniae* (22%) and *Enterobacter cloacae* (16%). Then the ceftazidime-resistant *Pseudomonas aeruginosa* (PARC) occupies the 2nd place with 5%, and finally methicillin-resistant *Staphylococcus aureus* (MRSA) and imipenem-resistant *Acinetobnacter baumanii* (ABRI) which occupy the 3rd place with rates at 3%. These BMR constitute a worrying problem, hence the need for rigorous application of hygiene rules and rational prescription of antibiotics. The knowledge of bacteriological profiles and the use of targeted antibiotic susceptibility testing will allow a management adapted to each hospital context.

Keywords: Urinary tract infection, uropathogenic bacteria, antibiograms.

INTRODUCTION

Urinary tract infection (UTI) is the aggression of a tissue of the urinary tract by one or more microorganisms generating an inflammatory response and symptoms of varying nature and intensity depending on the terrain. It is a frequent reason for consultation and a major public health problem [1]. The frequency of urinary tract infections is estimated at 150 million cases per year worldwide [2].

The cytobacteriological examination of urine remains the key examination for the positive diagnosis of this infection.

The emergence of multidrug-resistant bacteria (MDR) involved in UTIs limits the choice of antibiotics, hence the importance of adequate bacteriological examinations and appropriate antibiotic therapy [3].

The objective of this work is to propose, based on updated data, the microbial ecology of UTI, and to

follow the antibiotic susceptibility profile of uropathogenic bacteria, in a context of changing epidemiology of antibiotic resistance.

MATERIAL ET METHODS

We conducted a retrospective descriptive study over a period of 4 years (from January 1, 2014 to December 31, 2018), on 17607 urinary cytobacteriological examinations from inpatients and outpatients, done in the microbiology laboratory of the Avicenne Military Hospital in Marrakech. The samples are taken and collected in the concerned services and then sent to the laboratory, or directly collected at the laboratory for outpatients in compliance with the GBEA (guide to the correct execution of analyzes). Cyto-bacteriological examinations (ECBU) are carried out by traditional or automated techniques. The culture is done on agar plate.

For each urine received in the laboratory we realized a macroscopic examination, a microscopic examination and a bacteriological culture.

The antibiotic susceptibility test was done by automated technique (Phoenix 50 BectomDeckinson) and the interpretation of the antibiotic susceptibility test was done according to the recommendations of the EUCAST (European Committee on Antimicrobial Susceptibility testing). The statistical exploitation of the results was done on Excel.

RESULTATS

During the study period, out of the 17607 ECBUs examined, 2349 met the criteria for UTI, with a positivity rate of 13%.

Of the 2349 positive UTIs, 75% were from hospital patients and 25% from ambulatory consultants.

The female sex was the most affected with a rate of 1214 (52%) against 1135 (48%) for the male sex,means a sex ratio F/H of 1.1 (Figure 1).

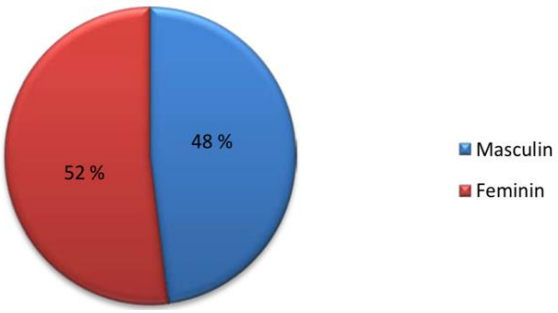

Figure 1: Distribution of urinary tract infection by gender

During our study, the bacterial species identified showed a predominance of Enterobacteriaceae with a rate of 80% (Figure 2), represented essentially by *Escherichia coli* (71%), followed by *Klebsiella pneumoniae* (15%), then *Enterobacter cloacae* (5%).

Non-fermentative BGN constitute 5% of isolated bacteria. They are mainly represented by *Pseudomonas aeruginosa* which is by far the most represented species (65%) as well as *Acinetobacter baumannii* (35%).

Gram-positive cocci represent 15% of the bacteria isolated and are distributed as follows: Streptococcus agalactiae (B) 32%; 20% of *Staphylococcus aureus*, the coagulase negative Staphylococci 20%.

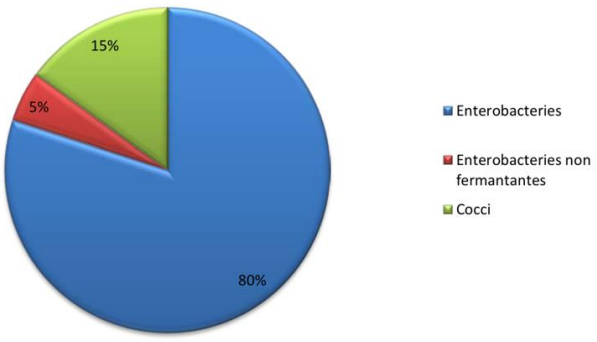

Figure 2: Distribution of uropathogenic germs according to bacterial species

The reading and interpretation of the antibiograms showed a resistance of *Escherichia coli* mainly to amoxicillin (68%) and to amoxicillin and clavulanic acid (51%). A varied resistance rate for the cephalosporin family: 14.7% for cefixime, 10% for cefotaxime and 8% for ceftazidime. A resistance rate to ciprofloxacin of 33%, and a low rate of resistance to aminoglycosides: 5% to amikacin and 12% to gentamicin (Figure 3).

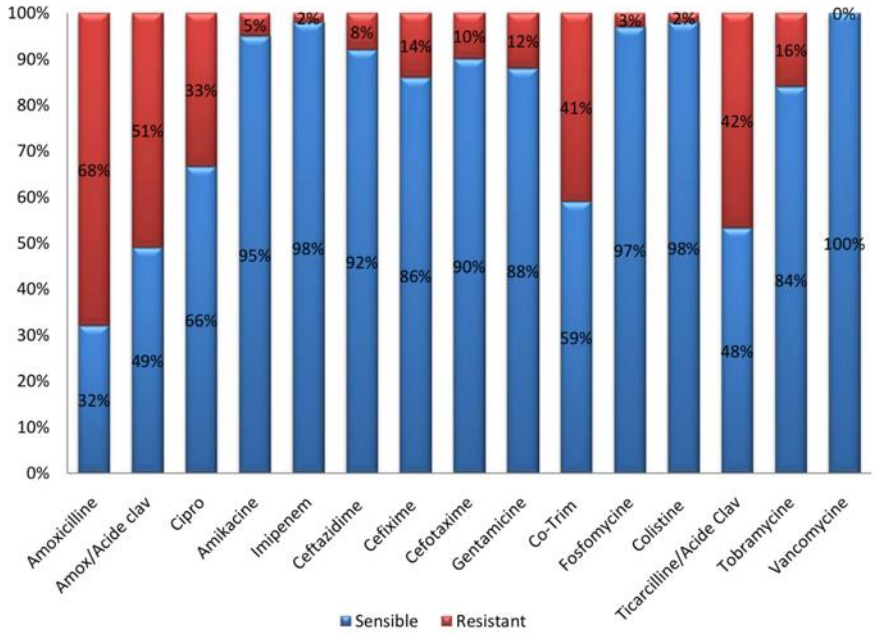

Figure 3: Susceptibility profile of Esherichia coli isolates to major antibiotics

Regarding the resistance of *Klebsiella pneumoniae* to antibiotics, we noticed a resistance to ceftazidime in 23% of cases and to cefotaxime in 22% of cases. A very low rate of resistance to the aminoglycoside family with 2% for amikacin and 15% for gentamicin and a rate of resistance to imipenem is 6% (Figure 4).

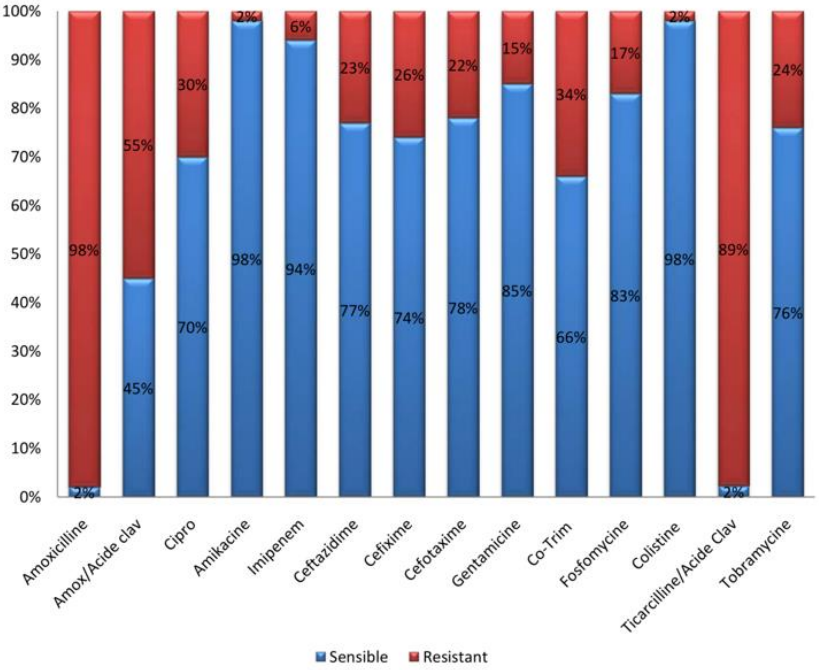

Figure 4: Susceptibility profile of Klebsiella Pneumoniae isolates

Resistance spectrum analysis of *Acinetobacter baumannii* showed resistance to ceftazidime in 25% of cases, to imipenem in 19% and to amikacin in 14% of cases. No resistance to colistin was noted.

Resistance to ceftazidime affecting *Pseudomonas aeruginosa* concerned 16% of cases. A varied rate of resistance to the aminoglycoside family with 10% for amikacin and 20% for gentamicin. A rate of 10% to imipenem. Concerning *Staphylococcus aureus*, the rate of resistance to oxacillin is 16.5%, 12% of resistance to cefoxitin and 33% of resistance to gentamicin.

The prevalence of MRB is 6.5%. They are represented by Enterobacteriaceae (EBLSE) which were isolated in 89% of cases (n=136), with a predominance of *Escherichia coli* (52%) followed by *Klebsiella pneumoniae* (22%) and *Enterobacter cloacae* (16%).

Ceftazidime-resistant *Pseudomonas aeruginosa* (PARC) is in second place with 5% (n=7), Finally, methicillin-resistant *Staphylococcus aureus* (MRSA) and imipenem-resistant *Acinetobacter baumanii* (ABRI) occupy the 3rd place with 3% (n=5).

DISCUSSION

Urinary tract infection (UTI) represents one of the main reasons for consultation, leading to the intensive use of antibiotics, with the consequence of increasing the cost of care and the selection of multi-resistant strains in both hospital and community settings [4].

Among the cytobacterioligical urine exam that arrived in our laboratory during the study period, the positivity rate of the urine examined was 13%. This rate is identical to that found at the Hassan II University Hospital of Fez in 2015 (13%), unlike a study conducted at the Hospital of Specialties of Rabat or the rate was higher (23%) [5, 6].

Rates closer to the order, 11% and 16% were reported by studies conducted respectively at the Mohammed V Military Hospital of Instruction (HMIMV) of rabat and the Moulay-Ismail Military Hospital of Meknes (HMMIM) [7, 8].

In our study, we counted 52% of female patients and 48% of male patients, means a Sex-ratio F/H= 1.1, which is in perfect agreement with the data in the literature both nationally and internationally: a Sex-ratio F/H of about 2 in an American study, 1.48 in Algeria and Mauritania in 2016, and 1.3 for the HMIMV of Rabat for the 2014 study [9-12].

The female predominance is confirmed by the study carried out in France in 2014 on 1223 ECBU, which found a frequency of UTI of 81% in women [13].

The epidemiological profile of the germs isolated in our study shows a clear predominance of Enterobacteriaceae which represented 80% of the isolates. At the head of the line, we find *Escherichia Coli* with a frequency of 71%, followed by *Klebsiella spp* with a frequency of 15%, *Enterobacter Cloa*cae with a rate of about 5% and then the Gram-positive cocci represented 15% of isolates, of which 32% were *Streptococcus agalactiae* and 21% of *Staphylococcus Aureus* and 20% of coagulase-negative Staphylococci and 19% of Enterococcus faecalis. Non-fermenting Gram-negative bacilli represented 5% of the total number of isolates, including 65% of *Pseudomonas Aeruginosa* and 35% of *Acinetobacter Baumanii*. Our results are similar to those found at the HMIMV of Rabat in 2014 and at the University Hospital of Fez in 2016 where *Escherichia coli* was predominant with respective rates of 56% and 63%, followed by *Klebsiella pneumoniae* with rates of 16% and 17%, the other species of enterobacteria presented only a small percentage in both studies [5, 12].

These data are also comparable to the results of the hygiene laboratory of Constantine in Algeria and the prospective study conducted in 3 medical analysis laboratories in the city of Nouakchott in Mauritania, [2] according to which the most frequently identified germs are: *Escherichia coli* at the top of the list with a rate of 64% in both studies, followed by *Klebsiella pneumoniae* (15% and 24%), *Proteus mirabilis* (5.1. 9%) and *Staphylococus aureus* (1%,5%) [10, 11].

Our results are similar to several European studies, as those of Mathai et al, and Grude et al, who also found a predominance of *Escherichia coli* with respective rates of 46.9% and 56.7% [14].

A 2016 French study on 1119 ECBU also showed that *Escherichia coli* were predominant with a frequency of 73%, followed by *Enterococci* at 7%, and *Klebsiella pneumoniae* at 6%. More rarely, *Proteus* was found at 3.5%, *Staphylococci* at 1%, *Streptococcus B* at 2% and *Pseudomonas aeuroginosa* infections represented 2% of isolates. Finally, various enterobacteria (*Citrobacter spp*, *Enterobacter spp*, *Providencia Rettgeri*, and *Shigella*) represented 4.5% of infections [15].

There is a high rate of resistance to ampicillin, which varies between 57.7% and 89.8% depending on the study, in our study we found 68% of resistant strains.

For the amoxicillin + clavulanic acid the resistance rate found in our study is 51%, a high level of resistance, compared to the one found in France in 2016 which is 10%, while in Morocco several studies have shown a high resistance to aminopenicillins + clavulanic acid including the HMIMV (32%), the Hospital of Specialties of Rabat (HSR) (65%) and the Hassan II University Hospital of Fez (50%) [5, 7, 15, 16].

This high rate of resistance can be explained by the abusive use of this antibiotic in our health structures but also by self-medication.

As for the resistance of this bacterial species to cephalosporins, the rate of resistance to cefotaxime found in our study is 10%. This rate is very close to that reported by the study conducted at HMIMV (12%) and HSR (18%), as well as those of some foreign hospitals such as those in Algeria (9%) and Mauritania (18%). On the other hand, a lower rate of resistance was reported by a French study conducted in 2016 (4.5%) [7, 6, 10, 11, 15].

The emergence of strains resistant to cefixime, which is one of the most active antibiotics on enterobacteria, is increasingly observed.

In our study, the rate of resistance of *Escherichia coli* to this antibiotic is 14%, contrary to what has been shown by other studies, which found a rate of resistance lower than 5% [16-18]

For the combination Trimethoprim + Sulfamethoxazole, the resistance of *Escherichia coli* is between 34.4% and 60% depending on the country, the rate found in our study is 48.1%, This result is comparable to the one found at the Hospital of Specialties in Rabat, the University Hospital of Fez and the HMIMV where the rates recorded were respectively 48%, 60% and 35% [5-7].

In our study, the rate of resistance of *Escherichia coli* to ciprofloxacin is 33%, a result close to that reported by Hailaji (28%).

The analysis of the resistance profile of *Klebsiella pneumoniae* strains to the different antibiotics showed a C3G resistance rate of 22%. This rate is very close to those reported in the study carried out at the IBN SINA University Hospital (25%) [19]. Higher rates of resistance were reported by the HSR (41%) and the HMIMV (46%) and the University Hospital of Fez (32%) [19, 6, 7, 5].

At the African level, Algeria and Tunisia report low rates of resistance of around 5 and 12%, however other countries such as Mauritania report rates exceeding 35% [10, 20, 11].

As for the resistance to Ciprofloxacin, the rate found in our study is 34%. This rate is very close to those reported in the studies carried out at the University Hospital of IBN SINA (24%) and the Hospital of Specialties of Rabat (40%), as well as those of some foreign hospitals such as those of Algeria (20%), and Mauritania (33%) [19, 6, 10].

For the combination Trimethoprim + Sulfamethoxazole, the rate found in our study is 34%, this rate is very close to the one found at the University Hospital of Fez (38%) and to the study done in Tunis (32%), other studies report higher rates such as Nouakchott and HSR where the resistance rates are higher than 50% [5, 20, 11, 6].

It can be concluded that *Klebsiella spp* has experienced a significant emergence of resistance to the antibiotics tested apart from fosfomycin and amikacin, which still have good activity.

The resistance of *Pseudomonas aeruginosa* occupies an important position in the problem of urinary tract infections. Analysis of its resistance profile has shown that it is highly resistant, in all studies, to most antibiotics [21]. As for the aminoglycosides, we note that amikacin has the lowest resistance rate of around 10%, whereas it is 20% for gentamicin.

These rates are similar to those reported by the HMIMV with a percentage of resistance of 14% for amikacin and 20% for gentamicin. However, the study carried out at the University Hospital of Fez reported a low rate of resistance to amikacin of around 3.3%.

These rates of acquired resistance to this family of antibiotics remain comparable to those of European countries where the rate of resistance to Gentamicin is 30 to 50%, that of Tobramycin 20 to 30% and finally 10 to 30% for Amikacin, the most constantly active molecule [15, 21].

In our study we found a resistance to ciprofloxacin at 40% while it is 66% for levofloxacin, this result is very high compared to the resistance rates reported in other studies such as Fez and Rabat where the percentage found is 18% and 23% [5, 12].

At the African level, a study carried out in 2015 in the town of Tébessa in Algeria found a rate of resistance of *Pseudomonas aeruginosa* to ciprofloxacin of 14% [22].

The resistance of *Acinetobacter baumanii* to many antibiotics is frequent. This resistance is found in certain strains in the form of multidrug resistance to β-lactamines and aminoglycosides. It is due to the production of β-lactamases and aminoglycoside-modifying enzymes [23].

In our study, the rate of *Acinetobacter baumanii* resistant to imipenem (ABRI) is 19%, this rate is comparable to that of the IBN SINA hospital which is 18%, nevertheless the HSR recorded a rate of resistance to imipenem at 75%, but this rate may be overestimated given the small number of strains [19, 6]. In France and Tunisia the rate of ABRI isolated in ECBU does not exceed 5% [15, 20].

The resistance to aminoglycosides is variable, it is 40% for Gentamicin and 14% for Amikacin. These rates are close to those found in some Maghreb countries such as Tunisia and other developing countries as well as some European countries such as France where a study was conducted at 4 university hospitals in Marseille and found a resistance rate of 58% to gentamicin and 54% to amikacin [24].

As for the resistance of this bacterial species to Ciprofloxacin, the rate found in our study is 57%. This rate is very close to that reported in the study conducted at the IBN SINA University Hospital (58%) and the HMIMV (67%), as well as those of some foreign hospitals such as those in Tunisia (53%) and France (68%) [19, 7, 20, 15].

In our study, 44 isolates (10.3%) of positive bacteriological samples correspond to strains of *staphylococcus aureus.*

Resistance to Cefoxitin in MRSA is about 12%. This rate is close to that reported by the HSR (15%), the CHU IBN ROCHD (10%) and by the Resaux Medqual (15%), nevertheless these rates remain low compared to that observed by the HMIMV in 2014 or the rate of MRSA was 23% [6, 25, 26, 12].

No resistance to glycopeptides (Vangomycin, teicoplanin) has been found. Two other antibiotics: Tetracycline and Trimethoprim + Sulfamethoxazole quite used in Morocco are more or less active with resistance rates of 35% and 10% respectively.

A study carried out at the HMIMV in Rabat showed 39.1% resistance to tetracycline and 15% to rifampicin. These results are similar to those reported in other studies in Africa [10, 11, 19, 27].

According to our study, the overall frequency of isolation of ESBL-producing Enterobacteriaceae is 14% (fig.42). This rate is comparable to that reported by Hlaiji (12.8%) [11]. European countries report low rates of EBLSE for example in France in 2016 the rate found is (4.2%), in Germany (2. 6%) and Great Britain (2%) [14, 15], however our rate is lower compared to those found in Tunisia (30.8%) or in the HSR 28% [6, 5], the HMIMV (25%) and in the CHU Ibn Rochd of Casablanca 19% [20, 6, 6, 28], The differences observed between these different countries are related to antibiotic therapy and in particular the use of broad-spectrum antibiotics as well as the means implemented to control infections, which vary from country to country and even from region to region [29].

In our study *Escherichia coli* represents 57% of ESBL-secreting Enterobacteriaceae, followed by *Klebsiella pneumoniae* (22%) and *Enterobacter cloacae* with 18%. These rates remain close to those reported in Mauritania 2016 where these germs represent successively 56%, 41%, 2%, and in France in 2016, with respective rates of 90% and 10% [11, 15]. However, the HSR study reports a predominance of *Klebsiella pneumoniae* at 40% followed by *Esherichia coli* at 30% and *Enterobacter cloacae* at 16.7% [6]. Our 14% prevalence of EBLSE should draw attention to the extent of dissemination of these strains in the absence of control and prevention measures, especially since the majority of our patients were ambulatory consultants. This would be related to the high prevalence of fecal carriage of EBLSE in our community patients. It is therefore clear that this type of strain is no longer the exclusive preserve of the hospital environment, as shown by the data in the world literature.

The prevalence of ceftazidime-resistant *Pseudomonas aeruginosa* (PARC) in our study is 15%, which is comparable to the rate found in France in 2015, which is 12.5% [30].

CONCLUSION

In Morocco, the study conducted at the Hospital of Specialties in Rabat found a rate of PARC to 30% while it is 11% at the military hospital of instruction Mohamed V in 2014, in Tunis the rate of PARC in 2010 is 23% [6, 12, 20].

Urinary tract infection remains a very frequent pathology throughout the world, and is one of the main reasons for consultation, microbiological explorations and antibiotic prescriptions, with consequences for the latter in terms of the cost of care and the development of bacterial resistance.

This retrospective study gave us an idea of the rates of antibiotic resistance in the main bacteria involved in urinary tract infections.

The bacterial ecology has not changed much in recent years, with *Escherichia coli* continuing to be the most common uropathogen. On the other hand, knowledge of the responsible bacteria is a valuable tool for the choice of first-line antibiotic therapy, which must be adapted to the site of the infection and the underlying terrain.

The appearance of increasingly frequent resistance in the classes of antibiotics prescribed as first-line treatment, particularly betalactam and

fluoroquinolones, has led to the widespread prescription of other molecules that are often more recent and/or have a broader spectrum, thus favoring the emergence of multi-resistant germs.

The isolation of these multi-resistant bacteria leads the clinician to an increasingly limited therapeutic choice. Thus, this alarming observation of multidrug resistance must lead practitioners to a rational prescription of antibiotics, preferably guided by the results of a correctly performed and interpreted antibiogram.

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