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Monitoring of the Evolution of Antibiotic Resistance in Urinary Tract Infection at the Mohamed VI University Hospital in Marrakech

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Abstract **Original Research Article**

Introduction: Urinary tract infections are a public health problem due to the excess mortality and the additional costs they entail. ***Objective:*** To monitor the evolution of antibiotic resistance of uropathogenic germs over the last three years in patients treated at the CHU Med VI of MARRAKECH. ***Materials and Methods***: Descriptive study carried out over a period of 3 years (from January 2018 to December 2020) including all urinary tract infections retained as meeting the criteria for microbiological and clinical infections in patients treated at the Mohammed VI University Hospital in Marrakech. ***Results:*** Out of a total of 37,394 ECBUs, the prevalence of UTI was 11% (n = 4275). The average age was 36 years, with a standard deviation of 25.9 years. The sex ratio M / F was 0.95. Uropathogenic germs were represented mainly by Enterobacteriaceae 78%. E. coli accounted for 66%. Enterobacteriaceae were resistant to third generation cephalosporins in 22% of cases, decreased sensitivity to Carbapenems in 7.2%, resistant to ciprofloxacin in 31%, to Cotrimoxazole in 42%, to Gentamicin in 17.5%, to Amikacin in 2%. Extended spectrum beta-lactamase production was 21%. Over the past three years, 895 multi-resistant bacteria have been identified, i.e. 23%. Klebsiella spp accounted for 41%. ***Conclusion:*** The results testify to the increased resistance of uropathogenic bacteria. Updated local studies are important to understand the state of play of bacterial ecology and resistance profiles in order to avoid treatment failures.

Keywords: Urinary tract infection, resistance, antibiotic.

INTRODUCTION

Urinary tract infections are the second leading cause of community-acquired bacterial infections and the leading cause of nosocomial infections, and account for up to 40% of all hospital acquired infections. They are characterized by their frequency but also by the variety of their clinical presentations, ranging from simple colonization to severe urinary tract infection with septic shock [1, 2].

Urinary tract infections are a real public health problem due to the excess mortality and the additional costs they entail, in particular with the growing emergence of strains resistant to antibiotics.

The problem of bacterial resistance arises in the face of the need to start early and effective probabilistic antibiotic therapy in order to reduce the risk of complications and kidney scarring, hence the importance of knowing the local microbial ecology and resistance profiles in order to guide the initial treatment [2, 3].

The objective of this study is to follow the evolution of antibiotic resistance of uropathogenic germs over the last three years in patients treated at the Hospital University Center Mohamed VI of MARRAKECH, to determine the most affected sectors of activity and to help orient the probabilistic antibiotic treatment of urinary tract infections in our context.

MATERIAL AND METHODS

This is a descriptive study carried out over a period of 3 years (from January 2018 to December 2020) including all the urinary infections retained as meeting the criteria for microbiological and clinical infections in patients treated at Mohammed VI University Hospital in Marrakech.

Each urine sample received at the laboratory was subjected to a cytobacteriological examination of the urine comprising:

- A direct examination to assess leukocyturia, hematuria, bacteriuria and the elements of

urine (crystals, kidney cells, etc.), performed by automated method (SYSMEX UF-1000i)
- A culture appreciating the positivity thresholds and the morphological and cultural characteristics of the germs
- An antibiogram studying the sensitivity of bacteria to antibiotics

The identification of the isolated strains was carried out by the PHOENIX 100 machine during the period 2018 and 2019 and from 2020 by the MALDI-TOF machine.

The antibiograms were carried out by PHOENIX M50 and the interpretation was carried out according to the standards of the Antibiogram Committee of the French Society of Microbiology (CA-SFM / EUCAST).

The data collected focused on age, gender, services, isolated germs and antibiotic resistance profiles.

Data processing was carried out using Excel software.

RESULTS

Out of a total of 37,394 cytobacteriological urine exams treated in the Microbiology Department during this period, the prevalence of urinary tract infection was 11% all sectors of activity combined (n = 4275).

The average age was 36 years, with a standard deviation of 25.9 years. The sex ratio M / F was 0.95.

Culture was sterile in 54% of patients (n = 20,056), poly microbial in 35% of patients (n = 13,055) and 46% of patients had significant leukocyturia.

Uropathogenic germs were mainly represented by Enterobacteriaceae, ie 78% of all germs found (n = 3335). The remainder is divided between Candida spp (8%), 5% Enterococci spp, 3% Pseudomonas aeruginosa and 2% Acinetobacter baumanii.

E. coli accounted for 66% of the Enterobacteriaceae isolated, 24% of Klebsiella pneumoniae and 6% of Enterobacter cloacae.

Of these documented urinary tract infections, 41% came from patients treated in emergency rooms, 24% from medical services, 13% from external patients, 8% from surgical services, 7% from pediatrics and 5% from various intensive care units.

Enterobacteriaceae were resistant to third generation cephalosporins.

In 22% of cases (n = 755), decreased sensitivity to Carbapenems in 7.2% (n = 241), resistant to ciprofloxacin in 31% (n = 1022), to Cotrimoxazole in 42% (n = 1323), Gentamycin in 17.5% (n = 540), Amikacin in 2% (n = 68).

Extended spectrum beta-lactamase (ESBL) production in isolated Enterobacteriaceae was 21%

Table I: Percentage of resistance to antibiotic families in Enterobacteriaceae susceptible to C3G versus Enterobacteriaceae producing ESBL

	% resistance of ESBL Enterobacteriaceae	% resistance of Enterobacteriaceae Sensitive to C3G
Ciprofloxacin	67,8	20
Cotrimoxazol	76	32
Gentamicin	62	5
Amikacin	7	0,8

Pseudomonas aeruginosa was resistant to Ceftazidime in 16% of cases and Acinetobacter baumanii in 92%.

Over the past three years, 895 multidrug-resistant bacteria have been identified, ie 23% of all uropathogenic bacteria isolated. Klebsiella spp accounted for 41% of all of these identified MRBs.

There were 163 MRBs in medical services, out of a total of 817 positive cultures, that is to say a percentage of 20%, 29% of these MRBs were isolated in nephrology service.

In the surgical department, 144 MRBs were isolated, representing a percentage of 34% of all mono-microbial cultures. Of which 58% in urology and 20% in general pediatric surgery.

In gyneco-obstetrics, there were 9 MRBs, ie a prevalence of 26.4% in the gynecology-obstetrics departments.

In intensive care units, there were 53 MRB, i.e. a prevalence of 25% including 30% in surgical intensive care, 34% in gynecological intensive care and 17% in pediatric intensive care

In the emergency room, there were 292 MRBs representing a percentage of 15% of the total positive cultures from emergency rooms, of which 60% from

adult emergencies, and 40% from pediatric emergencies.

In pediatrics, there were 95 MRBs, i.e. a prevalence of 36%, of which 84% (n = 80) in pediatrics B and 16% (n = 15) in pediatrics A.

In the neonatal department, there were 58 MRBs, ie a percentage of 56%

Concerning samples from patients seen externally, there were 81 MRBs, ie a percentage of 15%.

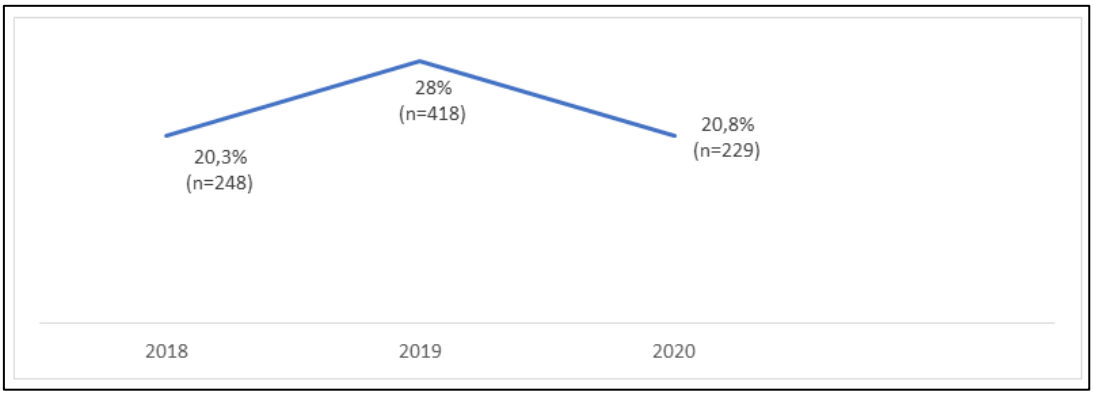

Figure 1: Evolution of the percentage of Uropathogenic BMRs over the three years (n = 895) at the Marrakech University Hospital

Table II: General distribution of Uropathogenic Germs isolated between 2018 and 2020 at the Marrakech University Hospital by sector of activity

Department	Prevalence of urinary tract infection (%)	Main isolated germs (%)	Enterobacteriaceae (%)
Medicine	19 (n=817)	Enterobacteriaceae : 77 (n=626) Candida spp :7 (n=63) Enterococcus spp : 5% (n=44) Pseudomonas aeruginosa :3 (n=23) Acinetobacter baumanii : 3 (n=24) S. aureus : 2% (n=14) Other : 2% (n=23)	E. coli : 66,5 (n=416) Klebsiella spp : 25 (n=157)
Surgery	10 (n=427)	Enterobacteriaceae :65 (n=277) Candida spp :10,7 (n=46) Enterococcus spp : 6,5% (n=28) Pseudomonas aeruginosa :6 (n=27) Acinetobacter baumanii : 6,5 (n=28) S. aureus : 1,4 (n=6) Other : 3,5 (n=15)	E. coli : 53 Klebsiella spp : 31
Obstetric-gynecology	0,9 (n=34)	Enterobacteriaceae : 91 (n=31) Candida spp : 3 (n=1) Pseudomonas aeruginosa :3 (n=1) Acinetobacter baumanii : 0 Enterococcus spp : 3 (n=1) S. aureus : 0	E. coli : 64,5 (n=20) Klebsiella spp : 16 (n=5) Enterobacter spp :13 (n=4)
Intensive care	4,9 (n=209)	Enterobacteriaceae : 44,5 (n=93) Candida spp :34,5 (n=72) Enterococcus spp : 3,5(n=7) Pseudomonas aeruginosa :3 (n=6) Acinetobacter baumanii : 10,5 (n=22) S. aureus : 2 (n=4) Other : 2 (n=4)	E. coli : 52 (n=48) Klebsiella spp :32 (n=30) Enterobacter spp :12 (n=11)
Emergency room	44,5 (n=1901)	Enterobacteriaceae : 84 (n=1598) Candida spp : 6 (n=109) Acinetobacter baumanii : 0,7 (n=13) Pseudomonas aeruginosa : 2 (n=42) Enterococcus spp : 3,5 (n=68) S. aureus :1,6 (n=32) Other : 2 (n=39)	E. coli : 74 (n=1175) Klebsiella spp :19 (n=298) Enterobacter spp :4 (n=62)

Pediatrics	6,2 (n=264)	Enterobacteriaceae: 68 (n=180) Candida spp : 15 (n=40) Acinetobacter baumanii : 0 (n=0) Pseudomonas aeruginosa : 3 (n=8) Enterococcus spp : 10 (n=27) S. aureus : 1,5 (n=4) Other 2 (n=5)	E. coli : 45 (n=82) Klebsiella spp :45 (n=82) Enterobacter spp :3 (n=4)
Neonatology	2,4 (n=103)	Enterobacteriaceae : 81,5 (n=84) Candida spp : 8,7 (n=9) Acinetobacter baumanii : 0 (n=0) Pseudomonas aeruginosa : 0 (n=0) Enterococcus spp : 8,7 (n=9) S. aureus : 1 (n=1)	Klebsiella spp :52 (n=44) Enterobacter spp :26 (n=22) E. coli : 16,6 (n=14)
External patients	12 (n=520)	Enterobacteriaceae : 86 (n=447) Candida spp : 2,5 (n=13) Acinetobacter baumanii : 1 (n=6) Pseudomonas aeruginosa : 2 (n=11) Enterococcus spp : 5,3 (n=28) S. aureus : 1 (n=5) Other : 2 (n=10)	E. coli : 72 (n=323) Klebsiella spp :19 (n=85)
Total	99,9 (n=4275)	Enterobacteriaceae : 3335 Candida spp : 353 Acinetobacter baumanii : 93 Pseudomonas aeruginosa : 118 Enterococcus spp : 212 S. aureus : 68 Other : 94	

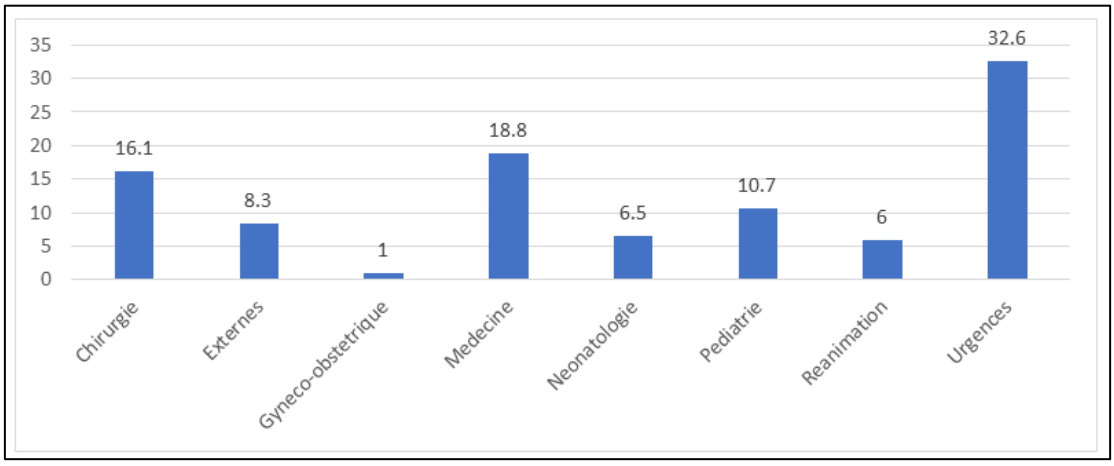

Figure 2: Percentage distribution of Uropathogenic MRBs at the Marrakech University Hospital according to departments (n = 895)

Table III: Percentage of multiresistance within the species in Gram-negative Uropathogenic bacteria isolated between 2018 and 2020 at the Marrakech University Hospital

Department	% of strains resistant to C3G in EBs	% of SDC strains in EBs (%)	% Multi resistance in Pseudomonas	% Multi resistance in A.baumaanii
Medicine	21 (n=132)	8,4 (n=53)	22 (n=5)	66,6 (n=16)
Surgery	40 (n=112)	18 (n=50)	44 (n=12)	71 (n=20)
Gyn-obstetrics	29 (n=9)	25,8 (n=8)	0	0
Intensive care	32 (n=30)	9,7 (n=9)	0	82 (n=18)
Emergency room	15,6 (n=249)	4,2 (n=68)	40 (n=17)	69 (n=9)
Pediatrics	47 (n=85)	9 (n=16)	50 (n=4)	0
Neonatology	68 (n=57)	19 (n=16)	0	0
External patients	14 (n=81)	4,7 (n=21)	36 (n=4)	66 (n=4)
Total	N=755	N=241	N=42	N=67

DISCUSSION

Urinary tract infection is one of the main reasons for consultation, microbiological tests and antibiotic prescriptions with their consequences on the cost of care and the development of bacterial resistance. The frequency of these infections is estimated at 150 million cases per year worldwide and the proportion of antibiotics prescribed to treat urinary tract infections represents 12% of antibiotic prescriptions [3-5].

Knowledge of local bacteriological data is essential for the proper initial treatment of patients and to minimize the risk of complications related to urinary tract infections, particularly in patients at risk of complication (organic or functional abnormality of the urinary tract, male sex, pregnancy, elderly, severe immunosuppression, severe chronic renal failure) [6].

Epidemiologically, the results are consistent with the literature regarding the predominance of women, this can be explained by the anatomy of the female genital system (short urethra, proximity between urethral and anal orifice) and certain physiological states such as pregnancy that promotes sagging muscles [7, 6].

The predominance of Enterobacteriaceae, mainly E. coli is also consistent with the data in the literature, except for the neonatology department where there is a predominance of Klebsiella spp, this result is consistent with a study conducted within the same department revealing the predominance of Klebsiella spp in neonatal infections with a percentage of 50.8%, this predominance decreases with advancing age in favor of E. coli [8-12].

The high rate of non-fermentative BGN in intensive care units compared to other wards, as well as the high rate of resistance to CAZ are also consistent with the data in the literature. A study carried out in the intensive care unit of the CHU Med VI in Marrakech showed that 33% of the germs isolated were non-fermenting BGNs, and that they were responsible for urinary tract infection in 8.35% of cases. A study carried out in Cameroon showed a resistance rate to CAZ of 69% [13, 14].

On all the studied samples, the prevalence of MRBs was 23% with Klebsiella spp leading. It was high in neonatology with a percentage of 56%, followed by pediatric departments 36%, these results agree with studies carried out in the same departments in 2014 and 2019 respectively [11, 12].

The lowest prevalence was observed in emergency rooms (15%), this can be explained by the fact that urinary tract infections seen in emergency rooms are mainly community-based.

MRB's prevalence in medical wards were 20%, including 29% in nephrology wards. This result is explained by the frequency of urinary invasive medical procedures, as well as by the patients' condition, which represents a risk factor for complication of urinary tract infections. This prevalence is higher in comparison with the data in the literature [15, 16].

In surgical departments, 58% of MRBs in surgical departments were in urology, with a prevalence within the department of 34%. This increase is due to the frequency of invasive urological maneuvers in the department, as well as the long hospital stay of the patients. This result is higher than the study conducted in 2018-2019 in the same department [8].

The same is true in pediatric visceral surgery where patients generally hospitalized in this department may present malformative uropathies leading to recurrent urinary tract infections with selection of resistant mutants. A Moroccan multicenter study showed that in 18.69% of urinary tract infections identified in the different hospital university centers, patients had an underlying malformative uropathy, and that 60% of UTIs in infants under one year old are related to malformative uropathies [17, 18].

Regarding the resistance profile of Enterobacteriaceae to C3G, it was 22% of the total isolates. The prevalence of enterobacteriaceae resistant to C3G was increased in neonatology 68%, in pediatrics 47%, in intensive care 34%, in emergency departments it reached 15%, these data are consistent with the literature [12, 19, 13, 14, 20].

The resistance of Enterobacteriaceae to Ciprofloxacin was 31%, to Cotrimoxazole 42%, these results agree with local data. They are lower than the sub-Saharan countries where resistance reaches 52.9% in Niger for Ciprofloxacin and 82.3% for Cotrimoxazole, and higher compared to the data collected in France where resistance to Ciprofloxacin is 10.5% and 21% Cotrimoxazole [21-23, 9, 14, 4].

Considering the emergence of resistance to Fluoroquinolones, which are valuable for their efficacy and bioavailability, it is currently recommended for the treatment of simple UTIs without risk of complications to use furans and Fosfomycin in the first lines in order to spare them [3].

CONCLUSION

The results of this study testify to the increased resistance of uropathogenic bacteria to different families of antibiotics, particularly in the pediatric population and in patients hospitalized for pathology of the urinary tract or who have undergone invasive urinary procedures.

The execution of a good quality sample, the clinical-biological comparison and the rationalized and guided use of antibiotics are essential to fight against excessive antibiotic therapy with the risk of selection of resistant mutants.

Updated local studies are essential to understand the state of play of bacterial ecology and resistance profiles in order to avoid treatment failures.

It is important to establish a collaboration between clinicians and biologists in order to set up personalized recommendations based on epidemiological and bacteriological data to improve therapeutic management and quality of care, particularly in services with patients at high risk of urinary complications.

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