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Epidemiology and Antibiotic Resistance of Enterobacteriaceae Isolated in Urinary Tract Infections at Oued Eddahab Military Hospital Agadir

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Abstract **Original Research Article**

Objective: Determine the current bacteriological profile of urinary tract infections and the antibiotic resistance of the main enterobacteria isolated in urine. ***Methods***: Retrospective study over a period of 18 months from January 1, 2022 to June 30,2023 including all urinary cytobacteriological examinations of patients hospitalized in the various departments of the Oued Eddahab Military Hospital in Agadir, as well as outpatients. ***Results***: Out of 4483 urine samples, 487 met the criteria for UTI (10.86% of total samples). The microorganisms were predominantly Enterobacteriaceae (421/487 86.44%). Of the infections, 75% originated from outpatients. The sex Ratio F/M was 1.35. E.Coli dominated the epidemiological profile for both inpatients and outpatients (63% vs. 77%). There was a high frequency of resistance to the main families of antibiotics, while quinolones, fosfomycin, nitrofurans, and aminoglycosides retained good activity. Resistance to third-generation cephalosporins through the production of extended-spectrum betalactamase was present in 09% of Enterobacteria. Finally, no resistance to imipenem and colistin was detected.

Keywords: Urinary tract infections, Retrospective study, cytobacteriological urine examinations.

INTRODUCTION

Urinary tract infection (UTI) is the attack of the urinary tree by one or more microorganisms, generating an inflammatory response and symptoms of varying nature and intensity, depending on the terrain, and very common in both inpatient and outpatient settings. It is the second most common site of community-acquired bacterial infection, after the respiratory tract and the leading site of nosocomial infections [1]. The bacteria most often implicated are enterobacteria, the natural hosts of the intestine and the environment (Escherichia coli, Proteus, Klebsiella). Escherichia coli (E. coli) accounts for 70-80% of bacteria isolated in urinary tract infections [2-4]. The study we propose concerns urine cytobacteriological examinations (ECBU) presenting UTI criteria collected in the Medical Biology Department of the Oued Eddahab Military Hospital Agadir over an 18-month period. This work includes a bacteriological study of the microorganisms isolated, as well as a antibiotic susceptibility to enable a better therapeutic approach.

MATERIALS AND METHODS

Location and Study Period

We conducted a retrospective study in the Medical Biology Department of the Oued Eddahab Military Hospital Agadir. It involved 4483 cytobacteriological urine examinations (ECBU), performed over an 18-month period from January 1, 2022 to June 30, 2023. Urine samples were taken from the hospital's various medical and surgical departments or from outpatients.

Bacteriological Analysis

Each urine sent to the Medical Biology Department underwent a routine urinary cytobacteriological examination (UCE) including:

- Uroculture with germ count (bacteriuria);

- Direct examination to assess leukocyturia and figurative elements in the urine (red blood cells, crystals, etc.).

Biological diagnosis of urinary tract infection was based on the classic Kass criteria:
leukocyturia greater than 10^4/ml and bacteriuria greater than 10^5 CFU/ml. Depending on clinical context, the bacteriuria thresholds of 10^3 CFU/ml for coliform cystitis and 10^4 CFU/ml for enterobacteria, more commonly involved in nosocomial urinary tract infections. Bacteria were identified on the basis of their culture and biochemical characteristics (API 20E strips, bioMérieux).

Antibiotic Susceptibility Testing

Antibiotic susceptibility was determined by diffusion method on Müller Hinton medium. The interpretation was carried out according to the standards of the Antibiogram Committee of the French Society of Microbiology (CA-SFM) [5]. Extended-spectrum ß-lactamase (ESBL) detection was performed using the synergy test between the following antibiotics: amoxicillin-clavulanic acid, aztreonam, cefotaxime, ceftazidime and cefepime or cefpirome.

Data Collection and Processing

For each patient, various parameters were collected from the registers of the Medical Biology Department of the Military Hospital Oued Eddahab Agadir: name, date of sampling, origin of sampling (outpatient/inpatient, department, etc.), bacteriological profile of urinary tract infection and antibiotic resistance status. Data collection was followed by data entry on Excel 2013. All data were analyzed using SPSS software. The results were presented as percentages.

RESULTS

During the study period, we received a total of 4483 urine samples, 487 of which met the positivity criteria for urinary tract infection (10,86%). 421 strains of Enterobacteriaceae were found, corresponding to 86,44% of isolates. These UTIs involved patients hospitalized in theurology, nephrology, internal medicine departments (25%) and, above all, outpatients (75%). The sex ratio (F/M) was 1.35. The Escherichia coli species dominates the epidemiological profile for both hospital and community-acquired Enterobacteriaceae.

In fact, among the 316 strains of enterobacteriaceae isolated from consultant patients, Escherichia coli was the predominant species (77%), followed by Klebsiella spp. (11%) and various other species (12%): Proteus mirabilis, Enterobacter cloacae. On the other hand, among the 105 strains of Enterobacteriaceae isolated from hospitalized patients, Escherichia coli still represented the predominant species (63%), followed by Enterobacter cloacae (22%), Klebsiella spp (11%) and various other species (04%) : Proteus mirabilis, Citrobacter Freundii.

Distribution of Enterobacteriaceae species in hospital and community settings are shown in Table 1. 09 % of Enterobacteria isolated were ß-lactamase extended-spectrum (ESBL) producers strain. Urology and Nephrology departments were the main source (58%), and the main species isolated were as follows: K.pneumoniae (67%), E. coli (22%), and E. cloacae (11%) for hospital strains and E. coli (67%), K. pneumoniae (33%) for community strains. Distribution of Enterobacteriaceae species ß-lactam extended-spectrum (ESBL) and the percentages of antibiotic resistance of Enterobacteriaceae isolated are shown in Tables 2,3.

Table 1 : Distribution of Enterobacteriaceae species in hospital and community settings

Enterocaecaeae species	Consultants	Hospitalized
Escherichia coli (309)	243	66
Klebsiella spp. (46)	35	11
P. mirabilis (26)	22	4
Enterobacter cloacae (33)	10	23
C. freundii (7)	6	1
Total (421)	316	105

Table 2 : Distribution of Enterobacteriaceae species ß-lactam extended-spectrum (ESBL) in hospital and community settings

Enterocaecaeae species	Consultants	Hospitalized
Klebsiella pneumoniae (21)	4	17
Escherichia coli (14)	8	6
Enterobacter cloacae (3)	0	3
Total (38)	12	26

Table 3 : The percentages of antibiotic resistance of Enterobacteriaceae isolated in hospital and community settings

Antibiotic	Community strains	Nosocomial strains
Amoxicillin	51	59
Amoxicillin + Clavulanic Acid	43	46
Cefotaxime	4	25
Ciprofloxacin	30	36
Gentamicin	7	13
Amikacin	1	3
Sulfamethoxazole + trimethoprim	38	48
Nitrofurans	6	10
Fosfomycin	13	18
Imipenem	0	0
Colistin (Acquired resistance)	0	0

DISCUSSION

The epidemiological profile of uropathogenic bacteria varies from region to region. As a result, knowledge of the local epidemiology and its evolution remains to choose an effective first-line antibiotic therapy suited to each region. In our series, urinary enterobacteriaceae were predominantly found in consultants (75%), as urinary tract infection is the second most common bacterial infection in the community, after respiratory tract infections. Among consultants, we found many female UTIs (F/M = 1.47). This is due to specific factors (short urethra, pregnancy...) [5]. In hospitalized patients, the difference was less marked (F/H = 1.06), because there are many common favouring factors (catheters, diabetes, etc.), and above all because of the demand from the urology department, where the majority of patients are men.

The Escherichia coli species dominates the epidemiological profile for both nosocomial (63%) and community-acquired (77%) enterobacteria, follow-up Klebsiella pneumoniae and Proteus mirabilis. The ascending pathophysiology of UTI and the heavy colonization of the perineum by enterobacteria of digestive origin, particularly Escherichia coli, combined with specific uropathogenic factors such as bacterial adhesins capable of binding to the urinary epithelium and prevent its elimination through bladder emptying, explain this predominance [5]. Klebsiella and Proteus secrete a urease that alkalinizes urine, whose naturally acidic pH prevents the proliferation of germs.

ß-lactam antibiotics are well distributed in the urinary tract. For this reason, they have long been widely used in the first-line treatment of uncomplicated community-acquired UTI. Currently, the increase in resistance to this family of family of antibiotics is worrying. Our hospital recorded a high rate of resistance to aminopenicillins (amoxicillin and ampicillin) of 59%, about the same as the rate reported in a study carried out at the Marrakech Military Hospital (65%) [7] and lower than that of the Meknes Military Hospital (85%) [8]. This increase resistance to amoxicillin has been noted worldwide, leading to the elimination of this molecule from the list of recommended probabilistic treatments for UTI [9]. The acquisition of resistance to AMC, an antibiotic with a very high prescription in Morocco, is a worldwide phenomenon reported at highly variable rates [10]. In our study, resistance to amoxicillin-clavulanate was 45%, similar to that in Marrakech (43%) [7], and lower than the rates found in the Meknes and Rabat studies [8-11], respectively 70 and 60 %. Because of this high level of resistance, these antibiotics are no longer the first choice for empirical treatment of uncomplicated UTIs. ESBL production in Enterobacteriaceae was observed in 38 strains, corresponding to a prevalence of 09%. This rate is similar to that observed in a study in Rabat [11], significantly lower than that of Meknes [8], and higher than that of Marrakech [7]. Fluoroquinolones occupy a privileged place among molecules in the treatment of urinary tract infections, particularly in the probabilistic treatment of acute treatment of acute uncomplicated cystitis in women [12].

As with any other antibiotic, the relationship between increased consumption of fluoroquinolones and the increase in bacterial resistance to these molecules is demonstrated [12]. The resistance rate of Enterobacteriaceae to ciprofloxacin was 32% in our hospital, 27% in Rabat [11], and 38% in Meknes [8]. Multivariate studies have identified risk factors for the acquisition of these resistances: recent prescription of quinolones in the preceding 6 to 12 months, residence in a nursing home, advanced age, recent hospitalization or an invasive urinary tract procedure [13, 14] .Our study shows that the aminoglycosides are among the most active antibiotics with resistance rates as low as 2 % for Amikacin. Gentamicin, on the other hand, shows an increase in resistance to this antibiotic, observed mainly in ESBL-producing strains of Enterobacteriaceae but still retains good activity (13%). The high rates of resistance of uropathogenic Enterobacteriaceae to Sulfamethoxazole trimethoprim reported in our study (48%) and in other Moroccan studies [1-8], argues in favor of the importance of antibiotic susceptibility testing before prescribing this molecule in our context. Nitrofurans are still of interest in the short treatment of lower UTIs, although they are less effective than other

molecules in vitro [15]. The sensitivity rates found in our study were high. The same is true of fosfomycin, an antibiotic that is not widely used due to its restricted indications for UTI. Prescribing these two molecules in towns and cities should therefore be encouraged, in order to minimise overuse of other antibiotic families, particularly fluoroquinolones [16]. On the other hand, nitrofurans have activity against ESBL-producing E. coli in 94% of cases [17], making their use interesting for cystitis. No resistance to imipenem has been demonstrated in any of the Enterobacteriaceae strains identified. However, the rational use of this molecule in hospitals is essential to avoid the emergence of carbapenemase producing Enterobacteriaceae strains. No acquired resistance to colistin has been detected.

CONCLUSION

The study we carried out enabled us to drawing up an assessment of resistance of enterobacteria involved in urinary tract infections in our hospital and in the community. The spread of multiresistant uropathogenic bacteria is a real public health problem and a challenge for microbiologist, clinicians, hygienists and health authorities. Surveillance of antibiotic resistance must be continuous and systematic, based on each department's antibiotic prescription policy, the prevention of nosocomial infections and epidemiological studies. In this field, more practically speaking, permanent cooperation between clinicians and microbiologists is necessary for a dual objective: therapeutic and prophylactic objectives.

REFERENCES

1. Sekhsokh, Y., Chadli, M., & El Hamzaoui, S. A. (2008). Fréquence et sensibilité aux antibiotiques des bactéries isolées dans les urines. *Médecine et maladies infectieuses*, *38*(6), 324-327.
2. Debre, B., saigh, D., & peyromaure, M. (2004). Abrégée Urologie, Paris, Masson, 3eme Edition, 80-82.
3. Philippon, A., & Arlet, G. (2005). Beta-lactamases in Gram-negative bacilli: so many new developments in 15 years! *Antibiotics* , *7* (4), 247-259.
4. Etienne, M., Lefebvre, E., Frebourg, N., Hamel, H., Pestel-Caron, M., Caron, F., & Bacyst Study Group. (2014). Antibiotic treatment of acute uncomplicated cystitis based on rapid urine test and local epidemiology: lessons from a primary care series. *BMC infectious diseases*, *14*, 1-8.
5. Recommandations du Comité d'Antibiogramme de la Société Française de Microbiologie CASFM/EUCAST 2023.
6. Larabi, K., Masmoudi, A., & Fendri, C. (2003). Étude bactériologique et phénotypes de résistance des germes responsables d'infections urinaires dans un CHU de Tunis: à propos de 1930 cas. *Médecine et maladies infectieuses*, *33*(7), 348-352.
7. Arsalane, L., Kamouni, Y., Yahyaoui, H., Bennouar, N., Berraha, M., & Zouhair, S. (2014). Current antibiotic resistance profile of uropathogenic Escherichia coli strains and therapeutic consequences. *Advances in Urology* , *24* (16), 1058-1062.
8. Lahlou, A. I., Chegri, M. L., & Kassmi, H. (2009). Épidémiologie et résistance aux antibiotiques des entérobactéries isolées Uro'Andro - Volume 1 N° 4 Juillet 2015 Page 171 d'infections urinaires à l'hôpital militaire Moulay-Ismail de Meknès. *J. antib*, *11*(2), 90-96.
9. Agence française de sécurité sanitaire des produits de santé. Recommandations pratiques : diagnostic et antibiothérapie des infections urinaires bactériennes communautaires chez l'adulte. Med Malad Infect 2008, 38S:203-52
10. Ferjani, A., Marzouk, M., Ben Moussa, F., & Boukadida, J. (2010). Résistance des souches d'Escherichia coli isolées de prélèvements d'origine urinaire vis-à-vis de l'association amoxicilline–acide clavulanique et divers antibiotiques. *J. medmal*, *40*(3), 129-84.
11. Tagajdid, MR, Boumhil, L., Iken, M., Adnaoui, M., & Benouda, A. (2010). Study of the resistance of Escherichia coli strains isolated in urine to fluoroquinolones and third-generation cephalosporins. *Medicine and Infectious Diseases* , *40* (2), 70-73.
12. Čižman, M., Oražem, A., Križan-Hergouth, V., & Kolman, J. (2001). Correlation between increased consumption of fluoroquinolones in outpatients and resistance of Escherichia coli from urinary tract infections. *Journal of Antimicrobial Chemotherapy*, *47*(4), 502-502.
13. Colodner, R., Kometiani, I., Chazan, B., & Raz, R. (2008). Risk factors for community-acquired urinary tract infection due to quinolone-resistant E. coli. *Infection*, *36*, 41-45.
14. Chaussade, H., Sunder, S., Bernard, L., Coloby, P., Guy, L., Karsenty, G., ... & Bruyère, F. (2013). Antibiotic drugs in urology. *Progress in Urology* , *23* (15), 1327-1341.
15. Bruyère, F., Cariou, G., Boiteux, J. P., Hoznek, A., Mignard, J. P., Escaravage, L., ... & Coloby, P. (2008). Cystites aiguës. *Progrès en Urologie*, *18*, 9-13.
16. Honderlick, P., Cahen, P., Gravisse, J., & Vignon, D. (2006). Quelle sensibilité aux antibiotiques pour les bactéries responsables d'infections urinaires? Que penser de fosfomycine et nitrofuranes?. *Pathologie Biologie*, *54*(8-9), 462-466.
17. Fournier, D., Chirouze, C., Leroy, J., Cholley, P., Talon, D., Plésiat, P., & Bertrand, X. (2013). Alternatives to carbapenems in ESBL-producing Escherichia coli infections. *Médecine et maladies infectieuses*, *43*(2), 62-66.