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Research Article

CURRENT ANTIBIOTIC SUSCEPTIBILITY PROFILE OF *ESCHERICHIA COLI* STRAINS FROM COMMUNITY ACQUIRED URINARY TRACT INFECTIONS IN MOROCCO

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ABSTRACT

Introduction: Urinary tract infection (UTI) constitute the first reason for consultation and medical prescription and the leading cause of infection in community medicine justifying antibiotic treatment.

To our best knowledge this first Moroccan study which aims to evaluate the frequency of isolation and antimicrobial susceptibility of uropathogenic *Escherichia coli* strains isolated from non-hospital settings in Morocco.

Patients and Methods: This a multicentre prospective study conducted in 20 medical analysis laboratories in eight major cities in Morocco (Rabat, Sale, Kenitra, Marrakech, Meknes, Settat, El-Jadida, Tanger).

Results: In this study, 3,400 uropathogenic enterobacteriaceae were isolated, including 2555 non-repetitive strains of *E. coli*, an overall isolation rate of 67%. Women represent 73% of infected patients, confirming the frequency of urinary infections in women. The susceptibility rate of *E. coli* toamoxicillin, amoxicillin-clavulanic acid, céfixime, cefotaxime, ceftriaxone, ceftazidime, ertapenem, imipenem, nalidixic acid, ofloxacin, norfloxacin, ciprofloxacin, gentamicin, cotrimoxazole, nitrofurans and fosfomycine was 35.3%, 56%, 82.4%, 85%, 78.7%, 85.5%, 84.5%, 99%, 69.7%, 66.5%, 65.3%, 70%, 86%, 54%, 91.1% and 97% respectively.

E. coli producing extended spectrum β-lactamase constituted 2.3% of all uropathogens *E. coli*.

Conclusion: The emergence and dissemination of multiresistanturopathogens *Escherichia coli* are a real public health problem and a real challenge for biologists, clinicians, hygienists and health authorities. The adoption of policy for the proper use of antibiotics, updated through regular monitoring programs of the susceptibility of bacteria to antibiotics, remains one of the key tools for reducing the magnitude of the phenomenon of bacterial resistance to antibiotics.

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INTRODUCTION

Urinary tract infection (UTI) constitute the first reason for consultation and medical prescription and the leading cause of infection in community medicine justifying antibiotic treatment. Excessive and / or inappropriate use of antibiotics such as fluoroquinolones and third generation cephalosporins (C3G) in the treatment of UTIs was rapidly followed by the emergence of multidrug-resistant strains. *Escherichia coli (E. coli)* urinary tract infections are a priority for surveillance and antibiotic resistance studies because of their high frequency and severity. The aim of this work is to evaluate the frequency of isolation and antimicrobial susceptibility of uropathogenic *E. coli* strains isolated from non-hospital settings in Morocco.

PATIENTS AND METHODS

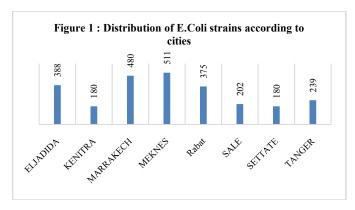
This a multicentre prospective study conducted in 20 medical analysis laboratories in eight major cities in Morocco (Rabat, Sale, Kenitra, Marrakech, Meknes, Settat, El-Jadida, and Tangier). The study was conducted on a period of a year (2017), each laboratory provides exhaustive antibiogram data of all the *E. coli* isolated from urine. Duplicates were eliminated. All ages of both sexes were included; Patient samples from health care facilities (hospitals, private clinics) are excluded from the study. The various stages of the preanalytical phase have been mastered (sampling, conservation, transport, identification, clinical information), seeding and identification methods are specific to each laboratory.

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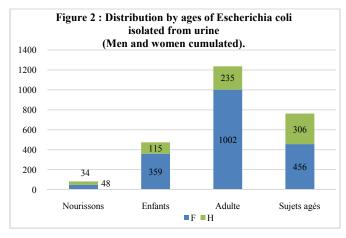
The antimicrobial susceptibility of *E.coli* and the interpretation the results were carried out according to the recommendations of the REMIC 2015 edition (Reference in Medical Microbiology 5th edition) concerning community medicine [1]: leucocyturia ≥104 / mL and bacteriuria = 103 CFU / mL. The analysis of the resistance rates is performed on the interpreted results: sensitive, intermediate and resistant. The antibiotics tested were amoxicillin (AMX), amoxicillinclavulanic acid (AMC), cefixime (CXM), cefotaxime (CTX), ceftriaxone (CRO), ceftazidime (CAZ), ertapenem (ERT), imipenem (IPM), nalidixic acid (NA), ofloxacin (OFL), norfloxacin (NOR), ciprofloxacin (CIP), gentamicin (G), cotrimoxazole (SXT), nitrofurans (FU) and fosfomycin (FOS). Most antibiotics are tested by all laboratories following the recommendations of CASFM. The production of extended spectrum β-lactamases (ESBL) was confirmed by the diffusion method involving the synergy test between AMC and a thirdor fourth-generation cephalosporin and / or aztreonam. This synergy is characterized by a "champagne cork" image and signifies the presence of an ESBL. The statistical analyzes used are based on the Pearson Chi2 method using the IBM SPSS statistics 23 software.

RESULTS

In this study, 3,400 uropathogenicentero bacteriaceae were isolated, including 2555 non-repetitive strains of *E. coli*, an overall isolation rate of 67%. The frequency of isolation of *E. coli* strains according to the cities is shown in (Figure 1).



Women represent 73% of infected patients, witnessing the frequency of urinary infections in women. In both sexes, the number of isolated strains increases with age (Figure 2).



The prevalence of UTI in men reflects the reality of the frequency of infections occurring with age, especially on prostatic obstruction. In young women, simple urinary infections are underestimated because they are treated without urine culture. In our study, 556 *E. coli* were isolated from children under 15 years, mainly in girls (73.2%).

Since 2015, the results for aminopenicillins can be interpreted in consist of those of ampicillin or amoxicillin, in our study we presented only the results of Amoxicillin. The susceptibility profile in this class of antibiotic was low (overall susceptibility of the AMX is 35%). The addition of clavulanic acid only restored the sensitivity to 20.7% of the strains (susceptibility for AMC: 56%). The cephalosporins of 3rd generation keep a good activity with susceptibility rate up to 85% for cefotaxime and 78.7% for ceftriaxone. Strains remain very susceptibility to and imipenem. The susceptibility fluoroquinolones ranges from 66.5% for ofloxacin to 70% for ciprofloxacin. Urinary-specific antibiotics remain among the most effective, including fosfomycin and nitrofurans (susceptibility rate =94% for both molecules) (Figure 3).

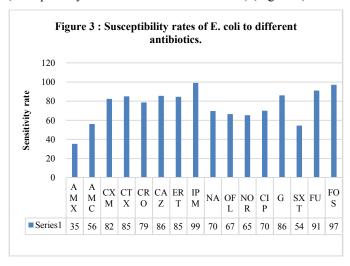
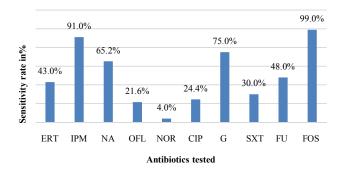


Figure 4: Sensitivity Rates for the Different Antibiotics of Escherichia coli ESBL producers in the entire study population.



Analysis of the susceptibility rate to antibiotics depending on the age and sex of the studied population (men and women over 15, children under 15) show less favorable outcomes in the population of men especially antibiotics such as fluoroquinolones (ciprofloxacin susceptibility: 71.2%, 48.1% and 84% respectively among women, men and children) or the C3Gbut to a lesser degree (susceptibility to cefixime 85%, 76.4% and 83% respectively) (Table 1).

Table 1 Susceptibility rates for different antibiotics in men, women, and children and under 15 year's patients.

	AMX	AMC	CXM	CTX	CRO	CAZ	ERT	IPM	NA	OFL	NOR	CIP	G	SXT	FU	FOS
children	30.0%	53.4%	83.0%	83.6%	75.1%	83.3%	88.0%	97.0%	81.6%	77.7%	80.0%	84.0%	86.2%	50.0%	98.2%	98.2%
Women	38.0%	58.0%	85.0%	88.7%	60.0%	89.0%	85.6%	99.0%	68.2%	69.0%	72.0%	71.2%	60.0%	58.6%	92.5%	96.0%
men	32.7%	53.0%	74.1%	76.4%	74.7%	79.0%	77.1%	99.0%	55.6%	48.7%	40.0%	48.1%	80.1%	48.1%	86.3%	98.3%

The number of $E.\ coli$ strains resistant to C3G by producing extended spectrum β -lactamase "ESBL" was 60, an average frequency of 2.3% of all uropathogens $E.\ coli$ isolated. In ESBL-producing $E.\ coli$, imipenem has a good activity (susceptibility: 91%). For the antibiotics specific to the treatment of urinary infections, fosfomycin maintains its activity (susceptibility: 99%) while nitrofuran shows a low susceptibility (susceptibility: 48%). The activity of fluoroquinolones becomes very limited (susceptibility for IPC: 24.4%, OFL: 21.6% and NOR: 4%). (Figure 4)

DISCUSSION

The frequency of urinary tract infections is high, estimated at 150 million cases per year worldwide and 2 million annual cases in France [2]. This frequency varies according to gender, in our study 73% of cases of UTI is observed in women. It is also variable according to age, especially the young woman (0.5 to 0.7 episodes of acute cystitis / year) and the elderly. Sexual activity and pregnancy are two well-identified risk factors of UI [3]. Data on the epidemiology of IU come from networks of city laboratories ONERBA (National Observatory of Epidemiology of bacterial resistance to antibiotics) but all UI are not subject to an URINE CULTURE with simple acute cystitis being underrepresented [4].

Medications that can be used to treat urinary tract infections are numerous, however, community-acquired urinary tract infections are a major provider of antibiotics in community medecine. *E. coli*, a bacterium of the intestinal flora, is subject to the pressure of antibiotic selection and is also the leading cause of urinary tract infection. The evolution of resistance in this bacterial species is a little evidence of the effectiveness of antibiotic management policies in city or hospital medicine [4].

The study of the susceptibility of isolated strains in our study revealed variable susceptibility levels to the tested antibiotics, including the main molecules used in the treatment of urinary tract infections. A low rate of susceptibility to aminopenicillins (amoxicillin, S: 35.3%) was recorded. Similar lower rates of amoxicillin sensitivity up to 25% have been reported in other studies [5, 6] and others at 50% [4].

The acquisition of amoxicillin resistance protected by clavulanic acid (AMC), a highly consumed antibiotic in Morocco on medical prescriptions and self-medication [7, 8], is a worldwide phenomenon reported at variable rates [4]. In our study, sensitivity to AMC was 56%, a similar rate was reported in another study in Tunisia at 53% [9]. Thus, the use of amoxicillin alone or in combination with clavulanic acid is not recommended in UTI probabilistic treatment, but only on documentation in the few cases where the strain will be sensitive. [4, 10]. Third generation cephalosporins remain active and resistances are mainly due to the production of ESBL. In our study the proportion of ESBL phenotype is generally 2.3% versus 4.73% in a study conducted in France [4], and 9% in another study in Tunisia [9].

Fluoroquinolones (FQ) occupy a privileged place among the molecules prescribed in the treatment of urinary tract infections and in particular in the probabilistic treatment of simple acute cystitis in women [10]. Like any other antibiotic, the relationship between increasing use of fluoroquinolones and the increase of bacterial resistance to these molecules is well established [11]. The susceptibility of E. coli to ciprofloxacin was 70% in our study, the global epidemiological situation of the susceptibility of *E.coli* strains to FQ remains variable with a susceptibility rates of 87.7 in France [4], 84% in Tunisia [9] and 50% in China [12]. In the presence of ESBL, the tested FQs have a low susceptibility of 4% for NOR, 21% for OFL and 24% for CIP. This decrease in sensitivity is observed in other publications [4, 13]. This can be explained by the fact that ESBL genes, usually carried by plasmids, are often associated with antibiotic resistance genes, especially fluoroquinolones [14].

Escherichia coli present in our study a susceptibility rate of 54.4% to cotrimoxazole, while 60% was observed in Tunisia [9] and 77.5% in France [4]. The recommendations place this antibiotic only on bacteriological documentation especially in cases of male IU [10] where the susceptibility rate is 48.1% in our study.

Molecules with urinary specificity deserve special interest. Indeed, they are particularly effective: nitrofurans and fosfomyc in susceptibility of 94% for the two molecules in our study, 98.7%z and 99% in France and Tunisia respectively [4, 9]. They are antibiotics that are not selective for the intestinal macrobiota [15]. They thus maintain excellent activity even in the presence of an ESBL (FOS 99%, FU 48%).

Imipenem has good activity against the identified *E. coli* strains, a susceptibility of 99%. However, the rational use of this molecule is mandatory in order to avoid the emergence of carbapenemase producing *E. coli* strains.

The limits of our study remain in the difficulty of carrying out a study of bacterial resistance in community medecine. The clinical circumstances were not collected. It should be pointed out that for simple acute cystitis, first-intention URINE CULTURE is not necessary, so the bacteria isolated in the laboratories are not the exact reflection of all urinary infections with probably an overestimation of popular resistance during therapeutic failures, recurrent cystitis, UI, with risk factors, precisely the circumstances under which the urinalysis was made. The data presented in this study are global and do not allow to highlight any differences in the resistance phenotypes according to the clinical pictures.

CONCLUSION

Controlling antibiotic resistance requires a good use of antiinfective treatment. Although studies are frequent in hospitals, they are rarer in community medicine where private laboratories have a primordial role. The emergence and dissemination of multiresistanturopathogens *Escherichia coli* are a real public health problem and a real challenge for biologists, clinicians, hygienists and health authorities. The adoption of policy for the proper use of antibiotics, updated through regular monitoring programs of the susceptibility of bacteria to antibiotics, remains one of the key tools for reducing the magnitude of the phenomenon of bacterial resistance to antibiotics.

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