



## Urinary tract infection at the service of urology: Epidemiological and bacteriological aspects at the Marrakech University Hospital

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### ABSTRACT

**Introduction:** Urinary tract infection is one of the most frequent infections in hospital practice. It covers a range of clinical situations, symptomatology and gravity ranging from simple asymptomatic bacteriuria to complicated acute pyelonephritis. In urology, it is a constant concern because of their frequency, their morbidity, the lengthening of their stay and the resistance of the germs to antibiotics. **OBJECTIVE:** To assess the incidence of urinary tract infection in hospitalized patients in urology, to determine the bacteriological characteristics and risk factors of urinary tract infection in urology. **MATERIAL AND METHODS:** Prospective study carried out over a period of 6 months (July 2016 - December 2016) at the microbiology laboratory of the CHU Mohammed VI in Marrakech, including all urinary infections documented by a positive ECBU from the urology department of CHU Med VI. Identification and antibiogram were performed using the Phoenix 100 (Becton Dickinson) and by manual methods. Interpretation of antibiotic sensitivity was made according to the recommendations of the CA-SFM. The age and clinical and bacteriological data of the patients included were recorded on a farm record. **RESULTS:** During the study period, 121 records meeting the urinary tract infection criteria were selected. The prevalence of urinary tract infection in urology was 25.6%. The average age of patients was 52.2 years with a sex ratio of 0.9. 17% of patients were smoking and 8% were diabetic. The most common reason for hospitalization was bladder tumors (43%) followed by stenosis of the urethra (14%). Urinary signs were dominated by voiding burns (78.5%), followed by pollakiuria (61%). 51% of patients received endoscopic surgery and 19% were surgical. 60% of the patients were surveyed. 50% of patients received probabilistic antibiotic therapy covering the invasive procedure. 62% of urinary infections were nosocomial. The appearance of urine was cloudy in 58.6% of cases, with significant leukocyturia in 90% of cases, and significant hematuria in 92%. 90% of the strains isolated were Gram-negative bacilli with a predominance of *Escherichia coli* (41%) and *Klebsiella pneumoniae* (30%). In enterobacteriaceae, the resistance to amoxicillin-clavulanic acid was 73%, and that to C3G was 43.75%. For non-fermentative Gram-negative bacilli, the resistance to Cefazidime was 43%, and to the Imipenem of 36%. Fluoroquinolone resistance in uropathogenic isolates was 58.8%. **CONCLUSION:** The results of this study highlight the problem of urinary infections in hospitals, particularly in the urology department, where the use of invasive urological maneuvers is frequent. Timely microbiological surveillance and assessment of antibiotic resistance is a defense against the emergence of new bacterial strains increasingly resistant to broad-spectrum antimicrobials, making therapeutic options increasingly limited.

**Keywords :** Urinary infection, Enterobacteriaceae, resistance.

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## INTRODUCTION

Urinary tract infection (UTI) is one of the most frequent infections in hospital practice. It corresponds to the aggression of a tissue of the urinary tree by one or more microorganisms generating an inflammatory response and symptoms of nature and intensity that vary according to the terrain. It covers a range of clinical situations, symptomatology and severity ranging from simple asymptomatic bacteriuria to complicated acute pyelonephritis. In urological surgery, it is a parameter of quality, thus constituting a constant concern by its frequency, its morbidity, the prolongation of its duration of stay, and the resistance of the germs to the antibiotics.

Urinary tract infections represent, according to current definitions, about 40% of nosocomial infections. This is a real public health problem that interests all actors [1]. In recent years, there has been an increase in the incidence of resistance to antibiotics from germs responsible for urinary tract infections. The emergence of Streptococcus secreting enzymes (ESBL) is increasingly prevalent [2].

The objective of the study is to evaluate the prevalence of urinary tract infections in patients hospitalized in urology, to determine the epidemiological and bacteriological characteristics as well as the risk factors associated with their occurrence.

## MATERIALS AND METHOD

This prospective study was carried out in the microbiology laboratory of the Marrakech CHU Mohammed VI and included all urinary infections documented by a positive ECBU from the Urology Department of MedU CHU for a period of 6 months (July 2016 - December 2016).

Each specimen sent to the laboratory was subjected to a urinary cytobacteriological examination (ECBU) including a micro-culture with germ counts and a microscopic examination evaluating leucocyturia and hematuria.

The biological diagnosis of UI was carried out on a leucocyturia greater than or equal to 104 / ml associated with a significant bacteriuria which was interpreted according to the bacterial species involved and the sex of the patient. In a symptomatic patient with leukocyturia  $\geq 104$  UFC / ml, the bacteriuria thresholds are noted in Table I [3].

The identification and the antibiogram were carried out using the Phoenix 100 (Becton Dickinson) and by the manual methods (standard antibiogram by diffusion on agar and galleries Api). Interpretation of antibiotic sensitivity was made according to the latest CASFM-EUCAST recommendations.

The following were recorded on a farm record: age, sex, history, hospitalization, clinical symptomatology, ECBU biological data, bladder sampling and duration of exposure, Risk factors studied were: anterior antibiotic treatment less than 6 months, surgical or endoscopic invasive intervention and the nosocomial or community nature of the infection (the nosocomial character was retained on a positive ECBU after 48 h hospitalization).

## RESULT AND DISCUSSION

### General epidemiology of urinary tract infection in urology:

During the period studied, 121 cases meeting the criteria for urinary tract infection were selected. The prevalence rate of urinary tract infection in the urology department was 25.6%. The mean age

of the patients was 52.2 years (Table II), 41.3% were between 41 and 60 years of age. The sex ratio M / F was 0.9. 17% of patients were smoking and 8% were diabetic. The most common reason for hospitalization was bladder tumors (43%) followed by stenosis of the urethra (14%) (Figure 1).

Urinary signs were dominated by micturition burns (78.5%), followed by pollakiuria (61%), renal colic (49%), dysuria (49%), and hematuria (27%). , Pelvic pain (14%), fever (12%) and pyuria (4%).

51% of patients received endoscopic surgery and 19% were surgical. 60% of the patients were surveyed, with a sampling time exceeding three months in 26% of the cases (Table III).

50% of the patients received an antibiotic prophylaxis covering the invasive procedure, in the form of a dose of cephalosporin of first generation when it was a sterile preoperative ECU. Otherwise treat and sterilize the urine before any gesture was the rule. Urological UTIs were nosocomial in 62% of cases.

The appearance of the urine was cloudy in 58.6% of cases, with the presence of significant leucocyturia in 90% of cases, and significant hematuria in 92%.

#### **Distribution of uropathogenic species isolated in urology:**

Enterobacteriaceae were the leader of uropathogenic isolates (80%). The distribution of the different strains isolated is illustrated in Table III. Escherichia coli occupied first place (41%) in isolated enterobacterial strains followed by Klebsiella pneumoniae (30%).

#### **Study of the sensitivity of uropathogenic enterobacteriaceae:**

The resistance to amoxicillin-clavulanic acid was 73%, and that to C3G was 44%. The strains resistant to ertapenem accounted for 14.5%, and 3% of the isolates had decreased sensitivity to imipenem (Figure 2).

In Enterobacteriaceae, Klebsiella Pneumoniae occupied second place (30%) after Escherichia Coli (51.5%).

Of 97 strains of isolated enterobacteriaceae, 35% were resistant to C3G by production of ESBL. C3G resistance mainly affected isolates of K. pneumoniae (61%), followed by Escherichiacoli (30%), Enterobacter cloacae (6%), and Citrobacter freundii (3%).

Resistance to fluoroquinolones in enterobacteriaceae was 59%. The resistance to amikacin was 32% and the sulfamethoxazole-trimethoprim combination was 59%. Multi-resistant strains accounted for 40% of all isolates with three strains resistant to tigecycline.

#### **Study of antibiotic susceptibility of isolates of Escherichia Coli and Klebsiella pneumoniaeuropathogens:**

High levels of resistance to the various antibiotics tested were found in Klebsiella pneumoniae compared to E. coli: 8% of Klebsiella pneumoniae isolates had decreased sensitivity to imipenem, 6% intermediate sensitivity to amikacin, and 66% Of resistance to C3G (Figure 3).

#### **Comparison of the antibiotic sensitivity profile of uropathogenic enterobacteriaceae in nosocomial versus community urinary infections:**

Nosocomial urinary enterococcal infections dominated the urology UI profile (58%). High levels of resistance have been found in nosocomial strains compared to community strains, affecting betalactamins, aminoglycosides, fluoroquinolones and sulfamethoxazole + trimethoprim.

Resistance to C3G in Enterobacteriaceae was 37% in strains isolated from nosocomial UI and 6% in strains isolated from community UI. Strains with decreased sensitivity to carbapenem were mainly found in nosocomial UTIs (Figure 4).

#### **Study of the sensitivity to antibiotics of uropathogenic non-fermentative BGN:**

For non-fermentative Gram-negative bacilli, the resistance to Ceftazidime was 43%, Imipenem 36%, and ciprofloxacin 35.7%. Resistance to gentamycin was 43%. The multiresistance of *Pseudomonas aeruginosa* was found in 12% of cases and all isolates of *Acinetobacter Baumannii* were multiresistant.

#### **Discussion:**

The epidemiological profile of uropathogenic bacteria varies from one region to another and is still influenced by different risk factors. Knowledge of local epidemiology and its evolution remain essential for the choice of antimicrobial therapy. Effective first-line and adapted for each region [4]. The results of this study highlight the problem of urinary infections in hospitals, particularly in the urology department, where the use of invasive urological maneuvers is frequent. Timely microbiological surveillance and assessment of antibiotic resistance is a defense against the emergence of new bacterial strains increasingly resistant to broad-spectrum antimicrobials, making therapeutic options increasingly limited.

The prevalence of UI in this series was in the order of 25.6%. This high prevalence could be explained by a number of risk factors for UI: frequent recruitment of patients who have stayed in the emergency department and who have been subjected to an iterative urinary sampling, a relatively long average length of hospital stay, Profile of pathologies supported in urology (organic and functional anomalies of the urinary tree ...). However, this prevalence has dropped considerably compared to a local study performed at the same department in 2011, with an incidence rate of 42.2% [5].

The female predominance found in UU in the urological patient is related to the anatomical characteristics of women: shortness of the urethra, proximity of genital and anal orifices, inadequate hygiene practices, sexual intercourse and pregnancy [6].

Patients over 40 years of age were more prone to urinary tract infection (78%). This could be explained by the increased age of bladder trauma, dehydration, poor hygiene and But also by the frequency of the tumor pathology of the bladder at this age, which is the main reason for hospitalization in the urology department.

UTI signs were dominated by urinary disorders. In patients surveyed, symptoms lose much of their diagnostic value, nevertheless there is a good correlation suggestive of urinary tract infection with probe and bacteriuria greater than 10 5UFC / ml [8].

60% of the patients underwent a bladder catheter, the acquisition of the germ in these patients can be done either by endoluminal route, because of bacteria that reach the bladder via the inner wall of the probe [8], or by The digestive bacteria colonize the meatus and then progressively migrate towards the urethra and the bladder by capillarity in the fine mucous film adjacent to the external surface of the probe. Lymphatic or haematogenic acquisition remains possible.

The duration of the catheterization depends on the indication: routine surgery (1-7 days), measurement of diuresis in an intensive care unit (7-30 days), acute and chronic urinary retention (1 day at > 30 days), and urinary incontinence (> 30 days) [10]. In our context the duration of the sampling exceeded three months in 43% of the cases, this is explained by the high rate of patients

with bladder tumors for whom the surgery is kept the time to program the surgery, and to prepare them. This also explains the high rate of urinary infections in these patients.

50% of the patients were given antibiotic prophylaxis, it was intended only for uninfected and non-colonized patients who will undergo surgical or invasive surgery with an infectious risk either at the surgical site (infection of the surgical site) or Distance [11]. The authors concluded that all endoscopic prostate resections require antibiotic prophylaxis, even if patients do not have any risk factors [12].

Biologically, urine was disordered in 58.6% of cases, bacteriuria  $\geq 10^5$ UFC / ml was present in 88% of cases and leukocyturia was present in 90% of cases. Leukocyturia translates the normal inflammatory response to a bacterial infection in the urinary tract but is not specific. Hematuria was present in 92% of the samples but is often influenced by urological pathology.

For isolated uropathogenic germs, Gram-negative bacilli were the most frequently infected with mainly *E. coli* and *Klebsiella pneumoniae*. This has also been reported by several national and international series [13-14].

The study of the susceptibility of hospital and community enterobacteriaceae to the antibiotics tested reveals several points: a high level of resistance for most of the antibiotics tested outside of amikacin, especially with the increase in resistance to C3G. These levels of resistance are disturbing and alarming. This situation is the consequence of the selection pressure due to the massive and unreasonable prescription of broad spectrum antibiotics, both in hospitals and community settings, as well as the cross-transmission of acquired resistance to plasmid determinism. Antibiotic self-medication is a serious problem in developing countries such as ours, where these medicines are readily available often without a medical prescription [15].

The C3G resistance rate (44%) remains higher than those reported in other studies [14-16-17-18]. This high level of resistance is related to the non-negligible number of ESBL-producing strains recovered, which is 35% in this series compared to a previous local study (30%) [16]. These resistance rates are significantly higher than those reported in the Mauritanian (12.8%) [18], or Tunisian (9%) series [17]. This is explained by the increased consumption of third-generation cephalosporins, and consequently the resistance of uropathogenic enterobacteria to these molecules has increased.

Resistance to ertapenem affected 14.5% of enterobacteriaceae and 3% of strains had intermediate sensitivity to imipenem. In view of the increased resistance to C3G in the germs responsible for UI in patients in urology, the use of carbapenems has become more and more frequent, leading to the emergence of carbapenem-resistant strains. The rational use of these so-called last resort molecules is mandatory in order to avoid the emergence of carbapenemase-producing strains.

Fluoroquinolones and sulfamethoxazole + trimethoprim were the molecules most affected by resistance. Resistance to these antibiotics in uropathogenic isolates was 59%. This high figure compared to other local studies [14-16] can only be explained by the high use of these molecules, especially in the community. A treatment with fluoroquinolones in the previous 6 months exposes the risk of selection of strains less sensitive to these molecules. The important ecological impact of fluoroquinolones on the intestinal microbiota requires a saving strategy and limits their use to specific indications.

Although rarely isolated in urinary infections, *P. aeruginosa* accounted for 7.4% of all the strains isolated, it posed therapeutic problems with *Acinetobacter baumannii* because of their natural and acquired resistances. The levels of resistance to ceftazidime and imipenem were respectively 43%

and 35.7%, these levels remained high compared to those reported by Dia mel et al. [19]. The sensitivity rates to ciprofloxacin (64, 3%) could be related to the large use of quinolones in city antibiotics.

### CONCLUSION

Urological urinary tract infection in the urology is a particular situation favored by a multitude of risk factors, mainly urological pathology, multiple hospitalizations and broad spectrum antibiotics, but also aggressive urological maneuvers and surgery. All these factors weaken the urinary tree and expose it to external aggression such as infection.

The problem of urinary tract infection in urology is dominated by the high level of resistance to C3G in enterobacteriaceae but also by resistance levels becoming more and more worrying with other antibiotics that can be given as an alternative. However, the impact of widespread use of C3Gs is felt. This delicate and rather frequent situation complicates the therapeutic decision and obliges the clinician to prescribe a broad spectrum antibiotherapy such as carbapenems, which has led to the emergence of strains of decreased sensitivity to carbapenems. It is essential not to abuse these molecules and to reserve them to the last resort in the absence of any other therapeutic alternative, to compare the biological results with the clinical context before treating the patient and systematically control the ECBU at 48 hours for any urinary infection With resistant germs. Urology UI is a parameter of quality of care and remains a real challenge for biologists, clinicians, hygienists and health authorities.

**Table I:** Bacteriuria thresholds retained in symptomatic patients with leukocyturia  $\geq 10^4$  CFU / ml: [3]

Bacterial Species	Seuil de significativité	sex
E.Coli, s.saprophyticus	$10^3$ UFC/ml	Man or woman
Enterobacteriaceae other than E. coli, enterococci, C. urealyticum, P. aeruginosa, S. aureus	$10^3$ UFC/ml $10^4$ UFC/ml	Man Female

**Table II:** Distribution of patients with UI by age group in urology (n = 121):

Age range	Number of Patients	%
<20 years	2	1,6
20-40 years	25	20,5
41-60 years	50	41,3
61-80 years	42	35
> 80 years	2	1,6

**Table III:** Distribution of patients with UI according to the duration of urinary catheter placement (n = 121):

	number	%percentage
<1month	25	34,7
1-3 months	16	22,3
> 3 months	31	<b>43</b>

Bacterial Species		number	%
Enterobacteriaceae		97	<b>80,1</b>
	<i>Escherichia coli</i>	50	<b>41,3</b>
	<i>Klebsiella. pneumoniae</i>	35	<b>30,0</b>
	<i>Morganella. morganii</i>	2	1,6
	<i>Citrobacter spp</i>	1	0,8
	<i>Protéus spp</i>	2	1,6
	<i>Enterobacter spp</i>	7	5,8
	<i>Acinetobacter baumannii</i>	5	4,0
	<i>P. aeruginosa</i>	9	7,4
	<i>Staphylocoque aureus</i>	5	4,0
	<i>Entérocoque</i>	3	1,9
	<i>Streptocoque alpha hémolytique</i>	1	0,8
	<i>Candida albicans</i>	1	0,8

**Tableau IV** : Distribution of isolated bacterial species in patients with UTI in urology (n= 121):

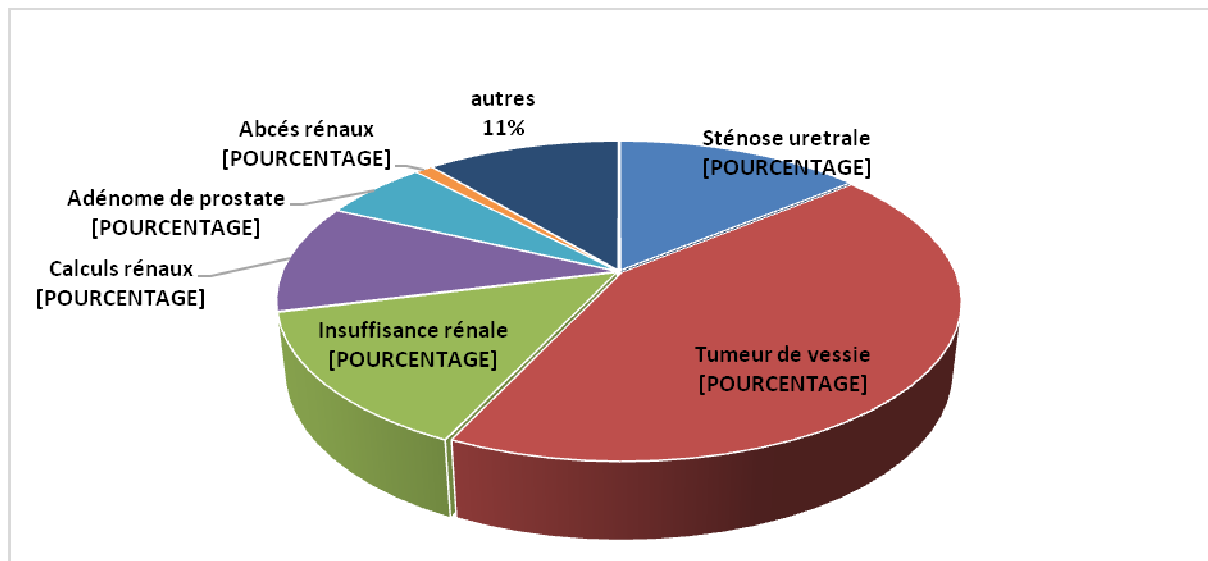


Figure 1: Distribution of patients hospitalized in urology (n= 121) by type of hospitalization

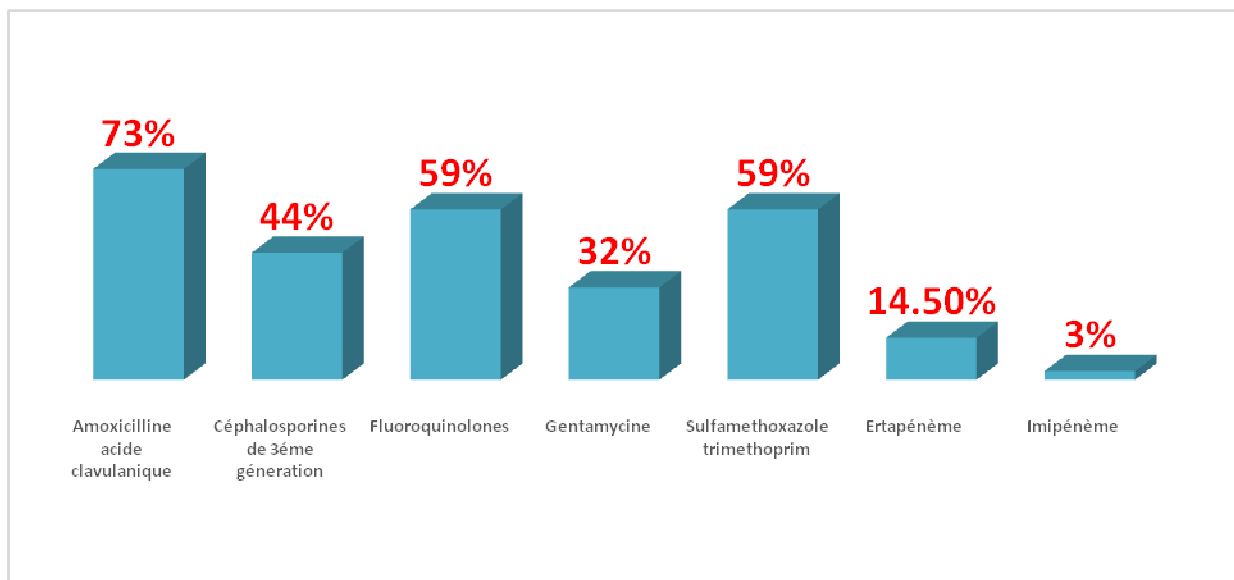
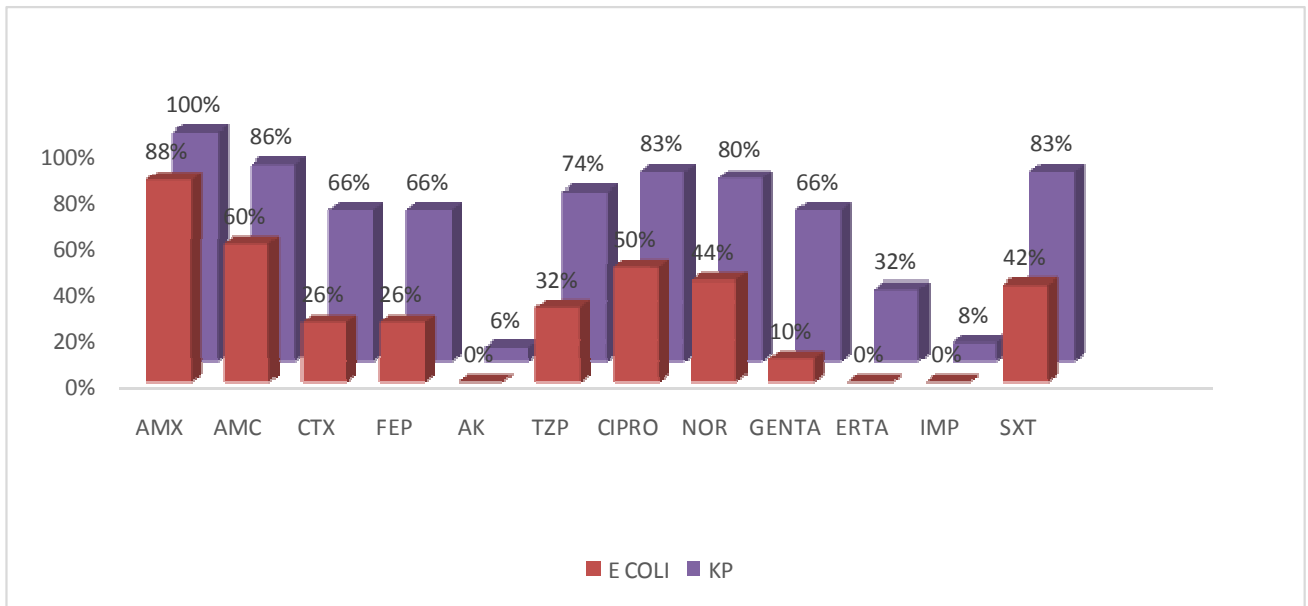
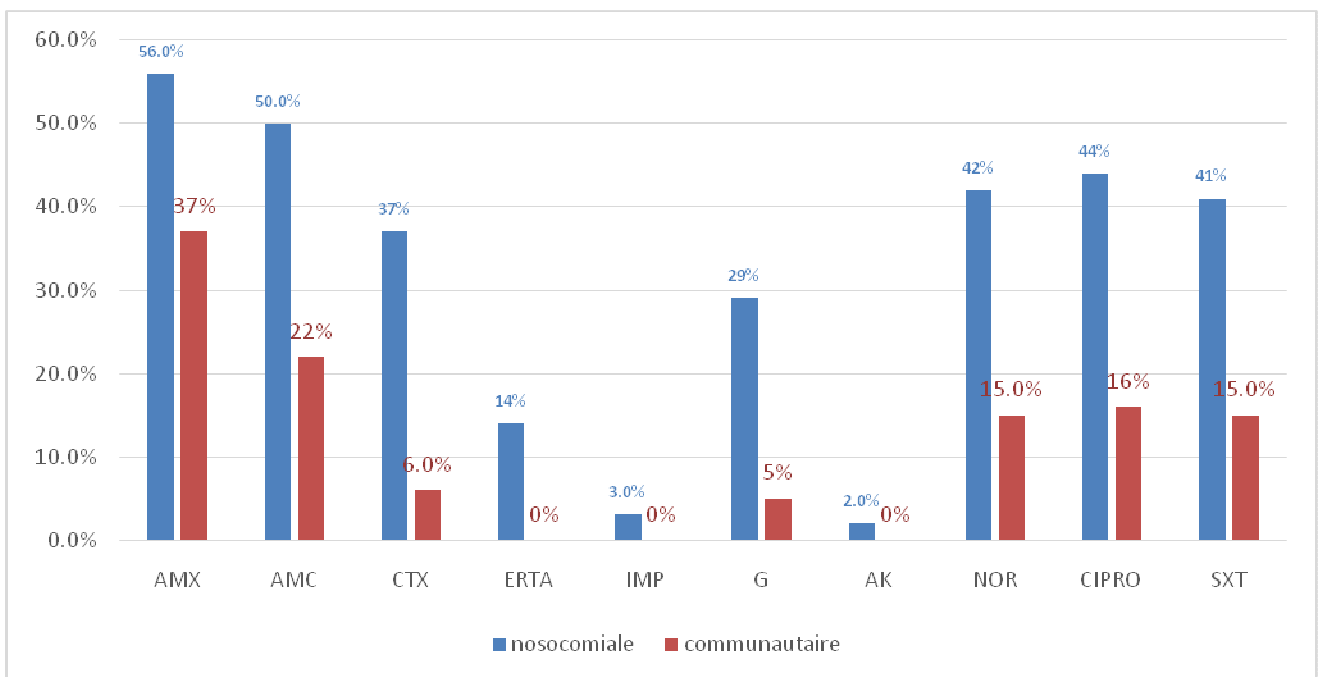


Figure 2: Antibiotic resistance profile of uropathogenic enterobacterial isolates in urology patients (n = 97)





**Figure 3:** Comparison of% resistance to antibiotics in E.coli and K.pneumoniae isolated in urology UI (n = 85)



**Figure 4:** Resistance profile in uro-pathogenic enterobacteria in nosocomial urinary tract versus community urinary infection (n = 97)

**AMX : amoxicilline, AMC : amoxicilline acide clavulanique ,CTX : céfotaxime, ERTA : értapénème, IMP : imipénème, G : gentamycine, AK : amikacine, NOR : norfloxacin, CIPRO : ciprofloxacine, SXT : sulfaméthoxazole triméthoprim**

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