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Advances in Biochemistry and Biotechnology

Research Article

Kouara S, et al. Adv Biochem Biotechnol 4: 1094.
DOI: 10.29011/2574-7258.001094

Epidemiology and Antibiotic Resistance of Community Urinary Tract Infections at CHU HASSAN II in Fez

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Citation: Kouara S, Rotbi MF, Yahyaoui G, Mahmoud M (2019) Epidemiology and Antibiotic Resistance of Community Urinary Tract Infections at CHU HASSAN II in Fez. Adv Biochem Biotechnol 4: 1094. DOI: 10.29011/2574-7258.001094

Received Date: 22 October, 2019; **Accepted Date:** 27 November, 2019; **Published Date:** 02 December, 2019

Summary

Urinary Tract Infection (UTI) is a common pathology both in the community and in the hospital. In recent years, there has been an increase in the incidence of antibiotic resistance of UI-causing organisms, particularly due to the emergence of enterobacteria with Extended-Spectrum Beta-Lactamase (ESBL).

Goal: The aim of this work was to study the epidemiology of germs responsible for urinary tract infections, as well as their sensitivity to antibiotics at the University Hassan II Center of Fez in all patients presenting for ECBU during a period from March 2018 to May 2018.

Materials and Methods: This is a prospective study conducted at the level of the microbiology laboratory, over a period of two months in all patients presenting to this structure for ECBU during this period. The culture was made according to the usual techniques, and the antibiogram was performed according to the recommendations of the Committee of the antibiogram of the French Society of Microbiology (CA-SFM).

Results: Out of 520 urine samples, 63 met the criteria for urinary tract infection (12, 12%). The sex ratio F / H is 2.5. The epidemiology of urinary tract infections in our laboratory is broadly comparable to literature data for age, sex, field, and the most frequently responsible organism *Escherichia coli* 76.2 %. However, differences in resistance are observed: higher resistance to betalactamines, quinolone regeneration, fluoroquinolones and cotrimoxazole. The UI was common in patients with the concept of abuse of antibiotics (64.9%), hospital (58.73%), diseases of the urinary tract (50.79%), the survey (30, 16%) and diabetes (34.92%). The prevalence of ESBL-producing enterobacterial urinary tract infections in our study was 16.6 % among all urinary enterobacterial infections. The strains of *E. coli* and in *Klebsiella pneumoniae* isolated ESBL expressed respectively in 12.5 and 28.5% of cases.

Conclusion: The distribution of strains in our study is comparable to the literature, however, antibiotic resistance is higher in our series, a result probably of inappropriate use of these molecules in our country, hence the need to foresee a good strategy of supply and dispensing of these molecules as well as the revision of the empirical treatment of IU in our country.

Abbreviations

UTI: Urinary Tract Infection; ESBL: Extended-Spectrum Beta-Lactamase; CA-SFM: The Committee of the Antibiogram of the French Society of Microbiology

Introduction

Infectious urinary pathology is common in both community and hospital settings. About 150 million cases of urinary tract infections worldwide are reported annually. As such, they constitute a public health concern [1]. The data in the literature show that *Escherichia coli* is the predominant bacterium in urinary tract infection [2-4]. In our country the Cytobacteriological Examination of Urine (ECBU), which is the only diagnostic element of certainty, is only rarely requested in case of suspicion of IU, self-medication is also a common practice of our patients. These factors, among others, led to a strong selection of multidrug-resistant bacteria. For these reasons, the study of the epidemiology of the bacteria responsible for community UI and especially their sensitivity to antibiotics seems necessary to us to reach therapeutic recommendations of UI in our context. The purpose of our work is to study the epidemiological profile and antibiotic resistance of community

urinary tract infections isolated in the microbiology laboratory of Hassan II University Hospital Center in Fez over a period of two months (March 2018-May 2018), which will make it possible to adapt the antibiotic treatment protocol for urinary tract infections, according to local epidemiological data.

Material and Methods

We report the results of a prospective descriptive study carried out for two months at the level of the bacteriology laboratory of the Hassan II University Hospital Center of Fez, in all the patients presenting to these structures for ECBU during this period. To avoid any contamination by the commensal flora, the sampling protocol has been well explained to the patients or, where appropriate, to the medical staff.

Criteria for Inclusion and Exclusion

Included in our study were all patients with leukocyturia greater than or equal to 10^4 / mL associated with:

Bacteriuria greater than or equal to 10^3 CFU / mL in humans.

Bacteriuria greater than or equal to 10^3 CFU / mL in women if the isolated germ is *Escherichia coli* or *Staphylococcus saprophyticus*.

Bacteriuria greater than or equal to 10^4 CFU / mL in women if the isolated germ is other than the two preceding species.

All patients with negative or positive ECBU associated with parasitosis were excluded.

The identification was carried out according to the morphological, cultural and metabolic characters of the germs, and the antibiogram was performed according to the recommendations of the Committee of the antibiogram of the French Society of Microbiology (CA-SFM) [3]. The search for the secretion of Extended Spectrum ß - Lactamases (ESBL) was established by the synergy test between a central amoxicillin - acideclavulanic disk 30 mm distant from the cefotaxime, ceftazidime and ceftriaxone disks.

Results

We conducted 520 urine cultures, 63 met criteria for UTI is 12,12% positivity. The average age in our series was 51 years with extremes of 20 days and 98 years.

The female sex was predominant with 68.46% (45) of women and 31.54% (18) of men, which corresponds to a sex ratio F / H of 2.5.

Of the patients, 85.71% (53 patients) had at least one of the following urinary symptoms (urinary burning, dysuria, pollakiuria, hematuria), while ten patients had no symptoms of urinary tract infection. Among symptomatic patients we noted prevalence of pollakiuria frequency (58.73%) followed by abdominal pain (55.6%).

The most common antecedents in patients with community-acquired urinary tract infection were predominantly antibiotic abuse (92.06%), previous hospitalization (58.73%), urinary tract (50.79%), probing (30.16%) and diabetes (34.92%). Out of 354 women, 18 were pregnant and 3 developed one IU (4.76 %). Of the 45 women with urinary tract infection 25 are menopausal or 56.82%.

Gram-negative *bacilli* accounted for 95.24% of isolated bacterial strains and gram-positive cocci represented 4.76%. The *Escherichia coli* species dominates the epidemiological profile of community urinary tract infection. In fact, among the 60 strains of enterobacteria isolated from consulting patients, *Escherichia coli* represents the predominant species (80%), followed by *Klebsiella pneumoniae* (11.6%) and various other species (8.3 %) as the *Proteus mirabilis* and the *Enterobacter cloacae*.

ESBL production was observed in eight strains of enterobacteria with an overall prevalence of 13.3 %. The strains of *E. coli* and *Klebsiella pneumoniae* producing ESBL respectively 12.5 and 28.5 % of cases. The distribution of ESBL-producing enterobacteria within each isolated species is shown in Table 2.

In regards to resistance profile *E. coli* we found higher resistance to aminopenicillin, quinolone to 1st generation, and cotrimoxazole, and that the strains of *Klebsiella pneumoniae* isolated were rarely resistant to sulfamethoxazole trimethoprim.

The percentages of antibiotic resistance of strains of *E. coli* and *K. pneumoniae* isolated are shown in Table 3.

Seeds	Effective	Percentage%
Escherichia coli	48	76.2
Klebsiella pneumoniae	7	11.1
Proteus mirabilis	3	4.8
Staphylococcus aureus	2	3.1
Eenterobacter cloacae	2	3.1
Staphylococcus saprophyticus	1	1, 6

Table 1: Frequency of distribution of bacterial strains isolated from cytobacteriological examinations of urine.

Strain	E-ESBL	*Enterobacteriaceae*	Percentage %
Escherichia coli	6	48	12.5
Klebsiella pneumoniae	2	7	28.5
Proteus mirabilis	0	3	0
Enterobacter cloacae	0	2	0
Total	8	60	13.3
ESBL: Betalactamase Extended Spectrum; E-ESBL: ESBL-Producing Enterobacteria.			

Table 2: Percentage of ESBL strains within each enterobacterium.

Antibiotic	*Escherichia coli*	*Klebsiella spp.*
Amoxicillin	83, 3	RN (Natural Resistance)
Amoxicillin + clavulanic acid	2 7	57, 1
Cephalothin	18, 7	42. 8
Cefotaxime	16.6	42.8
Imipenem	0	0
Gentamicin	6.2	14.2
Amikacin	0	0
Nalidixic acid	31.2	42.8
Ciproflox	27	28, 5
Cotrimoxazole	62, 5	57, 1

Table 3: Percentage of antibiotic resistance of strains of *Escherichia coli* and *Klebsiella pneumoniae* isolated.

Discussion

Our study shows that the epidemiology of urinary tract infections in our laboratory is broadly comparable to the world literature with respect to age, sex, terrain and the most frequently responsible *E. coli*. The latter dominated the epidemiological profile (76.2%).

Our positive ECBU rate, which is 12.2%, is comparable to that found by Romli in Morocco (11%) [5] and lower than that found by Ben Haj Khalifa, et al. In Tunisia (15,44%) [6] and by Hailaji, et al. in Mauritania (18.4%) [6]. *Bacilli* Gram égatif, in our study, accounted for 95.24% of all bacteria isolated. They are represented mainly by enterobacteria with head list of *E. coli*. Our finding is shared by other authors with variable rates [6-9]. The upward pathophysiology of IU as well as the strong colonization of the perineum by enterobacteria of digestive origin, associated with the specific factors of uropathogenicity, such as bacterial adhesins capable of binding to the urinary epithelium, explain this predominance [10,11].

Among the enterobacteria isolated in our study, *Klebsiella pneumoniae* comes in second place with 11.1%, a result lower than that found by other studies with variable rates [6,12,13]. The prevalence rate of E-ESBL in our study was 13.3 %. In fact, this rate varies from one country to another and from one center to another. For example, southern European countries recorded rates above 10 %, while those in the North recorded less than 5% [14]. In Morocco, Lahlou, et al. have found a rate of 9% [15]. In 2010, a study in the urology department at the hospital Ibn Sina Rabat thy showed a rate of 17.5% [16]. Our prevalence rate of 13,3% must draw our attention to the scale of the inevitable spread and possibly dramatic of these strains in the absence of excessive control and prevention, especially that these are external consultants. This would be related to the importance of the prevalence of faecal carriage of E-ESBL in our patients in community. It is obvious that this type of strain is no longer the prerogative of the hospital environment, as evidenced by the data of the world literature. Our study focuses on the major role of *Klebsiella* with approximately 28.5 % of E-ESBL isolates; *Klebsiella* is at the same time the most abundant bacterium of ESBL followed by *E. coli* 12.5 %, as reproduced by Lahlou, et al. [15] For Ben Haj Khalifa, et al. *Klebsiella* produced ESBL in 20.2% of cases [16], whereas for Romli, et al. This rate affected 25% of cases [7]. However, some authors report a decline in this dominance in favor of Enterobacter or *E. coli* [17,18]. The distribution of ESBL-producing enterobacteria as well as the percentage of ESBL phenotype for each species are shown in Table 2.

Our study confirms the disturbing character of the evolution of *E. coli* resistance to Aminopenicillins. Thus, it appears that only 17,7% of strains of *E. coli* are sensitive to amoxicillin. This observation is consistent with the results of some particular African authors: Podie in Cotonou got 19.9% of susceptible strains to amoxicilline [19], for Aknaf 17.2% of strains of *E. coli* sensitive the amoxicillin [20]. This high resistance rates can be explained by the improper medical use of this antibiotic in our health facilities but also by self-medication. The emergence of cefotaxime-resistant strains, which is one of the most active antibiotics on

enterobacteria, is increasingly being observed [5]. In our study, the of resistance rates *E. coli* to this antibiotic was 16, 6 %, in contrast to what has been shown by other studies that have found a resistance rate of less than 5% [21-23]. The resistance rates of *E. coli* to cotrimoxazole was 62,5 %, it is markedly higher than that noted in Europe (20 to 30%) [23,24]. This molecule is to be avoided in first intention by our practitioners because its rate of resistance is quite high. Aminoglycosides retain a good activity, mainly amikacin and to a lesser extent gentamicin reaching respectively 100% and 93.8%. The resistances acquired mainly concern the ESBL-producing enterobacteria, this finding is shared by other authors [5,15].

In Bamako, Tahirou found that the sensitivity of *Klebsiella pneumoniae* to third generation cephalosporins is 58% for cefotaxime [25]. Comparable results were found in our study, we recorded 57,2 % sensitivity for cef otaxime. This resistance rate for cefotaxime is explained by the large number of ESBL producing strains among isolated *Klebsiella* strains. It should be noted that the production of ESBL. It should be pointed out that the production of ESBLs alone cannot explain the high level of resistance to cephalosporins in our series, other resistance mechanisms such as the production of cephalosporinase plasmids would probably be associated [26].

The sensitivity of *Klebsiella* isolates to gentamicin is 85.7%, slightly higher than that described in France (65-70%) [27]. The massive use of ciprofloxacin and norfloxacin to treat urinary infections caused by enterobacteria in urban medicine, explains the resistance rates obtained for community strains 27 % for *E. coli* and 28.5% for *Klebsiella pneumoniae*.

Levels of resistance to quinolones and fluoroquinolones have evolved in recent years to reach in France in 2003, 12 to 15% resistance to quinolones and nearly 10% of strains of enterobacteria resistant to fluoroquinolones [28]. It is therefore essential to insist on the rational use of fluoroquinolones to reduce the selection pressure of resistance genes because the risk of spreading resistance to this therapeutic family is to be feared.

Conclusion

The isolation of multidrug-resistant bacteria responsible for community urinary tract infections leads the clinician to an increasingly limited therapeutic choice. In addition, the isolation of strains of *Escherichia coli* and *Klebsiella pneumoniae* that produce ESBL in community settings is noted in our study. The spread of ESBL bacteria is and will remain a major issue in the coming decades. This alarming finding of multidrug resistance should lead practitioners to a rational prescribing of antibiotics, guided preferably by the results of an antibiogram correctly performed and interpreted, and this, to reduce the selection pressure exerted by a broad spectrum antibiotic, sometimes abusive and inadequate. Compliance with the rules of good officinal practice for the dispensing of drugs, the major role that pharmacist of the city must play as antibiotic therapy advisers are all elements to promote in the control of the spread of multidrug resistance in the community. Maintaining an increased monitoring of the evolution of resistance is therefore mandatory within our training to define new therapeutic strategies adapted to local epidemiology.

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