RISK FACTORS FOR THE ACQUISITION OF ESBL PRODUCING ENTEROBACTERIACEAE AMONG PATIENTS WITH COMMUNITY-ACQUIRED URINARY TRACT INFECTIONS.

[1,3]A. Aouam, [1,3]A. Toumi, [2]Y. Kadri, [1,3]H. Ben Brahim, [1]C. Loussaief, [2]H. Ben Abdallah, [1,3]M. Chakroun.
1 Infectious Diseases Department, 2 Microbiological Department, 3 UR 12SP41 – University Hospital Monastir – Tunisia.

INTRODUCTION-OBJECTIVE

The changed epidemiology of extended spectrum beta-lactamases, the spread to the community and the need for prudent use of carbapenems require updated knowledge of risk factors for infection with ESBL producing Enterobacteriaceae (ESBL-E).

The aim of this study was to describe the epidemiology, clinical and microbiological features of urinary tract infections and to determine risk factors of uropathogenic ESBL-E.

METHODS

Retrospective study including patients admitted for community-acquired urinary tract infections at infectious diseases department in the university hospital of Monastir between 2009 and 2013. Antimicrobial susceptibility was performed by agar diffusion according to CA-SFM. A case control study was performed: cases were patients with ESBL-E (group A), control patients with susceptible strains (group B). Cases and controls were matched 1:2 based on age and gender. Covariates found to be associated with ESBL-E on univariate analysis at a level of significance $p < 0.1$ were eligible for inclusion in a multivariate logistic regression model.

RESULTS

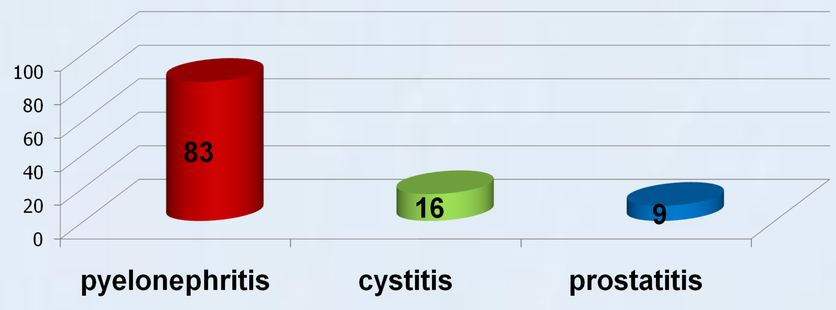
108 patients were included, 72 (66.6%) in group B and 36 (33.4%) in group A. Gender and age distribution were uniform in the two groups ($p > 0.05$). Diabetes was noted in 37 cases (51.4%) in group B and in 18 cases (50%) in group A (p=0.52). Recurrent urinary tract infection was noted in 27 cases (37.5%) in group B and in 24 cases (66.6%) in group A (p=0.004) and urinary lithiasis in 14 (19.4%) in group B and in 10 (27.7%) in group A (p=0.23). Previous hospital admission and previous antibiotics use were significantly associated with ESBL-E. (Table 1)

Table 1. Comparison of characteristics of patients in 2 groups

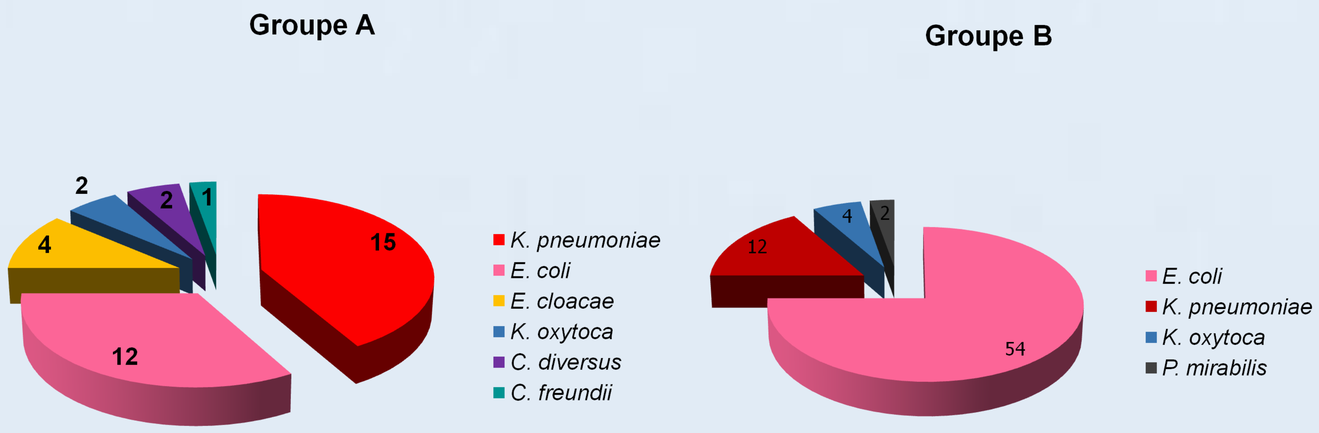
	Group B	Group A	*P* value
Patients (nb, %)	**72 (66.6%)**	**36 (33.4%)**	
Mean age (years)	**55.49**	**55.44**	0.99
Sex ratio (male/female)	**27/45**	**13/23**	1
Diabetes (nb, %)	**37 (51.4%)**	**18 (50%)**	0.52
Recurrent urinary tract infection (nb, %)	**27 (37.5%)**	**24 (66.6%)**	**0.004**
Urinary lithiasis (nb, %)	**14 (19.4%)**	**10 (27.7%)**	0.23
Hospitalization < 1 year (nb, %)	**19 (26.3%)**	**17 (47.2%)**	**0.027**
Antibiotic therapy < 6 months (nb, %)	**21 (29.1%)**	**27 (75%)**	**< 0.001**

Pyelonephritis was diagnosed in 83 cases (76.8%), cystitis in 16 cases (14.8%) and prostatitis in 9 cases (8.3%). Figure 1

Figure 1: clinical feature



K. pneumoniae was predominant in group A (41.6%) and *E. coli* in group B (79.2%). The different microorganisms in the 2 groups are indicated in figure 2.



The frequency of resistance to gentamicin, amikacin, fluoroquinolones and cotrimoxazol was significantly higher in group A. No strains in the two groups were resistant to imipenem. (Table 2)

Table 1. Comparison of frequency of resistance to antibiotic treatment of patients in 2 groups

	Resistance to antibiotics		P value
	Group A	Group B	
Gentamicin	61.1%	8.3%	< 0.0001
Amikacin	13.9%	2.7%	0.04
Fluoroquinolones	88.9%	15.3%	< 0.0001
Cotrimoxazol	83.3%	38.9%	< 0.0001
Imipenem	0%	0%	

A biantibiotherapy was prescribed in 12 cases (16.6%) in group A and in 7 cases (19.4%) in group B (p=0.7).

Multivariate analysis identified recurrent urinary tract infection, previous hospital admission and previous antibiotics use as risk factors for ESBL-E infection. (Table 3)

Table 3: Risk factors for the acquisition of ESBL producing enterobacteriaceae

Risk factors	OR	CI	*P* value
Recurrent urinary tract infection	3.33	1.43-7.73	0.004
Hospitalization < 1 year	2.49	1.07-5.77	0.027
Antibiotic therapy < 6 months	7.28	2.93-18.1	< 0.001

DISCUSSION - CONCLUSION

❖ In gram-negative pathogens, beta-lactamase production remains the most important contributing factor to antimicrobial resistance. Cases of infections with extended–spectrum ESBL-E were first reported during the late 1980s and have subsequently spread worldwide. The emergence of ESBL-E is not restricted to the health care setting but also involves the community, especially among E. coli.

❖ the survey published in 2009, has highlighted a significant increase in ESBLE in the French community setting, up to 1.1% of the urinary enterobacteria.

❖ Most of the ESBLE were resistant to the other classes of antibiotics, in particular fluoroquinolones and/or cotrimoxazole, which are commonly prescribed by general practitioners. In our study, fluoroquinolones and cotrimoxazole resistance was 88.9% and 83.3%, respectively. C. Arpin et al has revealed in his study the presence of plasmid-mediated broad-spectrum resistances co-existing with ESBLs, such as the plasmid-mediated cephalosporinase DHA-1 in one CTX-M-15-producing E. coli, and in the SHV-12-producing K. oxytoca. Another CTX-M-15 E. coli harboured the gene armA encoding 16S rRNA methylase which confers pan-aminoglycoside resistance. Although most of the ESBLE were resistant to fluoroquinolones, a single strain carried a qnr determinant, the qnrB4 allele. However, other plasmidmediated resistances such as aac(60)-Ib-cr genes have been reported to confer quinolone resistances.

❖ Our case–control study confirmed that a recent hospitalization and recurrent urinary tract infection are a major risk factor for developing community-onset ESBL-producing bacterial infections. The previous use of fluoroquinolones and b-lactams was also a risk factor for selection of ESBLE.

❖ These risk factors were found to be related with increased incidence of ESBL-E. Identifying these risk factors may help identifying which patients may warrant empiric ESBL-targeted antimicrobial drug therapy as a means to limit carbapenem use.

References:

1-K. Rzazi, LP Derde, P. Verachten et al. Clinical impact and risk factors for colonization with extended-spectrum β-lactamase-producing bacteria in the intensive care unit. Intensive Care Med 2012; 38: 1769-78.

2- C. Arpin, C. Quentin, F. Grobost et al. Nationwide survey of extended-spectrum b-lactamase-producing Enterobacteriaceae in the French community setting. Journal of Antimicrobial Chemotherapy 2009;63: 1205–1214.