Risk factors for community-acquired acute pyelonephritis caused by Extended-Spectrum beta-Lactamase-producing *Escherichia coli* in a University Hospital in Tunisia.

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Background

Escherichia coli is the most common pathogen in community-acquired acute pyelonephritis (CA-AP). The changed epidemiology of extended-spectrum beta-lactamases (ESBL), the spread to the community and the need for prudent use of carbapenems require updated knowledge of risk factors for infection with ESBL-producing *E. coli* (ESBL-E). The aim of this study was to describe the epidemiology, clinical and microbiological features of CA-AP and to determine risk factors of uropathogenic ESBL-E.

Methods

Study included all patients admitted for CA-AP caused by *E. coli,* at Infectious Diseases department in the University Hospital of Monastir between 1999 and 2014. Clinical and epidemiological features were collected. Patients aged > 14 years who presented temperature ≥ 37,8° C, flank pain and/or costovertebral tenderness, urinary tract symptoms, leukocyte count > 10^4/ml and bacteriuria > 10^5/ml were enrolled. Identification of *E. coli* was performed by API20E. The study of antibiotic susceptibility was performed by agar diffusion according to CA-SFM. Univariate analyses were run to describe the distribution, central tendency and variability. Covariates found to be associated with ESBL- producing *E. coli*, on univariate analysis at a level of significance p < 0.01, were eligible for inclusion in a multivariate logistic regression model. SPSS version 17.0 was used for analysis.

Table 1; Comparison of characteristics of patients in 2 groups (univariate analysis)

	All (n = 484)	Non ESBL (n = 442)	ESBL (n = 24)	*p-Value*
Diabetes	117 (24.2%)	105 (22.8%)	12 (50%)	**0.02**
Menopause	94 (27%)	84 (26.2%)	8(50%)	**0.037**
History of UTI	145(30%)	135 (29.3%)	10 (41.7%)	0.199
Antibiotics < 3 months	68 (14%)	58 (12.6%)	10 (41.7%)	**<0.001**
Urinary catheterisation	12 (2.4%)	9 (2%)	3 (12.5%)	**0.001**
Uropathology	31 (6.4%)	26 (5.7%)	5 (20.8%)	**0.001**
Urolithiasis	43(8.9%)	40 (8.7%)	3 (12.5%)	0.52
Complicated AP	309 (63%)	290(63%)	19 (79.2%)	0.1

Table 2: Associated resistances to ESBL producing *E. coli*

Antibiotics	Non ESBL (n = 442)	ESBL (n = 24)	*p-Value*
Gentamicine	16 (3.5%)	16 (66.7%)	<0.001
Amikacin	4 (9%)	5 (20.8%)	< 0.001
Fluoroquinolones	25 (5.5%)	4 (91.3%)	< 0.001
Cotrimoxazol	162 (35.3%)	18 (85.7%)	<0.001
Imipeneme	2 (4%)	3 (12.5%)	0.001

Table 3: Risk factors for the acquisition of ESBL producing *E. coli* (multivariate analysis)

Risk factors	OR	95% IC	p
Diabetes	**0.032**	**1.09 - 8**	**0.032**
Urinary catheterisation	3.01	0.61 - 14.73	0.17
Uropathology	**3.46**	**1.04 - 11.52**	**0.043**
Complicated AP	0.88	0.26 - 3.01	0.84
Antibiotics < 3 months	**4.04**	**1.6 - 10**	**0.003**

Results

- A total of 484 cases of CA-AP were included.
- Mean age was 45 years (14-89) and 309 (63.8%) were female.
- Mean Duration of hospitalisation was 12 days (5-90).
- History of hospitalisation in the last six months: 37 cases (7.6%).
- History of hospitalisation < 6 months was not correlated to ESBL-E isolation (p = 0.48).
- Antibiotic resistance :
  - Fluoroquinolones resistance : 46 strains (9.5%)
  - **ESBL producing : 24 (5%)**

Conclusion

- In gram-negative pathogens, beta-lactamase production remains the most important contributing factor to antimicrobial resistance.
- 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.
- Our case-control study confirmed that the use of antibiotics in last months is a major risk factor for developing community-onset ESBL-producing bacterial infections.
- Identifying these risk factors may help identifying which patients may warrant empiric ESBL-targeted antimicrobial drug therapy as a means to limit carbapenem use.