618

Augusto K L[1], Bezerra L R P S[2], Martins A G[3], Ferreira T W M[3], Façanha N C[3], Ogawa E[4], Vasconcelos Neto J A[1], Vasconcelos C T M[4], Karbage S A L[5], Bilhar A P M[6], Girão E S[4], Ohi C A[7]

***1.** Hospital Geral de Fortaleza, **2.** HOSPITAL GERAL CESAR CALS, Universidade Federal do Ceará (UFC), **3.** Universidade Estadual do Ceará (UECE), **4.** Universidade Federal do Ceará (UFC), **5.** Universidade de Fortaleza (UNIFOR), **6.** Universidade Federal de Sào Paulo (UNIFESP), **7.** Hospital Geral Cesar Cals*

ANTIMICROBIAL SUSCEPTIBILITY FROM OUTPATIENT URINE CULTURES AND TRENDS IN PRODUCTION OF ESTENDED SPECTRUM BETA-LACTAMASE (ESBL) AMONG ESCHERICHIA COLI IN BRAZILIAN TERTIARY HOSPITAL (2010-2013)

Hypothesis / aims of study

To evaluate the incidence and susceptibility of organisms found in urine cultures of outpatient women in a tertiary Hospital. Additionally the study provides evolutionary data regarding prevalence of (Extended spectrum beta-lactamase) ESBL-producing *E coli* and susceptibility to potentially active drugs.

Study design, materials and methods

An observational, transversal study was conducted at a microbiology laboratory in Brazilian tertiary hospital. Laboratory records (january 2010 to december 2013) were assessed. Clean voided midstream urine samples were collected into sterile universal bottles from suspected to have a urinary tract infectin (UTI). Only colonies showing a significant growth of 10^5 CFU/ml per or more of urine samples were considered. Antibiotic susceptibility and ESBL production were studied according to Clinical Laboratory Standards Institute (CLSI) guidelines. Each isolate was tested using the VITEK 2 system with the ESBL test panel (bioM' erieux). The proportional reduction in growth in wells containing cephalosporin plus clavulanate compared with those containing the cephalosporin alone is considered indicative of ESBL production. Data were submitted to descriptive statistics, using Statistical Package Social Science (SPSS), version 20.0. Chi-square test for linear trends was used to evaluate the distribution of *E. coli*, its antimicrobial resistance and the trends in production of ESBL (only 2010-2012) over the years studied. The level of significance was $p< 0.05$.

Results

Of a total of 2852 positive urine cultures, 1193 (41.8%) were from outpatient women. From this, *Escherichia coli* was the most frequent (59,8%), followed by *Klebsiella pneumonia (13.2%)*, *Streptococcus agalactie (9.5%)*, *Staphylococcus sp (4.2%)*, *Proteus mirabilis (3.5%)* e *Enterococcus sp (3.4%)* (table 1). There was a trend to an increased incidence of E. coli during the period studied (p<0.001) (graphic 1). *E coli* strains found in the outpatient women showed high resistance (>20%) to ampicillin, sulfametoxazol-trimetropin, ciprofloxacin and cephalotin over the studied period. We observed a trend of increasing resistance of *E. coli* only to sulfametoxazol-trimetropin and cephalotin (p<0.001)(table 2). *E coli* showed significant temporal trend of increasing resistance of amoxicillin-clavulamic acid and nitrofurantoin and a temporal trend of decreased resistance of Cefotaxime e Cefepime (p<0,001) (table 2).Cefotaxime, cefepime, amoxicillin-clavulanic acid, nitrofurantoin, amicacin, gentamicin, ertapenem and meropenem retained significant activity. Of a total of 713 *E coli* strains, 71 (9,9%) were ESBL positive. ESBL-producing E. coli significantly increased from 10.7% (2010) to 18.6% (2012) isolates per year (P value for trend < 0.001). (graphic 2).

Interpretation of results

This survey defines the current epidemiology of ESBLs among laboratory records of community patients in this population. In addition, also provides evolutionary data regarding prevalence and distribution of ESBL-producing species, types of produced enzymes, and susceptibility to potentially active drugs. The results demonstrate the amoxicillin- clavulanate and nitrofurantoin appear to be effective for community cystitis caused by E coli. In addition, we demonstrated the continued susceptibility of *E coli* to nitrofurantoin, amoxicillin-clavulamic acid, amicacin, gentamicin, second and third generation cephalosporin, ertapenem and meropenem. On the other side, we reported a widespread and increasing resistance to ampicilin, fluoroquinolona, sulfametoxazole-trimetropin and first generation cephalosporin. The high level of resistance to the quinolones and first generation cephalosporin limits the options for this drugs to effective empirical treatment of UTI within this study area. The prevalence of ESBLs is clearly increasing, despite a significant decrease between 2012 and 2013, leading to an increased resistance to cephalosporins for example.

Concluding message

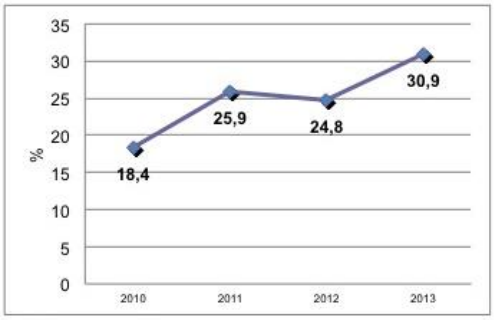
In recent years, true community-acquired infections caused by ESBL-producing enterobacteria have been described. There is a few local data about the real prevalence of ESBL-producing E coli in community, and the main agent of urinary tract infection. Data concerning risk factors, clinical features, and therapeutic options for such infections are scarce in Brazilian population. Knowledge of local antimicrobial resistance patterns in E. coli and the appearance of ESBL-positive enterobacteria is important as a guide to physician in selecting empirical antimicrobial therapy to ITU.

Table 1. Frequency of bacteria in outpatient urine culture for 2010-2013

	Frequency	%
Acinetobacter sp.	2	0,2
Escherichia coli	713	59,8
Enterobacter sp.	22	1,8
Enterococcus sp.	41	3,4
Klebsiella pneumonia	157	13,2
Morganela morgani	9	0,8

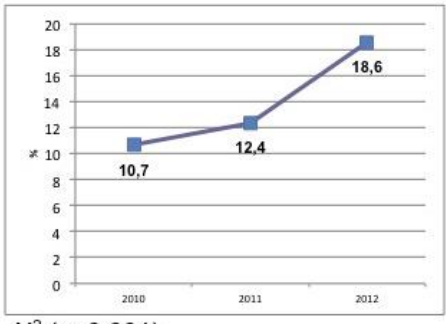
Proteus mirabilis	42	3,5
Providencia sp.	3	0,3
Pseudomonas aeruginosa	21	1,8
Staphylococcus sp.	50	4,2
Streptococcus agalactie	113	9,5
Others	20	1,7
Total	1193	100,0

Graphic 1: Incidence of *E. coli* in outpatient urine culture over the years studied (2010-2013).



X^2 (p=0,001)

Graphic 2: Trends in production of ESBL among *E. coli* over the years studied (2010-2012).



X^2 (p=0,001)

Table 2: Resistance incidence of *E. coli* present in the positive urine cultures of outpatients women between 2010 and 2013

Antimicrobial	2010		2011		2012		2013		p
	n	%R	n	%R	n	%R	n	%R	
Ampicillin	83	63,4	107	57,8	93	52,5	149	67,7	0,16
Gentamicin	14	10,7	18	9,7	14	7,9	23	10,5	0,91
Ciprofloxacin	34	26	46	24,9	50	28,2	78	35,5	0,44
sulfametoxazole-trimetropin l	57	43,5	85	45,9	88	49,7	110	50	0,00
Amoxicillin-clavuc acid	6	4,6	10	5,4	03	1,7	13	5,9	0,00
Cephalotin	29	22,1	50	27,0	48	27,1	66	30	0,00
Ceftaxime	13	9,9	18	9,7	17	9,6	11	5,0	0,00
Cefepime	13	9,9	03	1,6	07	4,0	03	1,4	0,00
Ertapenem	00	0,0	01	0,5	00	0,0	217	0,3	0,73
Nitrofurantoin	02	1,5	08	4,3	06	3,4	08	3,6	0,00
Meropenem	00	0,0	01	0,5	00	0,0	01	0,5	0,31

Disclosures
Funding: no disclosure **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Comite de Etica em Pesquisa do Hospital Geral de Fortaleza **Helsinki:** Yes **Informed Consent:** Yes