1451. Change in Clinical Characteristics of Community-Acquired Acute Pyelonephritis in South Korea: Comparison Between 2010–2011 and 2017–2018

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Background. The aim of this study was to examine the change in clinical characteristics of community-acquired acute pyelonephritis (CA-APN) in South Korea between 2010–2011 and 2017–2018.

Methods. We recruited all CA-APN patients with age ≥19 years who visited 4 hospitals in South Korea from September 2017 to August 2018, prospectively. The inclusion criteria were: (i) presence of fever (body temperature ≥37.8°C), (ii) pyuria [≥5–9 white blood cells per high power field (WBC/HPF)], and (iii) clinical symptoms or signs relevant to APN. Patients diagnosed with APN more than 48 hours after admission, those transferred from other hospitals during treatment of APN, those with other reasons for fever and pyuria, and those with insufficient data were excluded. Each patient was included for the first episode during the study period. The collected data were compared with those from the previous study with the same design in 2010–2012, in which the same hospitals were participated.

Results. A total of 349 and 472 patients were recruited during 2017–2018 and 2010–2011, respectively. *E. coli* was the most common causative pathogen for CA-APN in both periods (87.5% vs. 86.6%, $P = 0.727$). Significantly higher antimicrobial resistance against fluoroquinolone (33.5% vs. 21.0%, $P = 0.001$), cefotaxime (34.8% vs. 7.6%, $P = 0.040$) were observed for *E. coli* isolates in 2017–2018 compared with those in 2010–2011. The patients in 2017–2018 were older (60.71±17.29 vs. 55.77±18.60, $P < 0.001$) and had higher Charlson's comorbidity index (1.04±1.39 vs. 0.68±1.17, $P<0.001$) than those in 2010–2011. Total duration of antibiotic treatment increased from 15.40 ± 6.35 days in 2010–2011 to 21.74 ± 11.72 days in 2017–2018, $P < 0.001$); the proportion of patients using carbapenem increased from 6.1% in 2010–2011 to 26.6% in 2010–2011 ($P < 0.001$). The median days of admission was higher for patients in 2017–2018 than those in 2010–2011 (10 vs. 8, $P < 0.001$).

Conclusion. Patients with CA-APN in South Korea were aging. Antimicrobial resistance of *E. coli* to almost all antibiotic classes, especially third-generation cephalosporin, increased significantly and total duration of antibiotic treatment and proportion of carbapenem usage increased, consequently.

Table 1. Comparison of antibiotic susceptibility between *E. coli* isolates in 2010-2011 and those in 2017-2018

	2010-2011 (n=291)		2017-2018 (n=248)		
	Sensitive (%)	Resistant (%)	Sensitive (%)	Resistant (%)	*P*
Amikacin (AMK)	288 (99.0)	3 (1.0)	248 (100)	0 (0)	0.253
Amoxicillin/clavulanate (AMC)	**152 (80.9)**	**36 (19.1)**	**155 (72.4)**	**59 (27.6)**	**0.047**
Ampicillin (AMP)	**101 (35.6)**	**183 (64.4)**	**61 (24.6)**	**187 (75.4)**	**0.006**
Ampicillin/sulbactam (SAM)	**55 (51.9)**	**51 (48.1)**	**39 (38.2)**	**63 (61.8)**	**0.048**
Aztreonam (ATM)	**260 (91.2)**	**25 (8.8)**	**172 (69.4)**	**76 (30.6)**	**<0.001**
Cefazolin	**120 (82.2)**	**26 (17.8)**	**111 (61.7)**	**69 (38.3)**	**<0.001**
Cefepime (FEP)	**262 (92.3)**	**22 (7.7)**	**169 (68.1)**	**79 (31.9)**	**<0.001**
Cefotaxime (CTX)	**269 (92.4)**	**22 (7.6)**	**161 (65.2)**	**86 (34.8)**	**<0.001**
Cefoxitin (FOX)	174 (96.1)	7 (3.9)	231 (93.1)	17 (6.9)	0.184
Ceftazidime (CAZ)	**267 (92.1)**	**23 (7.9)**	**171 (69.0)**	**77 (31.0)**	**<0.001**
Fluoroquinolone (FQ)	**229 (79.0)**	**61 (21.0)**	**165 (66.5)**	**83 (33.5)**	**0.001**
Gentamicin (GEN)	**231 (79.4)**	**60 (20.6)**	**166 (66.9)**	**82 (33.1)**	**0.001**
Imipenem (IPM)	289 (99.7)	1 (0.3)	248 (100)	0 (0)	1.000
Meropenem (MEM)	218 (99.5)	1 (0.5)	102 (100)	0 (0)	1.000
Piperacillin (PIP)	69 (35.0)	128 (65.0)	21 (30.9)	47 (69.1)	0.534
Piperacillin/tazobactam (TZP)	274 (95.1)	14 (4.9)	234 (94.4)	14 (5.6)	0.684
Trimethoprim/sulfamethoxazole (SXT)	**184 (71.6)**	**73 (28.4)**	**114 (62.3)**	**69 (37.7)**	**0.040**
Tobramicin (TOB)	**230 (79.3)**	**60 (20.7)**	**62 (61.4)**	**39 (38.6)**	**<0.001**

Table 2. Comparison of demographic data and risk factors between patients with community-acquired acute pyelonephritis in 2010-2011 and those in 2017-2018

	2010-2011 (n=472)	2017-2018 (n=349)	*P*
Demographic data			
Age (years), mean ± SD	**55.77±18.60**	**60.71±17.29**	**<0.001**
Female sex (%)	441 (93.4)	317 (90.8)	0.166
Underlying co-morbidities (%)			
Charlson's comorbidity index, mean ± SD	**0.68±1.17**	**1.04±1.39**	**<0.001**
Diabetes mellitus	**119 (25.2)**	**113 (32.4)**	**0.024**
Hemiplegia	9 (1.9)	3 (0.9)	0.216
Cerebrovascular accident	36 (7.6)	34 (9.7)	0.283
Congestive heart failure	25 (5.3)	12 (3.4)	0.205
Connective tissue disease	**8 (1.7)**	**22 (6.3)**	**0.001**
Malignancy	**15 (3.2)**	**32 (9.2)**	**<0.001**
Chronic pulmonary disease	9 (1.9)	11 (3.2)	0.253
Liver disease	**11 (2.3)**	**19 (5.4)**	**0.019**
Renal disease	**17 (3.6)**	**25 (7.2)**	**0.025**
Dementia	15 (3.2)	16 (4.6)	0.296
Pregnancy	0 (0)	1 (0.3)	0.425
Menopause	**256/441 (58.0)**	**147/326 (45.1)**	**<0.001**
Bedridden state	14 (3.0)	13 (3.7)	0.547
Underlying urinary tract conditions (%)			
Intubated urinary tract	7 (1.5)	8 (2.3)	0.392
Intermittent catheterization	3 (0.6)	0 (0)	0.266
Benign prostatic hyperplasia	**4/31 (12.9)**	**13/32 (40.6)**	**0.013**
Neurogenic bladder	**2 (0.4)**	**14 (4.0)**	**<0.001**
Urolithiasis	9 (1.9)	6 (1.7)	0.843
Urinary retention	0 (0)	3 (0.9)	0.076
Vaginal wall prolapse	1/441 (0.2)	2/326 (0.6)	0.578
Polycystic kidney	4 (0.8)	0 (0)	0.141
Renal tumor	0 (0)	3 (0.9)	0.076

Table 3. Comparison of clinical characteristics between patients with community-acquired acute pyelonephritis in 2011-2012 and those in 2017-2018

	2010-2011 (n=472)	2017-2018 (n=349)	*P*
Clinical characteristics			
Pitt's score, mean ± SD	**0.48±0.99**	**0.67±0.95**	**0.008**
Urinary tract infection symptoms (%)	**318 (67.4)**	**180 (51.6)**	**<0.001**
Costovertebral angle tenderness (%)	305 (64.6)	230 (65.9)	0.703
Back pain (%)	**147 (31.1)**	**53 (15.2)**	**<0.001**
Vomiting/diarrhea (%)	124 (26.3)	84 (24.1)	0.473
Hematuria (%)	245 (51.9)	166 (47.6)	0.219
Azotemia (%)	**77 (16.3)**	**98 (28.1)**	**<0.001**
Bacteremia (%)	**154 (32.6)**	**137 (39.3)**	**0.050**
Duration of total antibiotics, days, mean ± SD	**15.40±6.35**	**21.74±11.72**	**<0.001**
Patients underwent following antibiotic regimen			
ESCs (%)	**273 (57.8)**	**303 (86.8)**	**<0.001**
FQs (%)	**119 (25.2)**	**167 (47.9)**	**<0.001**
Carbapenems (%)	**29 (6.1)**	**93 (26.6)**	**<0.001**
BL/BLIs (%)	**47 (10.0)**	**114 (32.7)**	**<0.001**
Outcomes			
Clinical failure (%)	17/452 (3.8)	7/342 (2.0)	0.162
Hospitalization days, median (IQR)	**8 (6-11)**	**10 (7-14)**	**<0.001**
Febrile days, median (IQR)	**2 (1-3)**	**3 (1-4)**	**<0.001**
Medical cost, 1,000 KRW, median (IQR)	N/A	3,100 (2,213-4,984)	-

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1452. Is Carbapenem-Sparing Therapy as Effective as Carbapenems Against Extended-Spectrum β-Lactamase Producing Enterobacteriaceae in UTI?

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Background. With the emergence of carbapenem-resistant strains of Enterobacteriaceae, non-carbapenem antibiotics are suggested as the alternative treatment of extended-spectrum β-lactamase (ESBL) producing Enterobacteriaceae infection. In this study, efficacy of non-carbapenem antibiotics on acute pyelonephritis (APN) with ESBL-producing Enterobacteriaceae was compared with that of carbapenems.

Methods. The medical records of patients who had diagnosed to have acute pyelonephritis with ESBL-producing Enterobacteriaceae on their urine culture, from January 2011 to December 2018, were reviewed retrospectively. Patients were classified as carbapenem and non-carbapenem group according to the definitive antibiotics they had treated with.

Results. Total number of patients was 141, including 112 (79.4%) who had received carbapenem, and 29 (20.6%) received non-carbapenem as definitive therapy against to APN with ESBL-producing Enterobacteriaceae. The duration of hospitalization was shorter for non-carbapenem group (median 9.93 days) than for carbapenem group (median 14.39 days) ($P < 0.001$). The duration of negative conversion of culture was shorter for carbapenem group (median 40.73 hours) than for non-carbapenem group (median 56.79 hours). There was no significant difference in time to febrile period and duration of definitive therapy between two groups.

Conclusion. Non-carbapenem therapy against APN with ESBL-producing Enterobacteriaceae has no significant difference in clinical outcome compared with carbapenem therapy.

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1453. Cephalexin and Cefadroxil Are Not Therapeutic Equivalents for Uncomplicated Cystitis (uUTI): Further Analysis of Cefazolin Surrogate Susceptibility Testing Criteria

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Background. Cephalexin (CLEX) and cefadroxil are first-generation oral cephalosporins (OC's) with similar antimicrobial spectrums, side-effects, and high urine concentrations; and are US-FDA approved for uUTI. Some stewardship programs are replacing CLEX (4 × daily) with cefadroxil (2 × daily) for dosing convenience. The US Committee on Antimicrobial Susceptibility Testing (USCAST) and CLSI recommend a cefazolin (CZOL) UTI surrogate breakpoint (≤16 mg/L; ≥15 mm) to predict susceptibility (S) for 7 OC's against indicated Enterobacteriaceae. Direct cefadroxil antimicrobial S testing (AST) does not exist in US breakpoint interpretive documents, limiting specific results.

Methods. We reanalyzed and compared the CZOL surrogate testing for cefadroxil, CLEX and 5 other OC's using AST data previously reported (Schuetz et al., 2013; IHMA). Broth microdilution AST was used against 205 isolates: *E. coli* (92; 40% with β-lactamase), *K. pneumoniae* (62), *P. mirabilis* (31; 10% with β-lactamase), and other enteric bacilli (20). A CZOL surrogate S breakpoint (≤16 mg/L) was used to infer S for OC's.

Results. CZOL X cefadroxil cross-S accuracy rate was only 91.6% (unacceptable; < 95%) and the false resistance was 1.0% (acceptable). Cross-S accuracy was ≥ 97.0% for all tested OC's except cefadroxil and cephradine (80.1%). CZOL spectrum vs. tested, indicated species (81.0%) was essentially identical for CLEX, cefprozil, cefaclor and loracarbef (80.0–81.0%). In contrast, cefdinir, cefpodoxime, and cefuroxime axetil S rates were underestimated 5.3 to 10.7% by the surrogate test. CLSI and USCAST did not list cefadroxil or cephradine for CZOL surrogate uUTI prediction; however

the current (2019) US-FDA website document states "cefadroxil may be deduced from testing CZOL" regardless of clinical indication.

Conclusion. Cefadroxil -S for guiding uUTI therapy cannot be accurately predicted by CZOL results at ≤16 mg/L (unacceptable surrogate accuracy and compromised spectrum/potency). Furthermore, direct cefadroxil AST does not exist in United States due to lack of breakpoint criteria (CLSI, USCAST) and reagent materials (MIC products or disks). CLEX or other OC's remain preferred, more active (table) uUTI treatment choices having quality direct or surrogate AST guidances.

Table 1 Cross S analysis for cefazolin (≤16 mg/L) versus cephalexin or cefadroxil (≤16 mg/L)

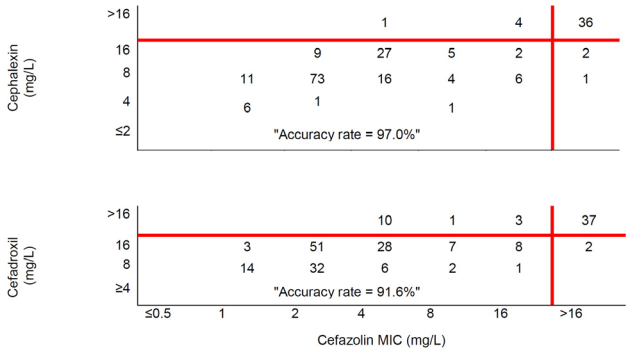

Table 2. Key antimicrobial analyses from 205 Enterobacteriaceae tested against cefazolin and nine orally administered cephalosporins [Schuetz et al; CLSI; USCAST]

Cephalosporin [a]	MIC_{50} (mg/L)	% susceptible at ≤16 mg/L	% cefazolin surrogate accuracy	Listed for surrogate testing
Cefazolin [b]	2	81.0	NA[b]	NA[b]
Cefpodoxime	≤0.25	91.7	100.0	Yes
Cefdinir	≤0.25	89.8	100.0	Yes
Cefuroxime axetil	2	86.3	98.8	Yes
Cefaclor	2	81.0	98.8	Yes
Loracarbef	2	81.0	98.8	Yes
Cefprozil	2	80.0	97.0	Yes
Cephalexin	8	80.0	97.0	Yes
Cefadroxil	16	75.1	91.6	No
Cephradine	16	66.8	80.0	No
Cefixime, Ceftibuten [c]	-	-	-	No

a. Cefixime and ceftibuten were not tested in this experiment
b. NA = not applicable (surrogate agent)
c. Excluded from surrogate use list due to poor accuracy (unacceptable false-susceptibility rates)

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1454. Cephalosporins and Quinolones Account for 95 Percent of Oral Antibiotic Treatment for Uncomplicated Cystitis in Japan

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Background. Uncomplicated cystitis (UC) imposes a large burden on antimicrobial use due to its high morbidity. IDSA/ESCMID guidelines recommend nitrofurantoin, sulfamethoxazole/trimethoprim (SMX/TMP), fosfomycin trometamol, and pivmecillinam for treating UC, but only SMX/TMP and fosfomycin calcium (FOM-C) are available in Japan. Therefore, we examined the antibiotics use to treat UC in Japan.

Methods. We obtained data from the JMDC Inc. claims database, which includes data of corporate employees and their family members. We extracted all records of oral antibiotic prescriptions for the treatment of acute cystitis (ICD-10 code: N300) between 2013 and 2016, and excluded prescriptions for male individuals and inpatients because they were considered to have complicated cystitis. Prescriptions for durations >7 days were also excluded because they were potentially prophylactic. Furthermore, we defined treatment failure as cases that required re-prescription within 13 days after the first prescription and estimated the treatment failure rate (TFR) of each antibiotic.

Results. Cephalosporins and quinolones accounted for 41.5% and 53.2% of the total number of antibiotic prescriptions (48,678). SMX/TMP and FOM-C only accounted for 0.7% and 0.8%. Third-generation cephalosporins accounted for 93.8% of total cephalosporins. TFR was less than 10% across almost all antibiotic categories, with the only exception being FOM-C.

Conclusion. Cephalosporins and quinolones accounted for 94.7% of oral antibiotic treatment for UC in Japan between 2013 and 2016. To avoid spreading antimicrobial resistance, approval of new antibiotics with good efficacy or an official recommendation for the use of narrower-spectrum antibiotics for treating UC may be required.

Table. Proportion of prescription and treatment success rate of each antibiotics

Drug name	Proportion of total prescription (%)	Treatment failure rate (%)
penicillin-combinations	0.4	8.5
first generation cephalosporins	0.5	8.8
second generation cephalosporins	1.9	4.1
third generation cephalosporins	37.9	6.3
faropenem	0.9	8.4
sulfamethoxazole/trimethoprim	0.7	6.6
quinolones	53.6	5.2
fosfomycin calcium	0.8	10.7
Others	3.3	-

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1455. Epidemiology, Empiric Treatment, and Outcomes Among Hospitalized Patients With Complicated Urinary Tract Infections in the United States, 2013–2018

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Background. Complicated urinary tract infection (cUTI) is common among hospitalized patients. Though carbapenems are an effective treatment in the face of rising resistance, overuse drives carbapenem resistance (CR). We hypothesized that resistance to routinely used antimicrobials is common, and, despite the frequent use of carbapenems, associated with an increased risk of inappropriate empiric treatment (IET), which in turn worsens clinical outcomes.

Methods. We performed a multicenter retrospective cohort study in ~180 hospitals in the Premier database, 2013–2018. Using an ICD-9/10-based algorithm we identified all adult patients hospitalized with cUTI and a positive blood or urine culture (CR excluded). We examined with the impact of triple resistance (TR; resistance to >3 of the following drugs/classes: third-generation cephalosporin [C3R], fluoroquinolones, trimethoprim-sulfamethoxazole, fosfomycin, and nitrofurantoin), on the risk of receiving IET. We derived multivariate models to compute the impact of IET on hospital outcomes.

Results. Among 23,331 patients with cUTI (96.2% community-onset), 3,040 (13.0%) had a TR pathogen. Compared with those with non-TR, patients with TR were more likely male (57.6% vs. 47.7%), black (17.9% vs. 13.6%), and in the South (46.3% vs. 41.5%), $P < 0.001$ each; had a higher median Charlson score (3 vs. 2), and were more likely to need early ICU (22.3% vs. 18.6%) and mechanical ventilation (7.0% vs. 5.0%), $P < 0.001$ each. Patients with TR were hospitalized at centers with higher median prevalence of both C3R (16.3% vs. 14.4%) and TR (15.1% vs. 12.2%), $P < 0.001$ each. IET was more frequent in TR than non-TR group (19.6% vs. 5.4%) despite greater empiric carbapenem use in TP (43.3% vs. 16.2%), $P < 0.001$ each. Though IET did not have an impact on adjusted hospital mortality or 30-day readmission rate, it was associated with excess adjusted resource utilization ($1,364 in costs and 0.66 day in length of stay).

Conclusion. Among hospitalized patients with cUTI, TR is common, and is associated with a nearly 4-fold increase in exposure to IET, which in turn contributes to excess resource utilization. Given the high prevalence of TR, clinicians should consider a lower threshold for broader empiric treatment in appropriate patients.

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1456. Increase in Resistance to Antibiotics in Enterobacteriaceae from Ambulatory Urinary Samples in Buenos Aires City

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Background. During the last years, an increase in the rates of resistance among causal agents of urinary tract infection (UTI) has been reported, even in community-acquired infections. This increase in resistance is problematic since it affects most therapeutic agents used in the ambulatory setting and often implies the lack of oral options for treatment. The aim of this study was to determine whether there were changes in the prevalence of resistance among samples from patients with UTI in the ambulatory setting caused by the most common *Enterobacteriaceae*.

Methods. We analyzed the resistance profiles of the three most common *Enterobacteriaceae* recovered in cultures from urinary samples of ambulatory adult patients, processed in a reference Laboratory in Buenos Aires City; according to