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TREND OF ESBL-PRODUCING *ESCHERICHIA COLI* ATA TERTIARYCARE UNIVERSITY HOSPITAL IN THE CENTRAL REGION OF JAPAN FROM 2008 TO 2010

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Abstract

The issue of extended–spectrum beta-lactamase (ESBL) production is one of the most serious problem for control of various bacterial infection disease through the world. This study was conducted to find out thetrend of characteristics of ESBL-producing *Escherichia coli* isolates at tertiary care university hospital in the central region of Japan from 2008 to 2010. *Escherichia coli* was identified by standard laboratory procedure. Antibacterial susceptibility testing was performed by micro dilution assay according to CLSI recommendation and isolates showing *in vitro* resistance to ceftazidime or cefotaximewere classified as ESBL-producing organism. Two hundred six *Escherichia coli* isolations were determined as ESBL-producing bacteria for three years. One hundred nine bacteria were isolated from female. The majority of age incidence were from sixty to eighty years age group. One hundred two isolates were from inpatient. The major source of isolates were urine and positive samples were received mostly from the urology. ESBL phenotype showed that cefotaxime-resistant isolates were greater than ceftazidime-resistant isolates.There were significant differences of trend of gender and the third cephalosporin resistant rates between 2008 and 2010. The continuous surveillance of ESBL-producing *Escherichia coli* is needed for treatment of *Escherichia coli* infectious disease.

Keywords: Escherichia Coli, Susceptibility, Antimicrobial Resistance, Extended-Spectrum Beta-Lactamase,

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INTRODUCTION

Escherichia coli is one of the most common pathogen bacteria that cause a variety of infections such as pneumonia, urinary tract and blood stream infections (Kang et al., 2013). The use of beta-lactams has become difficult in recent years as various classes of beta-lactamases such as extended-spectrum beta-lactamase (ESBL) have found in clinical *Escherichia coli* isolates (Bush et al., 1995). The present study was conducted to find out the trend of characteristics of ESBL-producing *Escherichiacoli* isolates at a tertiary care university hospital in the central region of Japan for three years.

MATERIALS AND METHODS

Strains and clinical data collection

A total of two hundred six *Escherichia coli* species were obtained from various clinical specimens at Nagoya City University hospital from 2008 to 2010. Nagoya City University hospital is an 808-bed tertiary care university hospital in the central region of Japan.

We used medical records appended to clinical species for the analysis of clinical feature at Nagoya City University Hospital. We considered several isolates from the same region of the same patient as one isolate per one patient for the analysis in this study. All *Escherichia coli* isolates were identified by standard conventional biochemical methods or the VITEK2 system (bioMérieux, Durham NC, USA). Our experimental design was approved by the ethics committee at Nagoya City University.

ESBL determination

Escherichia coli isolates were examined for CAZ; ceftazidime, and CTX; cefotaxime. Minimal inhibitory concentration (MICs) were determined using broth micro dilution methodology with the VITEK2 system. Evaluation of antibacterial resistance was based on Clinical Laboratory Standard Institute (CLSI) break point (M100-S20). For the purposes of this study, isolates showing *in vitro* resistance to CAZ or CTX were classified as ESBL-producing organism (Sohn *et al.,* 2011).

Statistical analysis of the data

The statistical analysis was conducted using a one-way analysis of variance (ANOVA) followed by Bonferroni/Dunnett's multiple t-test for the differences among multiple groups. Differences were considered significant when p was <0.05.

RESULTS

Total one thousand five hundred ninety three *Escherichia coli* was isolated in this study. Of them, two hundred six (12.9%) *Escherichiacoli* isolateswereclassified as ESBL-producing organism. One hundred nine isolates (52.9%) were from female and ninety-seven (47.1%) were from male for three years (Table 1).

Table 1. Demographic and clinical characteristics patterns of ESBL-producing *Escherichia coli*

		2008	2009	2010	Total
Gender					
	Female	31	33	45	109
	Male	23	31	43	97
Age					
	0-1	2	13	12	27
	1-10	1	1	4	6
	11-20	0	1	0	1
	21-30	1	1	2	4
	31-40	1	3	3	7
	41-50	5	1	5	11
	51-60	7	3	5	15
	61-70	10	14	18	42
	71-80	18	20	20	58
	81-90	7	7	19	33
	91-100	2	0	0	2
Hospitalization					
	Inpatient	20	32	50	102
	Outpatient	34	32	58	104
Department					
	Cardiology	0	1	4	5
	Cardiology	0	0	6	6
	Endocrinology	1	0	0	1
	Emergency room	5	3	5	13
	Gastroenterology	0	1	4	5
	General medicine	1	4	3	8
	Gynaecology	0	2	2	4
	Haematology	0	1	4	5
	ICU	4	2	0	6
	Nephrology	1	0	3	4
	Neurology	2	0	1	3
	Neurosurgery	2	0	0	2
	Ophthalmology	1	1	0	2
	Orthopaedics	0	2	1	3
	Otolaryngology	1	1	0	2
	Paediatric surgery	0	5	1	6
	Paediatrics	1	0	4	5
	Respiratory medicine	0	2	3	5
	Rheumatology	0	1	0	1
	Surgery	1	1	4	6
	Urology	34	37	43	114
Biological sources					
	Pharyngeal mucus	4	1	0	5
	Pus	1	1	3	5
	Secretion/effusion	1	9	6	16
	Blood	4	3	9	16
	Bile	0	1	2	3
	Urine	39	45	54	138
	Nasal discharge	0	9	4	13
	Sputum	5	4	10	19

There were significant differences of gender between 2008 and 2010 (p=0.03). The total age incidence among 0-1 years age group was 27 (13.1 %), among 1-10 years age group, 6(2.9%), among 11-20 years age group, 1(0.5%), among 21-30 years age group, 4(1.9%), among 31-40 years age group, 7(34%), among 41-50 years age group, 6(5.3%), among 51-60 years age group, 15(7.3%), among 61-70 years age group, 42(20.4%), among 71-80 years age group, 58(28.1%), among 81-90 years age group, 33(16%), among 91-100 years age group, 2(1%), (Table 1). One hundred two isolates (49.5%) were from inpatient and one hundred four (50.5%) were from outpatient (Table 1). In our study, urine 138 (67%) were the major source of *Escherichia coli* isolates (Table 1). Most of the *Escherichia coli* isolates were from the urology (114/55.3%) (Table 1).The results of cefotaxime and ceftazidimesusceptibility of ESBL-producing *Escherichia coli* isolates in this study are shown in Table 2.

Table 2. Ceftazidime (CAZ) - andcefotaxime (CTX) -resistant rates of ESBL-producing *Escherichiacoli*

		2008	2009	2010	Total
Antibiotics					
	CAZ	47	60	74	181
	CTX	53	61	85	199

Although we speculated all ESBL-producing *Escherichia coli* had both cefotaxime and ceftazidime resistant activities, ESBL phenotype showed that cefotaxime-resistant isolates were greater than ceftazidime-resistant isolates in our study. There were significant differences of the third-cephalosporin resistant rates between 2008 and 2010 (p=0.02)

DISCUSSION

In this study, we described the characteristics of ESBL-producing *Escherichia coli* isolates from 2008 to 2010 at a tertiary care university hospital in the central region of Japan. From the point of view of gender group, ESBL-producing *Escherichia coli* was isolated more from female than male. Furthermore, our study showed that there were significant differences of trendof gender group between 2008 and 2010.

Next, we clarified ESBL-producing *Escherichia coli* with age distribution. The present study revealed the major prevalence of ESBL-producing *Escherichia coli* were 28.1% (71-80 years age group), 20.4% (61-70 years age group), 16%(81-90years age group), 13.1% (0-1 years age group), respectively. Although young patients under 1 years frequently caused *Escherichia coli* infection, the about two-third of *Escherichia coli* was isolated from over 60 years age patients in our study. It is suggested to decrease immunity in the extremes of age groups. With respect to hospitalized group, there were no significant differences among hospitalization. Our result represented that ESBL-producing *Escherichia coli* was disseminated worldwide. In the analysis of biological sources, we found that biological sources where most patients with *Escherichia coli* was detected was urine. Furthermore, in the analysis of clinical departments, we found that department where most patients with *Escherichia coli* was detected was urology. Our result showed that urinary tract disease were usually popular as *Escherichia coli* infectious diseases. The disease burden of ESBL-producing *Escherichia coli* infections

has increased due to widespread emergence of antibacterial resistance in many countries from1980s (Turner *et al.,* 2005). Our study also demonstrated that there were significant differences of trend of the third cephalosporin resistant rates between 2008 and 2010. Previous worldwide study documented that ESBL-producing *Escherichia coli* was very prevalent in Eastern Europe (28.9%) followed by South America, southern Europe, and Asia (18.1 %, 16.0%, and 14.2%, respectively), and contrasting with the 7.5% and 6.2% in North America and northern Europe, respectively in MYSTIC studies (Turner *et al.,*1999).

In SMART study, 42.2% of *Escherichia coli* isolated from intra-abdominal infections in the Asia-Pacific region during 2007, was ESBL positive (Hawser et al., 2009). ESBL positivity of *Escherichia coli* isolates was 10.2% in tertiary-care hospitals in Korea (Ko *et al.*, 2008). The prevalence of Enterobacteriaceae isolates with ESBL was 14% in *Escherichia coli* in Taiwanese intensive care units (Jean *et al.,* 2009). The ESBL rates in India for *Escherichia coli* was 79% (Hawser *et al.*, 2009). Although other Japanese study showed that about 3% of *Escherichia coli* was ESBL positive in north eastern region of Japan (Yano *et al.*, 2013), our result is almost consistent with previous Asian result of ESBL-producing *Escherichia coli.* We need reassess the regional localization pf prevalence of ESBL-producing *Escherichia coli* in Japan. Systemic review and meta-analysis demonstrated that ESBL production is associated with increased mortality and a delay in effective therapy in *Escherichia col*i bacteraemia (Schwaber *et al.*, 2007). In Korean study, ESBL-producing *Escherichia coli* is a significant cause of bacteraemia even in patients with community-onset infections (Kang *et al.*, 2010). Furthermore, ESBL-positive infections led to significantly higher costs from hospitalization and intravenous antibiotics, as well as longer hospital stays (Hu *et al.*, 2010). Henceforth we need to focus on the characteristics in ESBL-producing *Escherichia coli* isolates.

Conclusion

Incidence of ESBL-producing *Escherichia coli* infection is increasing, both in healthcare institutions and throughout communities, in many countries such as Asia. Further continuous surveillance is essential for providing information on the trends in antibacterial resistance in Asia including Japan.

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