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**Original Article**

# International Comparison of Causative Bacteria and Antimicrobial Susceptibilities of Urinary Tract Infections between Kobe, Japan, and Surabaya, Indonesia

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**SUMMARY:** Variation by country in urinary tract infection (UTI)-causative bacteria is partly due to the differences in the use of antibiotics. We compared their frequencies and antibiotic susceptibilities in the treatment of patients with UTI from 2 cities, Kobe, Japan, and Surabaya, Indonesia. We retrospectively analyzed 1,804 urine samples collected from patients with UTI in 2014 (1,251 collected in 11 months at Kobe University Hospital in Kobe and 544 collected in 2 months at Dr. Soetomo Hospital in Surabaya). Surabaya data were divided into adult and pediatric patients because a substantial number of specimens from pediatric-patients had been collected. The results indicated that *Escherichia coli* was the most common uropathogen (24.1% in Kobe and 39.3% in Surabaya) and was significantly resistant to ampicillin and substantially to first- and third-generation cephalosporins in Surabaya adults but not in Kobe adults ($p < 0.01$). *Enterococcus faecalis* was often isolated in Kobe (14.0%), but not in Surabaya (5.3%). *Klebsiella* spp. were isolated at a higher rate in Surabaya pediatric patients (20.3%) than in Surabaya adults (13.6%) and Kobe adults (6.6%). The antibiotic susceptibilities of the isolates form Surabaya isolates tended to be lower than the ones from Kobe. Extended-spectrum β-lactamase-producing Gram-negative bacteria were detected at a significantly higher rate in Surabaya than in Kobe ($p < 0.001$). These results showed that the antimicrobial resistance patterns of UTI-causative bacteria are highly variable among 2 countries, and the continuous surveillance of trends in antibiotic resistance patterns of uropathogens is necessary for the future revision of antibiotic use.

## INTRODUCTION

Urinary tract infections (UTIs) are representative common infectious diseases, with nearly 10% of people will experience a UTI during their lifetime as well as respiratory tract infections (1). Importantly, the epidemiology of UTI varies among countries due to geography variation and antibiotic use (2). Rapid initiation of antibiotic-therapy with broad-spectrum antibiotics are important to treatment success, but the frequent use often results in an emergence of high-level antibiotic resistance bacteria (3,4). *Escherichia coli* is the most prevalent causative organism of both uncomplicated and complicated UTI. However, Gram-positive bacteria, such as *Enterococcus*, have become a representative causative agent of complicated UTIs in adults (5,6). On the other hand, pediatric UTIs are somewhat different from adult UTIs partly because of underlying diseases such as vesicoureteral reflux (VUR) (7). Thus, the UTI in a pediatric patient should be considered separately from one in adult patient. Pediatric UTIs are generally managed in a pediatric hospital in the Japanese medical system, whereas they are managed in the urological department in Indonesia (8).

There are many studies that reported epidemiology including antibiotic-susceptibility distributions of UTI-causative bacteria, but these studies usually showed results that were obtained from a single center or multicenter in one country (8). There are few studies that have investigated the between-country differences of UTI-causative bacteria, and that have focused on the comparison between developed and developing countries. In addition, for pediatric UTI, the characteristics of antibiotic susceptibilities of causative pathogens in this population have not been well-examined, despite the UTI being one of the leading

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cause of all pediatric infections in Surabaya (9).

In this study, we evaluated the UTI-causative bacteria and their susceptibility patterns to commonly administered antibiotics among UTI patients in 2 different cities of Asia, such as Kobe, Japan, and Surabaya, Indonesia (included pediatric UTI patients in Surabaya) and compared the results between these 2 distinct regions of Asia. This study was conducted as a part of the Kobe-Surabaya international collaborative study that was supported by the Japan Initiative for Global Research Network on Infectious Disease (J-GRID) project.

## MATERIALS AND METHODS

**Study setting:** Data were retrospectively gathered in the microbiology sections of Kobe University Hospital (Japan) and Dr. Soetomo Hospital (Surabaya, Indonesia). Kobe is located in the southern area of the Hyogo Prefecture and has a population of 1.5 million, with 105 local hospitals. Kobe University Hospital is a national university hospital that has 35 departments with over 900 beds, and at least 640 doctors who care for more than 497,000 outpatients and 306,000 inpatients annually. Surabaya is the second-largest city in Indonesia which is the capital of East Java and located in eastern Indonesia, with a population of 3 million. Dr. Soetomo Hospital is the largest hospital in eastern Indonesia and one of the central tertiary referral hospitals in Indonesia. Dr. Soetomo Hospital has over 1,500 beds and 26 departments. On average, the hospital cares for more than a half-million outpatients and over 40,000 inpatients. We chose these 2 cities for comparison because one represented a city in a developed country, and the other represented a city in a developing country.

In Surabaya, urine samples were collected from 544 patients with UTI (both inpatient and outpatients) and referred to the central clinical laboratory for urine culture from September to October 2014. Patient age ranged from 1.5 years to 65 years (mean age, 28.2 years). Patients aged 0 to 15 years were designated as children in this study. Samples were collected from children aged 0 to 3 years using sterile urine bags and from children aged 4 years to 15 years and adult patients aged 16 years or older by clean-catch midstream urine. In Kobe, 1,251 urine samples were collected from adult UTI inpatients and outpatients from January to November 2014.

**Ethical approval:** This study was approved by the institutional review board of Kobe University as an international study. All experiments were carried out in compliance with the relevant laws and guidelines, in accordance with the ethical standards of the Declaration of Helsinki.

**Sample collection:** Urine cultures were tested just after taking samples. Samples were inoculated on blood agar and MacConkey agar and incubated at 37°C overnight; for negative results, incubation was extended for 2 days. For semi-quantitative urine cultures, samples were inoculated on cysteine-lactose-electrolyte-deficient agar. Urine samples were considered positive for UTI when a single organism or 2 organisms were cultured at a concentration of $\geq 10^5$ colony forming unit (CFU) /ml, or when a single organism was cultured at a concentration of $>10^4$ CFU/ml and $\geq 5$ leukocytes per high-power field were observed on microscopic examination of the urine. The microorganisms isolated were identified by following standard biochemical procedures (10), and bacterial identification was based on the automatic diagnostic machine system BD Phoenix Automated Microbiology System (Becton Dickinson, Franklin Lakes, NJ, USA) according to the manufacturer's standard protocols (11).

**Antimicrobial susceptibility tests:** Antimicrobial susceptibility of isolates was tested by the disk diffusion method according to the Clinical and Laboratory Standards Institute (CLSI) recommendations, using Mueller-Hinton medium (12). Antimicrobial agents tested were ampicillin (AMP), cefazolin (CFZ), cefotaxime (CTX), ceftazidime (CAZ), imipenem (IPM), gentamicin (GEN), amikacin (AMK), levofloxacin (LVX), fosfomycin (FOF), and vancomycin (VAN) using BD BBL Sensi-Disc (Becton Dickinson, Sparks, MD, USA).

Extended-spectrum β-lactamase (ESBL)-producing bacteria were diagnosed with a positive ESBL test. Results were considered positive with the formation of inhibition zone by clavulanic acid (CLA) on the middle CAZ/CLA disc surrounded by the discs of CTX, CTX/CLA, cefpodoxime, and cefepime based on the double disc synergy test (13).

**Statistical analysis:** In the statistical analysis, discrete variables were expressed as percentages, and proportions were compared using the Chi-square test.

## RESULTS

**Bacterial isolation:** During a 2-month period, a total of 94 isolates were identified among the pediatric patients in Surabaya. All the data are shown in Table 1. Briefly, *E. coli* was the most often isolated (33/94, 35.1%) followed by *Klebsiella pneumoniae* (18/94, 19.1%)

Table 1. Isolated bacteria from pediatric UTI in Surabaya

| Bacteria | No. of isolates | % of total |
|---|---|---|
| *Escherichia coli* ESBL (−) | 10 | 10.6 |
| *Escherichia coli* ESBL (+) | 23 | 24.5 |
| *Klebsiella oxytoca* | 1 | 1.1 |
| *Klebsiella pneumoniae* ESBL (−) | 3 | 3.2 |
| *Klebsiella pneumoniae* ESBL (+) | 14 | 14.9 |
| *Klebsiella pneumoniae* spp. *ozaenae* ESBL (+) | 1 | 1.1 |
| *Enterococcus faecalis* | 8 | 8.5 |
| *Staphylococcus haemolyticus* | 5 | 5.3 |
| Coagulase-negative *Staphylococci*[1)] | 3 | 3.2 |
| *Staphylococcus aureus* | 1 | 1.1 |
| *Streptococcus* non-*haemolyticus* | 2 | 2.1 |
| *Enterobacter aerogenes* | 4 | 4.3 |
| *Enterobacter cloacae* | 1 | 1.1 |
| *Pseudomonas aeruginosa* | 4 | 4.3 |
| *Acinetobacter baumannii* | 2 | 2.1 |
| *Acinetobacter* spp.[1)] | 1 | 1.1 |
| *Proteus mirabilis* | 2 | 2.1 |
| Others | 9 | 9.6 |
| Total | 94 | 100.0 |

ESBL, extended-spectrum β-lactamase.

[1)]: Those excluding *Staphylococcus haemolyticus* and *Acinetobacter baumannii*, respectively.

and *Enterococcus faecalis* (8/94, 8.5%). Importantly, ESBL was detected in *E. coli* (23/33, 69.7% of all *E. coli*). In addition, interestingly, 83.3 % of isolates of *K. pneumoniae* including *K. pneumoniae* subsp. *ozaenae* had ESBLs (Table 1).

For the adult patients in Surabaya, data covering a 2-month period are shown in Table 2. Briefly, similar to the pediatric population, as to the frequency of isolates, *E. coli* was the most frequently isolated (181/450, 40.2%) followed by *K. pneumoniae* (59/450, 13.1%), *Pseudomonas* spp. (32/450, 7.1%), *Acinetobacter* spp. (32/450, 7.1%), and *Enterococcus* spp. (23/450, 5.1%). Therefore, *Pseudomonas* spp. were unique to the adult patients. Regarding the ESBL production, 63.5% (115/181) of *E. coli* and 76.3% (45/59) of *Klebsiella* spp. had ESBLs. Statistical analysis showed that significantly higher ESBL production ratio of *E. coli* (138/214, 64.5%) and *K. pneumoniae* (59/76, 77.6%) was seen in total Surabaya isolates compared to that in Kobe (*E. coli*: 70/302, 23.2%; *K. pneumoniae*: 2/66, 3.0%) ($p < 0.001$). These findings suggested that higher rates of ESBL production, especially in these 2 kinds of isolates, were seen in the Surabaya group, in both pediatric and adult patients. Regarding the total frequency of ESBL-producing isolates, the Surabaya group (200/544, 36.8%) showed significantly higher ESBL-production compared to the isolates in the Kobe group (72/1,251, 5.8%) ($p < 0.001$).

During more than 11-months of observation, a total of 1,251 isolates were detected in the Kobe group. Gram-negative bacilli were responsible for 39.6% (495/1,251) of cases, followed by Gram-positive cocci, which were responsible for 32.0% (400/1,251) of cases.

Analysis of the results indicated that although *E. coli* is the predominant isolated pathogen (302/1,251, 24.1%), followed by *E. faecalis, Pseudomonas aeruginosa, K. pneumoniae*, and *Enterococcus faecium* (175/1,251, 14.0%; 69/1,251, 5.5%; 66/1,251, 5.3%; and 35/1,251, 2.8%) (Table 3). In addition, as to *Staphylococcus* spp., *Staphylococcus aureus* was the most frequently isolated (51/1,251, 4.1%) followed by *Staphylococcus epidermidis* and *Staphylococcus agalactiae* (40/1,251 [3.2%] and 31/1,251 [2.5%], respectively). Regarding resistant strains, the ESBL-producers were most often seen in *E. coli* (70/302, 23.2%) followed by *K. pneumoniae* (2/66, 3.0%). As to methicillin-resistant strains, methicillin-resistant *S. aureus* (MRSA) was seen in 21 of 51 *S. aureus* strains (41.2%) and methicillin-resistant *S. epidermidis* (MRSE) was seen in 32 of 40 *S. epidermidis* strains (80.0%). MRSA and MRSE were detected only in Japanese samples.

**Antibiotic susceptibilities:** Antibiotic susceptibilities of representative isolates such as *E. coli*, *K. pneumoniae*,

Table 2. Isolated bacteria from adult UTI in Surabaya

| Bacteria | No. of isolates | % of total |
|---|---|---|
| *Escherichia coli* ESBL (–) | 66 | 14.7 |
| *Escherichia coli* ESBL (+) | 115 | 25.6 |
| *Klebsiella oxytoca* ESBL (+) | 2 | 0.4 |
| *Klebsiella pneumoniae* ESBL (+) | 45 | 10.0 |
| *Klebsiella pneumoniae* ESBL (–) | 14 | 3.1 |
| *Pseudomonas aeruginosa* | 27 | 6.0 |
| *Pseudomonas* spp.[1)] | 5 | 1.1 |
| *Acinetobacter baumannii* | 19 | 4.2 |
| *Acinetobacter* spp.[1)] | 8 | 1.8 |
| *Acinetobacter baumannii/calcoaceticus* complex | 5 | 1.1 |
| *Enterococcus faecalis* | 21 | 4.7 |
| *Enterococcus faecium* | 2 | 0.4 |
| *Staphylococcus haemolyticus* | 14 | 3.1 |
| *Staphylococcus epidermidis* | 2 | 0.4 |
| Coagulase-negative *Staphylococci*[2)] | 12 | 2.7 |
| *Staphylococcus aureus* | 5 | 1.1 |
| *Streptococcus* non-*haemolyticus* | 9 | 2.0 |
| *Enterobacter cloacae* | 15 | 3.3 |
| *Enterobacter aerogenes* | 11 | 2.4 |
| *Proteus mirabilis* | 9 | 2.0 |
| *Burkholderia cepacia* | 6 | 1.3 |
| *Providencia rettgeri* | 5 | 1.1 |
| *Aeromonas caviae* | 3 | 0.7 |
| *Citrobacter sedlakii* | 2 | 0.4 |
| *Serratia liquefaciens* | 2 | 0.4 |
| *Serratia marcescens* | 2 | 0.4 |
| *Morganella morganii* | 2 | 0.4 |
| Others | 22 | 4.9 |
| Total | 450 | 100.0 |

ESBL, extended-spectrum β-lactamase.
[1)]: Those excluding *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, respectively.
[2)]: Those excluding *Staphylococcus haemolyticus* and *Staphylococcus epidermidis*.

Table 3. Isolated bacteria from adult UTI patients in Kobe

| Bacteria | No. of isolates | % of total |
|---|---|---|
| *Escherichia coli* ESBL (–) | 232 | 18.5 |
| *Escherichia coli* ESBL (+) | 70 | 5.6 |
| *Enterococcus faecalis* | 175 | 14.0 |
| *Enterococcus faecium* | 35 | 2.8 |
| *Pseudomonas aeruginosa* MBL (–), MDRP (–) | 64 | 5.1 |
| *Pseudomonas aeruginosa* MBL (+) | 4 | 0.3 |
| *Pseudomonas aeruginosa* MDRP (+) | 1 | 0.1 |
| *Klebsiella oxytoca* | 16 | 1.3 |
| *Klebsiella pneumoniae* ESBL (–) | 64 | 5.1 |
| *Klebsiella pneumoniae* ESBL (+) | 2 | 0.2 |
| *Staphylococcus aureus* MRSA (–) | 30 | 2.4 |
| *Staphylococcus aureus* MRSA (+) | 21 | 1.7 |
| *Staphylococcus haemolyticus* | 23 | 1.8 |
| *Staphylococcus epidermidis* MRSE (+) | 32 | 2.6 |
| *Staphylococcus epidermidis* MRSE (–) | 8 | 0.6 |
| Coagulase-negative *Staphylococci*[1)] | 8 | 0.6 |
| *Streptococcus agalactiae* | 31 | 2.5 |
| *Streptococcus anginosus* | 4 | 0.3 |
| *Streptococcus dysgalactiae* | 4 | 0.3 |
| α-hemolytic *Streptococci* | 26 | 2.1 |
| *Enterobacter cloacae* | 25 | 2.0 |
| *Enterobacter amnigenus* | 8 | 0.6 |
| *Proteus mirabilis* | 12 | 1.0 |
| Others | 356 | 28.5 |
| Total | 1,251 | 100.0 |

ESBL, extended-spectrum β-lactamase; MBL, metallo-β-lactamase; MDRP, multiple-drug-resistant *Pseudomonas aeruginosa*; MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis*.
[1)]: Those excluding *Staphylococcus haemolyticus* and *Staphylococcus epidermidis*.

Table 4. Antimicrobial susceptibility of isolated bacteria

| Bacteria | No. of isolates | Ratio of susceptibility (%) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AMP | CFZ | CTX | CAZ | IPM | GEN | AMK | LVX | FOF | VAN |
| Surabaya pediatric group ($n$ = 94) | | | | | | | | | | | |
| *E. coli* ESBL (–) | 10 | 66.7 | 37.5 | 62.5 | 50.0 | 100.0 | 88.9 | 100.0 | 88.9 | 88.9 | – |
| *E. coli* ESBL (+) | 23 | 0.0 | 0.0 | 0.0 | 0.0 | 92.3 | 43.5 | 100.0 | 33.3 | 95.2 | – |
| *K. pneumoniae* ESBL (–) | 3 | 0.0 | 0.0 | 100.0 | 66.7 | 100.0 | 66.7 | 50.0 | 66.7 | 66.7 | – |
| *K. pneumoniae* ESBL (+) | 14 | 13.3 | 0.0 | 0.0 | 0.0 | 85.7 | 26.7 | 85.7 | 73.3 | 73.3 | – |
| *E. faecalis* | 8 | – | – | – | – | – | 0.0 | – | 0.0 | 40.0 | – |
| *P. aeruginosa* | 4 | 0.0 | 0.0 | 33.3 | 66.7 | 100.0 | 50.0 | 33.3 | 25.0 | 25.0 | – |
| Surabaya adult group ($n$ = 450) | | | | | | | | | | | |
| *E. coli* ESBL (–) | 66 | 11.7* | 30.9 | 67.2 | 72.3 | 95.5 | 82.8 | 100.0 | 63.5 | 81.5 | – |
| *E. coli* ESBL (+) | 115 | 0.0 | 0.0 | 0.0 | 0.0 | 93.9 | 57.7 | 99.1 | 10.9 | 83.5 | – |
| *K. pneumoniae* ESBL (–) | 14 | 0.0 | 62.5 | 64.3 | 76.9 | 87.5 | 78.6 | 100.0 | 69.2 | 71.4 | – |
| *K. pneumoniae* ESBL (+) | 45 | 0.0 | 2.33 | 4.35 | 6.67 | 91.7 | 50.0 | 97.6 | 35.9 | 58.1 | – |
| *E. faecalis* | 21 | 70.8 | – | – | – | – | 0.0 | – | 38.1 | 16.7 | 83.3 |
| *P. aeruginosa* | 27 | 0.0 | 0.0 | 0.0 | 50.0 | 89.5 | 48.0 | 95.5 | 36.0 | 20.0 | – |
| *E. cloacae* | 15 | 0.0 | 0.0 | 40.0 | 28.6 | 85.7 | 46.7 | 92.9 | 50.0 | 60.0 | – |
| Kobe adult group ($n$ = 1,251) | | | | | | | | | | | |
| *E. coli* ESBL (–) | 232 | 60.3 | 89.2 | 97.4 | 97.8 | 100.0 | 94.4 | 99.6 | 74.1 | 88.8 | – |
| *E. coli* ESBL (+) | 70 | 0.0 | 0.0 | 0.0 | 0.0 | 100.0 | 72.1 | 100.0 | 11.8 | 91.0 | – |
| *K. pneumoniae* ESBL (–) | 64 | 15.9 | 92.1 | 98.4 | 98.4 | 100.0 | 98.4 | 100.0 | 95.2 | 77.8 | – |
| *K. pneumoniae* ESBL (+) | 2 | – | – | – | – | – | – | – | – | – | – |
| *E. faecalis* | 175 | 100.0 | – | – | – | 100.0 | – | – | 88.6 | – | 100.0 |
| *P. aeruginosa* | 68 | – | – | – | 89.7 | 86.8 | 92.6 | 100.0 | 88.2 | 25.0 | – |
| *E. cloacae* | 25 | 12.0 | 0.0 | 60.0 | 52.0 | 100.0 | 100.0 | 100.0 | 72.0 | 56.0 | – |

*, $p < 0.01$. AMP, ampicillin, CFZ, cefazolin, CTX, cefotaxime, CAZ, ceftazidime; IPM, imipenem; GEN, gentamicin; AMK, amikacin; LVX, levofloxacin; FOF, fosfomycin; VAN, vancomycin; –, not done; ESBL, extended-spectrum β-lactamase.

or *E. faecalis* are shown in Table 4. Briefly, *E. coli* in the Surabaya adult patient group had a significantly lower susceptibility to AMP compared to that in the Surabaya pediatric patient group and Kobe patient group ($p < 0.01$). *E. coli* detected in both the adult and pediatric patients in the Surabaya group also tended to have lower susceptibilities to cephalosporins such as CFZ, CTX, and CAZ than that in the Kobe group. In many cases, the isolates in the Kobe group tended to have higher susceptibility rates than those in the Surabaya group, especially in not only *E. coli* but also *E. faecalis* or *P. aeruginosa* (Table 4).

## DISCUSSION

UTIs are common infectious diseases around the world. However, the diagnosis and treatment of UTIs by clinicians tended to be based on their experiences (14). In developing countries, guidelines for UTI treatment cannot always be referenced (15). Despite this situation, studies to utilize UTI guidelines and to properly manage UTIs in developing countries have not been fully investigated (16). Especially, these investigations are demanding because the guidelines were usually established on 2 important concepts: i) how to manage UTIs and ii) how to prevent the emergence of antibiotic-resistant strains. Importantly, there are variations in the use of UTI guidelines among countries, especially among developing countries.

Basically, there are natural differences in the medical issues among the countries in the world (17). These differences can be seen between developed and developing countries as well (18), partly because of the difference of the economy, amount of information, education, and medical insurance (19). Antibiotic usage is also varied owing to national economic issues (20). For instance, inadequate antibiotic uses such as sub-therapeutic drug concentrations, few kinds of drugs for selection, or poor adherence to therapy may result in the emergence of resistance, and possibly treatment failure, in the treated host (21). Therefore, the revision and comparison of antibiotic use between developed and developing countries are needed for the improvement of antibiotic susceptibilities or non-emergence of antibiotic resistances, especially in developing countries.

Our findings showed that UTI-causative bacteria detected from isolates in the Kobe and Surabaya groups and their antibiotic susceptibilities were different between the 2 cities. The most responsible pathogen for UTI was *E. coli* in the 2 countries, and the second most common in Kobe adults was *E. faecalis*, but in Surabaya adults was *K. pneumoniae*. This trend was also identified in the pediatric Surabaya group. Higher ESBL-production rates were partly or mostly led by inappropriate and/or unnecessary use of antibiotics with broad spectrum such as third-generation cephalosporins and fluoroquinolones (22). Generally, AMP, cephalosporines, and quinolones were used in UTI treatments in Indonesia (23), but third-generation cephalosporins and fluoroquinolones were usually used in Japan (24). Some studies indicated that period of dosing or antibiotic dose makes the difference among countries or regions (25,26); however, we have no available data investigating these factors between 2 cities in different countries.

We found a trend that more Gram-positive bacteria

such as *Enterococcus* spp. or *Staphylococcus* spp. were isolated in Kobe than in Surabaya. Reportedly, these bacteria were often detected in complicated UTIs (5), but in this study, we have no available data investigating whether the strains were from an uncomplicated UTI or a complicated UTI. Moreover, the distribution of these bacteria is possibly influenced by many kinds of factors including medical, educational, and economic issues as mentioned above (27). Perry et al. showed that in their study of developed and developing countries the production of community health workers' programs in each country around the world is important (28). For a definitive conclusion, further prospective investigation from broader viewpoints are needed to understand this difference between the 2 cities in the international epidemiology of antibiotic resistance.

Jean et al. reported that ESBL-producing Gram-negative bacteria were frequently detected from China, Vietnam, Malaysia, Singapore, Thailand, and the Philippines in the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2010 to 2013 (29). They also showed the highest ESBL-producing rate of *E. coli* was 59.9% in China, and that of *K. pneumoniae* was 61.3% in the Philippines. In this study, we found that ESBL-producing rates in Surabaya tended to be higher than other Southeast Asian countries. We also demonstrated that the susceptibilities of *E. coli* and *K. pneumoniae* to AMP, CAZ, CTX, and LVX in Surabaya were markedly lower than that of those countries, whereas in Kobe the susceptibility were higher. SMART survey also supports our results of high susceptibility to AMK and low susceptibility to LVX among ESBL-producing isolates in the Kobe group and Surabaya adult group. However, we found that *K. pneumoniae* had decreased susceptibility, especially in the Surabaya pediatric group. Further monitoring of antimicrobial susceptibility and ESBL-production is necessary to control the dissemination.

We would like to emphasize the limitations of this study. First, the period of study was different in the 2 countries. However, a short period of observation can be helpful in this kind of study because we could be aware of the trend of UTI-causative bacteria and their antibiotic susceptibilities. Second, there were no data on the patients' backgrounds, antibiotic dosing period, doses and types, and economic and educational issues. Third, no pediatric data were shown in the Kobe group. Fourth, data were not separated by uncomplicated UTI and complicated UTI. Fifth, there were no data on the differences between the 2 countries regarding the kind, period, and dose of administered antibiotics to explain why Gram-positive bacteria were isolated more often in Kobe than in Surabaya. These limitations will be overcome in our future research.

In conclusion, we showed that the antimicrobial-resistance patterns of UTI-causative bacteria are highly variable in Kobe and Surabaya especially regarding the ESBL-production rates. Continuous surveillance of trends in resistance patterns of UTI-causative bacteria is necessary for the future revision of the use of antimicrobial agents.

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**Conflict of interest** None to declare.

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