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Aspects of urinary tract infections and antimicrobial resistance in hospitalized urology patients in Asia: 10-Year results of the Global Prevalence Study of Infections in Urology (GPIU).

Choe HS[1], Lee SJ[2], Cho YH[3], Çek M[4], Tandoğdu Z[5], Wagenlehner F[6], Bjerklund-Johansen TE[7], Naber K[8]; GPIU Asian Investigators.

1 Department of Urology, St. Vincent's Hospital, The Catholic University of Korea College of Medicine, Suwon, South Korea.
2 Department of Urology, St. Vincent's Hospital, The Catholic University of Korea College of Medicine, Suwon, South Korea. Electronic address: lee.seungju@gmail.com.
3 Department of Urology, St. Mary's Hospital, The Catholic University of Korea College of Medicine, Seoul, South Korea.
4 Department of Urology, Trakya Medical School, Edirne, Turkey.
5 Northern Institute for Cancer Research, Newcastle University, Newcastle Upon Tyne, England, UK.
6 Clinic of Urology, Pediatric Urology and Andrology, Justus Liebig University Giesen, Germany.
7 Department of Urology, Oslo University, Oslo, Norway.
8 Technical University of Munich, Dept. of Urology, Munich, Germany.

Abstract

OBJECTIVES: To assess Asian data from Global Prevalence Study on Infections in Urology (GPIU study) which has been performed more than 10 years.

METHODS: Seventeen Asian countries participated in the GPIU study between 2004 and 2013. Data for these countries were collected from the web-based GPIU database. The point prevalence of urinary tract infections (UTI) and antimicrobial susceptibility of representative pathogens were analysed for Asian geographic regions.

RESULTS: A total of 6706 patients (5271 male, 1435 female) were assessed during the study period, and 659 patients were diagnosed with a UTI (9.8%). Of these UTI patients, 436 were male and 223 were female. Mean patient age was 54.9 ± 19.3 years. Pyelonephritis and cystitis were the most common clinical diagnoses, representing 30.7% and 29.9% of patients, respectively. Escherichia coli was the most frequently identified uropathogen (38.7%). For the patients with urinary tract infection, cephalosporins were the most frequently used antibiotics (34.4%), followed by fluoroquinolones (24.1%), aminoglycosides (16.8%). Fluoroquinolone resistance was relatively high (ciprofloxacin 54.9%, levofloxacin 39.0%), and cephalosporin resistance 42% (42.5-49.4%). Of the antibiotics evaluated, uropathogens had maintained the highest level of susceptibility to amikacin and imipenem (24.9% and 11.3% resistance rates, respectively).

CONCLUSION: Uropathogens in many Asian countries had high resistance to broad-spectrum antibiotics. Knowledge of regional and local resistance data and prudent use of antibiotics are important for proper management of UTI in Asian countries.

KEYWORDS: Antibiotic resistance; Asia; Prevalence; Surveillance; Urinary tract infections

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Aspects of urinary tract infections and antimicrobial resistance in hospitalized urological patients in Asia: 10-year Results of the Global Prevalence Study of Infections in Urology (GPIU)

Hyun-Sop Choe[1], Seung-Ju Lee[1], Yong-Hyun Cho[2],
Mete Cek[3], Zafer Tandogdu[4], Florian Wagenlehner[5],
Truls Erik Bjerklund-Johansen[6], Kurt Naber[7]
on behalf of the GPIU Asian Investigators

1 Department of Urology, St. Vincent's Hospital,
The Catholic University of Korea College of Medicine, Suwon, Korea
2 Department of Urology, St. Mary's Hospital,
The Catholic University of Korea College of Medicine, Seoul, Korea
3 Department of Urology, Trakya Medical School, Edirne, Turkey
4 Northern Institute for Cancer Research, Newcastle University, Newcastle Upon Tyne, England, UK
5 Clinic of Urology, Peditaric Urology and Andrology, Justus Liebig University Giesen, Germany
6 Department of Urology, Oslo University, Oslo, Norway
7 Technical University of Munich, Dept. of Urology, Munich, Germany

Address for Correspondence

Seung-Ju Lee, M.D. Ph.D.
Department of Urology, St. Vincent's Hospital,
The Catholic University of Korea College of Medicine,
Suwon, South Korea

Tel: +82.31-249-7473, Fax: +82.31-253-0949
E-mail: lee.seungju@gmail.com

Abstract

The epidemiological and clinical characteristics of urinary tract infections may differ within and between various countries; thus, it is necessary to assess Asian data from the Global Prevalence Study on Infections in Urology (GPIU-study). Seventeen Asian countries participated in the GPIU study between 2004 and 2013. Data for these countries were collected from the web-based GPIU database. The point prevalence of healthcare-associated urinary tract infections (HAUTI) and antimicrobial susceptibility of representative pathogens were assessed for Asian geographic regions. A total of 659 patients were diagnosed with urinary tract infection during the study period, including 436 males (66.2 %) and 223 (33.8 %) females. Mean patient age was 54.9 ± 19.3 years. Pyelonephritis and cystitis were the most common clinical diagnoses, representing 30.7 % and 29.9 % of patients, respectively. *Escherichia coli* was the most frequently identified uropathogen (38.7 %). Among urinary tract infection patients, cephalosporins were the most frequently used antibiotics (34.4 %), followed by fluoroquinolones (24.1 %), aminoglycosides (16.8 %). Resistance rates against fluoroquinolones were relatively high among uropathogens (ciprofloxacin 54.9%, levofloxacin 39.0%), and resistance rates against cephalosporins exceeded 42% (42.5 ~ 49.4 %). Of the antibiotics evaluated, uropathogens had maintained the highest level of susceptibility to amikacin and imipenem (24.9% and 11.3% resistance rates, respectively). Uropathogens in almost all Asian countries had high resistance rates to broad-spectrum antibiotics, a finding that was likely inevitable given increasing antibiotic usage. Knowledge of regional and local resistance data and prudent use of antibiotics are necessary to optimize antibiotic therapy in HAUTI.

Key Words

Healthcare-associated urinary tract infections (HAUTI); Antibiotic resistance; Asia

Introduction

Health-care associated urinary tract infections (HAUTI) surveillance

Healthcare-associated infections are defined as infections acquired during the course of receiving treatment for other conditions within a healthcare setting. HAUTIs are one of the most common types of healthcare-associated infections. The frequencies of HAUTIs have been reported as 12.9% (CI: 10.2–16%), 19.6% and 24% in the United States, Europe and developing countries, respectively [1-3]. Surveillance is very important in the management of HAUTIs. Various prevalence and antibiotic resistance surveillance programmes have been implemented [4-7]. In an effort to increase the body of evidence regarding HAUTI surveillance specifically in urological patients, the Global Prevalence Study on Infections in Urology (GPIU) study was conducted since 2003 [8, 9].

GPIU as a point-prevalence study and Asian data

The GPIU-study was an international internet-based study. All uploaded patients were anonymously collected and stored in a database (www.uroweb.org) following reporting by participating institutes and departments. GPIU is a worldwide, multicenter point-prevalence study of urogenital tract infection and antibiotic resistance. It is endorsed by the European Section for Infection in Urology (ESIU) and sponsored by the European Association of Urology (EAU). The aims of the GPIU study ware to assess urinary tract infections (UTI) and surgical site infections (SSI) in hospitalized urological patients. The prevalence of healthcare-associated infections (HAI) was investigated, as were causative uropathogens and the antibiotic resistance patterns. The use of antibiotics for UTI and SSI was also assessed in urology departments worldwide. Point prevalence has been defined as the proportion of a population with an existing condition at a defined moment in time [9, 10]. The aim of this paper is to assess Asian GPIU data from 2005 to 2013 (the years of Asian data collection) including prevalence and antibiotic resistance patterns of uropathogens causing HAUTIs.

Material and Methods

Enrolled Countries

A total of 17 Asian countries participated in the GPIU study. As displayed in the following map, the participating countries were evenly distributed throughout Asia.

Fig. 1. Enrolled Asian countries. The participating nations are distributed throughout Asia.

Performance of GPIU study

Data from the GPIU study from the period between 2005 and 2013 were analysed. During that period, Asian data were also collected as a part of the larger GPIU study. Data were collected to determine antibiotic use in urology departments and susceptibility of uropathogens causing HAUTIs. Participating institutes submitted data to the GPIU study on a single day of their choosing in November or December. At 8:00 AM on the chosen study day, prevalences of UTI and/or SSI were assessed according to CDC definitions for the course of the inpatient population's hospital stays. All data were entered into a web-based platform. Infectious conditions were assessed both retrospectively and prospectively. Patients were grouped according to their infection status prior to and following urological intervention. Antibiotics usage data were also evaluated within the same subgroups. All culture and antimicrobial susceptibility tests were completed in the local laboratories according to their microbiological standards.

Data collection from GPIU database

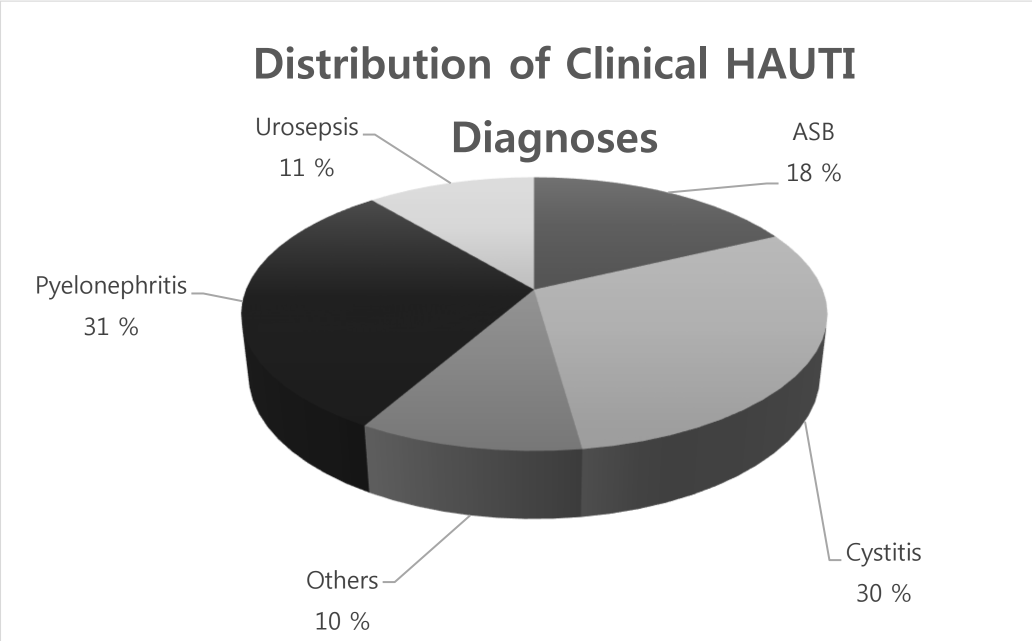
Collected data were imported from the web-based survey. Antimicrobial susceptibility data included the following species: *Escherichia coli*, *Klebsiella* spp., *Enterococcus* spp., *Pseudomonas aeruginosa*, *Proteus* spp., *Acinetobacter* spp., *Staphylococcus aureus*, *Enterobacter* spp., *Citrobacter* spp., and coagulase negative staphylococci (CoNS). Antibiotics assessed for resistance included the following: penicillin, aminopenicillin, aminopenicillin with a beta lactamase inhibitor (BLI; sulbactam or clavulanic acid); cephalosporins (first, second and third generation); carbapenem; aminoglycosides; fluoroquinolones; trimethoprim in combination with sulfamethoxazole (TMP-SMX); and phosphomycin.

Results

Clinical diagnosis of HAUTI (Patients (2004-2013))

A total of 6,706 patients were screened during the study period, and 659 patients were diagnosed with a HAUTI (9.8 %). Of these patients, 436 (66.2 %) were male and 223 (33.8 %) were female. Mean age was 54.9 ± 19.3 years, and 455/659 (69 %) UTIs were diagnosed by urine culture. Type of HAUTI included the following: pyelonephritis (PN, 30.7%); cystitis (29.9%); asymptomatic bacteriuria (ASB, 17.9%); urosepsis (11.1%); and other (10.5%). Whereas global GPIU results identified ASB as the most frequently diagnosed HAUTI [8], ASB was not the most frequently identified HAUTI in Asia. However, diagnoses of PN (31%) and cystitis (30%) were high.

Fig. 2. Rates of clinical diagnosis of HAUTI



Urological intervention status

Patient type was classified into an infection status and contamination status based on the type of urological intervention they underwent into following categories: clean, clean–contaminated (opening of urinary tract), clean–contaminated (opening of the bowel) and infected. Among the HAUTI cases, 464 underwent any intervention (70.4%), and 195 cases underwent no intervention. Among the cases who underwent an intervention, "clean–contaminated" procedures were consistently the most frequently reported (170 cases, 36.6%). For catheterization status, 179 cases had a urethral catheter, 80 cases had a suprapubic catheter, 57 cases had a ureteral catheter, 57 cases had a nephrostomy, 14 cases had other catheters, and no catheterization was reported for 272 cases. (Table 1)

Table 1

Urological interventions and contamination status

Year	Clean	Clean-contaminated (urinary tract)	Clean-contaminated (bowel)	Contaminated	Infected	No intervention	Total
2004	36	47	0	9	18	3	113
2005	0	13	12	6	1	0	32
2006	2	14	23	11	1	0	51
2007	0	19	21	4	19	2	65
2008	12	23	28	8	2	0	73
2009	14	12	4	1	2	38	71
2010	14	15	1	0	1	37	68
2011	20	27	2	1	3	67	120
2012	0	0	0	0	0	9	9
2013	14	0	0	0	4	39	57
Total	112	170	91	40	51	195	659

Clean procedures; Open or laparoscopic urological operations without opening of the urinary or genital tracts

Clean-contaminated procedures; Open or laparoscopic urological operations with opening of the urinary tract

Clean-contaminated or contaminated procedures; Open urological operations with bowel segment

Distribution of pathogens (%)

Bacterial spectrum

Escherichia coli was the most frequently identified uropathogen (255 of 659 isolates, 38.7 %); followed by *Klebsiella* (93 isolates, 14.1%); *Enterococcus* (84 isolates, 12.7%); and *Pseudomonas* (68 isolates, 10.4%)

Distribution of pathogens according to clinical diagnosis 2004–2013

In Asia, Acinetobacter detection rates were higher than those identified in other continents. (Table 2) This may be correlated with the fact that the proportion of HAIs caused by *Acinetobacter baumannii* has been gradually rising in Taiwan (22% in 2000 vs. 25% in 2005) [11] as well as in China [12] and Korea [13].

Table 2. Distribution of clinically diagnosed pathogens by HAUTI

	ASB		Cystitis		Pyelonephritis		Urosepsis		Other		Total	
E. coli	37	31.4%	77	39.1%	84	41.6%	36	49.3%	21	30.4%	255	38.7%
Klebsiella sp.	16	13.6%	32	16.2%	30	14.9%	10	13.7%	5	7.2%	93	14.1%
Enterococcus sp.	18	15.3%	31	15.7%	21	10.4%	8	11.0%	6	8.7%	84	12.7%
Pseudomonas aeruginosa	14	11.9%	26	13.2%	13	6.4%	6	8.2%	9	13.0%	68	10.3%
Proteus	5	4.2%	7	3.6%	7	3.5%	2	2.7%	3	4.3%	24	3.6%
Acinetobacter	5	4.2%	3	1.5%	10	5.0%	1	1.4%	5	7.2%	24	3.6%
Staphylococcus aureus	2	1.7%	5	2.5%	6	3.0%	2	2.7%	4	5.8%	19	2.9%
Enterobacter sp.	4	3.4%	5	2.5%	6	3.0%	1	1.4%	2	2.9%	18	2.7%
Citrobacter	2	1.7%	0	0.0%	3	1.5%	0	0.0%	2	2.9%	7	1.1%
Coagulase-negative sta	3	2.5%	1	0.5%	1	0.5%	1	1.4%	1	1.4%	7	1.1%
Other	12	10.2%	10	5.1%	21	10.4%	6	8.2%	11	15.9%	60	9.1%
Total	118	100.0%	197	100.0%	202	100.0%	73	100.0%	69	100.0%	659	100.0%

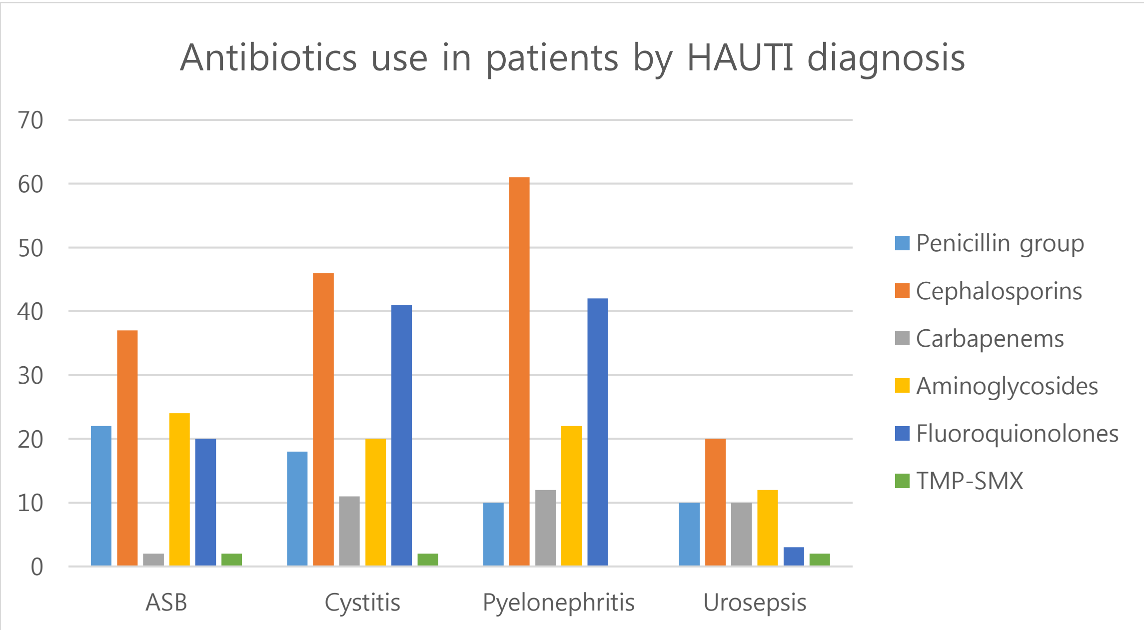
Choice of treating antibiotics

Among HAUTI cases, Cephalosporins were the preferred antibiotic treatment in 34.4 % of cases, followed by fluoroquinolones (24.1 %), aminoglycosides (16.8 %), penicillins (7.1%) and carbapenems (6.5%). Third generation cephalosporins were most frequently selected at 26.6% (Table 3). Cephalosporins were most frequently preferred antibiotics for all HAUTI diagnoses (Fig. 3).

Table 3. Antibiotics use in patients

	count	Percentage
Penicillin	47	7.1%
Aminopenicillin	12	1.8%
Aminopenicillin BLI	20	3.0%
Cephalosporins	227	34.4%
First generation	7	1.1%
Second generation	45	6.8%
Third generation	175	26.6%
Carbapenem	43	6.5%
Aminoglycosides	111	16.8%
Fluoroquinolones	159	24.1%
TMP-SMX	6	0.9%
Fosfomycin	3	0.5%
Others	31	4.7%
Total	659	100.0%

Fig. 3. Distribution of antibiotic use in HAUTI patients



Resistance rates among all pathogens (%)

The resistant rate of evaluated uropathogens against ciprofloxacin was 54.9% (185/337), and the resistance rate of levofloxacin was 39.0% (60/154). More than 42% of uropathogens were resistant to cephalosporins (42.5 ~ 54.7%). Second and third generation cephalosporins, which are widely used for UTI treatment, exhibited especially high resistance rates. Resistance rates against cefuroxime, cefotaxime, and ceftazidime were 49.4% (81/164), 42.5% (125/294), and 45.1% (110/244), respectively. The resistance rate against cefepime, which is classified as fourth generation cephalosporin, was 39.6% (55/139). Within the penicillin family, 55.0% of uropathogens were resistant to ampicillin plus beta lactamase inhibitor (111/202), and 37.3% of isolates were resistant to piperacillin plus tazobactam (47/126). Rates of resistance to TMP/SMX were higher at 58.8% (97/165). Within aminoglycoside antibiotics, 41.4% of isolates were resistant to gentamicin (144/348), and 24.9% of isolates were resistant to amikacin (69/277). Fosphomycin had a 39.4% (28/71) resistance rate. Imipenem had maintained effectiveness with the lowest, but already significantly elevated resistance rate of 11.3% (33/292). (Fig. 4.)

As previously identified, *E. coli* was the most frequently identified causative pathogen in this study. Table 4 shows resistance rates for *E. coli* against several antibiotics by study year. Trends could not be statistically analysed due to insufficient numbers of reported cases.

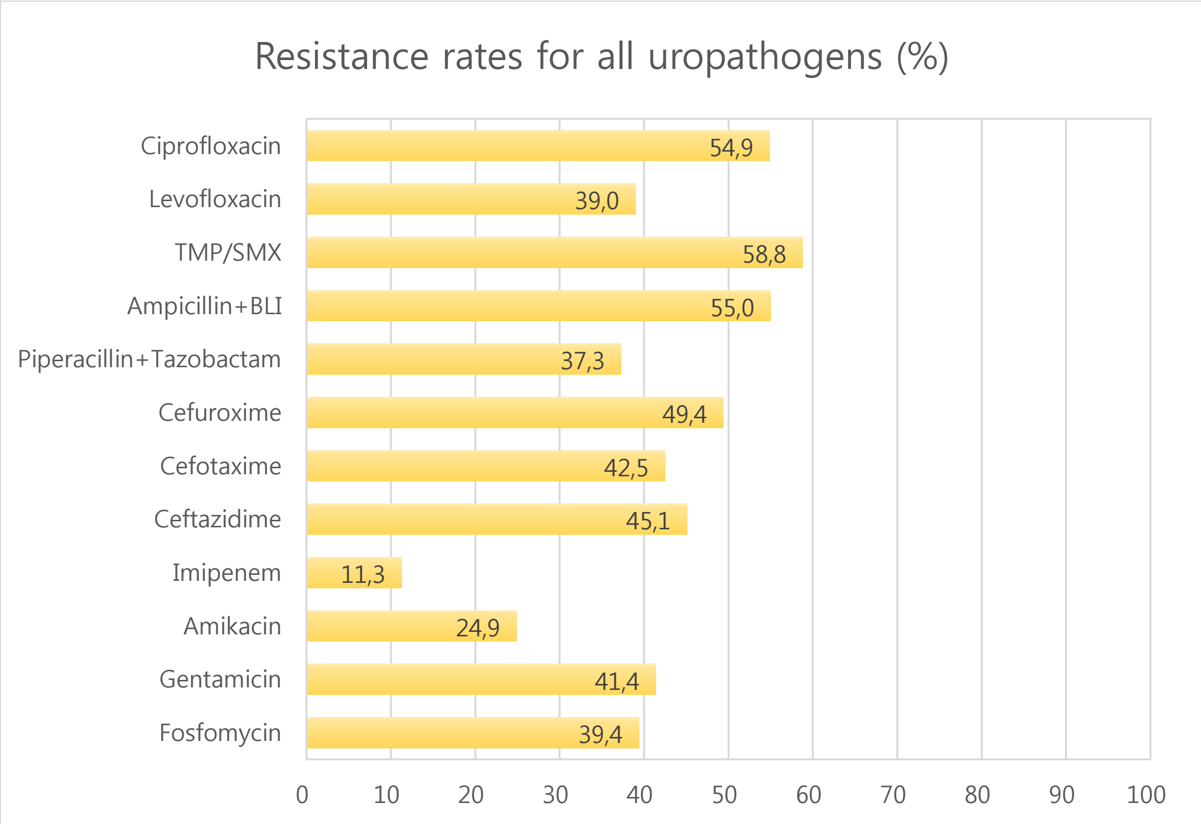


Fig. 4. Antibiotic resistance rates among uropathogens

Table 4. Annual rates of antibiotic resistance in *E. coli* isolates

	Cefotaxime		piperacillin-tazobactam		Ciprofloxacin		TMP-SMX	
2004	7/18	38.9%	2/7	28.6%	14/21	66.7%	10/13	76.9%
2005	1/7	14.3%	1/2	50.0%	1/9	11.1%	3/7	42.9%
2006	6/9	66.7%	2/2	100.0%	10/12	83.3%	5/5	100.0%
2007	5/19	26.3%	1/7	14.3%	7/21	33.3%	4/14	28.6%
2008	6/12	50.0%	1/3	33.3%	9/12	75.0%	1/4	25.0%
2009	10/27	37.0%	4/17	23.5%	10/29	34.5%	1/14	7.1%
2010	2/10	20.0%	1/1	100.0%	3/9	33.3%	3/4	75.0%
2011	3/20	15.0%	1/3	33.3%	1/7	14.3%	5/8	62.5%
2013	5/17	29.4%	2/13	15.4%	10/17	58.8%	7/12	58.3%
Total	45/139	32.4%	15/55	27.3%	65/137	47.4%	39/81	48.1%

Comparison between regional data with global resistance study.

Of the specific Asian regions, southwest Asian countries, Iran, Iraq, Oman had lower antibiotic resistance rates than other regions. The resistance rate for ciprofloxacin was 16.7% (5/30), and the resistance rate for cefotaxime was 33.3% (9/27); however, interpretation of these results is limited due to small sample sizes.

Determination of statistically significant differences between Asian and global data resulting was difficult. However, overall trend or pattern may be commented upon. While ciprofloxacin has been reported to have an increasing pattern of resistance, the resistance rate against this antibiotic among uropathogens identified in a previous GPIU study was 51% [9], but higher in the Asian data at 54.9%. Additionally, a higher resistance rate against piperacillin/tazobactam was identified in Asia (37.3%) relative to the global resistance rate (29%). Cefuroxime also was associated with a higher rate of resistance in Asia (49.4%) than globally (35%).

Discussion

This GPIU study is a point prevalence survey. The strengths of this study design are that it's easier to perform than incidence surveys and a practical alternative to optimize patient selection, prospectively collect desired variables, and collect data from subgroups across diverse settings. Point prevalence studies have been used widely in many disciplines [14, 15].

HAI and particularly HAUTI are major concerns in patient care. Prevalence surveys examining health-care associated infections have identified prevalence rates varying from 3.5 % to 9 % [4-7, 16-18]. Furthermore, the percentages of HAUTI among HAI overall in these surveys ranged from 8.64 to 57.8 % [17, 18]. A previous GPIU study estimated the global incidence of HAUTI to be 9.4 % (1,866 patients) within a total of 19,756 patients hospitalized in urology departments [8], and the Asian data revealed a similar prevalence for HAUTI, at 9.8% (659 of 6,706 patients)

A comparison of the diagnosis distribution between global and Asian data suggests that rates of PN and cystitis were relatively high and ASB was comparatively low in Asia. One reason for this difference could be that there might be some geographical differences on clinician awareness of ASB. Some articles related to ASB have reported that physician-related factors, including knowledge deficits, cognitive biases, and discrepancies between perception and practice, may affect ASB treatment [19-21]. Deductive reasoning suggests that geographical differences in ASB diagnoses might not be due to disease prevalence but due differences in ASB diagnosis due to a lack of clinician awareness.

Another comparison between global and Asian data suggested that antibiotic resistance was relatively higher in Asian countries, with the exception of some areas. It is known that multidrug-resistant *E. coli* has been increasing steadily worldwide, including in some Asian countries [22]. There are several hypotheses as to why antibiotic resistance among *E. coli* in Asia has reached such an excessive level. Three main contributing factors to the increasing prevalence of multidrug-resistant *E. coli* are antimicrobial use in humans and food-producing animals, international travel, and hospital and community hygiene. Antibiotic usage is one of the most important risk factors for acquisition of antibiotic-resistant pathogens [23-25]. In Asian countries, frequent usage of fluoroquinolones for prophylaxis has been reported in the GPIU dataset [26]. Recently, many Asian countries have implemented efforts to decrease antibiotic consumption through antibiotic stewardship programs that include creating public awareness, improving healthcare provider communication, improving diagnostic support, implementing strict guidelines, continuing education, and strengthening regulations [27, 28].

Asia is the largest and the most populated continent and can be divided into six regions; thus, there are diverse populations in Asia with different social, economic, historic backgrounds. One noteworthy finding was geographical differences in antibiotic resistance prevalence between East and West Asia. Southwest Asian countries have significantly lower antibiotic resistant rates. In this study, ciprofloxacin and cefotaxime resistance rates in Southwest Asian countries were 16.7% (5/30) and 33.3% (9/27), respectively. This phenomenon may reflect differences in antibiotic stewardship as well as in socioeconomic status. In Southeast Asia, antibiotics have been used frequently for treatment of minor ailments including diarrhoeal diseases; however, increased efforts have been focused on reducing antibiotics consumption as of late [29, 30]. Conversely, in some Southwest Asian countries, oral rehydration is more frequently used in the initial management of acute diarrhoeal conditions than antibiotics [31]. Antibiotic resistance is inevitably also affected by national wealth. High-income countries often have extensive surveillance systems to monitor antibiotic resistance [32, 33], and antibiotic use surveillance systems have also been developed in many of these countries [34, 35]. Surveillance of antibiotic use in low-income countries is challenging but important, as it may generate valuable information for public health interventions [36]. Many Asian countries are of developing status and have not implemented substantial surveillance systems, a finding that is reflected in the higher rates of antibiotic resistance in Asia relative to those previously identified in the global data.

Conclusion

GPIU is a well-established, web-based, point prevalence study with methodological strengths including the collection of data from many hospitals from globally various locations. While these data may not represent aspects of HAUTI in a specific country or locality, the trends and gross differences between regions can be assessed using GPIU data. In this study, it was informative to specifically access aspects of urinary tract infections and antimicrobial resistance in hospitalized urological patients within the Asian context. The resistance rates identified amongst evaluated uropathogens against the antibiotics tested varied by region in Asia. Many Asian countries had high resistance rates against broad-spectrum antibiotics, which may be an inevitable finding due to increasing antibiotic usage. It is necessary to bolster monitoring and assessment systems for antibiotic resistance in Asia. In an increasingly interdependent world, working with international partners to establish antibiotics stewardship will be increasingly important.

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Collaborators (214)

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