Sys Rev Pharm 2020; 11(3): 730 – 736
A multifaceted review journal in the field of pharmacy
E-ISSN 0976-2779 P-ISSN 0975-8453

Antibiotic Use in a Local Hospital in Vietnam: A Cross-Sectional Study Based on Medical Records among Urinary Tract Infection Patients

Dung Viet Nguyen[1], Tram Thi Huyen Nguyen[2], Thoai Dang Nguyen[3], Xuan Minh Ngo[4], Trung Quang Vo*[5], Thuy Phan Chung Tran[6], Tro Van Chau[7], Khoa Dang Nguyen[8], Hiep Tung Bui[9], Tri Dang Minh Bui[10], Chi Dang Phuong Bui[11], Hien The Pham[12]

[1]Tay Do University, Can Tho City 900000, Vietnam.
[2]Ear-Nose-Throat Hospital in Ho Chi Minh city, Ho Chi Minh City 700000, Vietnam.
[3]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[4]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[5*]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[6]Ear-Nose-Throat Hospital in Ho Chi Minh city, Ho Chi Minh City 700000, Vietnam
[7]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[8]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[9]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[10]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[11]Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
[12]Le Loi General Hospital, Ba Ria – Vung Tau province 790000, Vietnam

Article History: *Submitted: 12.03.2020* *Revised: 21.04.2020* *Accepted: 26.05.2020*

ABSTRACT
Urinary tract infection (UTI) is a commonly occurring disease that imposes a considerable burden on healthcare sectors all over the world. UTI-causing agents proliferate in hospital environments, but this condition can be treated entirely through the appropriate use of antibiotics. UTI is among the top five diseases worldwide that entail large-scale antibiotic treatment. This study was aimed at investigating antibiotic use as part of UTI treatment in An Giang General Hospital (AGGH) in Vietnam. This cross-sectional research was conducted from January to September 2019, with the medical records of inpatients at the Department of Urology as sources of data. Eighteen codes from the International Classification of Diseases, Tenth Revision, were referred to during the collection of data on diagnosis. The data were analyzed via descriptive statistical calculations run on Microsoft Excel 2010. This study assessed 552 eligible patients with an average age of 48.2±14.4. These patients were issued 2,992 prescriptions and treated with 5,177 antibiotics. The most frequently contracted disease was urolithiasis with infection. Among the cases, 130 switched to different antibiotics over the course of treatment. More than 52% of the prescriptions advised the use of one antibiotic, whereas 27 prescriptions directed the administration to use four or more antibiotics. The most common treatment combination comprised beta-lactam and beta-lactamase inhibitors. Antibiotic use at AGGH requires a comprehensive assessment because of the overuse of such medications in the institution.
Keywords: Aminoglycosides; Beta-lactam; Hospital; Quinolone; Resistance; Urolithiasis; Vietnam
Correspondence:
Trung Quang Vo (PhD.)
Department of Economic and Administrative Pharmacy, Faculty of Pharmacy, Pham Ngoc Thach University of Medicine, 02 Duong Quang Trung Street, Ward 12, District 10, Ho Chi Minh City 700000, Vietnam.
Email: trungvq@pnt.edu.vn ; voquangtrungdk@gmail.com
DOI: 10.31838/srp.2020.3.100

INTRODUCTION

Urinary tract infection (UTI) is a commonly occurring disease that can be contracted by a wide range of individuals, from newborns to the elderly, but especially by females (Nicolle, 2014). This disease poses considerable burdens on healthcare sectors all over the world, with seven million cases hospitalized per year (Foxman, 2002; Nicolle 2014). Its epidemiology has been shown to be associated with demographic characteristics, such as age, gender, and place of residence (Gundux & Altun, 2018). In Singapore, for example, 4% of young women and 7% of those over 50 years old are afflicted with UTI (Chee, 2016). Mature women are more easily infected than men of the same age, with half of the former experiencing at least one instance of UTI in their lifetime (Foxman, 2002).

UTI-causing agents proliferate in hospital environments. Among the most prevalent are *Escherichia coli*, *Klebsiella spp.*, *Proteus mirabilis*, *Staphylococci*, *Enterobacteriaceae*, *Enterococci*, and *Pseudomonas aeruginosa* (Jonathan, William, & Steven, 2010). In terms of risk factors, catheters are one of the most typical, being associated with 75% of hospital-acquired UTI (Nicolle, 2014). The condition can be treated entirely with the use of appropriate antibiotics as the concentration of such medications in urine plays a more important role than their level in plasma. Additionally, studies confirmed a strong correlation between bacterial sensitivity to antibiotics and urinary concentration (Vietnam Ministry of Health, 2015, 2016). Correspondingly, UTI is one of the top five diseases worldwide for which antibiotics are extensively used; the other conditions are lower respiratory tract infections, skin and skin structure infections, and abdominal infections (Versporten et al., 2018).

Treating UTIs among females in community-based outpatient clinics involves the administration of a substantial amount of oral antibiotics on a daily basis (Gupta, Hooton, & Stamm, 2001). Because *E. coli* accounts for up to 80% of community-acquired uncomplicated UTIs, these bacteria should be targeted when choosing empirical antibiotics (Kang et al., 2018). In 2011, the Infectious Diseases Society of America recommended that trimethoprim-sulfamethoxazole (cotrimoxazole), nitrofurantoin, fosfomycin, or pivmecillinam be used if the local resistance rates of uropathogens that cause acute uncomplicated UTIs do not exceed 20% or if the infecting strain is susceptible to these drugs (Gupta et al., 2011). Fluoroquinolones or beta-lactams, such as cephalosporins, are suggested alternatives. These recommendations indicate that awareness of regional susceptibility data regarding *E. coli* (antibiograms) is critical to the selection of appropriate empirical antibiotics. The problem is that the rate at which *E. coli* strains are developing resistance to a vast majority of these medications is increasing on a global scale.

Enterobacteriaceae harbor genes that confer resistance to almost all antibiotics (Harrison & Svec, 1998), and plasmids harboring these resistance determinants can be transferred between bacteria and even between species. Consequently, the development of resistance to new antibiotics may only be a matter of time. A considerably important issue, therefore, is to formulate practical rationales that govern interventions, including the prescription of antibiotics, when there is evidence of an infection, as this promotes the appropriate use of antibiotics and increases efforts to prevent UTIs. Following such strategies is essential because the abuse or misuse of antibiotics can give rise to resistance via the emergence of mutant strains (Baquero, 2001). Compounding this issue is the fact that unresolved or relapsed UTIs tend to be resistant to previously used antibiotics (Kim et al., 2016).

In consideration of the above-mentioned issues, this study investigated antibiotic use in a local hospital in southwestern Vietnam. The findings can be used by hospital decision makers as guidance in establishing a suitable plan for antibiotic usage and management.

MATERIALS AND METHODS

Study design and study site

This is a cross-sectional study conducted at An Giang General Hospital (AGGH). An Giang is one of the southwestern provinces located beside the Mekong River in the southern region of Vietnam. AGGH is the largest healthcare center not only for local residents but also for visitors from surrounding areas.

Data collection

From January to September 2019, data were collected from the medical records of patients who were admitted into the Department of Urology at AGGH. The sample was composed of patients diagnosed with UTI on the basis of the International Classification of Diseases, Tenth Revision (ICD-10). The ICD-10 codes applied in the diagnoses are listed in Table 1. Patients whose medical records had missing information, those admitted from another healthcare facility, pregnant and lactating women, patients under the age of 18 years, and those discharged without permission were excluded from the research.

Data analysis

General information on the patients included their ages, genders, main diagnoses, surgery/other procedures undergone, and glomerular filtration rates (GFRs, calculated on the basis of creatinine clearance using the Cockcroft-Gault formula [Cockcroft & Gault, 1976]). Clinical information included classes of antibiotics prescribed (as categorized on the grounds of chemical structure), antibiotic switches, and antibiotic combinations. The collected data were entered into Microsoft Excel 2010 for the calculation of descriptive statistics. The categorized variables were expressed as frequencies and percentages, and the continuous variables were indicated as mean values and standard deviations.

Ethical considerations

The study protocol was approved by the Ethical Council of AGGH. All personal information was coded for anonymity, and the data were used only for research purposes.

Table 1: ICD-10 codes referred to in the data collection

ICD-10 code	Diagnosis
A54.0	Gonococcal infection of lower genitourinary tract without periurethral or accessory gland abscess
A54.1	Gonococcal infection of lower genitourinary tract with periurethral and accessory gland abscess
A54.2	Gonococcal pelviperitonitis and other gonococcal genitourinary infections
A56.0	Chlamydial infection of lower genitourinary tract
A56.1	Chlamydial infection of pelviperitoneum and other genitourinary organs
A56.2	Chlamydial infection of genitourinary tract, unspecified
N10	Acute tubulo-interstitial nephritis
N11	Chronic tubulo-interstitial nephritis
N12	Tubulo-interstitial nephritis, not specified as acute or chronic
N20	Calculus of kidney and ureter
N21	Calculus of lower urinary tract
N22	Calculus of urinary tract in diseases classified elsewhere
N23	Unspecified renal colic
N30	Cystitis
N34	Urethritis and urethral syndrome
N39.0	Urinary tract infection, site not specified
N45	Orchitis and epididymitis
T83.5	Infection and inflammatory reaction due to prosthetic device, implant, and graft in urinary system

RESULTS

Over the study period, 637 medical records were examined, but only 552 were eligible for assessment. For these 552 patients, 2,992 prescriptions were issued, and 5,177 antibiotics were used in treatment. The majority were aged between 41 and 60 years old, making the average age

48.2±14.4. Urolithiasis with infection was the most frequently contracted disease, and approximately 60% of the patients suffered from mild kidney failure, as determined via creatinine clearance (Table 2). Beta-lactam was the most frequently used antibiotic class, including penicillins and cephalosporins with or without beta-lactamase inhibitors (Table 3). A total of 130 cases experienced the first antibiotic switch after an average of 2.52 days of hospitalization, and 20 went through a second switch after an average of 3 days of hospitalization (Figure 1). Over half of the prescriptions directed the intake of one antibiotic, but 27 prescribed the use of four or more such medications. Beta-lactam with beta-lactamase inhibitors was the most common combination adopted in UTI treatment (Table 4).

Table 2: Patient characteristics (N = 552)

Characteristics		n	%
Age	≤20	8	1.45
	21-40	143	25.91
	41-60	245	44.38
	>60	156	28.26
	Min - Max	18 - 87	
	Mean (SD)	48.2 (14.4)	
Gender	Male	219	39.67
	Female	333	60.33
Main diagnosis	Urolithiasis with infection	228	41.30
	Acute pyelonephritis	221	40.04
	Cystitis	60	10.87
	Epididymitis	10	1.81
	Urethritis	3	0.54
	Nonspecific	30	5.43
Number of surgeries/other procedures	0	272	49.28
	1	189	34.24
	2	44	7.97
	≥3	47	8.51
Renal function*	Normal	30	5.43
	Mild failure	213	38.59
	Moderate failure	83	15.04
	Severe failure	36	6.52
	No data for assessment	190	34.42
Antibiotic switches	0 switch	422	76.45
	1 switch	110	19.93
	2 switches	12	2.17
	3 switches	6	1.09
	4 switches	2	0.36

*Based on creatinine clearance (ClCr, mL/min)

Table 3: Antibiotics used per disease

Antibiotics	Total (N = 5177)	Urolithiasis with infection (N = 1823)	Acute pyelonephritis (N = 1807)	Cystitis (N = 551)	Epididymitis (N = 111)	Urethritis (N = 21)	Nonspecific (N = 170)
Beta-lactam	3789 (73.19)						
Amoxicillin	1073 (20.73)	541 (29.68)	376 (20.81)	82 (14.88)	19 (17.12)	5 (23.81)	50 (29.41)
Ampicillin	36 (0.7)	11 (0.60)	5 (0.28)	6 (1.09)	-	-	14 (8.24)
Cefuroxime	680 (13.14)	294 (16.13)	236 (13.06)	107 (19.42)	11 (9.91)	-	32 (18.82)
Cefoperazone	835 (16.13)	218 (11.96)	476 (26.34)	104 (18.87)	17 (15.32)	7 (33.33)	13 (7.65)
Cefotiam	8 (0.15)	-	-	7 (1.27)	-	-	1 (0.59)
Clavulanic acid	149 (2.88)	93 (5.1)	36 (1.99)	7 (1.27)	-	-	13 (7.65)
Sulbactam	1008 (19.47)	476 (26.11)	387 (21.42)	97 (17.6)	25 (22.52)	3 (14.29)	20 (11.76)
Quinolone	604 (11.67)						
Ciprofloxacin	208 (4.02)	61 (3.35)	86 (4.76)	47 (8.53)	7 (6.31)	4 (19.05)	3 (1.76)
Levofloxacin	396 (7.65)	122 (6.69)	147 (8.14)	82 (14.88)	32 (28.83)	-	13 (7.65)
Aminoglycoside	73 (1.41)						
Amikacin	67 (1.29)	7 (0.38)	47 (2.6)	4 (0.73)	-	-	9 (5.29)
Gentamicin	2 (0.04)	-	-	-	-	2 (9.52)	-
Neomycin	4 (0.08)	-	4 (0.22)	-	-	-	-
Peptide	4 (0.08)						

Polymyxin B	3 (0.06)	-	3 (0.17)	-	-	-	-
Vancomycin	1 (0.02)	-	-	-	-	-	1 (0.59)
5-nitro-imidazole	13 (0.25)						
Metronidazole	4 (0.08)	-	-	3 (0.54)	-	-	1 (0.59)
Tinidazole	9 (0.17)	-	4 (0.22)	5 (0.91)	-	-	-

*Data presented as n (%)

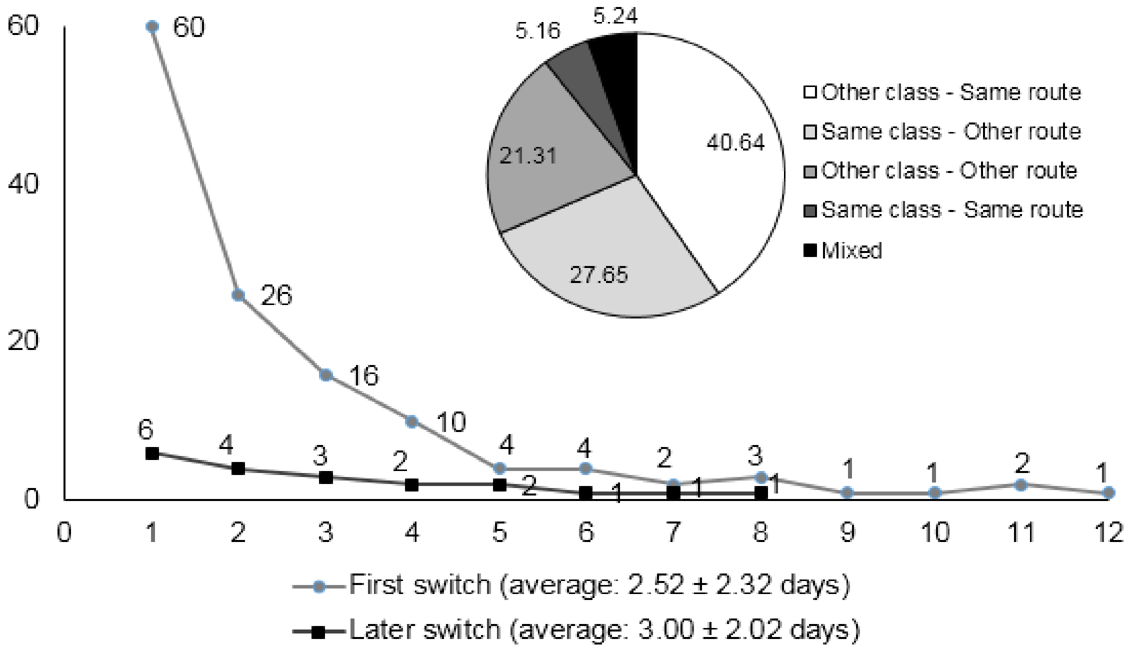

Figure 1: Antibiotic switches from the first day of admission

Table 4: Antibiotic combinations

No. of antibiotics per prescription	Antibiotic combinations	Each group n	Each group %	Total (N = 2992) n	Total (N = 2992) %
1				1580	52.81
2	Penicillins + Beta-lactamase inhibitors	917	74.13	1237	41.34
	Cephalosporins + Beta-lactamase inhibitors	75	6.06		
	2 Cephalosporins	25	2.02		
	Cephalosporine + Quinolones	201	16.25		
	Cephalosporine + 5-nitro-imidazoles	8	0.65		
	Cephalosporine + Aminoglycosides	2	0.16		
	Aminiglycosides + Quinolones	9	0.73		
3	Penicillins + Beta-lactamase inhibitors + Cephalosporins	70	47.30	148	4.95
	Penicillins + Beta-lactamase inhibitors + Quinolones	37	25.00		
	Penicillins + Beta-lactamase inhibitors + Aminoglycosides	3	2.03		
	Penicillins + Beta-lactamase inhibitors + 5-nitro-imidazoles	5	3.38		
	Cephalosporins + Beta-lactamase inhibitors + Quinolones	12	8.11		
	Cephalosporins + Quinolones + Aminoglycosides	13	8.78		
	Cephalosporins + Quinolones + 5-nitro-imidazoles	5	3.38		
	2 Cephalosporins +Quinolones	3	2.03		
4	Penicillins + Beta-lactamase inhibitors + 2 Cephalosporins	3	11.54	26	0.87
	Penicillins + Beta-lactamase inhibitors + 2 Quinolones	7	26.92		
	Penicillins + Beta-lactamase inhibitors + Cephalosporins + Quinolones	4	15.38		
	Penicillins + Beta-lactamase inhibitors + Aminoglycosides + Quinolones	3	11.54		
	Penicillins + Beta-lactamase inhibitors + Quinolones + 5-nitro-imidazoles	1	3.85		
	Cephalosporins + Beta-lactamase inhibitors + 2 Quinolones	8	30.77		
5	Penicillins + Beta-lactamase inhibitors + Cephalosporins + Quinolones + Aminoglycosides			1	0.03

DISCUSSION

Among the diseases diagnosed on the basis of 18 ICD-10 codes, only the following were reported: urolithiasis with infection, acute pyelonephritis, cystitis, epididymitis, and urethritis. Urolithiasis (41.30%) and acute pyelonephritis (40.04%) were the two most frequently acquired conditions. This result agrees with that derived from a national investigation into government guidelines for urology (Vietnam Ministry of Health, 2015). Of the medical records examined, 30 (5.43%) contained insufficient clinical and subclinical information for a precise diagnosis. Among the subjects, 280 (50.72%) underwent at least one medical procedure as part of their treatment. Surgery or other procedures are risk factors that directly or indirectly influence antibiotic use. In terms of direct effect, antibiotics are compulsory agents used in open surgery intended for prevention. As regards indirect influence, risks of infection arise after any type of intervention, thereby prompting the administration of antibiotics. The medical records did not explicitly differentiate between antibiotic use in primary diagnosis and antibiotic administration in surgery or other procedures.

Renal function is a determinant that should be considered when prescribing antibiotics, especially aminoglycosides and vancomycin. Among the cases, 65.58% had adequate information for GFR calculation (age, weight, gender, creatinine clearance) in their records. Using renal function as a basis, we found no case of incorrect dose adjustment—a positive feature of the practice in AGGH. Among these cases, however, 21.56% suffered from moderate or severe kidney failure, which should have been paid considerable attention during the establishment of antibiotic dosage.

Among five classes of antibiotics used in UTI treatment, beta-lactam was the most common, with 3.789 (73.19%) prescribed. Amoxicillin and its combinatorial counterpart, sulbactam, were the dominantly prescribed beta-lactam classes (20.73% and 19.47%, respectively). Beta-lactams encompass a wide range of medications for the treatment of UTI-causing agents, such as *Escherichia coli* (42%), *Enterococcus spp.* (17%), *Klebsiella spp.* (12.8%), *Pseudomonas spp.* (8.2%), and *Acinetobacter spp.* (5.6%) (Vietnam Ministry of Health, 2015). This tendency is consistent with the use of healthcare-related antibiotics in South and Southeast Asia, where beta-lactams are also the most commonly used antibiotics (Versporten et al., 2018).

Among the patients, 130 (31.92%) experienced at least one switch in antibiotic treatment; a maximum of four switches were implemented over the study period. The greater the number of modifications, the less the suffering of the patients. The switching of administration routes is appropriate when symptoms are accelerated and the treatment period has exceeded three days (Vietnam Ministry of Health, 2016). However, switches of up to three or four should be carefully considered because of issues related to costs, medication compliance, and medication efficacy (ibid.). This study did not inquire into the treatment duration of the patients, thus preventing the assessment of whether the switches were appropriate. Moreover, the average days at which switching was implemented (2.5 days for the first switch and 3 days for a subsequent modification) corresponded to existing guidelines (Laurence, Bjorn, & Randa, 2017). However, closer scrutiny revealed that certain switches occurred after only 1 day of treatment - an obviously inappropriate practice given the insufficiency of 24 hours for the evaluation of patients and the identification of suitable alternatives.

With respect to combination, two same-class antibiotics were prescribed in conjunction (e.g., penicillins and cephalosporins). This error not only decelerates the efficacy of antibiotics but also enhances resistance among cultures (ibid.). The combination of beta-lactams with quinolones or aminoglycosides can result in synergism (ibid.), owing to a widening spectrum. The beta-lactams–beta-lactamase inhibitor combination took the form of premixed products, which are reported to be effective against resistant cultures (Roberts, 2011).

The limitations of this work are worth noting. Dosage is also an important part of assessing the use of antibiotics, but this aspect was not explored in the study due to missing values and time constraints. Data collected from medical records may not reflect the actual process of treatment given errors in patient reports or typographical mistakes. Finally, a study conducted in a local hospital cannot be extrapolated for generalization to regional or national contexts.

CONCLUSION

Beta-lactam combined with beta-lactamase inhibitors dominated the antibiotics prescribed for UTIs at AGGH. Such overuse underscores the need for further and deeper assessment in the case hospital.

ACKNOWLEDGMENTS

We thank the Committee of AGGH for granting us approval to conduct the research. We also extend our appreciation to the board of directors of the hospital for their kind support.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES

1. Baquero, F. Low-level antibacterial resistance: A gateway to clinical resistance, Drug Resist Updat, vol. 2, 2001, pp. 93-105
2. Chee, W.T. Urinary tract infections in adults, Singapore Med J., vol. 57, no. 9, 2016, pp. 485-490.
3. Cockcroft, D.W. and Gault, M.H. Prediction of creatinine clearance from serum creatinine, Nephron, vol. 16, no. 1, 1976, pp. 31-41.
4. Foxman, B. Epidemiology of urinary tract infections: Incidence, morbidity, and economic costs, Am J Med, vol. 113, no. 1, 2002, pp. 5-13.
5. Gunduz, S. and Altun, H.U. Antibiotic resistance patterns of urinary tract pathogens in Turkish children, Glob Health Res Policy, vol. 3, no. 1, 2018, p. 10.
6. Gupta, K., Hooton, T.M., Naber, K.G., Wullt, B., Colgan, R., Miller, L.G., et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases, Clin Infect Dis, vol. 52, no. 5., 2011, pp. e103-e120.
7. Gupta, K., Hooton, T.M. and Stamm, W.E. Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections, Ann Intern Med, vol. 135, no. 1, 2001, pp. 41-50.
8. Harrison, J.W. and Svec, T.A. The beginning of the end of the antibiotic era? Part I. The problem: abuse of the "miracle drugs," Quintessence Int, vol. 29, no. 3, 1998, pp. 151-62.
9. Jonathan, C., William, P. and Steven, O. Infectious Diseases, 3rd edition, Elsevier: UK, 2010.
10. Kang, C-I., Kim, J., Park, D.W., Kim, B-N., Ha, U., Lee, S-J., et al. Clinical practice guidelines for the antibiotic treatment of community-acquired urinary tract infections, Infect Chemother, vol. 50, no. 1, 2018, pp. 67-100.
11. Kim, H.Y., Lee, S-J., Lee, D.S., Yoo, J.M., Choe, H-S., et al. Microbiological characteristics of unresolved acute uncomplicated cystitis, Microb Drug Resist, vol. 22, no. 5, 2016, pp. 387-391.
12. Laurence, L.B., Bjorn, C.K. and Randa, H-D. Goodman and Gilman's the pharmacological basis of therapeutics, 13th edition, McGraw-Hill Education/Medical: USA, 2017.
13. Nicolle, L.E. Catheter associated urinary tracinfections, Antimicrob Resist Infect Control, vol. 3, 2014, p. 23.
14. Roberts, K.B. Urinary tract infection: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months, Pediatrics, vol. 128, no. 3, 2011, pp. 595-610.
15. Versporten, A., Zarb, P., Caniaux, I., Gros, M-F., Drapier, N., Miller, M., et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: Results of an internet-based global point prevalence survey, Lancet Glob Health, vol. 6, no. 6, 2018, pp. e619-e629.

16. Vietnam Ministry of Health. Guidelines for antibiotics management at healthcare facilities (Decision 772/QD-BYT on 04/03/2016), Vietman MoH: Hanoi, 2016.
17. Vietnam Ministry of Health. Guidelines for diagnosis and treatment of urology disease (Decision 3931/QD-BYT on 21/09/2015), Vietman MoH: Hanoi, 2015