ANTIBIOTIC USE IN THE TREATMENT OF URINARY TRACT INFECTION AT TRUNG VUONG HOSPITAL

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ABSTRACT

Introduction: Urinary tract infection (UTI) is a common infectious disease. Inappropriate use of antibiotics in the treatment of UTIs can reduce treatment effectiveness and increase antibiotic resistance. **Objectives:** To investigate clinical and laboratory characteristics, antibiotic use pattern, and to identify factors associated with the length of hospital stay in the treatment of UTIs at Trung Vuong Hospital. **Methods:** A cross - sectional study was conducted on medical records of inpatients with UTIs (01/06/2022-31/05/2023) treated at the Department of Nephrology - Urology, Trung Vuong Hospital. The appropriateness of antibiotic use was evaluated using current guidelines. Logistic regression was used to determine factors related to the length of hospital stay. **Results:** A total of 213 medical records of UTI inpatients were included (male accounted for 55.4%). Mean age was 52.9 ± 14.5, with 79.3% of patients <65 years old. A great proportion of patients experienced common clinical symptoms, including flank pain and dysuria (75.6% and 43.7% respectively). There were 66.2% of patients with ≥25 leukocytes/μL urine. The most dominant bacteria isolated was *Escherichia coli*. The most common antibiotics used were β-lactams and fluoroquinolones (93.4% and 33.8%, respectively). Empiric antibiotics were properly indicated in 50.7% of patients. Age and surgical interventions were associated with prolonged hospital stays ($p<0.05$). **Conclusions:** The majority of patients exhibited common symptoms of UTI, and elevated urine leukocytes. The appropriateness of antibiotic use was suboptimal. Patients aged ≥65, undergoing surgical interventions were more likely to have longer hospital stays.

Keywords: *Urinary tract infection, antibiotic use*

I. INTRODUCTION

Urinary tract infection (UTI) is one of the most common infectious diseases, caused by both Gram-negative and Gram-positive bacteria. The disease can be complicated by several risk factors leading to treatment failure, recurrent infections, or increased morbidity and mortality [1] [2]. In 2019, there were approximately 404.6 million UTI cases and 236,786 deaths related to UTI worldwide [3]. Timely treatment with proper antibiotics can help quickly relieve symptoms and prevent serious complications, such as septic shock or death [1] [2]. However, the management of UTIs becomes more challenging due to antibiotic resistance, especially from extended-spectrum β-lactamase (ESBL)-producing Gram-negative bacteria, such as *Escherichia coli* and *Klebsiella pneumoniae* [2].

Several international and national organizations, such as European Urology Association (EUA 2022), Vietnam Urology and Nephrology Association (VUNA 2020), have published treatment guidelines on UTIs [1] [2]. These guidelines enable physicians to choose the best treatment options for specific UTI patients, thereby promoting high

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standards of care and rational medication use [1] [2]. However, recent studies have revealed that the use of antibiotics in the treatment of UTIs is suboptimal, with the rate of inappropriate antibiotic use around 50% [4] [5]. A study by Paige Chardavoyne (2020) found that 38.0% of UTI patients were treated with inadequate antibiotics [6]. In Vietnam, Pham Thuy Yen Ha (2022) also reported a high rate of inappropriate antibiotic use (45.5%), mainly due to antibiotic selection not aligning with guidelines and antimicrobial susceptibility [4]. The substandard use of antibiotics in the treatment of UTIs can result in ineffective and unsafe treatments, exacerbate or prolong the illness, and contribute to increased antibiotic resistance [2].

At Trung Vuong Hospital, the Department of Nephrology - Urology admits numerous UTI patients each year; however, little is known about the appropriateness of antibiotic use in the department. This highlights the need for a study to address this knowledge gap and provide deeper insights into antibiotic usage. Therefore, we conducted this research to investigate clinical and laboratory characteristics, antibiotic use pattern, and to identify factors associated with the length of hospital stay in the treatment of UTIs.

II. METHODS

2.1. Study design

A cross-sectional study was conducted to collect data from medical records of inpatients (aged ≥18 years), diagnosed with UTI, and treated with antibiotics at the Department of Nephrology - Urology, Trung Vuong Hospital, between June 01st, 2022 and May 31st, 2023. Patients were excluded if they met one or more of the following criteria:

- Pregnant or breast-feeding women
- Diagnosed with cancer or HIV/AIDS
- Having other concomitant infections (e.g. sepsis, genital tract infection, fungal infection)
- Treated with antibiotic for less than 48 hours
- Leaving the hospital without permission, requesting discharge, or being transferred to another hospital.

Data on patients' demographic, clinical and laboratory characteristics, patterns of antibiotic use, and treatment outcomes were recorded. The appropriateness of antibiotic use was evaluated using the guidelines of EUA 2022 [1], VUNA 2020 [2], Trung Vuong Hospital (2016) [7], Vietnamese National Drug Formulary (2022) [8], and the summary of product characteristics.

2.2. Statistical analysis methods

Data were analyzed using Microsoft Excel 2019 and Statistical Package for the Social Sciences (SPSS) version 20.0. Categorical variables were presented as frequencies and percentages. Numerical variables were presented as Mean ± Standard Deviation (for normal distribution) or Median (Interquartile Range) (for non-normal distribution). Logistic regression was performed to identify factors associated with the length of hospital stay. A p-value <0.05 was considered statistically significant.

2.3. Ethical considerations

The study was approved by the Ethics Committee in Biomedical Research of Trung Vuong Hospital (reference number: 123/HĐĐĐ-BVTV), signed on February 06th, 2023.

III. RESULTS

3.1. Patients' characteristics

A total of 213 eligible medical records were collected. Patients' demographic, clinical and laboratory characteristics were presented in Table 1 through Table 3.

Table 1. **Demographic characteristics of study population (n=213)**

Characteristics		Frequency	Percentage
Age (year)	Mean ± SD	52.9 ± 14.5	
	<65	169	79.3
	≥65	44	20.7
Gender	Male	118	55.4
	Female	95	44.6
Body Mass Index (BMI, kg/m^2)	Median (IQR)	23.4 (21.3-25.4)	
	Underweight (<18.5)	7	3.3
	Normal (18.5-<23.0)	95	44.6
	Overweight (23.0-<25.0)	50	23.5
	Obesity (≥25.0)	61	28.6
Creatinine clearance (mL/min)	<60	76	35.7
	≥60	137	64.3
Co-morbidities	Yes	105	49.3
	No	108	50.7

Notes: SD: Standard Deviation; IQR: Interquartile Range

The mean age of included patients was 52.9 ± 14.5 years, ranging from 19 to 88 years. Males accounted for 55.4%. A great proportion of patients (44.6%) had a normal BMI (18.5 - <23.0 kg/m^2). Additionally, about one-third of patients (35.7%) had a creatinine clearance <60 mL/min, and approximately half of patients (49.3%) had at least one co-morbidity.

Table 2. **Clinical characteristics of study population (n=213).**

Characteristics		Frequency	Percentage
Number of symptoms related to UTI	1	73	34.3
	2	59	27.7
	≥3	81	38.0
Symptoms related to UTI	Flank pain	161	75.6
	Dysuria	93	43.7
	Urinary frequency	44	20.7
	Hypogastric pain	34	16.0
	Urinary retention	33	15.5
	Hematuria/pyuria	22	10.3
	Fever	20	9.4
	Nausea/vomitting	20	9.4
	Bladder distension	19	8.9
	Chills	13	6.1
	Renal ballottement/palpation (+)	11	5.2
	Turbid urine	9	4.2
Classification of UTI	Uncomplicated	-	-
	Complicated	213	100.0
Diagnosis	Pyelonephritis	165	77.5
	Cystitis	48	22.5
Surgical interventions	None	105	49.3
	Temporary*	45	21.1
	Definitive**	63	29.6

Notes:

**Temporary surgical interventions: urethral dilation, urinary catheterisation, ureteral stenting (JJ stent), endoscopic dilation, and bladder urinary drainage.*

***Definitive surgical interventions: open surgery (for stone removal), laser lithotripsy, pyelolithotomy, ureterolithotomy, endoscopic stone extraction, percutaneous nephrolithotomy, nephrolithotomy, and cystoscopy clot evacuation.*

Of the patients, 81 (38.0%) suffered at least three symptoms. The most common clinical symptom was flank pain (75.6%). Moreover, 43.7% of patients experienced dysuria, while 20.7% reported urinary frequency. All patients had complicated UTIs, with pyelonephritis being the most common diagnosis (77.5%). About half (50.7%) underwent surgical interventions.

Table 3. **Laboratory characteristics of study population**

Characteristics			Frequency	Percentage
Blood test	White blood cells (K/μL) (n=213)	>10.8	94	44.1
		4.4-10.8	113	53.1
		<4.4	6	2.8
	C-reactive protein (mg/L) (n=159)	<5 mg/L	101	63.5
		≥5 mg/L	58	36.5
Urinalysis	Leukocytes (per μL) (n=213)	Negative	72	33.8
		≥25	141	66.2
	Nitrite (n=213)	Negative	188	88.3
		Postitive	25	11.7
Microbiological test (n=60)	Positive		19	31.7
	Escherichia coli		14	73.7
	Klebsiella pneumoniae		2	10.5
	Pseudomonas aeruginosa		2	10.5
	Proteus mirabilis		1	5.3
	Negative		41	68.3

Approximately half of study population (44.1%) had elevated WBC level. Of 159 patients indicated C-reactive protein (CRP) test, high CRP (>5 mg/L) was observed in about one-third (36.5%). The majority of the samples (55/60; 91.7%) were urine, while the others were blood (3/60; 5.0%) and pus (2/60; 3.3%). Among these, 19 samples (31.7%) tested positive for bacterial culture, all of which were Gram-negative bacteria. *E. coli* was the most prevalent species, identified in 73.7% of positive samples. Besides, 8 out of 19 positive samples contained ESBL-producing bacteria, including 7 samples of *E. coli* and 1 sample of *Proteus mirabilis*. Additionally, *E. coli* isolates were predominantly resistant to amoxicillin/clavulanate (12/14 samples), ceftriaxone (12/14), and ceftazidime (12/14).

3.2. The pattern of antibiotic use

The majority of patients received 1-2 antibiotics (74.6%), about one-fifth were treated with 3 antibiotics (20.7%), and a few patients (4.7%) received 4-5 antibiotics during their hospital stays. About half of patients (53.5%) were treated with antibiotics longer than 7 days. Table 4 presented specific antibiotics used in the treatment of UTIs.

Table 4. **Antibiotic use in UTI treatment (n=213)**

Antibiotic class	Antibiotic	Frequency	Percentage
β-lactam (+/- β-lactamase inhibitor) n=199 (93.4%)	Ampicillin/sulbactam	66	31.0
	Amoxicillin/clavulanate	1	0.5
	Cefoxitin	62	29.1
	Cefoperazone/sulbactam	58	27.2

Antibiotic class	Antibiotic	Frequency	Percentage
	Cefoperazone	31	14.6
	Cefotiam	6	2.8
	Ceftriaxone	6	2.8
	Ertapenem	31	14.6
	Imipenem/cilastatin	2	0.9
	Meropenem	1	0.5
Fluoroquinolone n=72 (33.8%)	Levofloxacin	39	18.3
	Moxifloxacin	19	8.9
	Ciprofloxacin	14	6.6
Aminoglycoside	Amikacin	21	9.9
Phosphonic acid derivative	Fosfomycin	51	24.0
Oxazolidinone	Linezolid	1	0.5

β-lactam and fluoroquinolone were the most commonly used antibiotic groups (93.4% and 33.8%, respectively). Of these, ampicillin/sulbactam (31.0%) and levofloxacin (18.3%) were the most frequently prescribed. In addition, fosfomycin was indicated for approximately one-fourth of patients (24.0%).

The pattern and appropriateness of empiric antibiotic use in the treatment of UTIs were presented in Table 5.

Table 5. **Empiric antibiotic use (n=213)**

Type of regimen		Frequency	Percentage
Monotherapy n=168 (78,9%)	β-lactam	136	63.8
	Phosphonic acid derivative (fosfomycin)	21	9.9
	Fluoroquinolone	10	4.7
	Aminoglycoside	1	0.5
Combination therapy n=45 (21,1%)	β-lactam + fluoroquinolone	25	11.7
	β-lactam + fosfomycin	13	6.1
	Fosfomycin + fluoroquinolone	4	1.9
	β-lactam + aminoglycoside	3	1.4
The appropriateness of antibiotic use			
Indication		136	63.8
Dosage		176	82.6
Administration route		213	100.0
Overall		108	50.7

Regarding empirical antibiotics, a larger proportion of patients received monotherapy compared to combination therapy (78.9% vs. 21.1%). Monotherapy with β-lactam was the most common regimen (63.8%), and ampicillin/sulbactam was the most frequently observed (26.3%). Besides, we noticed that the most favorable combinations were β-lactam + fluoroquinolone (11.7%) and β-lactam + fosfomycin (6.1%).

There were 136 patients (63.8%) indicated empiric antibiotics in accordance with the referenced guidelines. The main reason for inappropriate empiric treatment was antibiotic selection not aligning with the diagnosis (65.0%). Regarding dosage, 176 out of 213 patients (82.6%) received adequate empiric antibiotic dosage. Cases of incorrect dosing included longer dosing intervals than recommended (91.9%) and insufficient dosage adjustments in patients with renal failure (8.1%).

Additionally, all 213 patients received antibiotics via the appropriate route of

administration, with 69.5% treated intravenously and 30.5% orally. Overall, empiric antibiotics were prescribed properly in 50.7% of patients.

3.3. Treatment outcomes and factors associated with the length of hospital stay

The majority of patients stayed in the hospital for more than 7 days (62.9%), and nearly all patients (99.5%) were successfully treated.

Logistic regression was used to identify factors associated with the length of hospital stay (Table 6). The variables of the model included:

- Dependent variable: the length of hospital stay (≤7 days/>7 days)

- Independent variables: age group (<65 years/≥65 years), gender (male/female), diagnosis (cystitis/pyelonephritis), creatinine clearance (≥60 mL/min/<60 mL/min), co-morbidities (no/yes), urine leukocytes (negative/positive), surgical intervention (none/ temporary/definitive), the appropriateness of empiric antibiotics (no/yes).

Table 6. **Factors associated with the length of hospital stay**

Factors	OR (95% CI)	p-value
Age group		
≥65 years	***2.965 (1.122-7.835)***	***0.028***
Gender		
Female	*1.361 (0.664-2.789)*	*0.399*
Diagnosis		
Pyelonephritis	*1.251 (0.550-2.844)*	*0.594*
Creatinine clearance (mL/min)		
<60	*1.069 (0.493-2.316)*	*0.866*
Co-morbidities		
Yes	*1.852 (0.962-3.565)*	*0.650*
Urine leukocytes		
Positive	*1.080 (0.513-2.275)*	*0.839*
Surgical interventions		
Temporary	***4.502 (2.009-10.088)***	***<0.001***
Definitive	***11.149 (4.815-25.816)***	***<0.001***
The appropriateness of empiric antibiotic use		
Yes	*1.034 (0.547-1.955)*	*0.919*

Notes: OR: odds ratio; 95% CI: 95% confidence interval

Reference categories: the length of hospital stay (≤7 days), age group (<65 years), gender (male), diagnosis (cystitis), creatinine clearance (≥60 mL/min), co-morbidities (no), urine leukocytes (negative), surgical interventions (none), the appropriateness of empiric antibiotic use (no).

The results from logistic regression showed that patients aged 65 years or older (OR=2.965; 95% CI 1.122-7.835; p=0.028) and those underwent surgical interventions, including both temporary and definitive surgical treatments, were more likely to have longer hospital stays (OR=4.502; 95% CI 2.009-10.088; p<0.001, and OR=11.149; 95% CI 4.815-25.816; p<0.001, respectively).

IV. DISCUSSION

4.1. Patients' characteristics

The mean age of the study population was 52.9 ± 14.5 years. This aligns with the findings reported by Pham Thi Lanh (2023), where the mean age of patients was 51.7 ± 17.8 years [9]. Approximately 80% of patients were younger than 65 years, contrasting with the results from a study by Nguyen Thi Nhung (2021), which reported a

high proportion (60.0%) of elderly patients (≥65 years) [10]. This difference can be explained by the fact that most patients <65 years in our study had urinary tract abnormalities, which are considered significant factors associated with complicated UTIs [1]. We noted that male patients were predominant. Male gender is also a factor for complicated UTIs [1]. About one-third of the cases (35.7%) had reduced creatinine clearance (<60 mL/min), which may require antibiotic dose adjustment.

Our study revealed that 38.0% of patients experienced at least 3 symptoms, which is significantly higher than the figure reported by Pham Thuy Yen Ha (10.1%) (2022) [4]. Flank pain was the most common symptom (75.6%), surpassing the results of Pham Thuy Yen Ha (2022), with documented incidence of 59.6% [4]. This discrepancy is likely due to the high prevalence of pyelonephritis in the study population. Other common symptoms included dysuria (43.7%), urinary retention (20.7%), fever (9.4%), and chills (6.1%). Flank pain, fever, and chills are useful signs to differentiate between lower and upper UTIs [7].

All included patients were diagnosed with complicated UTIs, and 77.5% of the patients had pyelonephritis (upper UTIs). A study by Nguyen Thi Nhung (2021) also reported 100% of cases having complicated UTIs [10]. However, our findings differ from those of Vu Thi Thuy An (2022), where complicated UTIs observed in 75.8% of patients [5]. This variation might be explained by a high percentage of patients with urinary tract abnormalities in our study (96.2%).

A total of 108 patients (50.7%) underwent interventions, including temporary (21.1%) and definitive (29.6%) surgical treatments. According to the guidelines, surgical interventions on the urinary tract are a risk factor for multidrug-resistant organism infections. This should be considered when selecting empirical treatment [2].

About half of the patients (53.1%) had WBC within the normal range, which is comparable to the proportions reported by Vu Thi Thuy An (2022) and Pham Thuy Yen Ha (2022), i.e., 58.1% and 63.8%, respectively [4] [5]. A significant proportion (63.5%) exhibited elevated CRP levels, exceeding the figure reported by Pham Thuy Yen Ha (2022) (53.4%) [4]. WBC and CRP may be useful biomarkers in managing various infections, including UTIs [2].

The majority of the patients (66.2%) had elevated urine leukocytes. This finding is consistent with the results from studies by Nguyen Thi Nhung (2022) and Pham Thuy Yen Ha (2022), which reported proportions of 61.0% and 70.3%, respectively [4] [10].

Regarding microbiological testing, urine was the most common culture specimen (55/60; 91.7%). Guidelines recommend urine culture and antimicrobial susceptibility testing as useful diagnostic tools in UTI management, especially in pyelonephritis [1] [2], which was prevalent in our study. Approximately one-third of cultures (19/60; 31.7%) had positive results, and *E. coli* was the most frequently isolated bacterium (14/19; 73.7%). This is consistent with literature describing common etiologies of UTIs [1] [2]. Among the isolates, half (7/14) were ESBL-producing bacteria. Antibiotics with potential activity against ESBL-producing bacteria, such as imipenem/cilastatin, meropenem, cefoperazone/sulbactam, are recommended in the management of such cases [2].

4.2. The pattern of antibiotic use

Approximately 75% of patients were prescribed 1-2 antibiotics, while a smaller proportion (around 25%) received treatment with three or more antibiotics. β-lactams and fluoroquinolones were the most commonly used antibiotic groups (93.4% and 33.8%,

respectively), consistent with the findings of Vu Thi Thuy An (2022), where these antibiotics were also predominant [5]. Among the two groups, ampicillin/sulbactam (31.0%) and levofloxacin (18.3%) were the most frequently used agents.

Regarding empirical antibiotic use, monotherapy was more prevalent than combination therapy (78.9% vs. 21.1%). Our findings align with those of Vu Thi Thuy An (2022) and Pham Thuy Yen Ha (2022), who reported similar proportions of 73.0% and 73.5%, respectively [4] [5]. Among monotherapy regimens, ampicillin/sulbactam was the most commonly prescribed (26.3%). Several patients were treated with a combination of cefoxitin and fosfomycin, which is not recommended as empirical treatment according to the VUNA 2020 guidelines for managing complicated UTIs [2].

Approximately 40% of patients received inappropriate empiric antibiotic treatment, mostly due to improper antibiotic selection. For instance, fosfomycin was empirically prescribed for patients with pyelonephritis (38.0%), and moxifloxacin was used for patients with cystitis (24.0%). Guidelines do not advise fosfomycin as an initial antibiotic therapy for pyelonephritis [1]. Moxifloxacin is not recommended for the treatment of UTIs due to insufficient therapeutic concentrations in urine [1] [2] [8]. The remaining patients (35.0%) received antibiotics inconsistent with their risk stratifications. Most patients (82.6%) received the correct antibiotic dose. Among those with incorrect dosing, most cases (91.9%) involved longer dosing intervals for cefoxitin than recommended. This could lead to insufficient time above the microbial inhibitory concentration (MIC) and may result in treatment failure. The remaining cases involved insufficient dosage adjustments for antibiotics (e.g., amikacin, levofloxacin) in patients with renal failure. This resulted in higher doses than recommended, and increased the risk of drug toxicity, such as nephrotoxicity and/or ototoxicity by amikacin and tendinitis/tendon rupture by levofloxacin [8].

Overall, empiric antibiotics were appropriately prescribed in 50.7% of patients, similar to the findings of Pham Thuy Yen Ha (2022) (54.5%) [4]. Of the remaining (49.3%), most inappropriate cases (64.8%) were due to incorrect empiric antibiotic indications, while a smaller proportion (8.6%) involved both improper indication and dosage.

4.3. Treatment outcome and associated factors with the length of hospital stay

Nearly all patients (99.5%) improved after treatment. This is comparable with the results of Pham Thuy Yen Ha (2022) and Vu Thi Thuy An (2022), where the treatment success rates were observed in 100.0% of patients [4] [5]. A significant proportion of patients were hospitalized for more than 7 days (62.9%), which aligns with the rate reported by Nguyen Thi Nhung (2021) (87%). This similarity may be explained by the high percentages of complicated UTI patients in both studies [10]. According to guidelines, the duration of antibiotic treatment should be at least 7-14 days, depending on the individual response [2].

We found that age ≥65 years (OR=2.965; 95% CI 1.122-7.835; p=0.028) and undergoing surgical intervention (OR=4.502; 95% CI 2.009-10.088; p<0.001 for temporary interventions, and OR=11.149; 95% CI 4.815-25.816; p<0.001 for definitive interventions) were significantly associated with longer hospital stays (>7 days). A study by Jesús Redondo-Sánchez (2021) has indicated that older patients tended to have an increased duration of stay [11]. Furthermore, patients undergoing surgical procedures often experience severe

conditions and face a high risk of complications, which could contribute to prolonged hospital stays [12].

V. CONCLUSIONS

The majority of patients with UTIs exhibited common clinical symptoms and elevated urine leukocytes. The appropriateness of antibiotic use was suboptimal. Patients aged ≥65 or undergoing surgical intervention were more likely to have longer hospital stays.

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CONFLICT OF INTEREST

No potential conflicts relevant to this article to report.

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