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Original Research

ASSESSING ANTIMICROBIAL THERAPY IN TREATING HEALTHCARE-ASSOCIATED INFECTIONS AT A VIETNAMESE NATIONAL HOSPITAL

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ABSTRACT: To evaluate the appropriateness of antimicrobial therapy in treating healthcare-associated infections and identify factors associated with patient outcomes at a national hospital in Vietnam. A cross-sectional study was conducted on 122 medical records of patients who were diagnosed with healthcare-associated infection at Thong Nhat Hospital from January 2023 to December 2023, using data from the Infection Control Department. Appropriateness of antimicrobial therapy was defined as physician adherence to Thong Nhat Hospital guidelines for antibiotic use. The factors associated with the treatment outcome were identified using multiple logistic regression analysis. The median age of the patients was 75.5 (65-85). Hospital-acquired pneumonia was identified in 51.6% of patients. The most prevalent pathogens were Klebsiella pneumoniae and Escherichia coli. The overall appropriate rate of empiric antimicrobial therapy was 76.2%. The successful treatment outcome rate was 71.3%. Lower respiratory tract infection, sepsis/sepsis shock, cancer, and comatose state were factors associated with treatment failure. Active management and treatment are essential for patients with lower respiratory infection, sepsis or septic shock, cancer, and comatose states to improve treatment outcomes.

Keywords: healthcare-associated infection, antimicrobial therapy, treatment outcome

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1. INTRODUCTION

Healthcare-associated infections (HAIs) are infections that occur during a patient's hospital stay and were not present or incubating at the time of admission. Typically, infections developing more than 48 hours after admission are classified as HAIs [1]. These infections prolong hospital stays, exacerbate underlying conditions, contribute to antibiotic resistance, and increase mortality rates [2]. The distribution of infectious agents varies across patient populations, healthcare settings, and countries [1]. Overall, bacteria are the most common pathogens, followed by fungi and viruses. In Vietnam, approximately 70-80% of hospital-acquired infections are caused by gram-negative bacteria, while 14-30% are due to gram-positive bacteria, and about 11% are attributed to fungi [3].

Despite advancements in healthcare technology and the implementation of preventive measures, HAIs remain a significant challenge worldwide, posing substantial threats to patient safety and health. In 2022, the Centers for Disease Control and Prevention (CDC) estimated that one in 31 hospitalized patients and one in 43 nursing home residents in the U.S. acquired at least one HAI [4]. In developing countries, challenges such as inadequate sanitation, poor infrastructure, limited resources, insufficient infection control measures, and the irrational use of invasive devices and antibiotics further exacerbate the prevalence of HAIs [5]. In Vietnam, data on HAIs remain incomplete due to limited published surveillance. Studies from 2000 to 2013 reported HAI rates of approximately 4.2–8.4% in provincial general hospitals [6]. The risk is expected to be higher in tertiary hospitals, which often manage severe cases and perform numerous invasive procedures.

Antibiotics are essential for treating infections; however, increasing antibiotic resistance complicates the selection of effective treatments [7,8]. Appropriate antibiotic use has been shown to improve survival rates, shorten hospital stays, and reduce healthcare costs [9]. Therefore, we conducted this study to assess the appropriateness of antimicrobial therapy for HAIs and identify factors associated with patient outcomes at Thong Nhat Hospital. We suppose that knowing appropriate antibiotic rate and identification of factors associated with treatment outcomes may assist hospitals in establishing appropriate care strategies to improve treatment outcomes for patients with HAIs.

2. MATERIALS AND METHODS

2.1. Study design and setting

This cross-sectional study included in-patients aged 18 years or older who were diagnosed with healthcare-associated infections (HAIs) at Thong Nhat Hospital, a national hospital in South Vietnam, from January 2023 to December 2023. Data were obtained from the Infection Control Department. Exclusion criteria included: (1) patients diagnosed with HAIs within 48 hours of admission, (2) those transferred with HAIs from another hospital, (3) readmissions due to HAIs, (4) patients who did not receive antibiotic treatment for at least 2 days, and (5) cases where medical records were inaccessible.

We reviewed the patient's medical records and collected data, including demographic and baseline characteristics, causative pathogens, antimicrobial susceptibility testing, antimicrobial therapy regimen, and treatment outcomes. The demographic and baseline characteristics included age, gender, initial estimated glomerular filtration rate (eGFR), site of HAIs, onset date of HAIs, risk factors for HAIs, organ dysfunction status before HAIs, interventions before HAIs, and medications used prior to HAIs, as obtained from the medical records. The onset date of HAIs is defined as the first day on which HAIs were recorded in the medical record. Causative pathogens include the frequency and proportion of pathogens isolated. Antimicrobial therapy regimen includes the frequency and proportion of antibiotics/antibiotic groups used, as well as the frequency and proportion of monotherapy/combination antibiotic regimens. Antimicrobial susceptibility testing includes the number and proportion of bacteria susceptible to each antibiotic, the number and proportion of Extended-spectrum β-lactamase (ESBL)-producing bacteria, and the number and proportion of methicillin-resistant Staphylococci (MRS) strains. Treatment outcomes include the success rate of treatment, which consists of achieving a cure or remission. Treatment failure, on

the other hand, is defined as no change, worsening of the condition, including discharge from care, or death.

2.2. Appropriateness of antimicrobial therapy

We evaluated the appropriateness of antimicrobial therapy based on the selected antimicrobial agent, dosage, route of administration, and overall suitability. The criteria for assessing appropriateness in indication, dosage, and administration route were aligned with physician adherence to Thong Nhat Hospital's 2022 antibiotic use guideline [10]. For empirical antibiotic regimens, the choice of antimicrobial agents was deemed appropriate when it adhered to the guideline. For patients treated based on microbiological results and antibiotic susceptibility testing, an antimicrobial agent was considered appropriate if at least one antibiotic in the regimen remained susceptible according to the antibiogram results recorded in the medical records. Overall, antimicrobial therapy was classified as appropriate if the drug indication, dosage, and route of administration were all appropriate.

2.3. Statistical analysis

Data analysis was conducted using SPSS version 27.0 (IBM, Armonk, New York). Continuous variables following a normal distribution were expressed as mean ± standard deviation (SD), while non-normally distributed variables were reported as median (interquartile range [IQR]). Categorical variables were presented as proportions.

Factors associated with treatment outcomes, categorized as either success or failure, were evaluated. Initially, univariate logistic regression was performed to assess demographic and baseline variables, as well as antimicrobial therapy-related factors, including the overall appropriateness of the antimicrobial regimen, based on relevant literature. Variables with $p < 0.2$ were subsequently included in a multiple logistic regression analysis using a backward elimination approach to identify factors independently associated with treatment outcomes.

The dependent variable was treatment failure, and the independent variables included age, gender, initial eGFR, site of healthcare-associated infections (HAIs), risk factors for HAIs, organ dysfunction prior to infection, interventions before HAIs, medications administered before HAIs, and the overall appropriateness of antimicrobial therapy.

2.4. Ethics approval

The study protocol was approved by the Institutional Review Board of Thong Nhat Hospital, Ho Chi Minh City, Vietnam (128/2023/BVTN-HDYD). Patient confidentiality was strictly maintained, and all procedures adhered to the ethical standards set by the institutional and national research committees. The study also complied with the principles of the 1964 Declaration of Helsinki and its subsequent amendments or equivalent ethical guidelines.

3. RESULTS

3.1. Demographic and other baseline characteristics

Over a 12-month period, a total of 122 patients met the inclusion criteria and were enrolled in our study. The median age of the study population was 75.5 years, with 81.1% aged 60 years or older. Among the participants, 52.5% were female. Hospital-acquired pneumonia was the most prevalent type of HAI, accounting for 51.6% of cases. The primary risk factors identified were diabetes (40.2%) and chronic kidney disease (20.5%) (Table 1).

Table 1. Participants' baseline characteristics (n = 122)

Characteristics	Freq	%
Age, median (IQR)	75.5 (65-85)	
≥60 years old	99	81.1
<60 years old	23	18.9
Gender		
Female	64	52.5
Male	58	47.5
Initial eGFR		
≥60 mL/min/1.73 m2	68	55.7
<60 mL/min/1.73 m2	54	44.3

Characteristics	Freq	%
Site of HAIs		
Hospital-acquired pneumonia	63	51.6
Urinary tract infection	39	32.0
Sepsis/ septic shock	38	31.1
Surgical site infection	19	15.6
Ventilator-associated pneumonia	10	8.2
Other skin and soft tissue infection	5	4.1
Meningitis/central nervous system infection	4	3.3
Intra-abdominal infection	3	2.5
Onset date of HAIs, median (IQR)	8 (4.8-12.0)	
Risk factors for HAIs		
Diabetes	49	40.2
Chronic kidney disease	25	20.5
Cancer	19	15.6
Others1	23	18.9
Organ dysfunction status before HAIs		
No	62	50.8
Yes	60	49.2
Hematologic disorders*	26	21.3
Trauma	25	20.5
Coma	19	15.6
Respiratory failure	9	7.4
Acute kidney injury	7	5.7
Circulatory failure	2	1.6
Interventions before HAIs		
No	15	12.3
Yes	107	87.7
Oxygen therapy	56	45.9
Urinary catheter	55	45.1
Gastric/duodenal tube	54	44.3
Surgery	44	36.1
Endotracheal intubation	40	32.8
Sputum suctioning	39	32.0
Nebulization	29	23.8
Mechanical ventilation	25	20.5
Bag-valve-mask ventilation	18	14.8
Central venous catheter	15	12.3
Other procedures2	48	39.3
Medications used before HAIs		
No	22	18.0
Yes	100	82.0
Proton pump inhibitor	74	60.7
Intravenous sedative	38	31.1
Parenteral nutrition	31	25.4
Corticosteroid	26	21.3
Muscle relaxant	23	18.9

*When patient had at least one of the following test results: WBC < 4 K/µl, NEU < 0.5 K/µl, PLT < 100 K/µl, RBC < 3 M/µl before being diagnosed with HAIs

1Included: Cirrhosis, endotracheal intubation before admission, Cushing syndrome, NEU < 2 K/µL, alcohol addiction, use of cytotoxic drugs, chronic obstructive pulmonary disease, percutaneous biliary drainage, long-term urinary catheter, long-term gastric tube, dialysis

2Included: Pleural drainage, hemodialysis, radial artery cannulation, bladder irrigation, lumbar puncture, abdominal puncture, thoracentesis, knee joint injection, extracorporeal membrane oxygenation, invasive arterial blood pressure monitoring, jejunal feeding, biopsy, angioplasty, interventional angiography

Abbreviations: Freq Frequency; IQR. Interquartile range; eGFR: Estimated glomerular filtration rate; HAIs: Healthcare-associated infections

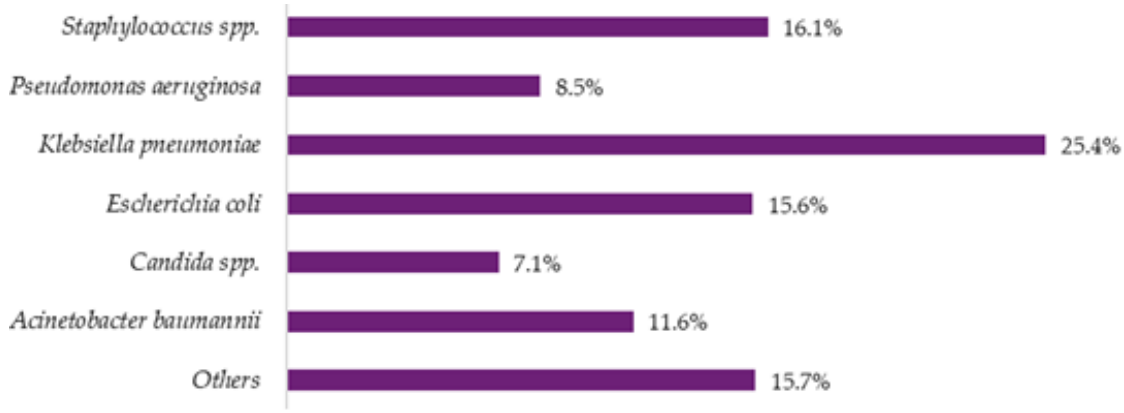

Figure 1. Suspected microbiological pathogens in 122 participants

Gram-negative bacteria were the most commonly identified pathogens in patient specimens, accounting for 74.6% of the total. The two most prevalent gram-negative bacteria were Klebsiella pneumoniae and Escherichia coli. Among gram-positive bacteria, Staphylococcus species were the dominant pathogens. Additionally, fungi constituted 7.1% of the total pathogens identified (Figure 1).

The analysis of microbiological data from patients with hospital-acquired infections reveals a high prevalence of resistant bacteria. Among Gram-negative pathogens, Klebsiella pneumoniae and Escherichia coli exhibited low susceptibility to third- and fourth-generation cephalosporins (20-21% and 25-37%, respectively) and fluoroquinolones (17-19% and 8-17%, respectively). Carbapenems remained moderately effective, particularly against Escherichia coli (85-92%). Acinetobacter baumannii also showed poor susceptibility across all tested antibiotics, with carbapenems at 30-36% and cephalosporins at 0-33%. Pseudomonas aeruginosa exhibited the highest susceptibility to cephalosporins (52%) among the studied antibiotics (Table 2). In contrast, Gram-positive bacteria, including Staphylococcus aureus, remain highly sensitive, with susceptibility rates of over 90% to first-line antibiotics used to treat Methicillin-Resistant Staphylococcus aureus (MRSA) (Table 3). For fungi, the susceptibility to antifungal agents is generally high, with all isolated strains of Candida being 100% susceptible to antifungal drugs, except for fluconazole (Table 4).

The median number of antibiotics initially prescribed to patients was 2 (IQR 1-2). The average duration of antibiotic treatment was 14 days (IQR 8.8-19.0). Additionally, the median number of antibiotic changes per patient during treatment was 1 (IQR 0-2). The most commonly used antibiotic classes were β-lactams and fluoroquinolones, with usage rates of 83.6% and 50.0%, respectively. Furthermore, 32.8% of cases received levofloxacin, and 22.1% were treated with ceftriaxone (Table 5).

Out of the 122 patients included in the study, 109 cases (89.3%) were treated with empirical regime, while 13 cases (10.7%) received treatment based on microbiological results and antibiotic susceptibility testing (Table 6).

3.2. Appropriateness of antimicrobial therapy

The initial administration of appropriate antimicrobial agents was found to be 86.9% (n = 106) (Table 7).

All cases of inappropriate antibiotic use involved empirical antibiotic regimens. The majority of inappropriate cases were due to the selected regimen targeting community-acquired bacteria instead of those associated with hospital-acquired infections (Table 9). For cases with appropriate antibiotic selection, we further evaluated the appropriateness of dosage and dosing intervals. In the study sample, 87.7% of cases met the criteria for appropriate dosage and dosing intervals. The most frequently associated with inappropriate dosing were vancomycin (n = 4), imipenem/cilastatin (n = 4), and piperacillin/tazobactam (n = 3) (Table 10).

Table 2. Antibiogram of gram-negative bacteria

Gram-negative bacteria	n	%	ESBL (%)	β-lactam															AGs			FQs		Others	
	161	75,6		Ampicillin	AMS	AMC	Ticarcillin	TCC	Piperacillin	PTZ	Cefazolin	Ceftazidime	Ceftriaxone	Cefepime	Ertapenem	Imipenem	Meropenem	Aztreonam	Gentamicin	Tobramycin	Amikacin	Ciprofloxacin	Levofloxacin	TMP/SMX	Colistin
Klebsiella pneumoniae	56	34,8	14	R	20	25	R	20	20	30	6	21	20	21	52	41	47	19	50	42	95	19	17	60	84
Escherichia coli	35	21,7	69	10	48	53	0	42	0	81	6	25	25	37	92	85	87	12	74	74	87	17	8	34	85
Acinetobacter baumannii	25	15,5	-	R	0	R	30	34	30	28	0	33	0	32	R	36	30	R	48	48	-	40	40	52	95
Pseudomonas aeruginosa	19	11,8	-	R	R	R	50	47	55	100	0	52	R	52	R	31	38	-	62	44	55	42	42	-	88
Enterobacter cloacae	9	5,6	-	R	R	R	0/9	0/9	0/9	2/9	R	0/9	0/9	3/9	7/9	5/9	6/9	6/9	3/9	3/9	9/9	1/9	0/9	6/9	9/9
Enterobacter aerogenes	4	2,5	-	R	R	R	0/4	0/4	0/4	0/4	R	0/4	-	0/4	-	0/4	0/4	0/4	0/4	0/4	4/4	0/4	0/4	0/4	1/4
Stenotrophomonas maltophilia	3	1,9	-	R	R	R	R	-	R	R	-	-	R	-	R	R	R	R	R	R	R	-	0/3	2/3	-
Serratia fonticola	2	1,2	-	-	-	-	0/2	0/2	2/2	0/2	-	0/2	-	2/2	-	2/2	0/2	0/2	0/2	2/2	2/2	2/2	2/2	2/2	0/2
Achromobacter xylosoxidans	1	0,6	-	-	-	-	1/1	1/1	1/1	1/1	-	1/1	-	1/1	-	1/1	1/1	0/1	0/1	0/1	1/1	0/1	0/1	1/1	0/1
Burkholderia cepacia	1	0,6	-	R	R	R	R	0/1	R	R	-	1/1	R	R	R	R	1/1	R	R	R	R	0/1	0/1	1/1	R
Citrobacter freundii	1	0,6	-	R	R	R	0	1/1	0/1	1/1	R	1/1	-	1/1	-	1/1	1/1	1/1	1/1	0/1	1/1	0/1	0/1	0/1	1/1
Citrobacter koseri	1	0,6	-	R	-	-	R	1/1	R	1/1	-	1/1	-	1/1	-	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
Comamonas testosteroni	1	0,6	-	-	-	-	0/1	1/1	1/1	1/1	-	1/1	-	1/1	-	1/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1
Proteus mirabilis	1	0,6	-	0/1	1/1	0/1	-	-	-	1/1	-	1/1	1/1	1/1	1/1	0/1	-	-	1/1	1/1	-	1/1	1/1	1/1	R
Ralstonia pickettii	1	0,6	-	-	-	-	0/1	0/1	1/1	0/1	-	1/1	-	1/1	-	1/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1
Serratia marcescens	1	0,6	-	R	R	R	1/1	1/1	1/1	-	R	1/1	-	1/1	-	-	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	R

For bacteria with a count of < 10, sensitivity rates are expressed as fractions. For bacteria with a count of ≥ 10, sensitivity rates are expressed as percentages
Interpret the table: green box: ≥ 80% of isolated bacteria are susceptible to the antibiotic, yellow box: ≥ 70% to < 80% of isolated bacteria are susceptible to the antibiotic, purple box: ≥ 50% to < 70% of isolated bacteria are susceptible to the antibiotic, red box: < 50% of isolated bacteria are susceptible to the antibiotic; (R): bacteria that are naturally resistant to the corresponding antibiotic; (-) indicates that the bacteria are not routinely tested for susceptibility to the corresponding antibiotic.
Abbreviations: n. frequency; ESBL. Extended-spectrum β-lactamase; FQs. fluoroquinolone; AGs.aminoglycoside; AMS. ampicillin/sulbactam; AMC. amoxicillin/clavulanate; TCC. ticarcillin/clavulanate; PTZ: piperacillin/tazobactam; TMP/SMX. trimethoprim/sulfamethoxazole

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Table 3. Antibiogram of gram-positive bacteria

Gram-positive bacteria	n	%	MRS (%)	β-lactam			FQs		Glycopeptid		TCs		Others						
	38	17,8		Benzylpenicillin	Oxacillin	Ampicillin	Ciprofloxacin	Moxifloxacin	Teicoplanin	Vancomycin	Tetracycline	Tigecycline	Gentamicin	Erythromycin	Linezolide	TMP/SMX	Clindamycin	Fusidic Acid	Rifampicin
Staphylococcus aureus	19	50,0	78	15	15	-	68	68	100	94	78	94	31	26	94	78	31	94	100
Staphylococcus haemolyticus	8	21,1	100	0/8	0/8	-	0/8	0/8	8/8	8/8	4/9	8/8	1/8	0/8	8/8	1/8	0/8	5/8	6/8
Staphylococcus epidermidis	6	15,8	83	0/6	0/6	-	3/6	3/6	6/6	6/6	5/6	6/6	4/6	2/6	6/6	3/6	4/6	6/6	5/6
Enterococcus faecalis	3	7,9	-	-	-	2/3	0/3	-	3/3	3/3	0/3	3/3	R	2/3	3/3	R	-	R	-
Staphylococcus hominis	1	2,6	-	0/1	0/1	-	0/1	0/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	0/1	0/1	1/1
Staphylococcus saprophyticus	1	2,6	-	0/1	0/1	-	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	0/1	1/1

For bacteria with a count of < 10, sensitivity rates are presented as fractions. For bacteria with a count of ≥ 10, sensitivity rates are presented as percentages

Interpret the table: green box: ≥ 80% of isolated bacteria are susceptible to the antibiotic, yellow box: ≥ 70% to < 80% of isolated bacteria are susceptible to the antibiotic, purple box: ≥ 50% to < 70% of isolated bacteria are susceptible to the antibiotic, red box: < 50% of isolated bacteria are susceptible to the antibiotic; (R): bacteria that are naturally resistant to the corresponding antibiotic; (-) indicates that the bacteria are not routinely tested for susceptibility to the corresponding antibiotic.

Abbreviations: n. frequency; MRS. methicillin-resistant Staphylococci; FQs. fluoroquinolone; AGs.aminoglycoside; TCs: tetracycline; TMP/SMX. trimethoprim/sulfamethoxazole

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Table 4. Antifungal susceptibility testing

Fungi	n	%	Fluconccccazole	Voriconazole	Caspofungin	Micafungin	Amphotericin B
	14	6,6					
Candida albicans	5	35,7	4/5	5/5	5/5	5/5	5/5
Candida spp.	4	28,6	4/4	4/4	4/4	4/4	4/4
Candida tropicalis	4	28,6	3/4	4/4	4/4	4/4	4/4
Candida lusitaniae	1	7,1	-	1/1	-	-	1/1

For fungi with a count < 10, susceptibility rates are presented as fractions. For fungi with a count ≥ 10, susceptibility rates are presented as percentages
Abbreviations: n. frequency

Table 5. Patterns of antimicrobial use in treatment of HAIs

Antibiotics	Frequency	Percentage case prescribed
β-lactam		
Ceftriaxone	27	22.1
Imipenem/cilastatin	25	20.5
Piperacillin/tazobactam	15	12.3
Meropenem	13	10.7
Others1	22	18.0
Fluoroquinolone		
Levofloxacin	40	32.8
Ciprofloxacin	20	16.4
Moxifloxacin	1	0.8
Glycopeptide		
Vancomycin	20	16.4
Teicoplanin	4	3.3
Aminoglycoside		
Amikacin	4	3.3
Gentamicin	1	0.8
Others2	8	6.6

1 Other β-lactams: amoxicillin/clavulanate, cefoperazone/sulbactam, ceftazidime, ceftizoxime, cefepime, cefuroxime, ticarcillin/clavulanate, ertapenem.

2 Other classes: colistin, linezolid, clindamycin, tigecycline, fosfomycin

Table 6. Antimicrobial therapy regimen

Antibiotic 1	Antibiotic 2	Antibiotic 3	Frequency
Empiric regimens (n = 109)			
Monotherapy (38,5%)			**42**
Ciprofloxacin	-	-	12
Ceftriaxone	-	-	11
Piperacillin/tazobactam	-	-	4
Othersa	-	-	15
Dual therapy (58,7%)			**64**
Levofloxacin (n = 30)	Piperacillin/tazobactam	-	8
	Imipenem/cilastatin	-	8
	Meropenem	-	5
	Othersb	-	9
Ceftriaxone (n = 15)	Vancomycin	-	4
	Levofloxacin	-	4
	Othersc	-	7
Vancomycin (n = 7)	Imipenem/cilastatin	-	4
	Meropenem	-	2
	Cefepime	-	1
Imipenem/cilastatin (n = 4)	Linezolid	-	1
	Ciprofloxacin	-	1
	Teicoplanin	-	1
	Gentamicin	-	1
Meropenem (n = 3)	Linezolid	-	1
	Ciprofloxacin	-	1
	Teicoplanin	-	1
Othersd	-	5	
Triple therapy (2,8%)			3
Vancomycin (n = 2)	Meropenem	Amikacin	1
	Levofloxacin	Imipenem/cilastatin	1
Imipenem/cilastatin (n = 1)	Ciprofloxacin	Teicoplanin	1
Regimens based on microbiological results and susceptibility testing (n = 13)			
Monotherapy (53,8%)			**7**
Vancomycin	-	-	5
Imipenem/cilastatin	-	-	1
Ceftazidime	-	-	1
Dual therapy (30,8%)			**4**
Imipenem/cilastatin	Amikacin	-	1
	Vancomycin	-	1
Colistin	Tigecyclin	-	1
Ceftriaxone	Clindamycin	-	1
Triple therapy (15,4%)			**2**
Levofloxacin	Meropenem	Teicoplanin	1
	Piperacillin/tazobactam	Ticarcillin/clavulanate	1

a vancomycin, levofloxacin, ertapenem, imipenem/cilastatin, cefepim, cefoperazone/sulbactam, ceftizoxime, amoxicillin/clavulanate, cefuroxime

b levofloxacin + cefepime/ceftazidime/cefoperazone/sulbactam/cefuroxime/ ceftizoxime

c ceftriaxone + meropenem/amikacin/ciprofloxacin/clindamycin/moxifloxacin

d (ciprofloxacin + cefoperazon/sulbactam), (piperacillin/tazobactam + ciprofloxacin), (linezolid + ticarcillin/clavulanate), (ticarcillin/clavulanate + fosfomycin)

Table 7. Appropriateness of antimicrobial therapy

Level of appropriateness	Frequency	Appropriate	Percentage
Empirical regime (n = 109)			
Antimicrobial agent	109	93	85,3
Dosage	93	83	89,2
Route of administration	93	93	100,0
Overall appropriateness	109	83	76,1
Regimens based on microbiological results and susceptibility testing (n = 13)			
Antimicrobial agent	13	13	100,0
Dosage	13	10	76,9
Route of administration	13	13	100,0
Overall appropriateness	13	10	76,9
Overall (n = 122)			
Antimicrobial agent	122	106	86,9
Dosage	106	93	87,7
Route of administration	106	106	100,0
Overall appropriateness	122	93	76,2

Table 9. Cases of inappropriate antimicrobial selection in empiric regimens (n = 16)

Antibiotics	Frequency	Site of HAIs
Ceftriaxone + levofloxacin	3	Hospital-acquired pneumonia
	1	Hospital-acquired pneumonia with sepsis
Ceftriaxone	2	Hospital-acquired pneumonia with sepsis
	1	Ventilator-associated pneumonia
Ceftriaxone + vancomycin	2	Hospital-acquired pneumonia
Ceftriaxone + amikacin	2	Hospital-acquired pneumonia
Ceftriaxone + moxifloxacin	1	Hospital-acquired pneumonia
Ceftriaxone + meropenem	1	Ventilator-associated pneumonia
Amoxicillin/clavulanate	1	Complicated urinary tract infection
Cefuroxime	1	Hospital-acquired pneumonia
Cefuroxime + levofloxacin	1	Complicated urinary tract infection

Abbreviations: HAIs. Healthcare-associated infections

Table 10. Cases of inappropriate dosing and dosing intervals (n = 13)

Antibiotics	Frequency	Reasons		
		Higher than the patient's renal function	Lower than the patient's renal function	Inappropriate dosing intervals
Vancomycin*	4	3*	1*	-
Imipenem/cilastatin	4	-	-	4
Piperacillin/tazobactam	3	-	-	3
Levofloxacin	2	-	-	2
Cefoperazon/sulbactam	2	2	-	-
Ticarcillin/clavulanat	2	-	-	2
Amikacin	1	1	-	-
Ciprofloxacin	1	-	-	1

The dosing of the medication is assessed based on creatinine clearance (CrCl). For patients without height and weight data, we evaluate the appropriateness of the dose based on eGFR

*The dosing of vancomycin is evaluated based on the target AUC/MIC range of 400 to 600 mg.h/l. Reasons for inappropriate dosing include being higher or lower than the target AUC/MIC

Table 11. Factors related to HAIs treatment failure (univariate analysis)

Factors	OR	95% CI	p-value
Age	1.011	0.983-1.040	0.432
Gender (Female)	1.303	0.591-2.872	0.512
Initial eGFR	0.992	0.977-1.007	0.254
Site of HAIs			
Lower respiratory tract infection (Yes)[1]	8.304	2.701-25.526	<0.001
Urinary tract infection (Yes)	0.430	0.169-1.095	0.077
Sepsis/ septic shock (Yes)	2.968	1.301-6.773	0.010
Surgical site infection (Yes)	0.113	0.014-0.880	0.037
Risk factors for HAIs			
Diabetes (Yes)	1.913	0.864-4.235	0.110
Chronic kidney disease (Yes)	1.536	0.605-3.901	0.367
Cancer (Yes)	2.665	0.976-7.276	0.056
Organ dysfunction status before infection			
Hematologic disorders (Yes)	3.364	1.362-8.308	0.009
Trauma (Yes)	0.277	0.077-0.995	0.049
Coma (Yes)	7.977	2.720-23.397	<0.001
Interventions before HAIs			
Oxygen therapy (Yes)	1.889	0.854-4.178	0.116
Urinary catheter (Yes)	1.218	0.555-2.674	0.623
Gastric/duodenal tube(Yes)	3.462	1.518-7.896	0.003
Surgery (Yes)	0.514	0.215-1.228	0.134
Endotracheal intubation (Yes)	2.211	0.979-4.991	0.056
Sputum suctioning (Yes)	3.978	1.732-9.138	<0.001
Nebulization (Yes)	3.200	1.333-7.681	0.009
Mechanical ventilation (Yes)	5.775	2.258-14.773	<0.001
Bag-valve-mask ventilation (Yes)	3.000	1.076-8.361	0.036
Central venous catheter (Yes)	2.469	0.820-7.433	0.108
Medications used before HAIs			
Proton pump inhibitor (Yes)	1.615	0.704-3.705	0.258
Intravenous sedative (Yes)	1.465	0.640-3.354	0.366
Parenteral nutrition (Yes)	1.867	0.787-4.429	0.156
Corticosteroid (Yes)	1.425	0.565-3.594	0.453
Muscle relaxant (Yes)	1.109	0.412-2.986	0.837
Overall appropriateness of antimicrobial therapy (Yes)	0.699	0.286-1.705	0.431

1 included hospital-acquired pneumonia and ventilator-associated pneumonia
Abbreviations: eGFR. Estimated glomerular filtration rate; HAIs. Healthcare-associated infections

Table 12. Factors related to HAIs treatment outcome (multivariable analysis)

Factors	p-value	OR	95%CI
Site of HAIs			
Lower respiratory tract infection (Yes)[1]	0.003	7.318	1.973- 27.148
Sepsis/ septic shock (Yes)	0.008	4.105	1.441- 11.700
Risk factors for HAIs			
Cancer (Yes)	0.019	4.675	1.292-16.919
Organ dysfunction status before infection			
Coma (Yes)	<0.001	11.944	3.256-43.812

1 included hospital-acquired pneumonia and ventilator-associated pneumonia
Abbreviations: HAIs. Healthcare-associated infections

3.3. Factors related to treatment outcome

According to medical records, the overall treatment success rate, defined as a cure or remission, was 71.3%. After univariate analysis, 19 factors related to treatment failure were found to be statistically significant ($p < 0.2$) and were included in the multivariate analysis. These factors were: lower respiratory tract infection, urinary tract infection, sepsis/septic shock, surgical site infection, diabetes, cancer, hematologic disorders, trauma, coma, oxygen therapy, gastric/duodenal tube, surgery, endotracheal intubation, sputum suctioning, nebulization, mechanical ventilation, bag-valve-mask ventilation, central venous catheter , and parenteral nutrition (Table 11).

Multivariable logistic regression using the backward method was performed (Table 12). Four factors related to poor outcomes were found to be statistically significant ($p < 0.05$): lower respiratory tract infection, sepsis/septic shock, cancer, and coma.

4. DISCUSSION

This study found that β-lactam antibiotics and fluoroquinolones were the most commonly prescribed medications, including third-generation cephalosporins, carbapenems, ciprofloxacin, and levofloxacin. These findings align with the fact that the two most prevalent infections in the studied population were hospital-acquired pneumonia and urinary tract infections. According to clinical guidelines, antimicrobial agents from these two classes are recommended as first-line treatments in empirical antibiotic regimens [5,6]. Furthermore, the risk factors for antibiotic-resistant bacteria and the current antibiotic resistance situation at Thong Nhat Hospital may explain the reliance on broad-spectrum antibiotics, such as carbapenems, glycopeptides (vancomycin, teicoplanin), colistin, and fosfomycin, to combat multidrug-resistant bacteria.

The most frequently used antibiotic in this study was levofloxacin, a fluoroquinolone effective against both methicillin-susceptible Staphylococcus aureus and Pseudomonas aeruginosa. It is particularly suitable for patients in units with a low prevalence of methicillin-resistant Staphylococcus aureus and resistant Gram-negative bacteria [12]. Levofloxacin is often used in combination therapy, primarily alongside piperacillin/tazobactam or imipenem/cilastatin, in accordance with guidelines for treating hospital-acquired pneumonia [10,11]. This finding aligns with the reality that hospital-acquired pneumonia is the most common type of infection.

More than half of the patients in the study were treated with two antimicrobial agents, followed by one antimicrobial agent, whereas triple therapy is relatively low. This finding contrasts with the study by Cai et al. (2017), which reported that 74.1% of patients received a single-drug regimen, 22.2% were treated with a two-drug regimen, and only 3.7% received a combination of three or more antibiotics [13]. This discrepancy may be attributed to differences in antibiotic resistance patterns at the research site. Furthermore, the microbiological situation at Thong Nhat Hospital indicates that most empirical antibiotic regimens for HAIs—except for uncomplicated urinary tract infection and mild to moderate skin and soft tissue infection—recommend using a combination of two antimicrobial agents [10]. The median duration of antimicrobial therapy in this study was 14 days, which aligns with recommendations suggesting a duration of 5 to 14 days depending on the site of infection [5,6].

In this study, 89.6% of patients received appropriate antibiotic regimens, the current finding was higher than other reports [14–16]. This difference may stem from variations in assessment methods and the characteristics of study populations (patients with HAIs versus patients with all types of infections) [14–16]. Appropriate empirical antibiotic therapy is defined as administering the antibiotic agent that aligns with the in vitro susceptibility of the isolated bacteria [17].

In cases of inappropriate dosing in this study, antibiotics were often prescribed and administered multiple times a day, necessitating adjustments based on renal function. Vancomycin, imipenem/cilastatin, and piperacillin/tazobactam were most commonly associated with inappropriate dosage. This is because vancomycin should be adjusted to achieve

an area under the curve to minimum inhibitory concentration (AUC/MIC) ratio of 400 to 600 mg·h/L, ideally within the first 24-48 hours [18]. The complexity of this dosing approach, however, often leads to inappropriate. Likewise, imipenem/cilastatin and piperacillin/tazobactam also require dose adjustments based on creatinine clearance. This intricate dosing process complicates proper antibiotic adjustments, leading to further inconsistencies. In addition, we also noted some cases of using antibiotic doses lower than the patient's actual renal function, which may reduce treatment effectiveness while using doses higher than the patient's renal function may cause drug toxicity [19].

Finally, we did not find an association between the appropriateness of antimicrobial therapy and the treatment outcome. This finding aligns with some studies [17,20,21] but contradicts existing recommendations [22]. We hypothesize that antibiotics are just one component in the healthcare chain, and treatment outcomes rely on factors beyond appropriate antibiotic use. Meanwhile, poor treatment outcome was associated with lower respiratory infection, sepsis/sepsis shock, cancer and coma ($p < 0.05$). This suggests that the outcomes for patients are influenced more by their condition before the infection or by the infection status itself, rather than by the care processes they received in the hospital before the infection. Currently, no studies have documented the relationship between coma and poor outcomes in patients HAIs. However, a systematic review by Liu et al. (2023) indicates that coma is a significant factor associated with these infections (OR = 5.12; 95% CI = 1.70-15.38) [23]. We hypothesize that many comatose patients before developing HAIs in this study do so due to underlying conditions such as stroke or intracerebral haemorrhage. These conditions may require invasive interventions and prolonged immobility, contributing to a decline in overall health. In comatose patients, the local defence mechanisms of the airways are altered, allowing microorganisms to more easily adhere to mucosal cells [24]. Cancer is also a factor associated with treatment failure (OR = 4.767; 95% CI = 1.292–16.919). In cancer patients, immune system suppression, combined with a range of factors such as organ dysfunction caused by tumor invasion, surgical interventions, comorbidities, malnutrition, psychological stress, and the adverse effects of treatments (surgery, radiation therapy, chemotherapy), synergistically impair the body's ability to defend against infections. This not only increases the overall susceptibility to infections within this patient population but also significantly elevates the mortality risk associated with infectious complications in cancer patients [25–27]. Meanwhile, lower respiratory infection (OR = 4.767; 95% CI = 1.199-18.946), and sepsis/sepsis shock (OR = 4.047; 95%CI = 1.400-11.699) were a significant predictor of poor treatment outcomes which aligns with the study by Fabbro-Peray et al. (2007), which found that patients with hospital-acquired pneumonia (OR = 3.4; 95% CI = 2.0-5.7), and those with sepsis (OR = 3.9; 95% CI = 2.0-7.4) have a higher risk of mortality [28]. Additionally, research by Koch et al. (2015) demonstrated that patients with lower respiratory tract infection have a higher risk of mortality within one year (HR = 1.7; 95% CI = 1.4-2.0) [29].

5. CONCLUSIONS

The rate of appropriate antimicrobial therapy remains moderate. It's important to note that the factors affecting treatment outcomes identified in our study cannot be changed. Therefore, it is vital to actively manage and treat patients with lower respiratory infection, sepsis or septic shock, and those in comatose states to enhance their chances of recovery significantly.

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