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Determinants of urinary tract infection in hospitalized patients with acute ischemic stroke

Pornpong Jitpratoom¹ and Adhiratha Boonyasiri^{2*}

Abstract

Background Stroke is a major cause of morbidity and mortality worldwide. Urinary tract infection (UTI) is a common post-acute ischemic stroke (AIS) complication. We assessed the incidence, determinant factors, infection characteristics, post-stroke complications, and outcomes of hospitalized AIS patients with UTI.

Methods This retrospective cohort study included AIS patients admitted within 7 days of stroke onset. The patients were divided into the UTI group and the non-UTI (control) group. Clinical data were collected and compared between the groups.

Results There were 342 AIS patients (31 with UTIs and 311 controls). The multivariate analysis showed that an initial National Institutes of Health Stroke Scale (NIHSS) score of ≥ 15 (odds ratio [OR] 5.00, 95% confidence interval [CI] 1.33–18.72) and Foley catheter retention (OR 14.10, 95% CI 3.25–61.28) were risk factors for UTI, whereas smoking (OR 0.08, 95% CI 0.01–0.50), an initial systolic blood pressure (SBP) of > 120 mmHg (OR 0.06, 95% CI 0.01–0.31), and statin use (OR 0.02, 95% CI 0.0006–0.42) were protective factors. Twenty cases (64.5%) were community-acquired and 11 cases (35.3%) were hospital-acquired. Ten patients (32.3%) had catheter-associated UTIs. The most common pathogen was *Escherichia coli* (13 patients, 41.9%). Post-stroke complications were significantly more common in the UTI group, including pneumonia, respiratory failure, sepsis, brain edema, seizure, symptomatic hemorrhagic transformation, congestive heart failure, atrial fibrillation with a rapid ventricular response, acute kidney injury, and hyponatremia. The median length of stay (LOS) in the UTI group was 12 days versus 3 days in the control group ($p < 0.001$). The median 3-month modified Rankin Scale score was higher (5 in UTI and 2 in control; $p < 0.001$) and the median 3-month Barthel Index was lower (0 in UTI and 100 in control; $p < 0.001$) in the UTI group than in the control group.

Conclusions The risk factors for post-AIS UTI included severe stroke (NIHSS score ≥ 15) and urethral catheter indwelling. An initial SBP of > 120 mmHg and statin use were protective factors. The UTI group had significantly worse post-stroke complications, a longer LOS, and worse 3-month outcomes. Smoking was protective, which requires further investigation.

Keywords Urinary tract infection, Acute ischemic stroke, Hospitalization, Predictor, Risk factor, Protective factor, Community-acquired, Hospital-acquired, Smoking, Statin

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Background

Stroke is ranked as the second leading cause of death worldwide. The burden of stroke includes both high mortality and high morbidity, which results in up to 50% of survivors having chronic disability [1, 2]. The injured brain can modify peripheral immunity and transition the functional status of the peripheral immune system from competent to suppressed following the acute phase of stroke [3]. Stroke can cause the transfer and ectopic colonization of specific intestinal flora, making stroke patients more susceptible to infection [4]. Urinary tract infection (UTI) is a common stroke-associated infection [5], with an incidence ranging from 3 to 40% [6–10]. UTIs are associated with poor outcomes [11], death, or disability [7, 12]. Data from previous studies show that the female sex, previous stroke [13], urinary catheterization [14], a higher initial modified Rankin Scale (mRS) score, a higher initial National Institutes of Health Stroke Scale (NIHSS) score [15, 16], older age [12], depressed consciousness, and diabetes mellitus [17] are associated with an increased incidence of infection, but there are many factors that have not been addressed, such as chronic kidney disease, the Barthel Index (BI), the Glasgow Coma Scale (GCS), vital signs, laboratory indicators, and stroke treatments. Therefore, we aimed to assess the determinant factors of UTIs and to explore the incidence, clinical features, and impact of UTIs on stroke outcomes in hospitalized patients with acute ischemic stroke (AIS).

Methods

This retrospective cohort study was conducted at Chumphon Khet Udomsakdi Hospital in Thailand between July 2019 and July 2020. All hospitalized patients aged ≥ 18 years who presented within 7 days of new-onset AIS were included. Patients were excluded if the information necessary for the study was incomplete. The requirement for informed consent was waived because of the absence of any adverse effect on the rights and welfare of the subjects, as approved by the ethics committee. The diagnosis of UTI was made during hospitalization if the patients developed acute dysuria alone, or fever plus one of the following symptoms: urinary frequency, urgency, or retention; incontinence; gross hematuria; change in urine characteristics; or tenderness in the suprapubic or costovertebral angle, combined with the presence of $\geq 10^3$ of any number of organisms in urine culture [18–22]. All included patients who were not assigned to the UTI group were assigned to the non-UTI (control) group. We classified UTIs into subcategories, with community-acquired UTIs defined as being present within < 48 h of hospital admission and hospital-acquired UTIs defined as being detected following 48 h of hospitalization [23, 24]. Additionally, catheter-associated UTIs (CAUTIs) were defined when patients had an indwelling

urinary catheter that had been in place for > 2 days, and either the catheter was in place on the date of infection or removed the day before UTI development [25, 26]. We collected the patients' demographic data, including age, sex, and vascular risk factors (arterial hypertension, diabetes mellitus, atrial fibrillation, hyperlipidemia, and smoking status). Initial data associated with acute stroke on admission were also collected, including neurological manifestations; laboratory findings, such as complete blood counts, blood urea nitrogen, and creatinine; GCS score, which was used to objectively determine the extent of consciousness impairment and ranged from 3 (coma) to 15 (normal) [27, 28]; NIHSS score, which is a tool for objectively quantifying stroke severity and ranges from 0 (normal) to 42 (coma with quadriplegia) [29, 30]; Trial of Org 10,172 in Acute Stroke Treatment (TOAST) classification [31]; mRS score, which represents the degree of disability because of stroke and ranges from 0 (no symptoms) to 6 (death) [32]; and BI, which was used to measure performance in activities of daily living (ADL), with scores ranging from 0 (totally dependent) to 100 (normal ADL) [33]. Data related to UTI, including urinary tract symptoms, urine analysis (pH, white blood cell count, red blood cell count), urine culture, and Foley catheter status, were also gathered. The impact of UTI on stroke complications, length of stay (LOS), discharge status, 3-month mRS score, and 3-month BI were compiled. To prevent bias, 3-month mRS and BI assessments were blinded to hospital inpatient data, including the history of UTIs. For stroke complications, brain edema was diagnosed when the patient had a new neurological deficit from brain swelling that was seen in a brain image [34]; progressive stroke was defined as gradual worsening of neurological function (NIHSS score increase from admission of ≥ 4) from ongoing ischemic processes [35–37]; and symptomatic intracranial hemorrhage was defined as any hemorrhage with neurologic deterioration, as indicated by an NIHSS score of > 4 points or greater than the baseline value [38].

Statistical analysis

Descriptive statistics were used to summarize the demographic features, such as patient age and sex. Quantitative data are presented as the mean \pm standard deviation or median (interquartile range [IQR]), and qualitative data are presented as frequency (percentage). The chi-square test or Fisher's exact test was performed on categorical variables, such as patient sex, across the control and UTI groups. LOS, complications, and treatment outcomes were compared between the two groups using Fisher's exact test and the Mann–Whitney U test. Multinomial logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) of the control and UTI groups via a manual backward step.

Factors with p values of <0.1 in the univariate analysis were considered for inclusion in the multivariate analysis. Multiple logistic regression based on the backward elimination method with removal of variables with p values of >0.2 was used for the adjusted model. All statistical analyses were performed using the PASW Statistics 18.0 package (Predictive Analytics Software, SPSS Inc., Chicago, IL, US).

Ethics approval

This study was approved by the human research ethics committee of the Faculty of Medicine, Thammasat University (Ref: MTU-EC-OO-0-124/63). All methods were performed in accordance with relevant guidelines and regulations, such as the Declaration of Helsinki, the Belmont Report, Council for International Organizations of Medical Sciences guidelines, and ICH-Good Clinical Practice guidelines.

Results

Demographic features of patients with AIS

A total of 342 hospitalized patients with AIS were recruited (Fig. 1). The median age (IQR) of the patients was 66 years, and 61% of the patients were male. The most common atherosclerotic risk factor was hypertension (72%), followed by dyslipidemia (54%), smoking (41%), obesity according to a body mass index of ≥ 25 kg/m² (36%), and diabetes mellitus (30%). The patients were categorized according to the TOAST classification into five subtypes: (1) large-artery atherosclerosis (30%); (2) cardioembolism (19%); (3) small-vessel occlusion (46%); (4) stroke of other determined etiology (3%); and (5) stroke of undetermined etiology (1%).

The lesion was in the anterior circulation in 248 patients (73%), in the posterior circulation in 77 patients (23%), and unknown (diagnosis of AIS without a definite lesion on imaging) in 17 patients (5%).

Factors associated with UTI

Patients were classified into two groups. If they were diagnosed with UTI during hospitalization, they were assigned to the UTI group (31 patients, 9%). Otherwise, they were assigned to the control group (311 patients, 91%). The univariate analysis of factors associated with UTI is shown in Table 1. The final multivariate analysis showed that an initial NIHSS score of ≥ 15 (OR 5.00, 95% CI 1.33–18.72) and Foley catheter retention (OR 14.10, 95% CI 3.25–61.28) were risk factors for infection, whereas smoking (OR 0.08, 95% CI 0.01–0.50), an initial systolic blood pressure (SBP) of >120 mmHg (OR 0.06, 95% CI 0.01–0.31), and statin use (OR 0.02, 95% CI 0.0006–0.42) were protective factors (Table 2).

Characteristics of UTIs

Of the 31 patients with UTIs, 20 cases (64.5%) were community-acquired and 11 cases (35.3%) were hospital-acquired. Ten patients (32.3%) had CAUTIs. The three most common UTI symptoms included fever (96.8%), turbid urine (45.2%), and urinary retention (41.9%). In 1991, the Sepsis-1 diagnostic criteria were established, and included infection or suspected infection, leading to onset of systemic inflammatory response syndrome (SIRS). SIRS criteria to identify sepsis have also been established, and include primarily tachycardia (heart rate of >90 beats/min); tachypnea (respiratory rate of >20 breaths/min); fever or hypothermia (temperature

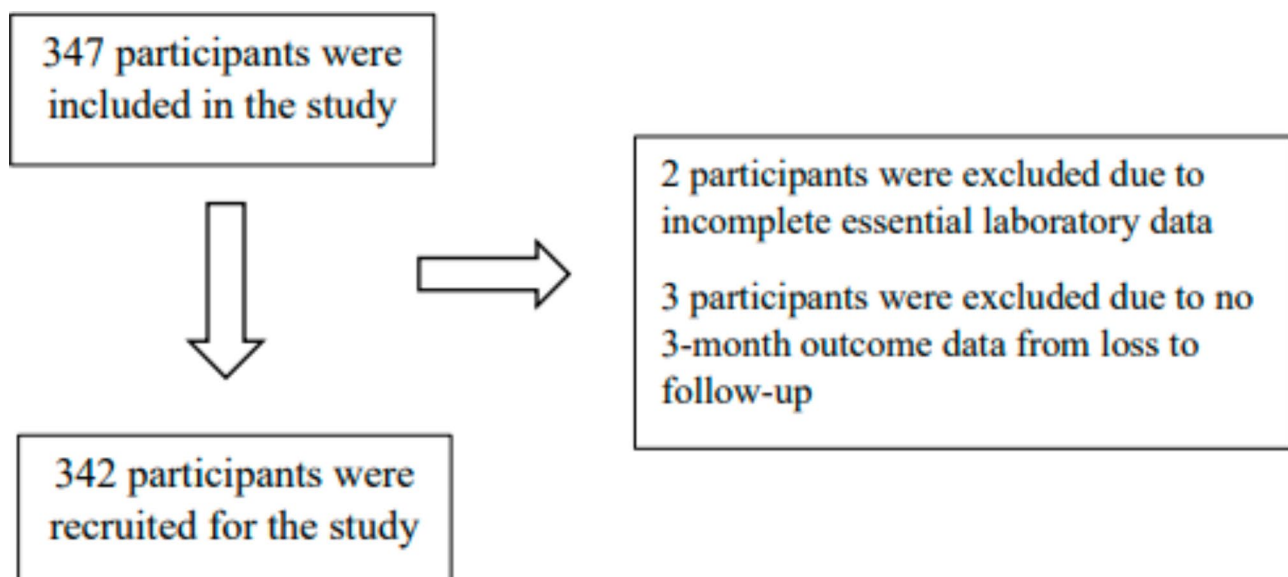


Fig. 1 Flow diagram showing study recruitment

Table 1 Univariate analysis of factors influencing UTI

Variables	Total (n = 342)	Controls (n = 311)	UTI (n = 31)	p value
Sex				
Male, n (%)	207 (60.5)	191 (61.4)	16 (51.6)	0.287
Age (years), median (IQR)	66 (54, 77)	65 (54, 76)	77 (63, 84)	0.002
Age ≥ 70, n (%)	141 (41.2)	121 (38.9)	20 (64.5)	0.006
Risk factors for stroke				
Alcoholism, n (%)	87 (25.4)	83 (26.7)	4 (12.9)	0.093
Smoking, n (%)	140 (40.9)	134 (43.1)	6 (19.4)	0.010
Hypertension, n (%)	246 (71.9)	225 (72.3)	21 (67.7)	0.59
Diabetes mellitus, n (%)	101 (29.5)	94 (30.2)	7 (22.6)	0.37
Chronic kidney disease, n (%)	79 (23.1)	68 (21.9)	11 (35.5)	0.086
Dyslipidemia, n (%)	185 (54.1)	167 (53.7)	18 (58.1)	0.64
Coronary artery disease, n (%)	42 (12.3)	34 (10.9)	8 (25.8)	0.038
Atrial fibrillation, n (%)	62 (18.1)	47 (15.1)	15 (48.4)	<0.001
Previous stroke, n (%)	52 (15.2)	47 (15.1)	5 (16.1)	0.80
Neurological manifestations				
Alteration of consciousness, n (%)	59 (17.3)	42 (13.5)	17 (54.8)	<0.001
Weakness, n (%)	303 (88.6)	272 (87.5)	31 (100)	0.035
Vertigo, n (%)	58 (17.0)	57 (18.3)	1 (3.2)	0.033
Aphasia, n (%)	54 (15.8)	44 (14.1)	10 (32.3)	0.017
Initial vital signs on admission				
SBP, mean ± SD (mmHg)	160 ± 31	162 ± 31	146 ± 31	0.006
SBP > 120 mmHg, n (%)	306 (89.5)	284 (91)	22 (71)	0.002
DBP, mean ± SD (mmHg)	92 ± 20	93 ± 20	83 ± 19	0.013
h, mean ± SD (beats/minute)	80 ± 19	80 ± 18	87 ± 26	0.043
Temperature, mean ± SD (°C)	36.8 ± 0.4	36.8 ± 0.4	37.0 ± 0.5	0.007
RR, mean ± SD (breaths/minute)	21 ± 3	21 ± 3	22 ± 5	0.034
Laboratory indicators				
Glucose, mean ± SD (mg/dL)	145 ± 76	144 ± 71	157 ± 117	0.69
BUN, mean ± SD (mg/dL)	16 ± 10	16 ± 9	21 ± 13	0.005
Creatinine, mean ± SD (mg/dL)	1 ± 0.6	1 ± 0.7	1 ± 0.4	0.45
Hemoglobin, mean ± SD (g/dL)	13 ± 2	13 ± 2	12 ± 2	0.092
White blood cell count, mean ± SD (cells/mm ³)	9,138 ± 3,384	9,047 ± 3,255	10,058 ± 4,443	0.11
Neutrophil count, mean ± SD (%)	64 ± 14	63 ± 14	70 ± 13	0.006
Lymphocyte count, mean ± SD (%)	25 ± 12	26 ± 12	20 ± 10	0.005
Initial score on admission				
mRS score, median (IQR)	4 (4, 5)	4 (3, 5)	5 (5, 5)	<0.001
BI, median (IQR)	50 (25, 70)	55 (35, 70)	10 (0, 35)	<0.001
GCS score, median (IQR)	15 (13, 15)	15 (14, 15)	10 (7, 13)	<0.001
NIHSS score, median (IQR)	6 (3, 14)	5 (3, 12)	22 (15, 28)	<0.001
NIHSS score ≥ 15, n (%)	83 (24.3)	58 (18.6)	25 (80.6)	<0.001
Treatment				
Thrombolysis (rt-PA), n (%)	47 (13.7)	40 (12.9)	7 (22.6)	0.17
Antiplatelets, n (%)	281 (82.2)	264 (84.9)	17 (54.8)	<0.001
Anticoagulants, n (%)	52 (15.2)	40 (12.9)	12 (38.7)	<0.001
Statins, n (%)	336 (98.2)	308 (99.0)	28 (90.3)	0.011
Devices				
Retained Foley catheter, n (%)	88 (25.7)	62 (19.9)	26 (80.6)	<0.001
NG tube placement, n (%)	82 (24.0)	56 (18.0)	26 (80.6)	<0.001
Failed WST, n (%)	85 (24.9)	59 (19.0)	26 (83.9)	<0.001

BI, Barthel Index; BPH, benign prostatic hyperplasia; BUN, blood urea nitrogen; cells/mm³, cells per milliliter; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; g/dL, grams per deciliter; GFR, glomerular filtration rate; HR, heart rate; ml/min, milliliters per minute; IQR, interquartile range; mg/dL, milligrams per deciliter; mmHg, millimeters of mercury; mRS, modified Rankin Scale; n, number; NG, nasogastric; NIHSS, National Institutes of Health Stroke Scale; p value, comparisons between the control group and the urinary tract infection group; RR, respiratory rate; rt-PA, recombinant tissue plasminogen activator; SBP, systolic blood pressure; SD, standard deviation; UTI, urinary tract infection; WST, water-swallowing test

Table 2 Multivariate logistic regression analysis of factors influencing UTI

Variables	OR (95% CI)	p value
Age \geq 70 years	3.51 (0.77–16.06)	0.106
Smoking	0.08 (0.01–0.50)	0.007
Underlying diseases		
Chronic kidney disease	0.35 (0.08–1.47)	0.150
Initial vital sign		
Systolic blood pressure $>$ 120 mmHg	0.06 (0.01–0.31)	0.001
Initial scoring system		
Initial GCS score \leq 8	4.18 (0.79–22.18)	0.093
Initial NIHSS score \geq 15	5.00 (1.33–18.72)	0.017
Treatment		
Antiplatelets	4.82 (0.45–51.44)	0.193
Anticoagulants	7.86 (0.69–89.86)	0.097
Statins	0.02 (0.0006–0.42)	0.013
Device		
Retained Foley catheter	14.10 (3.25–61.28)	$<$ 0.001

OR, odds ratio; CI, confidence interval; GCS, Glasgow Coma Scale; mmHg, millimeters of mercury; NIHSS, National Institutes of Health Stroke Scale; p value, comparisons between the control group and the urinary tract infection group

of >38 °C or <36 °C); and leukocytosis, leukopenia, or bandemia (white blood cell count of $>1,200/\text{mm}^3$ or $<4,000/\text{mm}^3$; bandemia of $\geq 10\%$). If patients met two or more of these criteria, they fulfilled the definition of SIRS [39]. In the present study, the median (IQR) of the SIRS criteria in patients with UTI was 3. Subsequently, a 2016 proposal defined the Sepsis-3 criteria as life-threatening organ dysfunction caused by a dysregulated host response to infection [40–42]. The quick Sepsis-Related Organ Failure Assessment (qSOFA) was designed to rapidly diagnose suspected sepsis, and it consists of three components, each worth 1 point, including a respiratory rate of ≥ 22 breaths/min; change in mental status; and SBP of ≤ 100 mmHg. A qSOFA score of 2 indicates organ dysfunction [43]. The median (IQR) qSOFA score in the present study was 1. Secondary bacteremia was observed in only two patients (6.5%). The three most common pathogens were *Escherichia coli* (*E. coli*) (41.9%), *Klebsiella pneumoniae* (16.1%), and *Enterococcus faecalis* (12.9%). The antibiotic susceptibility pattern of UTI-causative organisms was assessed. The susceptibility pattern of *E. coli* showed good sensitivity ($>80\%$ susceptibility) to amoxicillin/clavulanic acid, third-generation cephalosporins, piperacillin/tazobactam, and carbapenems. Over 30% of *E. coli* were resistant to gentamicin, trimethoprim/sulfamethoxazole, and quinolones. The antibiotic susceptibility of *E. coli* and the data described above are shown in Table 3. Most patients underwent antibiotic monotherapy, while only seven (23.3%) underwent combination therapy.

Complications following stroke and treatment outcomes

As shown in Table 4, the proportion of various post-stroke complications was significantly higher in the UTI group than in the control group, such as pneumonia,

respiratory failure, sepsis, brain edema, seizure, symptomatic hemorrhagic transformation, congestive heart failure, atrial fibrillation with a rapid ventricular response, acute kidney injury, and hyponatremia. The median LOS of patients in the UTI group was higher than in the control group (12 days vs. 3 days, respectively; $p < 0.001$). In terms of treatment outcomes, the proportion of patients without an improvement in discharge status and who died was higher in the UTI group (29% and 29%, respectively) than in the control group (5% and 3%, respectively). Regarding 3-month stroke outcomes, the mRS and BI scores, for which extensive evidence exists supporting their use as assessments of stroke outcomes, were poorer in the UTI group [32, 33]. Significantly higher median 3-month mRS scores (5 vs. 2, $p < 0.001$) and lower median 3-month BI scores (0 vs. 100, $p < 0.001$) were observed in the UTI group. With a significant p value of < 0.001 , 87.1% of patients in the UTI group had a 3-month mRS score of ≥ 3 , which indicates an unfavorable outcome in the assessment of disability [44–46], compared with 43.7% in the control group. The UTI group had a higher percentage of patients with a 3-month BI score of ≤ 40 than the control group (83.9% vs. 22.2%, respectively; $p < 0.001$). A BI score of ≤ 40 implies that performance in ADL is completely dependent on others [33].

Discussion

In this retrospective cohort trial of the determinants of UTI in hospitalized patients with AIS, we discovered that an initial NIHSS score of ≥ 15 on admission and Foley catheter retention during hospitalization were aggravating factors for infection. However, previous smoking, an initial SBP of >120 mmHg on admission, and statin use were preventive factors.

Table 3 Characteristics of UTIs

Characteristics of UTIs	Total (n = 31)
Type of infection	
• Community-acquired, n (%)	20 (64.5)
• Hospital-acquired, n (%)	11 (35.5)
Catheter-associated urinary tract infection, n (%)	10 (32.3)
Duration of retained Foley catheter since admission (days), median (IQR)	12 (5, 28.75)
Time to acquire urinary tract infection (days), median (IQR)	2 (1, 7)
Symptoms	
• Fever, n (%)	30 (96.8)
• Turbid urine, n (%)	14 (45.2)
• Urinary retention, n (%)	13 (41.9)
• Dysuria, n (%)	6 (19.4)
• Urinary incontinence, n (%)	2 (6.5)
• Gross hematuria, n (%)	1 (3.2)
SIRS criteria (points), median (IQR)	3 (2, 4)
qSOFA (points), median (IQR)	1 (1, 2)
Secondary bacteremia, n (%)	2 (6.5)
Pathogens	
• <i>Escherichia coli</i> , n (%)	13 (41.9)
• <i>Klebsiella pneumoniae</i> , n (%)	5 (16.1)
• <i>Enterococcus faecalis</i> , n (%)	4 (12.9)
• <i>Acinetobacter baumannii</i> , n (%)	3 (9.7)
Antibiotics susceptible to <i>Escherichia coli</i> (N = 13)	
• Amoxicillin/clavulanic acid, n (%)	11 (84.6)
• Ceftriaxone, n (%)	11 (84.6)
• Ceftazidime, n (%)	11 (84.6)
• Cefepime, n (%)	11 (84.6)
• Gentamicin, n (%)	8 (61.5)
• Amikacin, n (%)	13 (100)
• Ciprofloxacin, n (%)	5 (38.5)
• Trimethoprim/sulfamethoxazole, n (%)	9 (69.6)
• Piperacillin/tazobactam, n (%)	12 (92.3)
• Ertapenem, n (%)	13 (100)
• Meropenem, n (%)	13 (100)
Treatment (N = 30)	
Monotherapy, n (%)	23 (76.7)
• Ceftriaxone, n (%)	11 (36.7)
• Ceftazidime, n (%)	5 (16.7)
• Piperacillin/tazobactam, n (%)	7 (23.3)
Combination therapy, n (%)	7 (23.3)

IQR, interquartile range; n, number; N, number of patients who underwent antimicrobial susceptibility test; qSOFA, quick Sepsis-Related Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; UTI, urinary tract infection

The incidence of UTI in our study was 9% (31 patients), which is congruent with previous studies reporting incidence rates of 3.7–19% [13–15, 17, 47, 48]. According to the multivariate analysis in the present study, an NIHSS score of ≥ 15 on first admission is associated with an increased risk of UTI. Consistent with data reported by Li et al. in 2020, a higher NIHSS score was associated with UTI. Additionally, in 2022, Mukapa et al. found that an NIHSS score of 16–42 is a risk for UTI (OR 5.15, 95% CI 1.68–15.75; $p < 0.001$) [15, 16]. Therefore, stroke

severity, as evaluated using the NIHSS on admission, appears to be associated with the incidence of UTI.

Foley catheter retention is a well-established risk factor for healthcare-associated UTI. Moreover, AIS is associated with a high incidence of bladder dysfunction. These conditions have been observed in patients with large infarcts and in those with infarcts located in the cortex, which increase the likelihood of catheterization, thereby further increasing the risk of UTI [49, 50]. CAUTIs are a leading cause of secondary nosocomial bloodstream

Table 4 Complications, length of stay, discharge status, and 3-month outcomes of patients with and without UTIs

Variables	Total (n = 342)	Controls (n = 311)	UTI (n = 31)	p value
Complications				
Pneumonia, n (%)	62 (18)	40 (13)	22 (71)	< 0.001
Respiratory failure, n (%)	42 (12)	23 (7)	19 (61)	< 0.001
Sepsis, n (%)	64 (19)	36 (12)	28 (90)	< 0.001
Brain edema, n (%)	12 (4)	5 (2)	7 (23)	< 0.001
Seizure, n (%)	14 (4)	10 (3)	4 (13)	0.029
Progressive stroke, n (%)	10 (3)	10 (3)	0 (0)	0.61
Symptomatic hemorrhagic transformation, n (%)	7 (2)	2 (1)	5 (16)	< 0.001
Asymptomatic hemorrhagic transformation, n (%)	8 (2)	6 (2)	2 (6)	0.16
Gastrointestinal bleeding, n (%)	11 (3)	9 (3)	2 (6)	0.26
Myocardial infarction, n (%)	3 (1)	2 (1)	1 (3)	0.25
Congestive heart failure, n (%)	21 (6)	16 (5)	5 (16)	0.031
Atrial fibrillation with rapid ventricular response, n (%)	11 (3)	6 (2)	5 (16)	0.001
Hypoglycemia, n (%)	5 (1)	4 (1)	1 (3)	0.38
Hyperglycemia, n (%)	3 (1)	2 (1)	1 (3)	0.25
Acute kidney injury, n (%)	21 (6)	13 (4)	8 (26)	< 0.001
Hyponatremia, n (%)	9 (3)	5 (2)	4 (13)	0.005
Length of stay, median (IQR)	3 (2, 5)	3 (2, 4)	12 (6, 29)	< 0.001
Discharge status				
Complete recovery, n (%)	10 (3)	10 (3)	0 (0)	< 0.001
Improvement, n (%)	288 (84)	275 (88)	13 (42)	
No improvement, n (%)	25 (7)	16 (5)	9 (29)	
Death, n (%)	19 (6)	10 (3)	9 (29)	
3-month outcome				
mRS score, median (IQR)	2 (1, 4)	2 (1, 4)	5 (5, 6)	< 0.001
mRS score \geq 3, n (%)	163 (47.7)	136 (43.7)	27 (87.1)	< 0.001
BI score, median (IQR)	95 (35, 100)	100 (55, 100)	0 (0, 10)	< 0.001
BI score \leq 40, n (%)	95 (27.8)	69 (22.2)	26 (83.9)	< 0.001

BI, Barthel index; IQR, interquartile range; mRS, modified Rankin Scale; n, number; p value, comparisons between the control group and the urinary tract infection group; UTI, urinary tract infection

infection [51]. According to a 2009 report by Stott et al., post-stroke UTI is associated with urinary catheterization (OR 3.03, 95% CI 1.41–6.52) [12], which is comparable to the observation of the present study.

We identified smoking as a protective factor. Cigarette smoking is a well-known major risk factor for premature mortality because of cancer, cardiovascular disease, and chronic obstructive pulmonary disease. Smoking appears to be a risk factor for respiratory tract infections, although the risk of UTIs with smoking is unknown [52, 53]. According to a 2001 study by Alnaif et al. (in women) and a 2018 study by Yongzhi et al. (in patients with urolithiasis), smoking is not associated with UTIs [54, 55]. However, smoking may contribute to the development of lower urinary tract symptoms in women [56]. Despite these results, it should be noted that no related studies have previously been conducted in the post-stroke population. The effects of smoking on urinary tract microorganisms have been studied, and it was found that microorganism species differed between smokers and non-smokers [57]. The urobiota plays a role in bladder

homeostasis by maintaining the integrity of the urinary tract epithelium, protecting against infection, regulating neurotransmission, and promoting proper immune system functioning, which affects the occurrence of UTIs [58, 59]. Accordingly, smoking may influence UTIs through this mechanism.

Another protective factor was an initial SBP of >120 mmHg on admission, which can be explained by the fact that known UTIs can cause urosepsis, and approximately one third of these patients present with hypotension [60]. Moreover, when stroke occurs, blood pressure often increases because of various factors, including psychological stress, pain, urinary retention, and hypoxemia [61]. In addition, stroke can lead to permanent damage to the areas of the brain involved in the regulation of cardiovascular functioning, including blood pressure. An acute hypertensive response is observed in >60% of patients with AIS according to previous studies [62–64]. Therefore, the relative hypotension on admission from occult urosepsis, which is particularly common with community-acquired UTIs (64.5%) that present within 48 h, can

be just within the normal range of SBP (the mean initial SBP of the control and UTI groups was 162 mmHg and 146 mmHg, respectively). In contrast, high blood pressure may be a protective factor under these conditions. A review of previous literature revealed that initial blood pressure has not previously been examined in the context of the associations between UTIs and acute stroke [12–17, 48, 50, 65–67]. Therefore, this is the first report of this finding.

The present study supports the observation that statin use is a preventive factor for UTIs. Preclinical studies have indicated that statins can indeed reduce bacterial invasion [68–71]. In 2013, Pouwels et al. found that pravastatin can reduce the occurrence of recurrent UTIs [72]. The postulated mechanism is that bacterial invasion of the bladder epithelium requires the membrane-bound protein Rac1, the expression of which can be reduced by statins [71, 73, 74].

In our study, 64.5% of UTIs were community-acquired, 35.3% were hospital-acquired, and 32.3% were CAUTIs, which approximates the findings of Bogason et al. from 2017 [14]. The causative organisms most commonly involved in UTIs are those found in the colonic bacterial flora, primarily *E. coli*, which may be because of their capacity to attach to the uroepithelium. However, other Enterobacterales are also common [16, 75]. The high prevalence of *E. coli* was comparable to that reported in previous studies [16, 65, 67].

In 2019, the National Antimicrobial Resistant Surveillance in Thailand reported that *E. coli* urinary isolates from outpatients were susceptible to ciprofloxacin (30.1%), cotrimoxazole (42.2%), ceftriaxone (59.7%), and amikacin (98.8%) [76]. The susceptibility patterns to ciprofloxacin, cotrimoxazole, and amikacin were similar to those in our study, whereas the susceptibility to ceftriaxone (59.7%) was lower than in our study (84.6%). When we compared the antibiotic susceptibility patterns of *E. coli* in the present study with the antibiotic susceptibility patterns of community-acquired infections from another tertiary care hospital in the same region of Thailand within the same period [77], both antibiotic susceptibility patterns were similar, and low-level resistance to third-generation cephalosporins, amikacin, and carbapenems was observed. Therefore, according to the present study, third-generation cephalosporins remain an effective treatment option for post-stroke UTIs in Thailand. However, in other countries, the susceptibility of *E. coli* to third-generation cephalosporins in the context of UTI varies between 53.5% and 94.9%. As a result, antibiotic treatment should be based on the local antibiogram [78–83].

Various post-stroke complications were more prevalent in the UTI group than in the control group in the present study. These included infection; respiratory failure;

bleeding; and neurological, cardiovascular, metabolic, and renal complications. According to our review of the literature, no studies have addressed stroke complications in such patients [12–17, 48, 50, 65–67, 84, 85]. Sepsis can be caused by UTIs [86], and the severity of the UTIs appears to be increasing and is typically associated with hyponatremia [87, 88], acute respiratory distress syndrome [86] leading to respiratory failure [89], disseminated intravascular coagulopathy [86] leading to bleeding complications [90], sepsis-induced cardiomyopathy leading to heart failure [91], atrial fibrillation [92] leading to atrial fibrillation with a rapid ventricular response [93, 94], seizure [95], and acute kidney injury [86]. UTIs increase the odds of a decline in neurological status during hospitalization [11], and severe neurologic deficit increases the risk of stroke-associated pneumonia [96]. Although rare, UTIs can spread to the lungs, causing pneumonia [97]. One limitation of our study is that we did not document the temporal relationship between brain edema and UTIs. Brain edema is a severe stroke complication that is associated with prolonged hospitalization and poor outcomes [98, 99]. AIS with cerebral edema usually requires urinary catheterization for intensive urine output monitoring [100] and prolonged immobility, which can increase the risk of UTI [101]. This may be the reason why the UTI group had a greater number of patients with cerebral edema than the control group. Several studies have shown a longer LOS in the UTI population than in the control population [13, 14, 16, 50, 65]. Patients with UTI also have a poorer discharge status [16, 50] and 3-month outcomes [7, 12, 66], which is consistent with our study.

Although stroke severity itself may increase the risk of UTI [15, 16] and could explain some of the associations between UTIs and poorer outcomes, a causal effect of UTI on stroke recovery is also possible and may be multifactorial. It is well documented that fever in patients with brain injury of any etiology, including stroke, correlates with poorer outcomes in many measures, including mortality, mRS score, BI, and hospital LOS [102]. Additionally, increasing evidence from animal studies suggests that systemic inflammatory insults that simulate infection promote antigen presentation and autoimmunity against the brain, which are key elements in the pathobiology of stroke, and may also play a central role related to the clinical impact of post-stroke infection [103, 104]. This may lead to prolonged damaging cytokine production and microgliosis, which can have a profound effect on the onset and/or progression of neurodegenerative diseases [105–108], and these responses are associated with poorer stroke outcomes. However, evidence pertaining to this issue is scarce, and the exact pathophysiology remains to be investigated.

This study has some limitations that should be noted when interpreting the results. Only patients from hospitals providing tertiary care participated in the study. Therefore, theoretically, our findings may not be applicable to other populations receiving care at different facilities. Moreover, the number of patients included in this study was relatively small, resulting in unavoidable selection bias.

Conclusions

UTIs are a major infectious complication in hospitalized patients with AIS. Stroke severity and Foley catheter retention were re-established as risk factors for post-stroke UTI, while an initial SBP of >120 mmHg and statin use were newly recognized as protective factors that have not previously been described in this population. Smoking was associated with an increased risk of infection in many organs, particularly the respiratory tract. However, we found smoking to be another protective factor against UTI, which has not previously been reported in such patients. Accordingly, this phenomenon requires further study. Two thirds of all UTIs were community-acquired, and *E. coli* was the predominant pathogen. For the first time, we showed that many post-stroke complications (e.g., pneumonia, seizure, congestive heart failure, and acute kidney injury) in patients with AIS with UTI are significantly more frequent than in patients without UTI. Finally, the longer LOS and poorer outcomes of patients with UTI were reconfirmed in this study.

Abbreviations

ADL	activities of daily living
AIS	Acute Ischemic Stroke
BI	Barthel Index
BPH	Benign Prostatic Hyperplasia
BUN	Blood Urea Nitrogen
cells/mm ³	cells per milliliter
CI	Confidence Interval
CIOMS	Council for International Organizations of Medical Sciences
DBP	Diastolic Blood Pressure
<i>E. coli</i>	<i>Escherichia coli</i>
GCS	Glasgow Coma Scale
g/dL	grams per deciliter
GFR	Glomerular Filtration Rate
HR	Heart Rate
ICH-GCP	International Conference on Harmonization-Good Clinical Practice
IQR	interquartile range
LOS	length of stay
ml/min	milliliters per minute
mg/dL	milligrams per deciliter
mmHg	millimeters of mercury
mRS	modified Rankin Scale
n	number
NG tube	Nasogastric tube
NIHSS	National Institutes of Health Stroke Scale
OR	Odds Ratio
qSOFA	quick Sepsis-related Organ Failure Assessment
RR	respiratory rate
rt-PA	recombinant tissue Plasminogen Activator
SBP	Systolic blood pressure
SD	standard deviation

SIRS	systemic inflammatory response syndrome
SPSS	Statistical Package for the Social Sciences
TOAST	Trial of ORG 10172 in Acute Stroke Treatment
UTI	Urinary Tract Infection
USA	United States of America
WST	Water-Swallowing Test

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Authors' contributions

P.J. has been involved in research. By requesting permission for human research from ethics committee, including data collection, interpreted the patient data regarding the neurological disease, analyzed basic statistical data and was a major contributor in writing the manuscript. A.B. edited research proposal project, calculated the number of populations to be studied, interpreted the patient data regarding the infectious disease, analyzed data with advanced statistics, edited the manuscript and sent for submission. Both authors read and approved the final manuscript.

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Data Availability

Individual level data cannot be shared publicly because of patient confidentiality under current Thai legislation. The data that support the findings of this study are available from Chumphon Khet Udomsakdi Hospital, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from Dr. Pornpong Jitpratoom (Email: pornpong31@gmail.com) upon reasonable request and with permission of Chumphon Khet Udomsakdi Hospital and the appropriate ethics committee.

Declarations

Ethics approval and consent to participate

The study was approved by the human research ethics committee of the Faculty of Medicine, Thammasat University (Ref: MTU-EC-OO-0-124/63). Informed consent was waived due to no adverse effect on the rights and welfare of the subjects approved by the human research ethics committee of the Faculty of Medicine, Thammasat University (Ref: MTU-EC-OO-0-124/63). All methods were performed in accordance with relevant guidelines and regulations, such as the Declaration of Helsinki, the Belmont Report, Council for International Organizations of Medical Sciences guidelines, and ICH-Good Clinical Practice guidelines.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Warlow CJTL. Epidemiology of stroke. 1998;352:S1-S4.
- Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJJT. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. 2006;367(9524):1747-57.
- Shi K, Wood K, Shi F-D, Wang X, Liu QJS. neurology v. Stroke-induced immunosuppression and poststroke infection. 2018;3(1).
- Stanley D, Mason LJ, Mackin KE, Srikhanta YN, Lyras D, Prakash MD et al. Translocation and dissemination of commensal bacteria in post-stroke infection. 2016;22(11):1277-84.
- Chamorro A, Urra X, Planas AMJS. Infection after acute ischemic stroke: a manifestation of brain-induced immunodepression. 2007;38(3):1097-103.

6. Davenport R, Dennis M, Wellwood I, Warlow CPJS. Complications after acute stroke. 1996;27(3):415–20.
7. Aslanyan S, Weir C, Diener HC, Kaste M, Lees KR, Committee GIS et al. Pneumonia and urinary tract infection after acute ischaemic stroke: a tertiary analysis of the GAIN International trial. 2004;11(1):49–53.
8. Ersoz M, Ulusoy H, Oktar MA. Akyuz MJAJopm, rehabilitation. Urinary tract infection and bacteriuria in stroke patients: frequencies, pathogen microorganisms, and risk factors. 2007;86(9):734–41.
9. McLean, DEJAopm. Rehabilitation. Medical complications experienced by a cohort of stroke survivors during inpatient, tertiary-level stroke rehabilitation. 2004;85(3):466–9.
10. Hamidon B, Raymond A, Norlinah M, Jefferelli SJSmj. The predictors of early infection after an acute ischaemic stroke. 2003;44(7):344–6.
11. Rocco A, Pasquini M, Cecconi E, Sirimarco G, Ricciardi MC, Vicenzini E et al. Monitoring after the acute stage of stroke: a prospective study. 2007;38(4):1225–8.
12. Stott D, Falconer A, Miller H, Tilston J, Langhorne PJQAIJoM. Urinary tract infection after stroke. 2009;102(4):243–9.
13. Ovbiagele B, Hills NK, Saver JL, Johnston SC, Stroke CASPRIJJo, Diseases C. Frequency and determinants of pneumonia and urinary tract infection during stroke hospitalization. 2006;15(5):209–13.
14. Bogason E, Morrison K, Zalatio O, Ermak DM, Lehman E, Markley E et al. Urinary tract infections in hospitalized ischemic stroke patients: source and impact on outcome. 2017;9(2).
15. Li Y-m, Xu J-h, Zhao Y-xJM. Predictors of urinary tract infection in acute stroke patients: a cohort study. 2020;99(27).
16. Mukapa N, Mataruse A, Ngwende GW, Robertson VJlpip. Incidence, risk factors and microbiological aetiology of urinary tract infections in admitted stroke patients at a teaching hospital in Zimbabwe: A prospective cohort study. 2022;4(2):100210.
17. Johnsen P, Svendsen SL, Ingeman M. AJTOIDJ. Infection in patients with acute stroke. 2012;6(1).
18. Schmiemann G, Kniehl E, Gebhardt K, Matejczyk MM, Hummers-Pradier EJDÄI. The diagnosis of urinary tract infection: a systematic review. 2010;107(21):361.
19. Loeb M, Bentley DW, Bradley S, Crossley K, Garibaldi R, Gantz N et al. Development of minimum criteria for the initiation of antibiotics in residents of long-term-care facilities: results of a consensus conference. 2001;22(2):120–4.
20. Rowe TA, Juthani-Mehta MJIDC. Diagnosis and management of urinary tract infection in older adults. 2014;28(1):75–89.
21. Grigoryan L, Trautner BW, Gupta KJJ. Diagnosis and management of urinary tract infections in the outpatient setting: a review. 2014;312(16):1677–84.
22. Control, CfD. Prevention. Healthcare-associated infection surveillance protocol for Urinary Tract Infection (UTI) events for long-term care facilities. 2020.
23. Kabugo D, Kizito S, Ashok DD, Kiwanuka AG, Nabimba R, Namunana S, et al. Factors associated with community-acquired urinary tract infections among adults attending assessment centre. Mulago Hosp Uganda. 2016;16(4):1131–42.
24. Ahmed N, Hussain T, Biswal IJjogid. Comparison of etiological agents and resistance patterns of the pathogens causing community acquired and hospital acquired urinary tract infections. 2014;6(3):135.
25. Control CfD, CAUTI PJD-aM. Urinary tract infection (catheter-associated urinary tract infection [CAUTI] and non-catheter-associated urinary tract infection [UTI]) and other urinary system infection [USI]) events. 2015.
26. Chuang L, Tambyah PAJJoI, Chemotherapy. Catheter-associated urinary tract infection. 2021;27(10):1400–6.
27. Teasdale G, Jennett BJTL. Assessment of coma and impaired consciousness: a practical scale. 1974;304(7872):81–4.
28. Shobhit J. Iverson LJSPhwngbn. Glasgow Coma Scale. 2018.
29. Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J et al. Measurements of acute cerebral infarction: a clinical examination scale. 1989;20(7):864–70.
30. Goldstein LB, Bertels C, Davis JNJAon. Interrater reliability of the NIH stroke scale. 1989;46(6):660–2.
31. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST Trial of Org 10172 in Acute Stroke Treatment. 1993;24(1):35–41.
32. Banks JL, Marotta CAJS. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. 2007;38(3):1091–6.
33. Quinn TJ, Langhorne P, Stott DJJS. Barthel index for stroke trials: development, properties, and application. 2011;42(4):1146–51.
34. Nehring SM, Tadi P, Tenny S. Cerebral edema. 2019.
35. Anderson DCJS. Defining "progressive stroke". 1991;22(8):1085.
36. Rocha M, Jovin TGJS. Fast versus slow progressors of infarct growth in large vessel occlusion stroke: clinical and research implications. 2017;48(9):2621–7.
37. Seners P, Baron J-CJJon. Revisiting 'progressive stroke': incidence, predictors, pathophysiology, and management of unexplained early neurological deterioration following acute ischemic stroke. 2018;265(1):216–25.
38. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. 2008;359(13):1317–29.
39. Strom G, Halje M, Karlsson D, Jiwakanon J, Pringle M, Fernstrom LL, et al. Antimicrobial use and antimicrobial susceptibility in *Escherichia coli* on small- and medium-scale pig farms in north-eastern Thailand. *Antimicrob Resist Infect control*. 2017;6:75.
40. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):762–74.
41. Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the Third International Consensus Definitions for Sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):775–87.
42. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801–10.
43. Marik PE, Taeb AM. SIRS, qSOFA and new sepsis definition. *J Thorac disease*. 2017;9(4):943.
44. Sato S, Uehara T, Ohara T, Suzuki R, Toyoda K, Minematsu K, et al. Factors Assoc unfavorable outcome minor ischemic stroke. 2014;83(2):174–81.
45. Zhang C, Zhang W, Huang Y, Qiu J, Huang Z-XJRM, Policy H. A dynamic nomogram to predict the 3-Month unfavorable outcome of patients with Acute. *Ischemic Stroke*. 2022;15:923.
46. ElHabr AK, Katz JM, Wang J, Bastani M, Martinez G, Gribko M et al. Predicting 90-day modified Rankin Scale score with discharge information in acute ischaemic stroke patients following treatment. 2021;3(1).
47. Yan T, Liu C, Li Y, Xiao W, Li Y, Wang SJAJoIc. Prevalence and predictive factors of urinary tract infection among patients with stroke: a meta-analysis. 2018;46(4):402–9.
48. Westendorp WF, Nederkoorn PJ, Vermeij J-D, Dijkgraaf MG, de DvJbn B. Post-stroke infection: a systematic review and meta-analysis. 2011;11(1):1–7.
49. Kong K-H. Young SJAopm, rehabilitation. Incidence and outcome of post-stroke urinary retention: a prospective study. 2000;81(11):1464–7.
50. Poisson SN, Johnston SC, Josephson SAJS. Urinary tract infections complicating stroke: mechanisms, consequences, and possible solutions. 2010;41(4):e180–e4.
51. Maki DG, Tambyah PAJEid. Engineering out the risk for infection with urinary catheters. 2001;7(2):342.
52. Arcavi L, Benowitz NLJAoim. Cigarette Smok Infect. 2004;164(20):2206–16.
53. Jiang C, Chen Q, Xie MJTID. Smoking increases the risk of infectious diseases: A narrative review. 2020;18.
54. Alnaif B, Drutz HPJJoIgtD. The Association of Smoking with Vaginal Flora, urinary tract infection, pelvic floor prolapse, and post-void residual volumes. 2001;5(1):7–11.
55. Yongzhi L, Shi Y, Jia L, Yili L, Xingwang Z, Xue GJBU. Risk factors for urinary tract infection in patients with urolithiasis—primary report of a single center cohort. 2018;18(1):1–6.
56. Maserejian NN, Kupelian V, Miyasato G, McVary KT, McKinlay JBJJoU. Are physical activity, smoking and alcohol consumption associated with lower urinary tract symptoms in men or women? Results from a population based observational study. 2012;188(2):490–5.
57. Ma W, Zhang W, Shen L, Liu J, Yang F, Maskey N et al. Can smoking cause differences in urine microbiome in male patients with bladder cancer? A retrospective study. 2021;1:677605.
58. Ackerman AL, Chai TCJCbdr. The bladder is not sterile: an update on the urinary microbiome. 2019;14:331–41.
59. Kawalec A, Zwolińska DJJoMS. Emerging role of microbiome in the prevention of urinary tract infections in children. 2022;23(2):870.
60. Kalra OP, Raizada AJJoGID. Approach to a patient with urosepsis. 2009;1(1):57.
61. Ishitsuka K, Kamouchi M, Hata J, Fukuda K, Matsuo R, Kuroda J, et al. High blood pressure after acute ischemic stroke is associated with poor clinical outcomes. *Fukuoka Stroke Registry*. 2014;63(1):54–60.

62. Qureshi AI, Ezzeddine MA, Nasar A, Suri MFK, Kirmani JF, Hussein HM et al. Prevalence of elevated blood pressure in 563 704 adult patients with stroke presenting to the ED in the United States. 2007;25(1):32–8.
63. Qureshi AJC. Acute hypertensive response in patients with stroke: pathophysiology and management. 2008;118(2):176–87.
64. Jordan JD, Powers WJAJoh. Cerebral autoregulation and acute ischemic stroke. 2012;25(9):946–50.
65. Šabanović A, Slobodan J, Kostić MJJIDE. Risk factors for hospital-acquired urinary tract infections in patients with Acute Stroke. 2021;7:211.
66. Grabska K, Gromadzka G. Członkowska AJNri. Infections and ischemic stroke outcome. 2011;2011.
67. Vargas M, Horcajada JP, Obach V, Revilla M, Cervera A, Torres F et al. Clinical consequences of infection in patients with acute stroke: is it prime time for further antibiotic trials? 2006;37(2):461–5.
68. Burnham C-AD, Shokoples SE, Tyrrell GJJFml. Rac1, RhoA, and Cdc42 participate in HeLa cell invasion by group B streptococcus. 2007;272(1):8–14.
69. Zaas DW, Duncan M, Wright JR. Abraham SNJBeBA-MCR. The role of lipid rafts in the pathogenesis of bacterial infections. 2005;1746(3):305–13.
70. Horn MP, Knecht SM, Rushing FL, Birdsong J, Siddall CP, Johnson CM, et al. Simvastatin inhibits *Staphylococcus aureus* host cell invasion through modulation of isoprenoid intermediates. 2008;326(1):135–43.
71. Rosch JW, Boyd AR, Hinojosa E, Pestina T, Hu Y, Persons DA et al. Statins protect against fulminant pneumococcal infection and cytolytic toxicity in a mouse model of sickle cell disease. 2010;120(2):627–35.
72. Pouwels KB, Visser ST, Hak EJJoAC. Effect of pravastatin and fosinopril on recurrent urinary tract infections. 2013;68(3):708–14.
73. Cordle A, Koenigsnecht-Talboo J, Wilkinson B, Limpert A, Landreth GJJJoBC. Mechanisms of statin-mediated inhibition of small G-protein function. 2005;280(40):34202–9.
74. Rashid M, Tawara S, Fukumoto Y, Seto M, Yano K, Shimokawa HJJC. Importance of Rac1 signaling pathway inhibition in the pleiotropic effects of HMG-CoA reductase inhibitors. 2009;73(2):361–70.
75. Álvarez MD, Batista BA, Córdoba RP, Robledo EHJBDHldM. Urinary tract infection caused by Enterobacteriaceae and its relationship with vesicoureteral reflux. 2017;74(1):34–40.
76. NARST. : National Antimicrobial Resistance Surveillance Center T. Antimicrobial Resistance rates of *E.coli* by year. 2019.
77. Sangsuwan T, Jariyasoonthornkit K, Jamulitrat S. Antimicrobial resistance patterns amid community-acquired uropathogens in outpatient settings of a Tertiary Care Hospital in Thailand. *Siriraj Med J*. 2021;73(8):501–9.
78. Kibret M, Abera BJAhs. Antimicrobial susceptibility patterns of *E. coli* from clinical sources in northeast Ethiopia. 2011;11:40–5.
79. Naqid IA, Balatay AA, Hussein NR, Saeed KA, Ahmed HA, Yousif SHJJJoI. Antibiotic susceptibility pattern of *Escherichia coli* isolated from various clinical samples in Duhok city, Kurdistan Region of Iraq. 2020;7(3).
80. Cambrea SCJJJoPID. Antibiotic susceptibility of *Escherichia coli* strains isolated in a pediatric population from South East Romania. 2014;9(03):157–62.
81. Niranjana V, Malini AJTJJoMr. Antimicrobial resistance pattern in *Escherichia coli* causing urinary tract infection among inpatients. 2014;139(6):945.
82. Zúniga-Moya JC, Bejarano-Cáceres S, Valenzuela-Cervantes H, Gough-Coto S, Castro-Mejía A, Chinchilla-López C, et al. Antibiotic Sensit profile bacteria urinary tract infections. 2016;58(4):146–54.
83. Daoud N, Hamdoun M, Hannachi H, Gharsallah C, Mallekh W. Bahri OJC. Antimicrobial susceptibility patterns of *Escherichia coli* among Tunisian outpatients with community-acquired urinary tract infection (2012–2018). 2020;14(4):200–5.
84. Donkor ES, Akumwena A, Amoo PK, Owolabi MO, Aspelund T, Gudnason VJT et al. Post-stroke bacteriuria among stroke patients attending a physiotherapy clinic in Ghana: a cross-sectional study. 2016;12:457.
85. Ingeman A, Andersen G, Hundborg HH, Svendsen ML, Johnsen SPJS. In-hospital medical complications, length of stay, and mortality among stroke unit patients. 2011;42(11):3214–8.
86. Porat A, Bhutta BS, Kesler S, Urosepsis. StatPearls [Internet]: StatPearls Publishing; 2022.
87. Kompani F, Barati L, Samba MMJN-UM. Association of Electrolyte Changes and inflammatory markers with renal involvement in children with febrile UTI. 2022;14(1).
88. Park SJ, Oh YS, Choi MJ, Shin JI, Kim KHJPN. Hyponatremia may reflect severe inflammation in children with febrile urinary tract infection. 2012;27:2261–7.
89. Moore S, Weiss B, Pascual JL, Kaplan LJJSI. Management of acute respiratory failure in the patient with sepsis or septic shock. 2018;19(2):191–201.
90. Boral BM, Williams DJ. Boral LJJAjocp. Disseminated intravascular coagulation. 2016;146(6):670–80.
91. Sato R, Nasu, MJJoic. A review of sepsis-induced cardiomyopathy. 2015;3(1):1–7.
92. Induruwa I, Hennebry E, Hennebry J, Thakur M, Warburton EA, Khadjooi KJJoIM. Sepsis-driven atrial fibrillation and ischaemic stroke. Is there enough evidence to recommend anticoagulation? 2022;98:32–6.
93. Shaver CM, Chen W, Janz DR, May AK, Darbar D, Bernard GR et al. Atrial fibrillation is an independent predictor of mortality in critically ill patients. 2015;43(10):2104–11.
94. Moskowitz A, Chen KP, Cooper AZ, Chahin A, Ghassemi MM, Celi LAJS. Management of atrial fibrillation with rapid ventricular response in the intensive care unit: a secondary analysis of electronic health record data. 2017;48(4):436.
95. Alessandri F, Badenes R, Bilotta FJJJoCM. Seizures and sepsis: a narrative review. 2021;10(5):1041.
96. Assefa M, Tadesse A, Adane A, Yimer M, Tadesse MJSR. Factors associated with stroke associated pneumonia among adult stroke patients admitted to university of Gondar hospital. Northwest Ethiopia. 2022;12(1):12724.
97. Quarata F, Lelli D, Biancone DM, Gherardi G, Incalzi RAJTL. A urinary tract infection caused by *Escherichia coli* mucoid phenotype progresses to a pneumonia and respiratory failure. 2023;401(10380):950.
98. Chen S, Shao L, Ma LJFicn. Cerebral edema formation after stroke: emphasis on blood-brain barrier and the lymphatic drainage system of the brain. 2021;15:716825.
99. Thoren M, Azevedo E, Dawson J, Egido JA, Falcou A, Ford GA et al. Predictors for cerebral edema in acute ischemic stroke treated with intravenous thrombolysis. 2017;48(9):2464–71.
100. Knight J, Nigam Y, Jones AJNT. Effects of bedrest 4: renal, reproductive and immune systems. 2019;115(3):51–4.
101. Rogers MA, Fries BE, Kaufman SR, Mody L, McMahon LF. Saint SJBg. Mobility and other predictors of hospitalization for urinary tract infection: a retrospective cohort study. 2008;8(1):1–8.
102. Greer DM, Funk SE, Reaven NL, Ouzounelli M, Uman GCJS. Impact of fever on outcome in patients with stroke and neurologic injury: a comprehensive meta-analysis. 2008;39(11):3029–35.
103. Iadecola C, Anrather JJNm. The immunology of stroke: from mechanisms to translation. 2011;17(7):796–808.
104. Becker KJ, Kindrick DL, Lester MP, Shea C, Ye Z-CJJoCBF. Metabolism Sensitization to brain antigens after stroke is augmented by lipopolysaccharide. 2005;25(12):1634–44.
105. Püntener U, Booth SG, Perry VH, Teeling JJJJon. Long-term impact of systemic bacterial infection on the cerebral vasculature and microglia. 2012;9(1):1–13.
106. Sankowski R, Mader S, Valdés-Ferrer, SJFicn. Systemic inflammation and the brain: novel roles of genetic, molecular, and environmental cues as drivers of neurodegeneration. 2015;9:28.
107. Trzeciak A, Lerman YV, Kim T-H, Kim MR, Mai N, Halterman MW et al. Long-term microgliosis driven by acute systemic inflammation. 2019;203(11):2979–89.
108. Valdés-Ferrer SI, Benkendorff A, Sankowski RJCoIn. Persistent inflammatory states and their implications in brain disease. 2020;33(3):341–6.

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