EPIDEMIOLOGY OF CATHETER-ASSOCIATED URINARY TRACT INFECTIONS AT MAHARAJ NAKORN CHIANG MAI HOSPITAL, NORTHERN THAILAND

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Abstract. Catheter-associated urinary tract infections (CAUTI) are a common nosocomial infection. This study aimed to determine the incidence, etiology and outcomes of CAUTI at Maharaj Nakorn Chiang Mai Hospital, northern Thailand. This was a prospective cohort study conducted among inpatients at the medicine units from March 2015 to June 2016. Study subjects were patients aged ≥ 18 years with a urinary catheter (UC) who developed a CAUTI. A total of 120 patients meeting inclusion criteria during the study period were included in the study consisting of 127 episodes of CAUTI. Seventy-five patients (62.5%) were male; the median study subject age was 65.5 years (interquartile range: 54.5, 79 years). The incidence of CAUTI varied from 2.37 to 7.83 /1,000 catheter-days. Forty point nine percent of subjects had a UC placed to monitor hourly urine output. Twenty-three point six percent of patients had a UC placed without a medical indication. Enterobacteriaceae was the most common group of bacterial pathogen isolated (48 episodes, 37.8%), followed by enterococci (47 episodes, 37.0%). The in-hospital mortality rate among study subjects was 36.7%; the CAUTI probably accounted for 20 % of these. Multivariate analysis revealed that factors associated with death included: having a CAUTI due to multidrug-resistant bacteria (odds ratio (OR)=3.70; 95% confidence interval (CI): 1.13-12.09; p=0.030), *Candida* species (OR: 10.85; 95% CI: 2.85-41.30; $p < 0.001$), *A. baumannii* (OR=11.42; 95% CI: 2.54-51.38; $p = 0.002$), *K. pneumoniae* (OR=19.96; 95% CI: 1.96-203.50; p =0.011) and developing septic shock (OR=65.26; 95% CI: 7.45-571.89; $p < 0.001$). In summary, a CAUTI caused death in one-fifth of study subjects. One-fourth of study subjects had no medical indication for retaining a UC. It is important to develop and implement strategies to prevent CAUTI, such as early UC removal, when to place a UC, in order to prevent CAUTI and mortality.

Keywords: catheter-associated urinary tract infections, incidence, etiology, outcome, northern Thailand

INTRODUCTION

Urinary tract infections (UTI) are common nosocomial infections worldwide (Allegranzi *et al*, 2011), including in Thailand (Danchaivijitr and Chokloikaew, 1989). The majority of hospital-acquired

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UTI are catheter-associated UTI (CAUTI) (Klevens *et al*, 2007). In the US, the CAUTI rate in 2012 as reported to the National Healthcare Safety Network (NHSN) was 0.5-5.3/1,000 catheter-days on adult inpatient units and 1.2-5.0/1,000 catheter-days in the intensive care unit (ICU) (Dudeck *et al*, 2013). In Thailand, 12-16% of hospitalized patients have urinary catheters (UCs) (Thamlikitkul *et al*, 2001). The daily risk for bacteriuria among patients with UCs has been reported to be 3-7% (Weinstein *et al*, 1999). One study from a tertiary-care hospital in Thailand found 30% of patients with UCs had bacteriuria and 6% had a symptomatic UTI (Thamlikitkul *et al*, 2001). Having a CAUTI can increase mortality and length of hospital stay (Lindenauer *et al*, 2006; Fakih *et al*, 2010; Fakih *et al*, 2012). Non-infectious complications can also occur, such as mechanical trauma, nonbacterial urethral inflammation, and urethral strictures (Jain *et al*, 1995; Lo *et al*, 2008). Many catheters are placed without an appropriate medical indication (Jain *et al*, 1995; Lindenauer *et al*, 2006; Lo *et al*, 2008; Fakih *et al*, 2010; Fakih *et al*, 2012). One of the most common reasons for having persistent UC is the physician being unaware of the UC (Saint *et al*, 2009).

The primary objective of this study was to determine the incidence of CAUTI among patients admitted to the medicine unit of the study hospital. The secondary objectives were to:1) identify the indications for the UC; 2) identify the bacterial pathogen causing the CAUTI, and 3) determine the treatment outcomes of CAUTI in terms of length of hospital stay and mortality.

MATERIALS AND METHODS

Study setting and study population

This prospective study was conducted from March 2015 to June 2016 among patients admitted to the Internal Medicine Department, Maharaj Nakorn Chiang Mai Hospital; a 1,400-bed, tertiary-care hospital in northern Thailand. Patients were included in the study if they were aged ≥ 18 years, had a UC during hospitalization and developed a CAUTI. Patients were excluded if they: had been diagnosed with or treated for a urinary tract stone, had benign prostatic hypertrophy or urinary tract malignancy or had a UC present prior to admission.

Definitions

A CAUTI was defined as a UTI occurring in a person with a UC in place or in whom a catheter was removed within the previous 48 hours (Hooton *et al*, 2010). A UTI was defined as the presence of symptoms and signs compatible with UTI and a urine culture growing $\geq 10^3$ CFU/ml with ≥ 1 bacterial species (Hooton *et al*, 2010).

Multidrug-resistant (MDR) pathogen was defined as a bacterium resistant to ≥ 1 antimicrobial in ≥ 3 antimicrobial classes or resistant to one key antimicrobial agent, such as methicillin resistant *S. aureus* or vancomycin resistance in enterococci (Magiorakos *et al*, 2012).

Indications for retaining a UC followed those of the 2014 Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) practice recommendation for strategies to prevent CAUTI in acute care hospitals: 1) undergoing a selected surgery, 2) monitoring urine output, 3) management of urinary retention or obstruction, 4) assistance in pressure ulcer healing, and 5) improving patient comfort or end of life care (Lo *et al*, 2008).

Data collection

Data were prospectively collected using pre-printed data collection forms.

Data collected were: patient age, sex, presence of underlying disease, the reason (s) for retaining a UC, the results of a complete blood count (CBC), urinalysis, urine culture, blood culture, antibiotic prescriptions, treatment outcome, presence of any complications (septic shock, acute kidney injury, and death).

Statistical analysis

Data are reported as numbers, percentages, means ± standard deviations (SD), medians and interquartile ranges (IQR) where appropriate. Parameters were compared using the Student's *t*-test or Mann-Whitney *U* test for continuous data and the chi-square test or Fisher's exact test for categorical data. Factors associated with death on univariate logistic regression analysis with a p-value <0.10 were then entered into the multivariate logistic regression model using the backward stepwise procedure. All statistical analyses were performed using Stata statistical software, version 11.0 (StataCorp, College Station, TX). A two-sided *p*-value <0.05 was considered statistically significant.

Ethical considerations

The study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University.

RESULTS

Demographic data

During the study period, 120 patients developed 127 CAUTI; these were all included in our study. Seventy-five patients (62.5%) were male, and the median age was 66.5 (IQR: 54.5, 79) years (Table 1). Underlying diseases among subjects included hypertension in 47 patients (39.2%), diabetes in 29 patients (24.2%), dyslipidemia in 26 patients (21.7%), chronic kidney diseases in 23 patients (19.2%), and coronary artery disease in 16 patients (13.3%) (Table 1). The three most common admission diagnoses were pneumonia in 24 patients (20.0%), heart failure in 16 patients (13.3%), cerebrovascular disease in 16 patients (13.3%), malignancy in 16 patients, (13.3%) and meningoencephalitis in 10 patients (8.3%).

Incidence of CAUTI

The overall mean incidences of CAUTI varied by month during the study period from 2.37 to 7.83 infections/1,000 catheter-days. The incidences of CAUTI in the non-ICU setting varied by month from 2.85 to 9.58 infections/1,000 catheter-days and in the ICU from 1.81 to 7.20 infections/1,000 catheter-days (p=0.643).

Indications for retaining urinary catheters

The indications for placing a urinary catheter included monitoring urine output in 52 patients (40.9%), improving patient comfort or end-of-life care in 37 patients (29.1%), managing urinary retention in 5 patients (3.9%) and assisting in pressure ulcer healing in 1 patient (0.8%). There was no valid medical indication for having a UC in 30 patients (23.6%). A single episode of hematuria requiring bladder irrigation occurred among study subjects (Table 2).

Uropathogens

The Enterobacteriaceae was the most common group of uropathogens (48 episodes, 37.8%) consisting of *Escherichia coli* (27 episodes, 21.3%), *Klebsiella pneumoniae* (10 episodes, 7.9%) and *Proteus mirabilis* (6 episodes, 4.7%); this was followed by enterococci (47 episodes, 37.0%) consisting of *Enterococcus faecium* (37 episodes, 29.1%) and *Enterococcus faecalis* (10 episodes, 7.9%); then other gram-negative uropathogens consisting of *Acinetobacter baumannii* (20 episodes, 15.7%), and *Pseudomonas aeruginosa* (15 episodes, 11.8%).

Table 1
Demographic data of 120 patients (127 episodes) with catheter-associated urinary tract infections.

Characteristics	Number (%) (Total N=120)
Median age in years (IQR)	66.5 (54.5, 79)
Males	75 (62.5)
Underlying diseases	
Hypertension	47 (39.2)
Diabetes	29 (24.2)
Dyslipidemia	26 (21.7)
Chronic kidney disease	23 (19.2)
Coronary artery disease	16 (13.3)
Cerebrovascular disease	15 (12.5)
Atrial fibrillation	7 (5.8)
Chronic obstructive pulmonary disease	6 (5)
Cardiomyopathy	6 (5)
Cirrhosis	5 (4.2)
Human immunodeficiency virus infection	5 (4.2)
Systemic lupus erythematosus	4 (3.3)
Dementia	4 (3.3)
Valvular heart disease	3 (2.5)
Benign prostatic hypertrophy	3 (2.5)
Diagnosis on admission	
Pneumonia	24 (20.0)
Heart failure	16 (13.3)
Malignancy	16 (13.3)
Cerebrovascular disease	16 (13.3)
Meningoencephalitis	10 (8.3)
Ward	
ICU	40 (31.5)
Non-ICU	87 (68.5)

IQR: interquartile range; ICU: intensive care unit.

Candida spp were reported in 21 episodes (16.5%) (Table 3).

Thirty-two of the isolates (25.2%) were MDR: 8 were extended-spectrum β-lactamase (ESBL) producing *E. coli*, 4 were ESBL-producing *K.pneumoniae*, 12 were MDR-*A.baumannii*, 4 were MDR-*P. aeruginosa*, 3 were vancomycin-resistant enterococci (VRE) and 1 was methicillin resistant *Staphylococcus aureus* (MRSA).

Blood cultures grew the same organisms as the uropathogens in 6 patients: 2 grew *P. aeruginosa*, 2 grew ESBL-producing *K. pneumoniae*, 1 grew MRSA and 1 grew VRE.

Antimicrobial prescription

The most common antimicrobial prescription was carbapenems, followed by vancomycin (Table 4).

Mortality

Of the 120 subjects with CAUTI 44 (36.7%) died. The deaths of 24 subjects (20.0%) were most likely due to their CAUTI. Eleven patients (9.2%) were in

Table 2
Indications for retaining the urinary catheter.

Indications	ICU (*n*=40) Number (%)	Non-ICU (*n*=87) Number (%)
No indication	12 (30)	18 (20.7)
Monitoring urine output	18 (45)	34 (39.1)
Underwent surgery	0 (0)	1 (0.1)
Improved patient comfort or end-of-life care	9 (22.5)	28 (32.2)
Management of urinary retention	0 (0)	5 (5.7)
Assistance in pressure ulcer healing	1 (2.5)	0 (0)
Hematuria (continuous bladder irrigation)	0 (0)	1 (0.1)

Table 3
Uropathogens isolated from study subjects (*N*=127 episodes).

Pathogens[a]	Number (%)
Gram-negative bacteria	
Enterobacteriaceae	48 (37.8)
Escherichia coli (total)	27 (21.3)
ESBL-producing strains of *E.coli*	8 (6.3)
Klebsiella pneumoniae (total)	10 (7.9)
ESBL-producing strains of *K. pneumoniae*	4 (3.1)
Proteus mirabilis	6 (4.7)
Morganella morganii	3 (2.4)
Enterobacter cloacae	2 (1.6)
Acinetobacter baumannii (total)	20 (15.7)
Multidrug-resistant strains	12 (9.5)
Pseudomonas aeruginosa (total)	15 (11.8)
Multidrug-resistant strains	4 (3.1)
Chyseobacterium spp	1 (0.8)
Aeromonas hydrophila	1 (0.8)
Gram-positive bacteria	
Enterococci	47 (37.0)
Enterococcus faecium (total)	37 (29.1)
Vancomycin-resistant *E. faecium*	3 (2.4)
Enterococcus faecalis	10 (7.9)
Methicillin-resistant *Staphylococcus aureus*	1 (0.8)
Fungi	
Candida species	21 (16.5)
Candida albicans	8 (6.3)
Candida tropicalis	5 (3.9)
Candida spp	8 (6.3)

[a]23 infections were due to more than 1 uropathogen.

Table 4
Antibiotics prescriptions for study subjects.

Antimicrobials[a]	Number (%)
Beta-lactams	85 (66.9)
Piperacillin/tazobactams	12 (9.4)
Ceftriaxone	15 (11.8)
Ceftazidime	3 (2.4)
Imipenem/cilastatin	7 (5.5)
Meropenem	44 (34.6)
Ertapenem	3 (2.4)
Vancomycin	38 (29.9)
Colistin	25 (19.7)
Fluoroquinolones	
Ofloxacin	1 (0.8)
Ciprofloxacin	3 (2.4)
Fosfomycin	2 (1.6)
Linezolid	1 (0.8)
Fluconazole	5 (3.9)
Amphotericin B	1 (0.8)

[a]36 episodes of infections were prescribed more than 1 antimicrobial agent.

terminally ill and their relatives requested to take them home. One patient was referred to a local hospital in good condition to continue medical treatment. Of those with more than 1 episode of CAUTI, only the last episode was analyzed for factors associated with death. Fifteen patients (12.5%) developed acute kidney injury, and 21 patients (17.5%) developed septic shock, 4 patients (3.3%) re-admitted to the hospital after discharge due to an untreated CAUTI. Those who were terminally ill and taken home, they were assumed to have died. Of the total subjects who died, they were more likely to have an infection caused by MDR bacteria, an infection caused by *A. baumannii*, an infection caused by *K.pneumoniae*, an infection caused by *Candida* spp, a longer duration of UC before onset of infection or who developed shock. Those who survived were more likely to have had an infection caused by *E. coli* or an infection caused by *E. faecalis* (Table 5). On multivariate analysis, factors associated with death were: having an infection caused by MDR bacteria (OR=3.70; 95% CI: 1.13-12.09; p= 0.030), an infection caused by *Candida* spp (OR=10.85; 95% CI: 2.85-41.30; $p <$ 0.001), an infection caused by *A. baumannii* (OR=11.42; 95% CI: 2.54-51.38; p= 0.002), an infection caused by *K. pneumoniae* (OR=19.96; 95% CI: 1.96-203.50; p=0.011) and having septic shock (OR=65.26; 95% CI: 7.45-571.89; p< 0.001).

DISCUSSION

In our study, we found the incidence rate of CAUTI ranged from 2.37 to 7.83/1,000 catheter-days which were comparable to the incidence rate of CAUTI in medical or medical/surgical units reported to NHSN in 2008 (3.1 to 7.4/1,000 catheter-days) (Edwards *et al*, 2009). The incidence rates in our study were higher than the

Table 5
Characteristics of study subjects by mortality.

Characteristics	Death (n=55)	Survived (n=65)	p-value
Age	65.0 (56,78)	69 (53,79)	0.979
Male	24 (43.6)	21 (32.3)	0.257
Underlying diseases			
Hypertension	24 (43.6)	23 (35.4)	0.453
Diabetes	13 (23.6)	16 (24.6)	1.000
Dyslipidemia	14 (25.5)	12 (18.5)	0.381
Chronic kidney disease	10 (18.2)	13 (20.0)	0.821
Coronary artery disease	7 (12.7)	9 (13.8)	1.000
Cerebrovascular disease	8 (14.5)	7 (10.8)	0.588
Uropathogens			
Infections caused by multidrug-resistant stains	20 (36.4)	10 (15.4)	0.011
Escherichia coli	4 (7.3)	22 (33.8)	<0.001
ESBL-producing strains	3 (5.5)	4 (6.2)	1.000
Klebsiella pneumoniae	8 (14.5)	1 (1.5)	0.011
ESBL-producing strains	4 (7.3)	0 (0)	0.042
Pseudomonas aeruginosa	8 (14.6)	6 (9.2)	0.404
MDR strains	2 (3.6)	2 (3.1)	1.000
Acinetobacter baumannii	16 (29.1)	3 (4.6)	<0.001
MDR strains	10 (18.2)	2 (3.1)	0.012
Enterococcus faecalis	1 (1.8)	8 (12.3)	0.038
Enterococcus faecium	19 (34.5)	16 (24.6)	0.314
Vancomycin-resistant *E. faecium*	2 (3.6)	1 (1.5)	0.593
All *Candida* species	14 (25.5)	5 (7.7)	0.011
Candida albicans	6 (10.9)	2 (3.1)	0.140
Candida tropicalis	4 (7.3)	0 (0)	0.042
Unawareness of indwelling catheter	40 (72.7)	39 (60.0)	0.177
Catheter duration (days) (median, IQR)	3 (18, 64)	22 (11, 38)	0.017
Outcomes			
Length of hospital stay (days) (median, IQR)	42 (23, 70)	35 (18, 68)	0.168
Acute kidney injury	10 (18.2)	5 (7.7)	0.101
Septic shock	20 (36.4)	1 (1.5)	<0.001

ESBL, extended-spectrum β-lactamase; IQR, interquartile range.

incidence rate among medical/surgical units in 2012 (1.2 to 2.9/1,000 catheter-day) (Dudeck *et al*, 2013). Although some studies reported higher incidence rate of CAUTI in ICU than in non-ICU patients (Lewis *et al*, 2013), the incidence of CAUTI reported to NHSN was not different between ICU-settings (mean 1.2-2.9/1,000 catheter-days) and non-ICU settings (1.5/1,000 catheter-days) (Dudeck *et al*, 2013). Our study supported the evidence that the incidence rate of CAUTI between ICU and non-ICU settings was not different. These findings suggest that the prevention strategies should be for both the ICU and non-ICU settings.

The most common indications for retaining urinary catheter was for monitoring urine output (40.9%) in both ICU (45%) and non-ICU settings (39.1%). The overall rate of no indications for urinary catheters is 23.6%; 30.0% in ICU and 20.7% in non-ICU settings. This number is comparable to the report from a tertiary care hospital in Bangkok, which ranged 16-34% among medical/ surgical wards (both ICUs and non-ICU settings) (Apisarnthanarak *et al*, 2007). The most common reason for inappropriate use of urinary catheters in that study was inappropriate monitoring urine output among ICU patients (43%) and no clear indication in 21-39% among non-ICU patients. As the incidence of bacteriuria increases each day the urinary catheter is in place and can lead to urinary tract infection (Weinstein *et al*, 1999), urinary catheter removal if not indicated may help to reduce CAUTI rate.

The five most common uropathogens isolated in our study were *E. faecium* (29.1%), *E.coli* (21.3%), *Candida* spp (16.5%), *A. baumannii* (15.7%), and *P.aeruginosa* (11.8%). The reason why *E. faecium* was more common in our study than *E. coli* is unclear, since previous surveillance data from our hospital found *E.coli* to be the most common uropathogen isolated for many years (date not shown). *E. coli* was also the most common CAUTI uropathogen reported to the Centers for Disease Control and Prevention's National Healthcare Safety Network (NSHN), followed by *Candida* spp, and enterococci (Weiner *et al*, 2016). *E. faecium* and *E.coli* usually enter the bladder through extraluminal migration from the rectum colonizing the patient's perineum (endogenous source), but *A. baumannii* and *P. aeruginosa* usually enter the bladder through intraluminal reflux or migration because of failure to maintain a closed drainage system (exogenous source) (Tambyah *et al*, 1999; Saint and Chenoweth, 2003). The intraluminal reflux and failure to maintain a closed drainage system reflect a lapse in infection control at UC insertion or UC maintenance. Among our study patients, *Candida* spp may enter the bladder in a retrograde manner from the urethra rather than through hematogenous spread, since none of our patients had candidemia (Fisher, 2011). Six patients (6 episodes, 4.7%) had bacteremia, which supported the evidence that UTI-associated bacteremia occurred in few cases. A previous study that followed 1,233 patients with hospital-acquired UTI reported secondary bloodstream infections in 2.6% (Krieger *et al*, 1983).

In our study, 8.1% of *E.faecium* isolates were vancomycin resistant, 29.6% of *E.coli* isolates and 40% of *K.pneumoniae* isolates were ESBL-producing and 60% of *A. baumannii* and 26.7% of *P. aeruginosa* isolates were MDR. The National Antimicrobial Resistance Surveillance Center for Thailand (NARST), in a survey of uropathogens from 35 hospitals in Thailand found 10% of *E. faecium* isolates were resistant to vancomycin, 59.7% of *E. coli* and 63.8% of *K. pneumoniae* isolates were resistant to third generation cephalosporins, 82.1% of *A.baumannii* isolates were resistant to carbapenems, and 36.4% of *P. aeruginosa* isolates were resistant to anti-pseudomonal third generation cephalosporins (NARTST, 2016). The most common prescribed antimicrobial agents were carbapenems (42.5%) and vancomycin (29.9%).

The in-hospital mortality rate was 36.7%, of which 20.0% were probably due to a CAUTI. The mortality rate due to CAUTI is higher than that reported from India (18%) (Khan *et al*, 2016), and another tertiary hospital in Thailand (12.6%) (Apisarnthanarak *et al*, 2007). In our study, factors associated with death were having an infection due to MDR-bacteria, having an infection due to *Candida* spp, having an infection due to *A. baumannii*, having an infection due to *K. pneumoniae*, and having septic shock. Having an infection due to MDR-bacteria and having a high APACHE score have been reported to be associated with high mortality rates (DiazGranados *et al*, 2005; Schwaber and Carmeli, 2007; Tumbarello *et al*, 2012; Durante-Mangoni *et al*, 2013; Inchai *et al*, 2015).

Our study was conducted at a single tertiary care university hospital, so the results may not be applicable to other institutions.

In conclusion, CAUTI was associated with a high mortality rate at the study hospital. Clear indications for urinary catheter placement and early removal need to be implemented at the study hospital and further studies are needed to determine if these can reduce the mortality rate due to CAUTI.

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