

## Evaluation of Intensive Care Unit-acquired Urinary Tract Infections in Singapore

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### Abstract

**Introduction:** Urinary tract infections remain one of the most frequently encountered acquired complications in an intensive care unit (ICU). The objective of this study was to determine the incidence, risk factors, microbial sensitivity patterns, and clinical outcomes of patients with UTIs acquired during their admission to an ICU in an acute care hospital in Singapore. **Materials and Methods:** This was a 14-week prospective study. All ICU patients  $\geq 18$  years who remained in the ICU for  $\geq 48$  hours were eligible for this study. Patients were reviewed daily and the presence of an ICU-acquired UTI was identified via urinary microscopic examination or culture results. Other data collected included patient demographics, ICU admission criteria, concomitant illnesses, presence of invasive lines, microbial sensitivity and treatment outcomes. **Results:** Thirty-five (13.7%) cases of ICU-acquired UTI occurred in 256 separate ICU admissions. The most common micro-organisms isolated were *Candida* spp. (34%). Female gender and prior exposure to antibiotics were independent risk factors for developing an ICU-acquired UTI ( $P < 0.01$ ). Both mean length of ICU stay and duration of catheterisation were significantly longer for patients with ICU-acquired UTI ( $P < 0.001$ ). The mortality rate of patients with ICU-acquired UTIs (12.1%) was slightly higher than those without (9.9%). **Conclusions:** The incidence of ICU-acquired UTIs was similar to figures reported for nosocomial UTIs from the previous studies. Significant risk factors for developing an ICU-acquired UTI were female gender and history of antibiotic exposure prior to ICU admission. The insignificant link between ICU-acquired UTI and mortality requires further investigation in larger cohorts.

Ann Acad Med Singapore 2010;39:460-5

**Key words:** Medical and surgical ICUs, Nosocomial UTI, Outcomes, Risk factors

### Introduction

Urinary tract infection (UTI) is one of the most common types of nosocomial infections encountered in the inpatient settings including intensive care unit (ICU). Amongst patients admitted to ICU, studies have revealed the incidence of nosocomial UTIs to range from 9% to 29%.<sup>1-3</sup> The risk of patients acquiring a UTI in an ICU was approximately 2.5-fold higher than that of patients in a general hospital ward. Complicated nosocomial UTIs may lead to urosepsis, and increase patient morbidity and mortality.<sup>4</sup> In 2007, UTIs were the ninth most common cause of death amongst hospitalised patients in Singapore, and the incidence of UTI-related deaths remained consistent at 2% in 2005 and 2.2% in 2007.<sup>5</sup>

Over the past few years, several studies conducted overseas have identified the presence and the prolonged use of urinary catheterisation, female gender, and increased length of ICU stay to be the risk factors associated with ICU-acquired UTI.<sup>6-8</sup> In addition, emerging antibiotic-resistant strains of some of the most frequently observed causative organisms of urinary infections, such as *Escherichia coli*, *Pseudomonas aeruginosa*, and other Gram-negative micro-organisms as a result of prolonged use or previous exposure to broad-spectrum antibiotics in the ICU patients is also becoming a growing concern.<sup>9</sup>

Currently in Singapore, data on the prevalence, the risk factors and the antibiotic resistance patterns associated with ICU-acquired UTI are still lacking. Since the complications

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of ICU-acquired UTI can be fatal and increase the unnecessary burden to the cost and the overall well-being of the patients,<sup>10,11</sup> the objective of this study was to determine the incidence, risk factors, microbial sensitivity patterns, and clinical outcomes of patients with ICU-acquired UTI in the context of Singapore.

## Materials and Methods

This was a prospective study conducted in the 18-bed medical intensive care unit (MICU) and 19-bed surgical intensive care unit (SICU) of a secondary, adult acute care hospital.

All patients 18 years and older admitted to the MICU or SICU between September 2008 and December 2008 were recruited. Only patients who remained in the ICU for 48 hours or longer were eligible for this study. Patients who passed away or were discharged within 48 hours of ICU admission were excluded from this study.

All patients admitted to MICU or SICU underwent an initial review upon admission; follow-up reviews were conducted several times weekly until the patients were discharged from the ICUs. Data such as patient demographics, history of chronic diseases, cause of ICU admission, history of prior ICU admission, details of surgical procedure, and the presence of urinary catheter *in situ* were collected. Potential risk factors evaluated were age, gender, length of ICU stay, duration of catheterisation, prior exposure to antibiotics and diabetes mellitus (DM). The presence of an ICU-acquired UTI identified via urinary microscopic examination or culture results and the clinical outcomes were also collected. Instruments such as Simple Acute Physiology Score (SAPS II) and Acute Physiology and Chronic Health Evaluation (APACHE II) used to measure the severity scores of patients based on their physiological state were not available as they were not used routinely in the ICUs.

In this study, an ICU-acquired UTI was defined as a urinary infection identified at least 48 hours after ICU admission and confirmed by bacteriuria ( $>10^5$  colony forming units/mL or cfu/mL) and a positive urine culture containing not more than 2 isolated micro-organisms.

Catheter-associated UTI (CAUTI) was defined as bacteriuria with  $>10^2$  cfu/mL of organisms detected in a urine sample sterilely aspirated from a urinary catheter port.

### Data Analysis

All data collected was recorded on Microsoft Excel® 2007 (Microsoft Inc., Redmond) and analysed using SPSS Statistics version 17.0 (SPSS Inc., Chicago). The formulae utilised for calculating the incidence rate of ICU-acquired UTI, CAUTI rate, device utilisation rate and relative risk

were as follow:

Incidence of ICU-acquired UTI =

$$\frac{\text{No. of newly developed UTIs}}{\text{No. of patients in 3.5 mo}} \times 100\%$$

CAUTI Rate =

$$\frac{\text{No. of CAUTIs}}{\text{No. of urinary catheter days}} \times 1000 \text{ days}$$

Device Utilisation Rate =

$$\frac{\text{No. of urinary catheter days}}{\text{No. of patient days}} \times 100$$

Relative Risk (RR) =

$$\frac{\% \text{ of UTI patients with risk factor}}{\% \text{ of UTI patients without risk factor}} \times 100$$

Both mean and median values were computed for quantitative data. Differences in means and medians were compared using the Student's *t*-test and Mann-Whitney U-test, respectively. Differences in proportions for categorical data were compared using chi-square ( $\chi^2$ ) test or Fisher's exact test. A multivariate logistic regression model was also used to pinpoint the risk factors associated with ICU-acquired UTI, and to evaluate factors independently associated with mortality in the ICU.

## Results

### Patient Demographics

A total of 697 patients were admitted to the MICU and/or SICU over the 14-week study period, and of which 256 patients (36.7%) met the inclusion criteria (Table 1).

A significantly greater proportion of patients admitted to the MICU were found to require incubation in order to facilitate mechanical ventilation compared to the SICU patients (70.8% vs 44.1%). While no patient admitted to the MICU underwent any major surgical procedure, almost two-thirds of all SICU patients experienced at least one major surgical operation, mostly preceding their admission to the ICU. The primary admitting diagnoses most commonly seen in the SICU and MICU were gastrointestinal diseases (30.8%) and cardiac-related conditions (50.4%), respectively.

### Incidence of ICU-acquired UTI

A total of 35 cases of ICU-acquired UTIs involving 33 patients were observed in this study; 2 patients experienced two separate episodes of ICU-acquired UTI. Nine of the

Table 1. Demographics of Patients Admitted for  $\geq 48$  hours in the Intensive Care Units (ICUs)

	Overall	SICU	MICU	P
Total no. of admissions (%)	256*	143	113	-
Gender				
Male (%)	166 (64.8)	96 (67.1)	70 (61.9)	0.4
Female (%)	90 (35.2)	47 (32.9)	43 (38.1)	
Age (y)				
Mean $\pm$ standard deviation	62.1 $\pm$ 17.5	59.8 $\pm$ 18.2	65.0 $\pm$ 16.2	<0.05
Median	66	62	69	<0.05
Range	19 - 97	19 - 97	23 - 93	-
Race				
Chinese (%)	161 (63.0)	91 (63.6)	70 (62)	0.3
Malay (%)	50 (19.5)	26 (18.2)	24 (21.2)	
Indian (%)	19 (7.4)	14 (9.8)	5 (4.4)	
Others (%)	26 (10.1)	12 (8.4)	14 (12.4)	
Presence of catheter use (%)	239 (93.4)	134 (93.7)	105 (92.92)	0.8
Mechanical ventilation at any one time (%)	143 (55.9)	63 (44.1)	80 (70.8)	<0.001
Percentage with surgery (%)	93 (36.3)	93 (65.0)	0	-
Total duration of catheterisation (days)				
Mean $\pm$ standard deviation	5.6 $\pm$ 5.6	5.9 $\pm$ 6.4	5.3 $\pm$ 4.5	0.4
Median	4	4	4	-
Total length of ICU stay (days)				
Mean $\pm$ standard deviation	5.9 $\pm$ 6.3	6.3 $\pm$ 7.5	5.6 $\pm$ 4.3	0.4
Median	4	4	4	-

\* 8 patients admitted twice, 1 patient admitted thrice, and 1 patient admitted 4 times in the ICU.

33 patients (27.3%) who developed an ICU-acquired UTI were also diagnosed with sepsis. There were 2 cases (6.1%) of concurrent bacteraemia detected amongst the patients who had developed an ICU-acquired infection. Of the 35 cases of ICU-acquired UTIs, 26 (74.3%) and 9 (25.7%) occurred in the SICU and MICU, respectively.

The overall incidence of ICU-acquired UTIs was 13.7% with SICU having more incidence than MICU ( $P < 0.05$ ). The overall percent of days of catheter device utilisation rate was 94.3 (SICU: 93.4; MICU: 95.5), and the overall CAUTI rate per 100 days was 23.7 (SICU: 29.9; MICU: 15.0).

#### Risk Factors Associated with ICU-acquired UTI

Table 2 describes the variables evaluated as potential risk factors for the development of ICU-acquired UTI. Women were at a significantly higher risk for getting ICU-acquired UTI compared to men (RR, 3.12; 95% CI, 1.65-5.90;  $P < 0.001$ ). Prior antibiotic exposure or surgical procedure and history of DM and/or stroke were also associated with the development of ICU-acquired UTI ( $P < 0.05$ ). Both mean

length of ICU stay and mean duration of catheterisation were significantly longer for patients with ICU-acquired UTI ( $P < 0.001$ ).

After adjusting for other covariates via multivariate logistic regression (Hosmer-Lemeshow Goodness of Fit test,  $\chi^2 [(8 \text{ df}) = 3.841, P = 0.87]$ , only female gender (OR, 4.24; 95% CI, 1.86-9.68;  $P < 0.001$ ) and prior antibiotic exposure (OR, 3.27; 95% CI, 1.39-7.67;  $P < 0.01$ ) independently increased the chances of developing ICU-acquired UTI.

#### Micro-organisms and Microbial Sensitivity Patterns

Of the 35 ICU-acquired UTI cases, 4 patients had 2 repeat urine cultures with either identical or different micro-organisms, making up a total of 39 positive urine cultures. The most common causative micro-organism of ICU-acquired UTI was *Candida* spp. (Table 3). The median period from ICU admission to the development of a first UTI was 6 days.

Of the 39 isolates, only 4 (10.3%) were highly antibiotic-resistant (3 extended-spectrum beta-lactamase [ESBL]-producing strains of *Klebsiella* spp. and 1 ESBL-producing

Table 2. Univariate Analysis of Risk Factors for Intensive Care Unit (ICU)-acquired Urinary Tract Infection (UTI)

Possible risk factors	UTI (n = 35)	Non-UTI (n = 221)	P
Female:Male (% F)	22:13 (62.9)	68:153 (30.8)	<0.001
Mean age ± standard deviation	65.0 ± 16.1	61.6 ± 17.7	0.3
Median age	69	64	0.3
Percentage with surgery (%)	18 (51.4)	75 (33.9)	<0.05
Mechanical ventilation at any one time in ICU (%)	20 (57.1)	123 (55.7)	0.9
Presence of catheter use (%)	33 (94.3)	206 (93.2)	0.8
Early catheterisation (%)	9 (25.7)	22 (10)	<0.05
Prior exposure to antibiotics at least 3 days before ICU admission (%)	12 (34.3)	37 (16.7)	<0.01
Renal impairment (%)	19 (54.3)	89 (40.3)	0.1
Diabetes mellitus (%)	20 (57.1)	82 (37.1)	<0.05
Immunocompromised (%)			
History of benign prostatic hypertrophy (BPH) (%)	2 (15.4) (n = 13 men)	11 (7.2) (n = 153 men)	0.3
Neurological impairment/stroke (%)	8 (22.9)	24 (10.9)	<0.05
Duration of catheterisation (days)	333	1102	-
Mean ± standard deviation	9.5 ± 6.9	5.1 ± 6.2	<0.001
Median	7	4	<0.001
Length of ICU stay (days)	339	1183	-
Mean ± standard deviation	9.7 ± 6.7	5.4 ± 6.1	<0.001
Median	7	4	<0.001

Table 3. Common Aetiologies of ICU-acquired UTI

Organism	SICU	MICU	Total occurrence* (%)
Mixed bacterial growth	12	3	15 (37)
<i>Candida</i> spp.	10	4	14 (34)
<i>Klebsiella</i> spp.	3	0	3 (7)
<i>E. coli</i>	1	2	3 (7)
<i>Pseudomonas aeruginosa</i>	2	0	2 (5)
<i>Acinetobacter baumannii</i> complex	1	0	1 (2)
<i>Citrobacter koseri</i>	0	1	1 (2)
<i>Enterococcus</i> † spp.	0	1	1 (2)

\* 39 positive infections were diagnosed among 35 patient admissions; One had 2 organisms co-isolated.

† Co-isolated with *E. coli* UTI from MICU.

strain of *E. coli*). Although all 3 ESBL-producing *Klebsiella* spp. were relatively resistant to ciprofloxacin and one of them was resistant to piperacillin/tazobactam; all were sensitive to imipenem. The ESBL-producing *E. coli* was sensitive to nitrofurantoin, co-trimoxazole, gentamicin and imipenem. The *Enterococcus* spp., co-isolated with *E. coli*, in one culture was sensitive to vancomycin but not ampicillin.

### Mortality

Of the 33 patients who had developed ICU-acquired UTIs, 4 patients (12.1%) died in the ICU (vs 22 [9.9%] without UTI), and 6 patients (18.2%) died in general wards (vs 35 [15.7%] without UTI) during the same hospital stay.

No significant association was found between ICU-acquired UTI and ICU-related mortality ( $P = 0.9$ ) after adjusting for age and length of ICU stay (Table 4). However, older age and the use of mechanical ventilation were independent risk factors for death in the hospital.

### Discussion

The overall cumulative incidence of ICU-acquired UTI was 13.7% during the 14-week study period, and this finding was consistent with those reported in the literature (6.5% to 28%).<sup>6,7,12,13</sup> Previous studies have brought up the possibility of under-reporting of UTIs and this factor cannot be entirely ruled out in this study as our protocol utilised an observational approach to the detection of UTIs. Thus, unless the patient displayed signs of sepsis, it would not have been possible to detect the presence of an asymptomatic UTI. Furthermore, the exact duration required for a UTI to develop in our patient population could not be established as patients were not followed-up after leaving the ICU.

Table 4. Independent Variables Associated with Hospital Mortality, using Multivariate Analysis

Variable	Odds ratio (95% CI)	P
Age	1.04 (1.02, 1.07)	<0.001
Length of ICU stay	0.94 (0.86, 1.03)	0.2
Post-surgical	0.96 (0.44, 2.12)	0.9
Mechanical ventilation at any one time during ICU stay	5.86 (2.39, 14.36)	<0.001
ICU-acquired UTI	0.95 (0.30, 3.01)	0.9

Despite these shortcomings, compliance to existing infection control practices and surveillance programmes have been shown to keep nosocomial infection rates low in the ICU.<sup>14,15</sup> Some of the measures that had been in place in our study even prior to the start of this study included limiting the nurse-to-patient ratio to 2:1 for patients receiving mechanical ventilation or 3:1 for patients requiring high-dependency care, prevention of backflow of urine through the catheter, not allowing urine collection bags to touch the floor or fill excessively, nursing staff required to wear gloves when handling urine bags and associated lines, nurses carefully observing for concentrated/blood-stained urine as well as for inflammation around the area of catheterisation.

Similar to other studies, female gender was also shown to be an independent risk factor for ICU-acquired UTI in this study.<sup>6-8</sup> This risk, however, may be attributed directly to the differences in the male and female body structures rather than ICU admissions. Compared to men, women have a shorter urethra, which predisposes easier access of perineal flora to the bladder along the periphery of the catheter.<sup>16</sup> In addition to gender, the patient's prior exposure to antibiotics was another risk factor found to be closely linked to ICU-acquired UTI in this study.<sup>9</sup> This was not surprising as most of the patients prior to ICU admission were already on antibiotics to treat other concomitant infections. However, unlike gender, prior exposure to antibiotics is a modifiable risk factor and it can be prevented if antibiotics are used appropriately. In our study, we found a fairly low rate of UTIs (7.7%) caused by bacteria displaying broad-spectrum resistance.

The most common micro-organism responsible for the ICU-acquired UTIs in this study was *Candida* spp. *Candida* spp. are ubiquitous and are the most common human commensal found near the perineal region where the urinary catheter is in close proximity. Most of the patients in our study received broad-spectrum antibiotics in the ICU. This could have inadvertently resulted in decolonisation of gut flora, allowing *Candida* spp. to be naturally selected as the dominant opportunistic micro-organism. It should be stated that intentional digestive decontamination to

prevent bacterial or fungal translocation, thereby possibly causing a nosocomial infection, was not carried out for any of the patients. This was due to the possible link between use of antibiotics for digestive decontamination and the development of antimicrobial resistance.

Studies have shown that the presence of UTI can increase the length of stay in ICU, which may further increase the risk of morbidity and mortality due to a higher chance of exposure to more debilitating forms of infections that are difficult to treat.<sup>17</sup> Patients who developed an ICU-acquired UTI required a longer ICU admission compared to those patients who were free of a UTI. Multivariate regression did not show any particular factor being directly responsible for the increased length of stay. However, it is noteworthy that a significantly higher proportion of patients with ICU-acquired UTIs had undergone surgery, had required catheterisation early in their admission, and had already received antibiotics at least 3 days before ICU admission compared to the group that did not exhibit any signs of a UTI.

The overall mortality rate amongst patients with ICU-acquired UTIs was lower compared to the rates described in the previous studies (12.1% vs 18-21%).<sup>3,6,7</sup> However, the mere occurrence of a UTI was not found to be an independent risk factor for death in ICU patients. This was perhaps not surprising since the principle cause of death in a patient with a serious UTI is usually related to some form of organ failure or sepsis. In this study, 9 of the 33 patients who developed an ICU-acquired UTI were also diagnosed with sepsis, of which two died. Two other cases of bacteraemia were detected in patients already experiencing a UTI; neither patient who had both a bacteraemia and ICU-acquired UTI died. Nevertheless, it cannot be excluded that the presence of a UTI could have played an indirect role in the death of the patients. Studies have shown that the presence of UTI can increase the length of stay in ICU, which may further increase the risk of morbidity and mortality due to a higher chance of exposure to more debilitating forms of infections that are difficult to treat.<sup>8,17</sup>

In this study, none of the patients with ICU acquired-UTI experienced deterioration in their clinical condition. It may be postulated that this was one reason why the mortality rate was lower compared to other studies. Another possibility was that the patient population and severity of clinical conditions in this study were different from those in other studies.

This study had several limitations. Firstly, the results were based on a single group of patients from a single institution. Therefore, the finding may not be representative of all ICU patients in Singapore hospitals. Small sample size, short study period and the observational nature of this study may also have affected the findings of this study. In addition, unlike other studies,<sup>6,7,11</sup> which included the use

of SAPS II or APACHE II score as one of the markers of severity of disease, the use of these instruments were not possible as the Glasgow Coma Scale (GCS), one of the vital parameters required, was not routinely determined for ICU patients other than those with neurological deficits, head trauma or required some form of neurological intervention in our hospital. A longer study period with a larger sample size using instruments such as SAPS II or APACHE II that define the disease severity and predict the outcome may be better suited to provide more substantial results to confirm the findings in this study.

Future studies should involve more ICUs from more than one institution; treatment regimens and comparisons of antibiotic resistance patterns between ICUs and general wards and across institutions should also be carried out to further evaluate patients with ICU-acquired UTI in Singapore.

### Conclusion

ICU-acquired UTIs remain as one of the most frequently encountered complications in ICU. In this study, the incidence of ICU-acquired UTI was similar to figures reported for nosocomial UTIs in previous studies conducted in other countries. Significant risk factors for developing an ICU-acquired UTI were female gender and history of antibiotic exposure prior to ICU admission. The insignificant link between ICU-acquired UTI and mortality requires further investigation in larger cohorts.

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