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ORIGINAL ARTICLE

The relationship of seasonality and the increase in urinary tract infections among hospitalized patients with spinal cord injury

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Background: Urinary tract infection (UTI) is the most frequent complication in patients who have spinal cord injury (SCI). The occurrence rate of UTI in this type of hospitalized patients was correlated to seasonality, age, and gender.

Methods: Patients hospitalized during the 4-year study period with underlying SCI were identified from Taiwan's National Health Insurance Research Database. Patients with a discharge diagnosis of UTI were identified as those with SCI and UTI; they were divided into the following four age groups: <18 years, 18 to 44 years, 45 to 64 years, and ≥65 years. The gender, monthly number of cases, major complication rate, seasonal differences, and odds ratios (ORs) of associated factors were analyzed.

Results: Data of 30 149 hospitalized patients diagnosed with SCI were retrieved. SCI and UTI were diagnosed in 3405 (11.3%) patients, of them 2296 were males (67.4%) and 1109 were females (32.6%). The UTI occurrence rate in hospitalized SCI patients was higher in males (11.8%) than in females (10.4%) (OR: 1.24; 95% CI: 1.15-1.34); it was highest in the ≥65-year-old age group (12.8%) and lowest in the <18-year-old age group (5.8%) (OR: 2.51; 95% CI: 1.83-3.44). The UTI occurrence rate varied from 7% to 18%, and it was highest in the summer (13.0% ± 2.6%) and lowest in the winter (10.2% ± 1.9%) (OR: 1.27; 95% CI: 1.15-1.40). Acute pyelonephritis was the most common complication in SCI and UTI cases.

Conclusion: The mean occurrence rate of UTI in hospitalized SCI patients was 11.3%; it was higher in males, in patients aged ≥65 years, and in the summer. Therefore, physicians should pay attention to the occurrence of UTI in aged male patients with SCI, especially in the summer.

Keywords: Age; Epidemiology; National health insurance research database; Seasonality; Spinal cord injury; Urinary tract infection

1. INTRODUCTION

Neurogenic bladder, a dysfunction in the coordination of bladder contraction and relaxation, following spinal cord injury (SCI) is an important clinical issue. Urinary tract infection (UTI) is the most frequent complication among SCI patients, and the prevalence of UTI in these patients is estimated to be an average of 2.5 times per year.[1]

UTI in patients with neurogenic bladder is considered as complicated UTI because of the functional urinary tract abnormalities.[2] Complications of UTI include development of acute pyelonephritis, epididymitis, orchitis, prostatic abscesses, and urosepsis. Once diagnosed with UTI, adequate antibiotics therapy should be started as early as possible. Recurrent UTI episodes may lead to renal scarring, decreased renal function, and urinary tract stone formation. However, repeated antibiotic therapy increases the risk of multidrug-resistant bacteria, without reducing the incidence or severity of symptomatic UTIs.[3] Understanding the epidemiological information on UTI in SCI can help in developing preventive strategies or interventions in clinical care.

The National Institute on Disability and Rehabilitation Research conference classified the risk factors of UTI in SCI patients into two broad categories: (1) functional and anatomical; and (2) sociologic and demographic.[4] The functional risk factors include high voiding pressure, failure to empty the bladder, bladder catheterization and instrumentation, and urinary tract stones.[5] Demographic and sociologic factors include the requirement of complete or maximal assistance (such as those with cervical level injuries) and personal hygiene.[6]

There is a significant seasonal fluctuation in the frequency of symptomatic UTIs in the general population of women who presented to general practitioners.[7] Nonclinical databases (web search data) that study the seasonality of UTI showed a higher incidence of UTI in the summer.[8] Growing studies that surveyed the seasonality of UTI in different populations were reported and collated into a large-scale validated database in the United Kingdom.[9,10] However, we are not aware of any investigation examining the seasonality of UTI in patients with SCI.

We studied the seasonal variability of UTI in SCI inpatients using the 4-year nationwide hospital admission data in Taiwan.

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2. METHODS

2.1. Study Population

The National Health Insurance Research Database (NHIRD) contains data on more than approximately 99.5% of 23.5 million Taiwanese people.[11,12] It contains comprehensive nationwide inpatient and outpatient medical claim data.

Taiwan's NHIRD provides disease diagnoses consistent with the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) dated 2016 and earlier. The database released from NHIRD was secondary deidentified data for research purposes. This study used the inpatient data from Taiwan's NHIRD. The local institutional Internal Review Board approved the study.

Hospitalized patients with a principal diagnosis of SCI (ICD-9-CM codes 952, 806, and 336) between January 2003 and December 2006 were identified. Among all the hospitalized SCI patients, the occurrence of UTI (ICD-9-CM code 599.0) and its complications including epididymitis/orchitis (ICD-9-CM code 604), prostitis (ICD-9-CM code 601), acute pyelonephritis (ICD-9-CM code 590), and urosepsis were identified. Urosepsis was defined as either combined UTI with sepsis (ICD-9-CM code 995.9) or septicemia (ICD-9-CM code 038). Recurrent episodes of UTI during one hospitalization admission were only counted once.

The monthly and seasonal proportions of incident UTI were defined as UTI events divided by the total number of SCI admissions in that specific month or season. The proportion of UTI complications was calculated as the number of UTI complications divided by the number of total UTI events.

The seasons are defined as spring (from March to May), summer (from June to August), autumn (from September to November), and winter (from December to February). The age of participants was categorized into four age groups: 0-17, 18-44, 45-64, and ≥65 years.

2.2. Data Setting and Statistical Analysis

The dataset from NHIRD was retrieved for database decoding using Microsoft SQL Server 2008 R2; SPSS (version 23.0, SPSS Inc., Armonk, NY, USA) and was used for data analysis. Characteristics of the participants were summarized using descriptive statistics; the percentages of the categorical variables and the means with SDs for the occurrence rate of incident UTI and age were shown.

We performed a mixed model analysis to evaluate the differences in the occurrence rates of incident UTI among the four seasons. Unconditional logistic regression was used to calculate the odds ratio (OR) of the four seasons in the categorized groups. Moreover, logistic regression was also used to calculate the ORs of UTI by age and gender. Graphpad Prism 7 (GraphPad Software, Inc. La Jolla, CA, USA) was used to create graphical representations. A two-sided p-value of <0.05 was considered statistically significant.

3. RESULTS

Overall, 30 149 hospitalized patients were diagnosed with SCI during the 4-year study period, and approximately two-thirds of them were male (19 476 patients, 64.6%). Among them, 3405 patients had a concomitant diagnosis of UTI (Table 1). The mean UTI occurrence rate in hospitalized SCI patients was 11.3% during the 4-year study period, and 11.8% were males and 10.5% females. In the different age groups, the UTI occurrence rates had an obvious difference between the ≥65-year-old group and the <18-year-old group (highest 13.8% vs lowest) (Table 1).

Among the 3405 UTI patients, 235 had urological complications (Table 2).The most common complications were acute pyelonephritis, followed by urosepsis, epididymitis, and prostitis (Table 2).

Figure 1 showed that the proportions on the monthly UTI occurrence rate had monthly variations and the peak proportions were in August 2004 to 2006 and July 2003 (Figure 1A, B). The peak proportions of the monthly UTI occurrence rates between male and female patients were both in August (Figure 1C). For the different age groups, the ≥65-year-old group was the highest all the year round, followed by the 45- to 64-year-old and 18- to 44-year-old groups. The <18-year-old group was the lowest during most of the months (Figure 1D).

For the seasonal differences shown in Table 3, the UTI occurrence rate was lowest in the winter (11.2% ± 1.9%) and highest in the summer (13.0% ± 2.6%). When divided on the basis of gender or age groups, almost all the UTI occurrence rates were significantly higher in the summer than in the winter ($p < 0.05$), except for the <18-year-old group ($p > 0.05$) (Table 3). Also the UTI occurrence rate of the ≥65-year-old group was significantly higher in autumn than in winter. The seasonal differences including different age groups were presented in Figure 2. For the complication rates, there was no significant difference among the four seasons ($p = 0.08$) (Table 3).

The ORs of UTI occurrence based on gender, age groups, and seasons in all hospitalized patients with SCI are listed in Table 4.The ORs of the males was 1.24 (95% CI: 1.14-1.34) compared with that of the females. With the <18-year-old SCI patients as the reference group, ORs for age groups 18 to 44 years, 45 to 64 years, and ≥65 years were 1.52, 2.12, and 2.51, respectively. For seasonality, with winter as the reference point, only summer showed a significant effect (OR = 1.27; 95% CI: 1.15-1.40).

When comparing the seasonal differences between both genders and the different age groups, the ORs was significant in the summer compared to winter except for the <18-year-old group

Table 1

Demographic characteristics and the occurrence rate of incident urinary tract infections among hospitalized patients with spinal cord injury

	SCI	SCI + UTI		
	Case No.	Case No.	Age, yMean ± SD	Occurrence Rate, %
All	30 149 (100%)	3405 (100%)	51.4 ± 19.1	11.3
Gender				
Male	19 476 (64.6%)	2296 (67.4%)	49.7 ± 18.4	11.8
Female	10 673 (35.4%)	1109 (32.6%)	54.6 ± 19.9	10.4
Age group, y				
<18	739 (2.5%)	43 (1.3%)	12.3 ± 4.9	5.8
18–44	10 158 (33.7%)	893 (26.2%)	32.1 ± 8.0	8.7
45–64	10 565 (35.0%)	1273 (37.3%)	54.5 ± 13.4	12.0
≥65	8687 (28.8%)	1196 (35.1%)	75.5 ± 14.9	13.8

Data are expressed as number (%), mean ± SD, or proportions where appropriate.
SCI = spinal cord injury; UTI = urinary tract infection.

Table 2

Major complication rates of the 3405 cases diagnosed as urinary tract infections among hospitalized patients with spinal cord injury

Complications (ICD-9)	N	%
Acute pyelonephritis (ICD-9:590)	145	61.7
Urosepsis (ICD-9:038 or ICD-9:995.9)	43	18.3
Epididymitis (ICD-9:604)	37	15.7
Prostitis (ICD-9:601)	10	4.3
Total UTI case numbers	235	100.0

ICD-9 = International Classification of Disease, Ninth Revision, Clinical Modification.

(Table 5). In addition to this, the ORs of the ≥65-year-old group were significant in autumn when compared to winter.

4. DISCUSSION

This study is based on a 4-year population dataset from Taiwan, a subtropical country. It showed that the proportion of UTI cases in hospitalized SCI patients was significantly associated with seasonality and was higher in males and in older patients. The proportion of UTI complications had no significant relation to seasonality. To the best of our knowledge, this is the first research that discusses the seasonality of UTI in SCI patients using a large longitudinal population database.

Our study showed a higher monthly proportion of incident UTI in the male (Figure 1) and elderly patients (Figure 2). Previous epidemiologic studies on the incidence of UTI in the general population showed higher rates in women than in men across all age groups.[13] The incidence of UTI reportedly decreases in middle-aged adults but rises significantly in older adults.[14] The prevalence of UTI in males was <1% until they develop prostatism, which contributes to the remarkable increase in UTI episodes.[15] Our study found that the monthly proportion of incident UTI was positively correlated with age. The ORs for those aged >65 years was 2.51 when compared to those aged <18 years. In the general older population, it is not surprising that prostatism in men and menopause in women can contribute to a higher risk of developing UTI. The results in our SCI patients show interesting new evidence that supports the idea that age is a risk factor of UTI occurrence, independent of SCI.

Bennett et al.[16] demonstrated that females with SCI on intermittent catheterization had significantly higher infection rates than males. The infectious organisms involved had a high percentage of *E. coli*, *Enterococcus*, *or Klebsiella*. The high incidence of UTI with *E. coli* or *Enterococcus* infection in female patients is possibly related to stool and proximal bowel contamination. Therefore, this anatomical difference causes females to be more susceptible to UTI.

However, we discovered a higher monthly proportion of UTI incidence in male SCI patients. To our knowledge, there are no other literature studies on patients after SCI about this contradictory phenomenon. However, there are many confounding factors that may explain this result. The SCI group is composed of patients with many heterogeneous characteristics, such as compromised bladder function, various neurological levels of SCI, a wide range of classifications based on the American Spinal Injury Association Impairment Scale (AIS), and other functional status evaluations. The NHIRD database did not contain data on this broad scope of patient characteristics. Moreover, patients who have taken preventive strategies toward UTI were not included in the database. For example, patients with recurrent UTI are encouraged to consume cranberry products; however, there is insufficient evidence proving the efficacy of such measures in preventing UTIs in both genders. Further analysis with a detailed history of the disease and more relevant data on the incidence of this combination is needed before it can be concluded that UTI is more predominant in males after SCI.

We noted that earlier studies showed different results on the seasonality of UTI between adult and children. There was a higher incidence of UTI in children in the winter, while

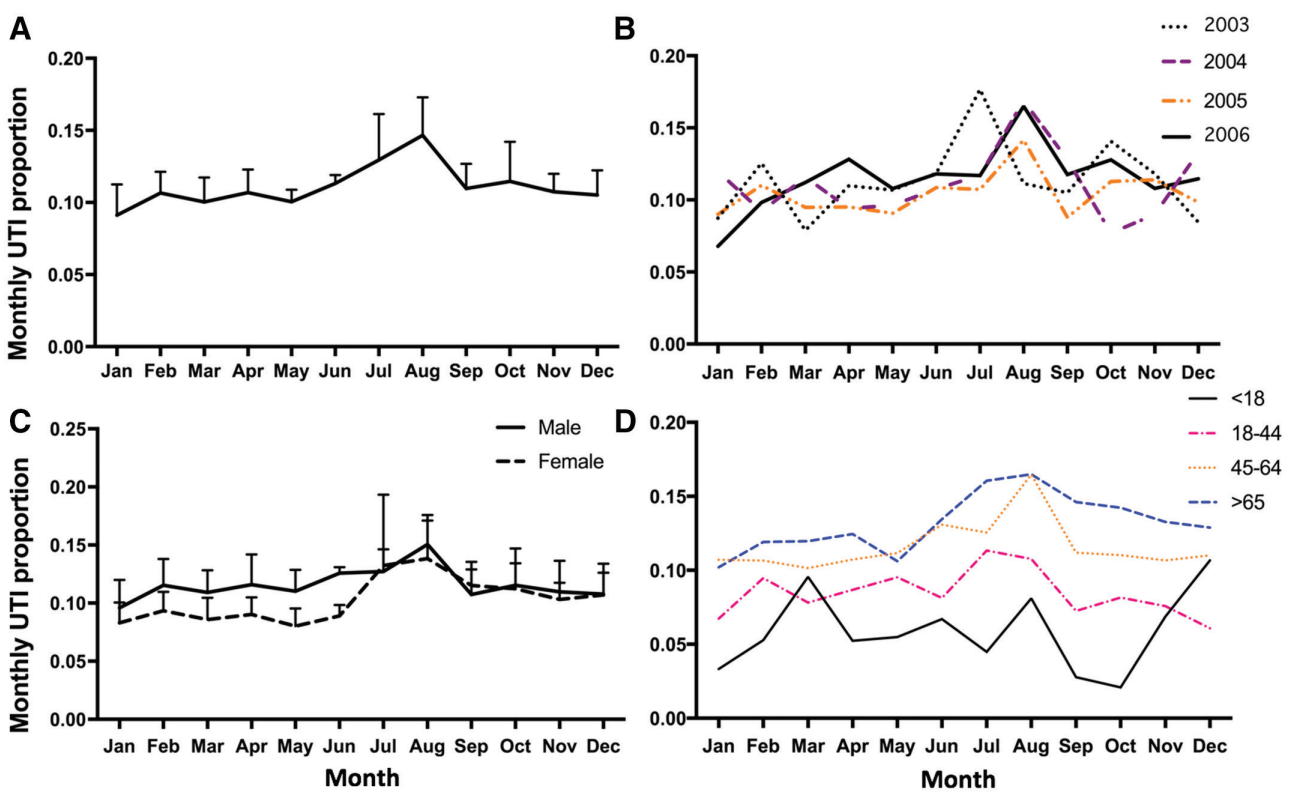

Fig. 1 Mean monthly proportion of UTI incidence in hospitalized patients with spinal cord injury (SCI). (A) Overall SCI patients; (B) Distributed by year; (C) Distributed by gender; (D) Distributed by age.

Table 3

Comparisons of the seasonal occurrence rate of urinary tract infections in patients with spinal cord injury based on gender, age, and complication events

Subgroup/Season	Spring	Summer	Autumn	Winter	F	*p*
Total case no. (UTI events)	7546 (763)	7937 (1068)	7482 (838)	7184 (736)		
Occurrence rate, %	10.3 ± 1.3	13.0 ± 2.6[a]	11.1 ± 1.8	10.2 ± 1.9	13.56	<0.001
Gender						
Male (UTI events)	4885 (535)	5162 (715)	4836 (556)	4593 (491)		
Occurrence rate, %	11.2 ± 1.9	13.5 ± 2.1[a]	11.1 ± 2.1	10.6 ± 2.4	12.69	0.002
Female (UTI events)	2661 (228)	2775 (353)	2646 (282)	2591 (235)		
Occurrence rate, %	8.5 ± 1.5	11.9 ± 4.3[a]	11.0 ± 2.4	9.4 ± 1.9	6.93	0.008
Age, y						
<18 (UTI events)	201 (12)	183 (11)	212 (10)	143 (10)		
Occurrence rate, %	6.8 ± 6.1	6.4 ± 4.3	3.9 ± 5.3	6.4 ± 8.9	0.07	0.99
18-44 (UTI events)	2571 (213)	2669 (302)	2468 (185)	2450 (193)		
Occurrence rate, %	8.7 ± 2.6	10.1 ± 4.0[a]	7.68 ± 2.3	7.4 ± 3.1	6.64	0.004
45-64 (UTI events)	2599 (284)	2828 (396)	2696 (301)	2442 (292)		
Occurrence rate, %	10.7 ± 2.6	14.0 ± 3.6[a]	10.9 ± 2.6	10.8 ± 2.0	4.95	0.02
≥65 (UTI events)	2176 (254)	2256 (359)	2106 (342)	2149 (241)		
Occurrence rate, %	10.2 ± 0.2	17.8 ± 1.4[a]	15.2 ± 3.4[a]	12.0 ± 0.4	7.6	0.009
Complication events	66	73	44	52		
Complication rate, %	8.6 ± 3.8	8.5 ± 3.2	5.6 ± 3.4	6.9 ± 3.0	3.69	0.08

UTI = urinary tract infections.
[a]$p < 0.05$ vs winter.

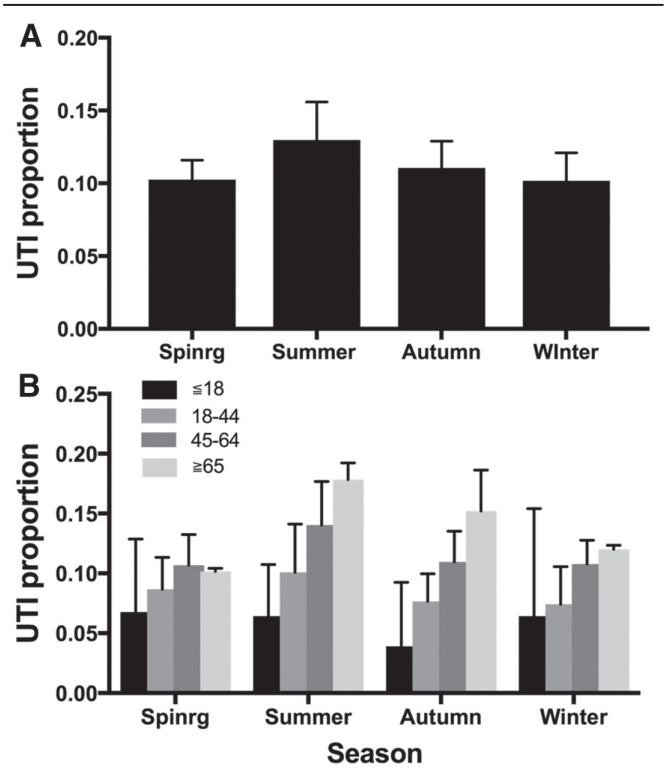

Fig. 2 Mean seasonal proportions of UTI incidence in hospitalized patients with spinal cord injury (SCI). (A) Overall SCI patients; (B) Categorized by age.

adult women had a higher incidence of UTI in the summer.[7,17] However, our results showed seasonal changes in UTI occurrence in adults, except for those aged <18 years. The small number of study participants combined with a high variation of monthly proportions in incident UTI may reduce precise observations on seasonality; hence, further studies on this topic are warranted. However, the proportion of UTI complications clearly showed no seasonal change. This implies that physicians should also be aware of possible complications in treating UTI in SCI patient regardless of the season. For those who have decreased or total loss of sensation after SCI, early

Table 4

Odds ratios in the occurrence of urinary tract infections based on gender, age, and seasons in patients with spinal cord injury

Variable	OR (95% CI)	*p*
Gender		
Female	1.00	
Male	1.24 (1.15-1.34)	<0.001
Age, y		
<18	1.00	
18–44	1.52 (1.10-2.09)	<0.001
45–64	2.12 (1.55-2.90)	<0.01
≥65	2.51 (1.83-3.44)	<0.001
Season		
Winter	1.00	
Spring	0.96 (0.87-1.07)	0.469
Summer	1.27 (1.15-1.40)	<0.001
Autumn	1.04 (0.93-1.15)	0.494

OR = odds ratio.

detection and monitoring of these complications are particularly important and the development of life-threatening conditions can be avoided.

It is noteworthy that only a few studies on the seasonality of UTI seem to exist. A retrospective analysis done in 1983 showed that there is an increased incidence of UTI in the summer in the female adult population.[7] A 1979 epidemiologic study on the incidence of UTI in children showed the highest rates in November and the lowest rates in the summer. The monthly frequencies showed a 2-fold difference. Several studies using time series analyses were conducted to survey the bloodstream infection of *E. coli*. It is noted to be the most prevalent pathogen in UTIs, and had a significant seasonality effect.[18–21] In addition to this, a higher ambient temperature was associated with the prevalence of *E. coli* bloodstream infection.[18,19,21]

One nonclinical method used to estimate the seasonality of UTI was to monitor the records of drug sales and internet searches. This method also showed a substantial seasonality for UTI, with a peak incidence in the summer.[8] However, the scarcity of specific studies on the seasonality of UTI in SCI patients makes our current results relevant in contributing to the epidemiology of this condition.

Table 5

Seasonal odds ratios in the occurrence of urinary tract infections among hospitalized patients with spinal cord injury in different gender and age groups

	Winter	Spring	Summer	Autumn
Subgroup/Season	OR	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gender				
Female	1.00	0.90 (0.75-1.09)	1.35[a] (1.13-1.60)	1.19 (0.99-1.42)
Male	1.00	0.98 (0.86-1.12)	1.23[a] (1.08-1.38)	0.98 (0.86-1.11)
Age, y				
<18	1.00	0.85 (0.36-2.02)	0.85 (0.35-2.07)	0.65 (0.27-1.61)
18-44	1.00	1.07 (0.88-1.31)	1.32[a] (1.09-1.60)	0.94 (0.76-1.16)
45-64	1.00	0.85 (0.71-1.01)	1.15[a] (1.01-1.31)	0.85 (0.72-1.01)
≥65	1.00	1.02 (0.85-1.23)	1.45[a] (1.21-1.73)	1.45[a] (1.20-1.71)

OR = odds ratio.

[a]$p < 0.05$ vs winter.

UTI is the most common complication after treatment of neurogenic bladder. It can interfere with the process of rehabilitation, increased medical cost burden, and it can even lead to lethal urosepsis.[22] Therefore, understanding its basic epidemiology and prevalence is important in determining appropriate clinical care and development and implementing effective prevention strategies.

The current clinical practice in treating neurogenic bladder is largely focused on adequate emptying methods. Preventive strategies for UTI include the use of a hydrophilic catheter[23,24] administration of weekly oral cyclic antibiotics,[25] consumption of cranberry products,[26] methenamine salt prophylaxis,[27] and bacterial interference with specific serotypes of *E. coli*.[28,29] There are several ongoing studies on the attempts in developing an *E. coli* vaccine for preventing recurrent UTI in women. If successfully developed, it may be applicable to the SCI population. With new epidemiologic evidence stating the incidence of UTI in SCI patient is higher in the summer, we are taking into account the seasonal factor in developing preventive strategies to decrease the incidence of UTI.

The mechanism of how seasonality influences UTIs is unclear. Previous studies on urinary tract diseases suggested that ambient temperature was also associated with incidences of urinary tract calculi and testicular torsion.[30,31] Our study showed a significant seasonal difference in the summer with an average ambient temperature that was higher than the other seasons. Possible explanations for the mechanopathogenesis are relative dehydration and insensible fluid loss in an environment with high temperatures. These can cause a decrease in urine output, which in turn contributes to an increase in UTI occurrence. Interestingly, a retrospective observational study of SCI patients showed that those with acute UTI had a significant decrease in urinary output for 7 days before UTI onset.[32]

Genital hygiene may be another contributory factor to the seasonal variations that we have observed. Increased perspiration and sebaceous secretion around the genital area in high temperatures result in a beneficial microenvironment for local bacterial colonization; hence, defeating the body's natural defenses can lead to UTI.

There are a few limitations in this study. First, the database we used was from 2003 to 2006. One might consider the data as outdated; however, it was the only database we could access. Moreover, since the ICD-9 coding for SCI and UTI had not been revised during the past decade, we believe our results were similar with the current diagnoses. Second, several patient characteristics were lacking in the NIH database. Only gender and age were included for the analysis. We were unable to obtain the following data from the database: neurological level, AIS classification, duration since the onset of SCI, etiologies, type of neurogenic bladder dysfunction (detrusor overactivity/underactivity, sphincter dysfunction, etc.), and method of bladder emptying. Third, the data we used were based on admitted SCI patients. For SCI patients who live in the community, information during their outpatient visits was unavailable. If possible, outpatient data can be included in future studies. It may be of importance because several differences exist between inpatients and outpatients. Generally, further studies with more detailed information are encouraged for a more comprehensive analysis of the epidemiology after SCI.

In conclusion, the mean occurrence rate of UTI incidence in hospitalized SCI patients was 11.3%. It was higher in males, in patients aged ≥65 years, and in the summer. Therefore, physicians should pay more attention on the potentially higher occurrence rate of UTI in aged male patients with SCI, especially during the summer season.

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