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Urinary tract infection in patients with chronic kidney disease

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Aim: Chronic kidney disease (CKD) has become a burden of health care globally. However, data on epidemiology, clinical features, and outcomes of urinary tract infection (UTI) in this population are scarce. This study aims to retrospectively review such data.

Materials and methods: A retrospective cohort study was conducted from 1 January 2005 to 31 December 2011 in patients with CKD requiring hospitalization. Patients who had upper and lower UTIs were compared for demography and clinical data. Logistic regression was used to assess which variables were associated with upper UTI.

Results: A total of 276 bacteriuria patients were admitted to our ward with upper and lower UTIs. The average ages of the upper and lower UTI patients were 59.21 ± 16.54 and 71.18 ± 14.77 years, respectively. The results of logistic regression analysis showed that age (OR 0.946, P < 0.001), female sex (OR 4.695, P < 0.001), and renal stones (OR 8.232, P < 0.001) were independently associated with upper UTI.

Conclusion: This study shows that patients with CKD and UTIs were elderly, and that females were prone to have more bacteriuria and upper UTIs than males. In addition, patients who had renal stones were more prone to have upper UTI than other bacteriuria patients. Aggressive treatment of renal stones should be considered in these patients.

Key words: Urinary tract infection, chronic kidney disease, renal failure, renal stones, bacteriuria

1. Introduction

Urinary tract infection (UTI) is not uncommon in females and patients who are diabetic, are immunocompromised, have anatomic abnormalities, are incontinent with indwelling catheter, or are of advanced age (1–7). It is also the most common bacterial infection acquired in the community and in hospitals (8). Recurrent UTIs are usually found in women and should receive further treatment to prevent kidney damage (9). Chronic kidney disease (CKD) may result from recurrent UTIs and retrospective infection to the kidneys. However, there are few studies of patients with CKD and UTI (10).

CKD has already become a burden of global health (11,12). With advances in hemodialysis and medical care, patients sustaining CKD have had prolonged survival. Even so, these patients may have some medical problems that cause CKD, such as diabetes mellitus (DM), uncontrolled high blood pressure, primary kidney diseases, or drug toxicities, which may result in chronic medical problems. They may have complications of reduced kidney function, such as hypertension, malnutrition, anemia, bone disease, and decreased quality of life (13). In addition, due to prolonged hemodialysis that may compromise their immune system, they are vulnerable to infection, including UTIs. Nevertheless, the incidence of UTIs in patients with CKD is unclear and the literature on the management of UTIs in these patients is sparse (14). Besides, to our knowledge, the literature has not addressed the differences of demographic and urological variables between upper and lower UTIs in patients with CKD.

In this study, we retrospectively reviewed patients who had CKD with UTIs and compared patient demography, medical histories, and infecting bacteria between upper and lower UTIs. The objectives of this study were to

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address some of the shortcomings of the literature and to seek to understand the differences of demographic and urological variables between upper and lower UTIs in patients with CKD.

2. Materials and methods

2.1. Study subjects and setting

We conducted a retrospective cohort study by reviewing the records for all patients who had CKD sustaining bacteriuria with UTI and were admitted to our nephrology ward in the middle county of Taiwan over the 6-year period from 1 January 2005 to 31 December 2011. The medical facility, located in the center of a county with a population of 547,709 people, provides health care with 1000 hospital beds, an outpatient department serving approximately 3800 persons daily, and an emergency department serving 260 persons daily. We included patients who had CKD sustaining bacteriuria with UTI during admission to our hospital from the emergency department or outpatient clinic. Patients on admission found to be without bacteriuria, who had CKD and were on dialysis therapy, who had been transferred from other facilities, who had received antibiotic treatments before urine culture, or who lacked complete chart records were all excluded.

Although this was a retrospective study, all data collected in this study were recorded prospectively when patients were admitted to the hospital. A standard form for chart review was used for data collection. To ensure the accuracy of the data, charts were reviewed and encoded by a senior training nurse for full-time research and double-checked by a nephrologist for demographic information and clinical data, including types of antibiotic treatment, stage of CKD, associated concomitant infections, management scheme, adjunctive treatment, and outcome. Review meetings were held to resolve disputed coding errors on a weekly basis.

Among patients with CKD, the stage of disease was assigned based on the level of kidney function, irrespective of diagnosis, according to the Kidney Disease Outcomes Quality Initiative CKD classification (15). We reviewed medical records of the patients and determined the stage of CKD when bacteriuria was diagnosed at our hospital. Stage I was kidney damage with normal or high glomerular filtration rate (GFR) of 90 mL/min or more; stage II was a mild decrease in GFR to 60 to 89 mL/min; stage III was a moderate decrease in GFR to 30 to 59 mL/min; stage IV was a severe decrease in GFR to 15 to 29 mL/min; and stage V was kidney failure with GFR of less than 15 mL/min or on dialysis.

The indications to culture the urine were tested in symptomatic patients with UTI or UTI suspicion, or under certain circumstances in risk groups with fever. A midstream clean-catch urine sample was collected by standard procedure. For catheterized specimens, a trained health care provider inserted a thin rubber tube or catheter through the urethra into the bladder and the urine sample was taken and placed in a sterile container at the other end of the tube. Bacteriuria was defined as any microorganisms present (growth of 100,000 CFU/mL bacteria in the culture) in the urine sample growing over the next 24 to 48 h as small circular colonies when urine was placed on 1 or more agar plates and incubated at body temperature. If there was more than 1 type of bacteria present in relatively large numbers, clinical symptoms were reviewed and it was determined by a nephrologist whether the colonies came from contamination of the skin picked up during the urine collection or by true infection. Bacteriuria patients who had pyelonephritis, renal abscess, and emphysematous pyelonephritis were defined as having upper UTIs, while cystitis and urethritis were defined as lower UTIs. Patients admitted to our ward with flank pain and fever received abdominal echogram and X-ray for further evaluation of the causes. Abdominal computed tomography (CT) was arranged according to further findings of a previous survey or if it was known from patient history that he or she suffered from renal stones. Patients who had renal stones were diagnosed by X-ray, abdominal CT, or echogram. Blood samples were drawn along with urine collection for laboratory tests and cultures for aerobic and anaerobic bacteria during admittance to the ward or our emergency department before antibiotics treatment.

In our hospital, patients with UTIs caused by bacteria are treated with antibiotics as suggested by the nephrologist or infection specialist. All patients with CKD included in this study received regular follow-up at our outpatient clinic and were followed for more than 6 months. If the patient's renal function deteriorated, hemodialysis was regularly performed at our hospital. Patients were considered for long-term Foley insertion if they had difficulty voiding without antibiotics treatment if no severe symptoms of infection were found.

2.2. Statistical analysis

Patient demographics, laboratory data, and selected variable relationships were characterized using descriptive statistics with the mean and standard deviations. Categorical variables were analyzed using chi-square analysis. One-way analysis of variance (ANOVA) was performed comparing stage of CKD against creatinine (Cr). Patients were divided into upper and lower UTI groups. The demographic and clinical characteristics between groups were evaluated using univariate analysis. For continuous variables, Student t-tests were used to compare means for normal distributed data, while the Pearson chi-square test was used for categorical variables; Fisher exact tests and continuity corrections were used where appropriate. A forward stepwise logistic regression was applied to determine the predictors for upper UTIs. All variables in the univariate analysis with 2-sided P-values of ≤0.20 were candidates for inclusion in the logistic regression model to assess which variables were associated with upper UTIs. Using a stepwise selection method, individual covariates were retained in the final model based on the maximization of model fit (r^2), while taking into account each additional covariate selected. A P-value of less than 0.05 was considered significant. All data were analyzed using qualified statistical software (SPSS for Windows 15; SPSS Inc., Chicago, IL, USA).

3. Results

A total of 276 bacteriuria patients were admitted to our ward with symptoms of upper UTIs and possible lower UTIs from 1 January 2005 to 31 December 2011. Among these patients, 73 patients (26.4%, 73/276) were confirmed to have upper UTIs and 203 patients were found to have lower UTIs (73.6%, 203/276) without progression to the kidneys. The average ages of the upper and lower UTI patients were 59.21 ± 16.54 and 71.18 ± 14.77 years, and so the patients who had upper UTIs were younger than those with lower UTIs (P < 0.001). There was significant difference in the numbers according to sex between patients of the 2 groups (P < 0.001). Females (36.1%, 60/166) were more prone to have upper UTIs than males (11.8%, 13/110).

Of these 276 patients, 38 (13.8%) had stage I CKD (Cr 1.40 ± 1.79), 91 (33.0%) stage II CKD (Cr 1.21 ± 1.00), 102 (37.0%) stage III CKD (Cr 1.79 ± 1.21), 37 (13.4%) stage IV CKD (Cr 2.94 ± 2.26), and 8 (2.9%) stage V CKD (Cr 4.97 ± 2.56). There was a statistically significant difference of Cr levels between the different stages of CKD (P < 0.001). Nevertheless, there was no significant difference in the stage between the 2 groups.

When the 2 groups were compared for DM, hypertension, liver cirrhosis, and renal stones (P = 0.396, 0.309, 0.604, and <0.001, respectively), only renal stones had a significant difference between the groups. Foley catheter insertion was also compared between the 2 groups (P < 0.001). However, 32 patients who had Foley insertion had UTIs and only 1 of these patients had an upper UTI (Table 1). When bacteria of infections between upper and lower UTIs were compared, there were no significant differences between the bacteria in the 2 groups (P = 0.903).

The results of logistic regression analysis showed that age (OR 0.946, 95% CI 0.926 to 0.967, P < 0.001), female sex (OR 4.695, 95% CI 2.173 to 10.146, P < 0.001), and renal stones (OR 8.232, 95% CI 3.450 to 19.646, P < 0.001) were independently associated with upper UTIs after adjustment for DM, liver cirrhosis, and Foley insertion (Table 2). The model adequately fitted the data with Hosmer–Lemeshow statistics (P = 0.110).

Table 1. Demographics, averaged physiological parameters, and variables in both UTI groups.

Variables	Upper UTI (n = 73)	Lower UTI (n = 203)	P-value
Age	59.21 ± 16.54	71.18 ± 14.77	<0.001†
Sex (Female)	60 (82.2%)	106 (52.2%)	<0.001*
Hypertension	26 (35.6%)	64 (31.5%)	0.523*
DM	25 (34.2%)	75 (36.9%)	0.396*
Liver cirrhosis	3 (4.1%)	9 (4.4%)	0.907*
Renal stones	25 (34.2%)	17 (8.4%)	<0.001v
Foley insertion	1 (1.4%)	31 (15.3%)	0.001*
Bacteria			
Escherichia coli	43 (58.9%)	104 (51.2%)	0.260*
Proteus	6 (8.2%)	6 (3.0%)	0.059*
Klebsiella	3 (4.1%)	16 (7.9%)	0.275*
Enterococcus	0 (0%)	12 (5.9%)	0.034*
Pseudomonas	2 (2.7%)	14 (6.9%)	0.192*
Staphylococcus	0 (0%)	1 (0.5%)	0.548*

P-values are based on the chi-square test (*) and on the Student t-test (†).

Table 2. Independent risk factors* associated with upper UTI.

	OR	95% CI	P
Age	0.954	0.935–0.973	<0.001
Sex (Female)	4.695	2.178–9.968	<0.001
Renal stones	7.927	3.372–18.635	<0.001
Foley insertion	7.167	0.884–58.121	0.065

*: The risk factors included in the logistic regression model were age, sex, renal stones, and Foley insertion.

4. Discussion

In our study, we found that patients who were younger, were female, and had renal stones with urobacteria were more prone to have upper UTIs, and patients who had indwelling urinary catheters were more prone to have lower rather than upper UTIs. However, we did not found any statistical differences of infective bacteria between the upper and lower UTI groups in patients with CKD.

In a study by Zhang et al., they found a high prevalence (17.4%) of CKD among older adults (50 to 74 years) from 9806 participants (13). In our patients with CKD, we found that although these patients were mostly seniors, patients who had upper UTIs (59.21 ± 16.54 years) were younger than those with lower UTIs (71.18 ± 14.77 years).

Females are prone to UTIs due to the shortness of the urethra, which is close to the vagina and anus; the lack of prostatic fluid, which has antibacterial activity; or the use of spermicides and/or diaphragms (16). In our study, we found that there were more females than males in both the upper and lower UTI groups. In addition, about 25% of our patients who had a lower UTI developed an upper UTI, and the number of females was triple that of males. Since women have up to a 10% risk of recurrent acute pyelonephritis in the year following the first acute episode and the equivalent risk in men is 6% (17), the findings may result from recurrent lower UTIs finally developing into upper UTIs.

In this study, we found that *Escherichia coli* was the bacteria infecting half of the patients regardless of sex. Since *Escherichia coli* is the most infective bacteria in UTI patients (18), it is not surprising that it also infected half of the patients with CKD. In addition, we found that there was no statistical difference in the bacteria cultured from upper or lower UTIs. In a previous study, the most frequent cause of upper UTI was also *E. coli* (19). Thus, empirical use of antibiotics in these patients with gram-negative infection is still effective in patients with CKD.

Urolithiasis was a potential cause of upper UTI in our patients with a higher odds ratio. In previous studies, urolithiasis was found to be one of the risk factors of subsequent treatment failure of or mortality from upper UTI (20,21). Due to patients with CKD being prone to having more medical problems, we suggest that early management of urolithiasis is critical in these patients to prevent further subsequent infection and damage to their kidneys.

Catheter-associated UTI is the most common of health care-associated infections (22). In our study, of the 32 patients with a urinary catheter, only 1 patient had an upper UTI. However, in patients with CKD who needed catheterization, the conditions were more complicated, with different underlying diseases. The relationship between catheterization and upper UTIs needs to be further determined.

There are some limitations of this study. One set of limitations is inherent in retrospectively reviewing medical records; therefore, the presence of symptoms could not be fully ascertained. However, although reviews were retrospective, the strengths of this study are the large number of patients included, its prospective collection, and the comprehensive clinical and microbiologic data gathered. Nevertheless, because this study was conducted at a single center and the sample size was relatively small for the subgroup of patients with catheter-associated urinary tract infection and the subgroup of bacterial infection, the results of statistic analyses may not be significant. Besides, as we defined “upper UTI” as emphysematous pyelonephritis, renal abscess, or acute pyelonephritis by image study or with typical features of urinary frequency/dysuria, flank tenderness, and high-grade fever accompanied by typical laboratory and microbiological findings, it is possible that this limitation may have hampered our ability to more precisely define the diagnostic role of upper UTIs. Another set of limitations may result from the patients with CKD having variants of underlying diseases with previous antibiotics treatment, which may confound the risk for upper UTI. This approach might lead to some underestimation of upper UTI in CKD.

In conclusion, in our study, females were more prone bacteriuria and upper UTIs than males among CKD patients. Bacterial infections between the upper and lower UTI groups showed no statistical difference. Therefore, an upper UTI infection may result from retrospective infection from a lower UTI. Treatment of CKD patients with upper UTIs can include empiric antibiotics according to the bacteriuria. Patients who had renal stones were more prone to having upper UTI as compared to other bacteriuria patients. Aggressive treatment of renal stones should be considered in such patients.

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The first 3 authors made equal contributions in this work and are all equally considered to be the "first author". The final 2 authors made equal contributions to this work and are both equally considered to be the "correspondence author".

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