



Original article

The gender specific risk factors for prolonged hospitalization due to acute pyelonephritis in a Japanese tertiary emergency center



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ABSTRACT

Objectives: The aim of this study is to characterize the potential differences between male and female patients with acute pyelonephritis (AP) and to predict the severity of AP based on the length of hospital stay.

Methods: We conducted a retrospective medical chart review of 172 consecutive adult patients who were hospitalized in Tsuyama Central Hospital due to AP from January 2007 through June 2012. We analyzed the length of hospital stay by the proportional hazard model.

Results: A total of 172 patients were identified who were admitted to our hospital with a diagnosis of AP. Of them, 62% (106/172) were female. Except for urological malignancy, there was no significant difference between men and women in underlying disease. Out of 26 variables, univariate analysis in male showed that only urolithiasis (OR 1.75, $p = 0.0294$) was significantly associated with longer hospital stay, while septic shock (OR 3.18, $P = 0.003$), urological malignancy (OR 2.94, $P = 0.002$), age over 65 (OR 1.66, $p = 0.018$) and neurogenic bladder (OR 1.92, $p = 0.014$) were all associated with longer hospital stay in female patients.

Conclusions: This is the first report to identify the risk factors for prolonged hospital stay for the patients who were admitted with AP in the Japanese population. The risk factors causing prolonged hospital stay were totally different between males and females. Reviewing the medical history based on sex gender might enable a clinician to predict the severity of acute pyelonephritis during the initial evaluation.

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1. Introduction

Urinary tract infections (UTIs) are considered the most common bacterial infections with an estimated annual global incidence of at least 250 million cases [1,2]. Acute pyelonephritis (AP) is one of the most severe forms of UTIs and can be lethal if it progresses to urosepsis or septic shock [3,4]. According to the data base of DPC/PDPS (Diagnosis Procedure Combination/Per-Diem Payment System) which included more than half of Japanese hospitals, in 2013

more than 50,000 patients were hospitalized due to AP with average hospital stay of 12.5 days in Japan [5].

Although numerous studies have focused on the antimicrobial resistance of bacteria that causes AP, limited studies are available to predict patients with AP who will respond poorly to treatment. Moreover, despite the fact that AP in women has been extensively studied, few studies regarding AP in men reported. One retrospective study found that several factors can be used to identify hospitalized patients with AP at greater risk of death or prolonged hospitalization as indicators of severity of AP [4]. Factors associated with death among men and women included age >65 years, septic shock, and bedridden status. Prolonged hospitalization, longer than 10 days, was noted among men and women with diabetes mellitus, long-term urinary catheterization, and change in initial antimicrobial therapy. However, the patients in this study tended to be

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more debilitated: 22.2% had evidence of septic shock at presentation. We compared and analyzed the characteristic of AP and risk factors of prolonged hospital stay due to AP between male and female patients in our Japanese tertiary emergency center.

2. Patients and methods

We conducted the study with retrospective medical chart review of all admissions to Tsuyama Central Hospital due to AP from January 2007 through June 2012. Data from 172 consecutive adult patients aged 20 years or older who were hospitalized with AP were analyzed. Criteria for diagnosis of AP was (1) fever, defined as an axillary temperature of 38 °C or greater; and (2) pyuria, defined as the presence of 5 or more leukocytes per high-power field in the centrifuged urine specimen. In all cases, a positive urine culture or pyuria was necessary for inclusion in the study. Factors that defined complicated AP included one or more of following; placement of catheter, structural or functional abnormalities of the urinary tract such as urothelial cancer, benign prostatic hyperplasia (BPH), neurogenic bladder (NB) and urolithiasis. Demographic data (age, gender, BMI), medical history (diabetes mellitus (DM), hypertension, cerebrovascular disease (CVD), coronary artery disease (CAD), dementia, Alzheimer's disease, psychiatric disease, chronic liver disease, genitourinary disease, genitourinary cancer, other cancer, urolithiasis, neurogenic bladder, abnormality of the genitourinary tract, bedridden status, disseminated intravascular coagulation (DIC), Septic shock, history of recent hospitalization, catheterization, benign prostatic hyperplasia, surgery), present symptoms (fever, altered level of consciousness, lower abdominal pain/back pain, CVA tenderness, vomiting/diarrhea, dysuria, pyuria, hematuria), laboratory data (CBC, basic metabolic panel, CRP, plasma glucose, HbA1c), and the resistance of microbes to antibiotics and treatment with antibiotics were recorded. Antimicrobial agents were administered empirically until the results of urine or blood cultures were known. This study was approved by the Institutional Review Board of Tsuyama Central Hospital (IRB136).

Urine sample for culture obtained by means of the midstream urine, in-and-out urethral catheterization, or pre-existing long-term indwelling catheterization, were incubated. For blood cultures, 10 mL of venous or arterial blood was obtained from patients and inoculated into aerobic and anaerobic bottles. At least 2 sets of blood cultures were obtained.

2.1. Statistical analysis

We compared demographics, each medical history, present symptoms and laboratory data between men and women using the chi-square for categorical data and t-test for continuous variables. All tests of significance were 2-tailed and a p-value of less than 0.05 was considered to be significant. We assessed differences in length of stay between all variables (demographic data, medical histories, laboratory results, present symptoms) by the Kaplan–Meier analysis and the proportional hazard model. In these analyses, we made adjustments of hospital stay based on duration of the treatment with intravenous antibiotics because patients who stayed hospital for other medical or social reasons would count as having a longer length of hospital stay.

3. Results

In the period January 2007–June 2012, a total of 172 patients were identified who were admitted to our hospital with a diagnosis of AP. Of them, 62% (106/172) were female, with the median age of 70 years old (interquartile range (IQR) 57–80) while the median age was 73 (IQR 58–78) in male patients. 119 (69%) patients had

complicated AP, defined as the presence of urolithiasis (48%, 63/119), urinary drainage issues including nephrostomy (14%, 18/128), ureteral stents (44%, 56/128), or urethral catheters (42%, 54/128). The proportion of complicated AP was significantly higher in the male group than in the female group [91% (60/66) vs. 56% (59/106); $p < 0.0001$]. Except for urological malignancy, there were no significant differences between men and women in underlying diseases. Regarding initial laboratory findings, male patients had higher CRP ($p = 0.0293$). On presentation, women had more frequent complaints of lower abdominal pain and vomiting/diarrhea ($p = 0.0351$ and 0.0200 , respectively) as shown in Table 1.

Of 133 patients with the positive urine culture, most infections were monomicrobial, with *Escherichia coli* (47%) being the most frequent causative organism. The other organisms included *Pseudomonas aeruginosa* (13%), *Klebsiella pneumoniae* (11%) and fourteen cases (11%) were caused by multi-drug resistant pathogens, including 11 extended spectrum beta-lactamase (ESBL) producing bacteria, 1 methicillin-resistant staphylococcus aureus (MRSA), 1 multi-drug resistant pseudomonas aeruginosa (MDRP), and 1 methicillin-resistant staphylococcus heamoliticus were more frequent in women ($p = 0.0001$) but *Pseudomonas* and *Enterococcus* species were more frequent in men ($p = 0.0043$ and 0.0050 , respectively) as shown Table 2.

Table 1
Patients' clinical and laboratory characteristics.

	Female	%	Male	%	p-value
Sex	106		66		
Age ≥ 65	69	65	45	68	0.6770
DM	16	16	15	28	0.0767
Hypertension	20	19	10	15	0.5322
Urolithiasis	34	32	29	44	0.1272
Neurogenic bladder	15	14	9	14	0.9556
Hydronephrosis	35	35	20	31	0.6513
Bedridden status	18	17	19	29	0.0669
Dementia/Alzheimer's disease	11	10	2	3	0.0763
Psychological disease	7	6	2	3	0.3061
CVD	17	16	18	27	0.0751
CAD	9	8	4	6	0.5577
Urologic anomaly	6	6	3	5	0.7495
Liver disease	8	6	2	3	0.2183
Urological malignancy	8	8	15	23	0.0044
Non-urologic malignancy	11	10	8	12	0.7227
BPH	NA	NA	8	12	NA
Complicated AP	59	56	60	91	<0.0001
Bacteremia	27	33	12	23	0.1683
Sepsis	6	6	2	3	0.4257
DIC	6	6	2	3	0.4257
Present symptoms					
Fever >39	47	55	28	52	0.6915
Lower abdominal pain	47	46	17	29	0.0351
Vomiting/diarrhea	30	28	8	13	0.0200
CVA tenderness	37	40	15	29	0.1878
Dysuria	20	20	14	23	0.6716
Hematuria	89	89	56	97	0.0959
Altered level of consciousness	16	15	6	9	0.2663
	Female		Male		
	Median	IQR	Median	IQR	p-value
Age	70	57–80	73	58–78	0.7720
BMI	22.9	19.8–25.1	26.1	20.0–26.0	
Initial laboratory findings					
WBC ($\times 10^3$)	11.9	9.3–15.6	13.4	9.9–18.9	0.1035
Hb	12	10.9–13.0	12.5	10.9–13.6	0.1885
CRP	11.6	6.1–19.6	15.2	9.5–21.7	0.0293
eGFR	53	38–68	50	36–71	0.6169

DM; Diabetes mellitus, CVD; cerebrovascular disease, CAD; coronary artery disease, BPH; benign prostate hyperplasia, DIC; disseminated intravascular coagulation, CVA; costovertebral angle, BMI; body mass index, WBC; white blood cells, Hb; hemoglobin, CRP; C-reactive protein, eGFR; estimated glomerular filtration rate.

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