박 사 학 위 논 문

Clinical and Genotypic Characteristics of Uropathogenic *Escherichia coli* Strains According to Gender in Korea

계 명 대 학 교 대 학 원

의 학 과

현 미 리

지도교수 김 현 아

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지도교수 김 현 아

이 논문을 박사학위 논문으로 제출함

2019년 8월

계 명 대 학 교 대 학 원

의학과 내과학 전공

현 미 리

현미리의 박사학위 논문을 인준함

주 심 류 성 열

부 심 김 현 아

부 심 김 유 철

부 심 이 지 연

부 심 홍 효 림

계 명 대 학 교 대 학 원

2 0 1 9 년 8 월

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저의 사랑하는 가족들에게 이 논문을 바칩니다.

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현 미 리

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1. Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections in the world. UTIs can be classified into three categories according to the site of infection: cystitis, pyelonephritis, and prostatitis (1). The admissions for UTI and the associated costs have been increasing in the United States (2). Also, UTIs are one of the major healthcare-associated infections (HAIs) (3) and account for up to 32% of all HAIs (4). Among the uropathogens, uropathogenic *Escherichia coli (E. coli)* account for up to 90% of community-onset UTIs (1) and 50% of healthcare-associated UTIs (5). Uropathogenic *E. coli* have many virulence factors, including adhesins and toxins, and properties such as iron acquisition and immune evasion that enable them to invade, colonize, and survive in the urinary tract. In addition, biofilm formation is an important mechanism that protects bacteria from the external environment (6). UTIs can occur in patients with the following predisposing factors: a neurogenic bladder, obstructive uropathies, such as benign prostate hyperplasia and uterine prolapse, and the use of urologic devices including Foley catheters (7). UTIs occur predominantly in females but can affect male patients as well; anatomical differences and various predisposing factors can vary according to gender. Complicated UTI is higher in males and clinical characteristics of UTI might be different according to gender (8). However, there are few studies that have investigated the association of UTI with gender. The purpose of this study was to compare the clinical characteristics, antimicrobial susceptibility, and genotypic factors of uropathogenic *E. coli* according to gender.

2. Materials and Methods

2.1. Patients and Bacterial Strains:

From February 2015 to June 2018, *E. coli* isolates from blood, urine, or pus were collected from patients at Keimyung University Dongsan Medical Center in Korea. This study was approved by the Institute Review Board of the Keimyung University Dongsan Medical Center (File No. 2019-05-075). Medical records were reviewed retrospectively. Only one isolate per patient was examined. Inclusive criteria for UTI were defined as both quantitative culture of $> 10^5$ CFU/mL for *E. coli* isolated from midstream urine or catheter, and the presence of urinary symptoms, such as urgency, frequency of urination, and dysuria. We relied on medical records for this information. Diagnostic criteria for upper UTI included fever, flank pain, urinary symptoms and/or tenderness of the costovertebral angle.

Susceptibility of *E. coli* strains, investigated using the interpretive criteria according to the Clinical and Laboratory Standard Institute (CLSI) guidelines, was determined for ampicillin, ampicillin/sulbactam, piperacillin/tazobactam, amikacin, gentamicin, cefazolin, cefoxitin, ceftazidime, cefepime, ciprofloxacin, ertapenem, imipenem, tigecycline and trimethoprim/sulfamethoxazole.

2.2. Phylogenetic analysis and detection of *Escherichia coli* virulence factors:

The phylogenetic grouping of the *E. coli* isolates was determined by the polymerase chain reaction (PCR)-based method developed by Doumith et al. *E. coli* isolates were assigned to one of the four main phylogenetic groups (A, B1, B2, and D) (9).

Crude DNA was prepared by lysis of colonies at 100 ℃ for 15 min in 500 μL of sterile distilled water, followed by centrifugation. The lysis supernatant was used for the PCR. The PCR conditions comprised an initial activation at 95 ℃ for 12 min, followed by 25 cycles at 95 ℃ for 30 s, 63 ℃ for 30 s, 68 ℃ for 4 min, and a final extension period at 72 ℃ for 10 min. The amplicons were separated at 100 V for 2 h on a 2% agarose gel containing ethidium bromide. The presence of the virulence factors, adhesion proteins (*papA, papC, papEF, papG, papG alleleI, papG alleleII, papG alleleIII, sfaS, fimH, afa/draBC, bmaE*), toxins (*hlyA, cdtB*), siderophores (*fyuA, iutA*), capsule synthesis proteins (*kpsMTII, kpsMTIII*), and uropathogenic-specific protein (*usp*), was analyzed by PCR using primers listed in Table 1 (10).

2.3. Definition of Terms:

Obstructive UTI was defined as urinary obstruction due to one of the following: benign prostate hyperplasia, uterine prolapse, or malignancy. Severe UTI was defined as severe sepsis or septic shock due to UTI. Complicated UTI was defined as UTI in the presence of factors that predispose the patient to persistent or relapsing infection, such as foreign bodies (e.g., indwelling urinary catheters or other drainage

devices), and obstructions. Acute kidney injury was defined as an increase in serum creatinine by > 0.3 mg/dL within 48 hours; or an increase in serum creatinine to > 1.5 times baseline, occurring within the first 7 days; or urine volume < 0.5 mL/kg per hour for 6 hours. Prior antibiotics within 3 months was defined as usage of antibiotics for at least 2 days within 3 months.

The early outcome was determined by persistent fever, defined as fever that persisted over 72 hours. The late outcome was determined by infection related 30-day mortality and relapsed UTI within 3 months. Infection related 30-day mortality was defined by death of the patient due to a uropathogenic *E. coli* UTI or complication of infection within 30 days.

2.4. Statistical Analysis:

Categorical variables were described using frequencies and percentages, while continuous variables were described using mean, median, and interquartile range (IQR). All statistical analysis was performed using Statistical Package for the Social Sciences software version 21.0 (SPSS Inc., IBM Corp., Armonk, NY, USA). The Pearson χ^2 test and Fisher's exact test were used for categorial data. Independent t-test was used to compare continuous variables. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Baseline Characteristics:

A total 351 patients were enrolled in this study; 289 cases were females and 62 cases were males. The mean age for females was 69.98±14.55 years and 70.92±13.36 years for males. Based on the category of infections, community-onset UTI was more observed in female. In underlying diseases, chronic liver disease, neurologic disease, and chronic lung disease were associated more with males, without significance. The incidence of diabetes mellitus was higher in females (Table 2).

3.2. Comparison of Predisposing Factors:

Neurogenic bladder and obstructive uropathy were observed more in males. Urogenic anomaly and nephrectomy were no significant differences between the two groups, respectively. Urinary catheter and intermittent catheterization were observed more in males, with significance. Urinary tract stone was observed more in males, without significance. Prior usage of antibiotics within 3 months were associated more with males (Table 2). Third generation cephalosporin (44.2% vs. 52.2%, p=0.525) and fluoroquinolone (46.2% vs. 47.8%, p=0.894) were commonly used antibiotics previously in both groups without significance.

3.3. Comparison of Clinical Characteristics:

Based on the category of disease, acute pyelonephritis was observed in 286 cases (99.0%) of females and 57 cases (91.9%) of males. Renal abscess was detected in 24 cases (8.3%) of females and 3 cases (4.8%) of males. In males, acute prostatitis and prostatic abscess were observed in 10 cases (16.1%) and 4 cases (6.5%), respectively. The concomitant bacteremia was observed more in males, with significance. Hydronephrosis was more frequent in females, without significance. Complicated UTI was associated more with males. The proportion of severe UTI was no significant differences between the two groups. Acute kidney injury was associated more with males, without significance (Table 3).

3.4. Comparison of Antimicrobial Resistance, Empirical Antibiotics, and Antibiotic adequacy:

Antibiotic resistance rates of amoxicillin/clavulanate, cefazolin, cefotaxime, cefepime, aztreonam, ciprofloxacin, and gentamicin were significantly higher in males. There were no significant differences between the two groups with regard to antibiotic resistance rates of piperacillin/tazobactam and trimethoprim/sulfamethoxazole. Rates of ESBL-producing *E. coli* were 64.5% in males and 34.7% in females (Table 4). In comparison of adequacy of empirical antibiotics according to antibiotic susceptibility, concordant rates of initial antibiotics were higher in females (73.7% vs. 48.4%, p=0.001).

3.5. Comparison of Treatment Outcomes:

In males, more patients had persistent fever than females. The need for invasive procedures was observed more in males, without significance. There were no significant differences between the two groups with regard to infection related 30-day mortality. Relapsed UTIs within 3 months were observed more in male. Hospital stay and total duration of antibiotics were longer in males than in females (Table 5).

3.6. Comparison of Phylogenetic Group and Virulence Factors:

In the phylogenetic group, B2 was the most common group in total patients including male and female. B2 was observed more in males and D was observed more in females, with significance. In virulence factors, *hlyA, cnf1* in toxin, *usp* in PAI, *iutA* in iron acquisition were more associated with male. *KpsMT II* in protectins was associated more with females (Table 6). Adhesins, *papA*, and *fimH* were present 65.2% and 97.6% in female, 68.9% and 100.0% in male, respectively. The toxins, *cnf1* and *hlyA* were present in 26.6% and 23.1% in females and 51.8% and 48.3% in males, respectively. Siderophores, *fyuA* was present in 96.2% in female and 96.7% in male, more present than *iutA*, 70.7% in female and 83.6% in male.

Table 1. Primers Used in This Study

Primer	Sequence
fimH	
Forward	5'-TGCAGAACGGATAAGCCGTGG-3'
Reverse	5'-GCAGTCACCTGCCCTCCGGTA-3'
iha	
Forward	5'-CTGGCGGAGGCTCTGAGATCA-3'
Reverse	5'-TCCTTAAGCTCCCGCGGCTGA-3'
papA	
Forward	5'-ATGGCAGTGGTGTTTTGGTG-3'
Reverse	5'-CGTCCCACCATACGTGCTCTTC-3'
sfa	
Forward	5'-CTCCGGAGAACTGGGTGCATCTTAC-3'
Reverse	5'-CGGAGGAGTAATTACAAACCTGGCA-3'
afaC	
Forward	5'-CGGCTTTTCTGCTGAACTGGCAGGC-3'
Reverse	5'-CCGTCAGCCCCCACGGCAGACC-3'
chuA	
Forward	5'-CCCAGAGATATCGAGGCTTGCA-3'
Reverse	5'-TCACGGATATCGCCGCGCATC-3'
fyuA	
Forward	5'-TGATTAACCCCGCGACGGGAA-3'
Reverse	5'-CGCAGTAGGCACGATGTTGTA-3'
iutA	
Forward	5'-CCTCTAGATGATGCGCAAAAAGTATATGC-3'
Reverse	5'-GGAAGCTTCAGAACAGCACTGAGTAGTT-3'
kpsMII	
Forward	5' GCGCATTTGCTGATACTGTTG-3'
Reverse	5'-CATCCAGACGATAAGCATGAGCA-3'
cnf1	
Forward	5'-AAGATGGAGTTTCCTATGCAGGAG-3'
Reverse	5'-TGGAGTTTCCTATGCAGGAG-3'
hlyA	
Forward	5'-AACAAGGATAAGCACTGTTCTGGCT-3'
Reverse	5'-ACCATATAAGCGGTCATTCCCGTCA-3'
usp	
Forward	5'-ATGCTACTGTTTCCGGGTAGTGTGT-3'
Reverse	5'-CATCATGTAGTCGGGGCGTAACAAT-3'

Table 2. Baseline Characteristics of Uropathogenic *Escherichia coli* Infection Classified by Gender

	Female (n = 289)	Male (n = 62)	p value
Age, years	68.98±14.55	70.92±13.36	NS
Category of infection			
Community-onset infection	220(76.1%)	35(20.6%)	< 0.05
Underlying diseases			
Solid tumor	39(13.5%)	10(16.1%)	NS
Chronic liver disease	39(13.5%)	13(21.0%)	NS
Cardiovascular disease	73(25.3%)	19(30.6%)	NS
Hypertension	157(54.3%)	17(50.0%)	NS
Neurologic disease	96(33.2%)	27(43.5%)	NS
Chronic renal disease	13(4.5%)	6(9.7%)	NS
DM	124(42.9%)	17(27.4%)	< 0.05
Chronic lung disease	29(10.0%)	11(17.7%)	NS
Solid organ transplantation	2(0.7%)	0(0.0%)	NS
Predisposing factors			
Neurogenic bladder	22(7.6%)	12(19.4%)	< 0.05
BPH or uterine prolapse	3(1.0%)	27(43.5%)	< 0.001
Urogenic anomaly	3(1.0%)	1(1.6%)	NS
Nephrectomy state (one kidney)	3(1.0%)	1(1.6%)	NS
Neutropenia	0(0.0%)	0(0.0%)	NS
Previous genitourinary surgery or procedure within 72 hours	0(0.0%)	0(0.0%)	NS
Recurrent UTI	34(11.8%)	5(8.1%)	NS
Presence of urologic devices	0(0.0%)	1(1.6%)	NS
Intermittent catheterization	0(0.0%)	2(3.2%)	< 0.05
Urinary catheter	29(10.0%)	14(22.6%)	< 0.05
Prior antibiotics within 3 months	53(18.3%)	23(37.1%)	< 0.001

DM: diabetes mellitus; BPH: benign prostate hyperplasia; UTI: urinary tract infection.

Table 3. Clinical Manifestation of Uropathogenic *Escherichia coli* Infection Classified by Gender

	Female (n = 289)	Male (n = 62)	p value
Bacteremia	172(59.5%)	46(74.2%)	< 0.05
Category of diseases			
Acute pyelonephritis	286(99.0%)	57(91.9%)	< 0.05
Cystitis	18(6.2%)	5(8.1%)	NS
Acute prostatitis	0(0.0%)	10(16.1%)	< 0.001
Renal abscess	24(8.3%)	3(4.8%)	NS
Prostatic abscess	0(0.0%)	4(6.5%)	< 0.001
Complicated UTI	18(6.2%)	47(75.8%)	< 0.001
Severe UTI	98(33.9%)	21(33.9%)	NS
Acute kidney injury	47(16.3%)	13(21.0%)	NS

UTI: urinary tract infection.

Table 4. Antibiotic Resistance of Uropathogenic *Escherichia coli* Classified by Gender

	Female (n = 289)	Male (n = 62)	p value
Resistance			
Amikacin	1(0.3%)	1(1.6%)	NS
Amoxicillin/clavulanate	97(33.7%)	32(51.6%)	< 0.05
Ampicillin	211(73.3%)	53(85.5%)	< 0.05
Aztreonam	99(34.4%)	40(64.5%)	< 0.001
Cefazolin	114(39.6%)	40(64.5%)	< 0.001
Cefepime	99(34.4%)	40(64.5%)	< 0.001
Cefotaxime	104(36.1%)	40(64.5%)	< 0.001
Cefoxitin	24(8.3%)	8(12.9%)	NS
Ceftazidime	99(34.4%)	40(64.5%)	< 0.001
Ciprofloxacin	113(39.2%)	43(69.4%)	< 0.001
Ertapenem	0(0.0%)	0(0.0%)	NS
Gentamicin	87(30.2%)	28(45.2%)	< 0.05
Imipenem	0(0.0%)	0(0.0%)	NS
Piperacillin/tazobactam	23(8.0%)	6(9.7%)	NS
Tigecycline	0(0.0%)	0(0.0%)	NS
Trimethoprim/sulfamethoxazole	116(40.3%)	25(40.3%)	NS
ESBL producer	100(34.7%)	40(64.5%)	< 0.001

ESBL: extended-spectrum beta-lactamase.

Table 5. Outcomes of Uropathogenic *Escherichia coli* Infection Classified by Gender

	Female (n = 289)	Male (n = 62)	p value
Persistent fever	54(18.7%)	25(40.3%)	< 0.001
Needs for invasive procedure	34(11.8%)	9(14.5%)	NS
30-day mortality	4(1.4%)	1(1.6%)	NS
Infection related 30-day mortality	2(0.7%)	0(0.0%)	NS
Total hospital stays, days	13.38±9.30	19.74±13.25	< 0.001
Total duration of antibiotics, days	21.47±11.18	24.95±10.80	< 0.05
Relapse within 3 months	19(6.6%)	7(11.3%)	NS

Table 6. Phylogenetic Groups and Virulence Factors of Uropathogenic *Escherichia coli* Classified by Gender

	Female (n = 289)	Male (n = 62)	p value
Phylogenetic group			< 0.05
A	3(1.0%)	2(3.2%)	
B1	11(3.8%)	1(1.6%)	
B2	216(75.3%)	55(88.7%)	
D	57(19.9%)	4(6.5%)	
Virulence factors			
usp	203(70.7%)	52(85.2%)	< 0.05
papA	187(65.2%)	42(68.9%)	NS
fimH	280(97.6%)	61(100.0%)	NS
kpsMT III	6(2.1%)	0(0.0%)	NS
papEF	38(13.2%)	10(16.4%)	NS
ibeA	15(5.2%)	3(4.9%)	NS
fyuA	276(96.2%)	59(96.7%)	NS
bmaE	3(1.0%)	0(0.0%)	NS
iutA	203(70.7%)	51(83.6%)	< 0.05
K1	80(27.9%)	12(19.7%)	NS
hlyA	65(23.1%)	29(48.3%)	< 0.001
kpsMT II	173(61.3%)	24(40.0%)	< 0.05
papC	193(68.4%)	47(78.3%)	NS
cnf1	69(26.6%)	29(51.8%)	< 0.001

4. Discussion

In our study, we found some differences in predisposing factors, clinical characteristics, antimicrobial resistant rates, and genotypic characteristics according to gender. Males were associated more with healthcare-associated UTI and predisposing factors, such as neurogenic bladder, obstructive uropathy, and indwelling urinary catheter. Males showed higher antimicrobial resistant rates, concomitant bacteremia, and persistent fever than females. In the phylogenetic group, B2 was observed more in males and D was associated more with females. In terms of virulence factors, *hlyA, cnf1* in toxin, *usp* in PAI, *iutA* in iron acquisition were observed more in male. *KpsMT II* in protectins was associated more with females.

Clinical spectrum of UTI ranged from asymptomatic bacteriuria to cystitis, pyelonephritis and prostatitis to septic shock (1). Complicated UTI was accompanied by several predisposing factors, such as urinary device and neurogenic bladder. Urinary catheters can be served as common predisposing substrates of UTIs (11). Residual urine volume can be associated with the development of UTI; greater than 100 mL resulted in a 4.9-fold increase in UTI occurrence compared to less than 100 mL (12). Increased intravesical pressure, such as neurogenic bladder, can result in bladder ischemia and delayed immune responses to uropathogens (13).

UTI is one of the most distinctive gender differences among infectious diseases. Classically, the anatomic differences, such as short urethral length in females, are well known causes for the vulnerable state of UTI in female. Premenoposal women experience UTI about 40 times more likely than the same aged men. The incidences of UTI are similar

between the genders in infants and the elderly (14). However, the clinical research about UTI has been focused on UTI in females. In our study, we found that the morbidity and predisposing conditions are important elements for the occurrence of UTI as well as anatomic differences, especially in males. For example, males had higher morbidity and used urinary catheter and prior antibiotics more frequently than females. Because of these differences, males and females may have shown different clinical characteristics and antimicrobial resistant rates. In a comparative study between males and females with UTI in Italy, males showed higher proportion of sepsis and mortality than females. *E. coli* was the most common uropathogen, followed by *Klebsiella* species, *Proteus* species, *Pseudomonas aeruginosa (P. aeruginosa)*, and *Streptococcus* species. The in-hospital mortality was more dependent on pathogens, especially *P. aeruginosa,* and female than comorbidity index and age (14). In a UTI study in males in Spain, which compared healthcare-associated and community-acquired UTIs, *E. coli* was the most common uropathogen, and was found in over 80% of the community-acquired UTIs and in nearly 50% of the healthcare-associated UTIs. *Klebsiella* species, *P. aeruginosa*, *Enterobacter* species, and *Enterococcus* species were more frequently associated with healthcare-associated UTIs than community-acquired UTIs. In-hospital mortality was associated with severe sepsis or septic shock, and liver cirrhosis (15). Ingersoll et al. proposed that the similar incidence of UTIs in male and female infants and the elderly is associated with the sex hormone, testosterone. This team conducted research on the inflammatory reaction and cytokine response associated with UTIs using male and female mice. In their study, females exhibited a more robust cytokine response as compared to males, and the increased severity of UTIs in males was due to the

testosterone-mediated suppression of the innate immune response (16).

E. coli was first described in 1885 by Theodor Escherichi, a German pediatrician. In 1893, Jensen found that *E. coli* species consist of pathogenic and non-pathogenic strains. Traditionally, pathogenic strains of *E. coli* were classified by the identification of O antigens, K antigens, and H antigens. Today, *E. coli* are classified according to genetic and clinical criteria into three main groups: commensal, intestinal pathogenic, and extraintestinal pathogenic strains (6). Among the extraintestinal pathogenic *E. coli*, some strains that had the ability to survive in the gut and colonize at the periurethral area and result in urinary tract infections were uropathogenic *E. coli*. A phylogenetic study revealed that *E. coli* can be separated into four major groups: A, B1, B2, and D (17). Uropathogenic *E. coli*, known as virulent strains, belong to the phylogenetic group B2 or D, and the less virulent strains mainly belong to A or B1 and are commensal strains (10). The phylogenetic group of uropathogenic *E. coli* mainly belong to B2, but the distribution could differ across countries. In an analysis of symptomatic UTIs in Mexico, phylogenetic group B2 was detected as the most frequent, followed by A and B1 (18). In a study of male febrile UTIs in Sweden, the phylogenetic group B2 was detected most frequently, followed by group D (19). In a study of community-acquired UTI in Korea, phylogenetic group B2 was detected as the most frequent, followed by groups D and A (20). In a comparative study about UTIs between genders conducted in Iran, phylogenetic group B2 was most frequently detected in both males and females with UTIs, and among them, the proportion of group D in males was higher than in females (21). Furthermore, phylogenetic group B2 was most frequently detected in our study, but the proportion of group D in females was higher than in males. Further studies are needed to determine whether there is a difference in phylogenetic groups

in males and females.

Uropathogenic *E. coli* have several virulence factors, such as adhesins, toxins, iron acquisition, immune evasion, and protectins (22). Many studies are being conducted to investigate the association of virulence factors, defense mechanisms, and infection in uropathogenic *E. coli* (6, 23-24). Adhesin molecules, such as type I fimbriae, play an important role during the attachment of the *E. coli* at the mucosal epithelium, initiate biofilm formation, and persist in the bladder (25). In our study, the adhesin *fimH* was the most frequently detected virulence factor among other adhesins, such as *papA*, *papG*, and *sfa/focED*, in both groups. In UTI in males in Iran, *pap* and *sfa/focED* were the most common virulence genes detected (21). In a comparative study about UTIs with bacteremia in Sweden, *papG* was observed more frequently in bacteremic UTI than nonbacteremic UTI (26). Toxins are important for mediating bacterial invasion and for the dissemination and persistence of bacteria in the bladder. The toxins *cnf1* and *hlyA* were present in 26.6% and 23.1% females, and 51.8% and 48.3% males in our study. *HlyA* is needed for initial bacterial invasion and *cnf1* is needed for dissemination and persistence of bacteria. Iron uptake systems and siderophores facilitate iron scavenging from the environment. Virulence factors, such as α-hemolysin, lipopolysaccharides, proteases, adhesins, aerobactin, and fimbriae, play an important role in biofilm formation (6). Biofilm production can increase resistance to antibiotics and virulence (27).

There were several limitations in this study. First, this study was retrospective; therefore, we had to rely on the medical records and it was difficult to evaluate the urinary function and identify the subjective urinary symptoms in all patients. Second, we acknowledge that the patients included in this study were at a tertiary hospital and their

condition might be more severe than that of patients in a primary medical center.

Despite these limitations, we found difference in the predisposing factors, clinical manifestations, antimicrobial susceptibility, and genotypic features of uropathogenic *E. coli* according to the gender in a tertiary hospital in South Korea.

In conclusion, in cases of pyelonephritis with uropathogenic *E. coli*, there were differences in the predisposing factors, clinical manifestations, and antimicrobial resistance rates according to gender. Comorbidity was observed more frequently in males than in females. We found that the incidence of *iutA, hlyA*, and *kpsMT II* in uropathogenic *E. coli* were different according to gender. Further studies will be needed to elucidate the virulence factors of uropathogenic *E. coli* according to gender and interaction with the host.

5. Summary

E. coli is a gram-negative bacillus that causes various infections, especially urinary tract infection. Urinary tract infection is a gender distinctive infection, however, there are only a few comparative studies about the gender-specific clinical characteristics of uropathogenic *E. coli*. The purpose of this study was to compare clinical characteristics, antimicrobial resistance rates, and genotypic characteristics according to gender. This study was performed on 351 *E. coli* isolates from patients with urinary tract infection, who were diagnosed at the Keimyung University Dongsan Medical Center between February 2015 and June 2018. The phylogenetic grouping of the *E. coli* isolates was determined by polymerase chain reaction (PCR)-based method. The presence of the virulence factors was assessed by multiplex PCR using specific primers. The clinical characteristics, antimicrobial susceptibility, phylogenetic groups, and virulence factors were compared according to gender. The males were more prone to healthcare-asssociated UTI and predisposing factors, and showed higher antimicrobial resistance rates, concomitant bacteremia, and persistent fever than the females. In the phylogenetic group, B2 was more observed in males and D in females. The virulence factors, *hlyA, cnf1* in toxin, *usp* in PAI, and *iutA* in iron acquisition were observed to be more in case of the males, while *KpsMT II* in protectins was observed to be more in females.

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Clinical and Genotypic Characteristics of Uropathogenic *Escherichia coli* Strains According to Gender in Korea

Hyun, Mi Ri

Department of Internal medicine
Graduate School

Keimyung University

(Supervised by Professor Kim, Hyun Ah)

(Abstract)

Escherichia coli (E. coli) is one of the most common uropathogens. The purpose of this study is to compare the clinical and genotypic characteristics of uropathogenic *E. coli* (UPEC) according to gender. We reviewed the medical records of pyelonephritis patients with UPEC retrospectively, between February 2015 and June 2018. We compared clinical and genotypic characteristics of UPEC according to gender. A total of 351 patients were identified, comprising 289 females and 62 males. The mean age of males was older than females. Neurogenic bladder, use of urinary catheter, and obstructive uropathy were observed more in males. Concomitant bacteremia and persistent fever were observed more in the males than the females. In the antimicrobial

susceptibility test, the UPEC were found to be resistant to cefotaxime and ciprofloxacin, more in males than females. Extended-spectrum β-lactamase producing UPEC were observed in 43.7% of the females and 64.5% of the males. Among the virulence genes, *PAI, iutA,* and *hlyA* were observed to be more in the males, while *KpsMT II* was observed to be more in the females; both were significant. We found that different clinical characteristics and the incidences of *iutA, hlyA,* and *KpsMT II* were different according to gender in UPEC.

성별에 따른 Uropathogenic *Escherichia coli* 감염의 임상적 및 미생물학적 특성 비교

현 미 리
계명대학교 대학원
의학과 내과학 전공
(지도교수 김 현 아)

(초록)

요로 감염 (UTI)은 가장 흔한 세균 감염 중 하나이고 대장균 (*Escherichia coli*)이 가장 흔한 원인균이다. 본 연구의 목적은 성별에 따른 uropathogenic *E. coli* (UPEC)의 임상적 및 미생물학적, 분자생물학적 특성을 비교하고자 함이다. 본 연구는 2015년 2월부터 2018년 6월까지 계명대학교 동산의료원에 내원한 환자 중 *E. coli*에 의한 신우신염 환자를 대상으로 실시하였다. Phylogenetic group과 virulence factor는 중합효소 연쇄반응검사로 확인하였다. 총 351명의 환자가 연구기간에 포함되었고 이 중 289명이 여성이었고 62명이 남성이었다. 남성의 평균 연령이 여성보다 높았으며 신경인성 방광, 요도 카테터 사용 및 폐쇄성 폐색증은 남성에서 더 많이 관찰되었다. 만성 간질환과 신경질환은 남성에서 더 흔했으며, 당뇨병은 여성에서 더 흔했다. 균혈증이 남성에서 더 많이 관찰되었다. Extended spectrum β-lactamase는 여성의 43.7%와 남성의 64.5%에서 관찰되었다. Virulence factor 중

PAI, iutA 및 *hlyA*는 남성이 많았고 *KpsMT II*는 여성이 더 많이 확인되었다. 성별에 따른 임상적, 분자 생물학적 차이를 확인할 수 있었고 이러한 특성은 여러 요인에 따른 영향이 있을 수 있으므로 이에 대한 추가 연구가 필요할 것으로 생각된다.

□ 저자 약력

1985년 대구 출생
계명대학교 의과대학 의학과 졸업
계명대학교 대학원 의학과 석사
계명대학교 동산의료원 감염내과 전임의
삼성서울병원 감염내과 전임의
계명대학교 동산의료원 감염내과 임상조교수 (현)

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