Journal of Microbiology, Immunology and Infection (2013) 46, 24–29

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

# Bacterial characteristics and glycemic control in diabetic patients with *Escherichia coli* urinary tract infection

**Ming-Cheng Wang [a,b], Chin-Chung Tseng [a], An-Bang Wu [a], Wei-Hung Lin [c], Ching-Hao Teng [d], Jing-Jou Yan [e], Jiunn-Jong Wu [f,g,*]**

[a] *Division of Nephrology, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan*
[b] *Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan*
[c] *Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan*
[d] *Institute of Molecular Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan*
[e] *Department of Pathology, National Cheng Kung University Hospital, Tainan, Taiwan*
[f] *Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, Tainan, Taiwan*
[g] *Center of Infectious Disease and Signaling Research, National Cheng Kung University, Tainan, Taiwan*

Received 1 July 2011; received in revised form 3 October 2011; accepted 13 October 2011

**KEYWORDS**
Bacterial virulence;
Diabetes mellitus;
*Escherichia coli*;
Glycemic control;
Urinary tract infection

*Background:* Patients with diabetes mellitus have an increased risk of infection. The roles of bacterial characteristics and glycemic control in diabetic patients with *Escherichia coli* infection have not been well investigated. The aims of this study were to examine the bacterial characteristics and glycemic control in diabetic patients with *E. coli* infections arising in the urinary tract.
*Methods:* A total of 271 *E. coli* isolates were collected from urine and bloodstream. Phylogenetic groups, the presence of virulence genes, and antimicrobial susceptibility of *E. coli* isolates were determined.
*Results:* There were few differences in *E. coli* bacterial characteristics between 190 diabetic and 81 nondiabetic patients. In diabetic patients with urosepsis, there was a higher hemoglobin $A_{1C}$ level, and the related *E. coli* strains had more *neuA*, *papG II*, *afa* and *hlyA* genes, and a lower prevalence of antimicrobial resistance to cephalosporins and fluoroquinolones than those with asymptomatic bacteriuria and urinary tract infection. Multivariate logistic regression analysis revealed that increased hemoglobin $A_{1C}$ and presence of *papG II* and *afa*

* Corresponding author. Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, No. 1 University Road, Tainan 70101, Taiwan.
*E-mail address:* jjwu@mail.ncku.edu.tw (J.-J. Wu).


doi:10.1016/j.jmii.2011.12.024

genes were independent factors associated with development of urosepsis in diabetic patients.
*Conclusion:* This study demonstrated that more virulent *E. coli* isolates, especially with *papG II* and *afa* genes, and poorer glycemic control were important determinants for development of urosepsis in diabetic patients.


## Introduction

*Escherichia coli* is the major pathogen in many extraintestinal Gram-negative bacillus infections. Several virulence factors of *E. coli* are responsible for colonization and invasion of the host, and/or serve to avoid or disrupt host defense mechanisms. Both *E. coli* virulence characteristics and host factors contribute to the development of *E. coli* bacteremia in upper urinary tract infection (UTI).[1]

Patients with diabetes mellitus have an increased risk for infections, including UTI, soft tissue infections, community-acquired pneumonia, necrotizing otitis externa, and bloodstream infections.[2,3] Impaired host defense, in both cell-mediated immunity and humoral immunity, increases the susceptibility to infection. Diabetes-associated functional and anatomical abnormalities of the host also contribute to it. Poor glycemic control increases the risk of community-acquired infections and acquiring asymptomatic bacteriuria (ABU).[4,5] Diabetes with poor glycemic control and urinary tract obstruction are important host factors predisposing to emphysematous pyelonephritis.[6] In most *E. coli* extraintestinal infections, host immunocompetence is associated with a relatively high prevalence of *papG II*, *afa* and *iha*, and relatively low antimicrobial resistance to fluoroquinolones.[7]

The role of bacterial characteristics and glycemic control in diabetic patients with *E. coli* infections related to urinary tract has not been well investigated. The aims of this study were to examine and compare the bacterial characteristics and glycemic control in diabetic patients with *E. coli* infections arising in the urinary tract.

## Materials and methods

### Subjects and bacterial strains

A total of 271 *E. coli* random isolates from urine or bloodstream of patients with urinary-tract-related colonization or infection at National Cheng Kung University Hospital, Taiwan were collected from July 2005 to December 2009.They were derived from 81 nondiabetic and 190 diabetic patients with available glycated hemoglobin ($HbA_{1C}$) values within 3 months before collection of *E. coli* isolates. Only one isolate per patient was accepted. Diabetes mellitus was diagnosed if fasting plasma glucose concentration was $\geq$ 7.0 mmol/L (126 mg/dL) on two separate occasions, or if the patient was being treated with insulin or oral hypoglycemic agents. ABU was defined as bacterial colonization of urine in the absence of clinical symptoms. UTI was diagnosed as a quantitative culture of $\geq 10^5$ CFU/mL for *E. coli* isolated from midstream urine or catheterization, and presence of symptoms or signs of lower UTI (i.e., urgency and frequency of urination, dysuria, and/or lower abdominal pain with normal body temperature) or upper UTI (i.e., body temperature $\geq$ 38.3°C, flank pain, and/or tenderness of the costovertebral angle). Urosepsis was defined as a patient with *E. coli* bacteremia arising from a urinary tract source.

The *E. coli* strains collected from urine and bloodstream were identified using standard methods, and stored in 20% glycerol at −70°C until used in all subsequent analyses. Susceptibility of *E. coli* strains, using the disk diffusion method and interpretive criteria according to the Clinical and Laboratory Standards Institute guidelines of 2006, was determined to ampicillin, gentamicin, cefazolin, second-generation cephalosporins (cefuroxime, cefoxitin or cefmetazole), third-generation cephalosporins (cefotaxime, ceftriaxone, ceftazidime, cefixime or cefpodoxime), fourth-generation cephalosporins (cefepime or cefpirome), and fluoroquinolones (ciprofloxacin, levofloxacin or lomefloxacin). Intermediate susceptibility was interpreted as resistance.

### Detection of *E. coli* K1 capsule and virulence genes

K1 capsule and 14 uropathogenic virulence factor genes of *E. coli* were detected using polymerase chain reaction (PCR). Primer pairs specific for K1 capsule gene, *neuA*, were K1-F: ATGATTACTCGACACTGTC; K1-R: AACAATCTCCGCT ATTTCG. The size of the PCR products was 812 bp. Primer pairs specific for the three PapG adhesion genes (*papG* class I—III) of P-fimbriae and genes for type 1 fimbrial adhesions (*fimH* ), S-/F1C-fimbriae (*sfa*/*foc*), afimbrial adhesions (*afa*), iron-regulated gene A homolog adhesion (*iha*), hemolysin (*hlyA*), cytotoxic necrotizing factor 1 (*cnf1*), catecholate siderophore receptor (*iroN* ), aerobactin receptor (*iutA*), outer membrane protease T (*ompT* ), and uropathogenic specific protein (*usp*) have been described previously.[6] The extraction of bacterial DNA and DNA amplification were performed. PCRs were carried out in duplicate and positive and negative control strains for the traits of interest were included in each assay.[6]

### Phylogenetic analysis

The phylogenetic grouping of the *E. coli* isolates was determined by a PCR-based method developed by Clermont et al.[8] The presence of the *chuA* and *yjaA* genes and DNA fragment TSPE4.C2 was examined and *E. coli* isolates were assigned to one of the four main phylogenetic groups (A, B1, B2 or D). These results were further confirmed using a dot-blot assay. Fifty microliters of extracted *E. coli* DNA was pipetted onto a nitrocellulose membrane together with

an equal volume of 0.2 N NaOH added to the DNA sample. The DNA was incubated at room temperature for 10 minutes, and the membrane washed with 50 μL buffer [0.5 M Tris—HCl (pH 7.5), 1.5 M NaCl solution] per well, and a vacuum was applied for 30 minutes. The DNA was cross-linked using a UV cross-linker device (Amersham Biosciences, Piscataway, NJ, USA) and the membrane rinsed with 2 × SSC buffer (30 mM sodium citrate, pH 7.0, 0.3 M NaCl). After hybridization reaction with a DNA probe at 60 °C for 1 hour, the membrane was exposed overnight to film for autoradiography.

### Statistical analysis

The Pearson $\chi^2$ test or Fisher's exact test (2-tailed) was used for comparison of categorical variables, whereas the Wilcoxon rank sum test or one-way analysis of variance was used for comparison of continuous variables. Multivariate logistic regression analysis was used to assess the independent factors for development of *E. coli* urosepsis in diabetic patients. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using JMP software (SAS Institute, Cary, NC, USA).

## Results

There were 63 ABU and 97 UTI *E. coli* strains derived from urine, and the number of *E. coli* strains from urosepsis was 111. Phylogenetic group B2 was the most common. The overall antimicrobial resistance rate was 77% for ampicillin, 33% for gentamicin, 30% for cefazolin, and 32% for fluoroquinolones (Table 1).

The sources of *E. coli* isolates and age and sex of the hosts were similar between diabetic and nondiabetic groups. Phylogenetic group B2 was most common in *E. coli* isolates. There was no significant difference in the overall virulence factors between the diabetic and nondiabetic groups, except a greater prevalence of *afa* gene in the diabetic group (Table 2).

The mean $HbA_{1C}$ value was highest in diabetic patients with urosepsis. Phylogenetic group B2 was most common in *E. coli* strains arising from a urinary tract source derived from diabetic patients. Virulence factor genes with *neuA*, *papG II*, *afa* and *hlyA* were more common in the urosepsis isolates, whereas they were relatively low in the ABU isolates (Table 3). Using $HbA_{1C}$ and *neuA*, *papG II*, *afa* and *hlyA* genes as confounding variables for development of *E. coli* urosepsis, multiple logistic regression analysis revealed

**Table 1** Demographic data of host and bacterial characteristics of urinary-tract-related *Escherichia coli* isolates

| | Total $n = 271$ |
|---|---|
| Host characteristic | |
| Age (y) | 68 ± 14 |
| Sex (female) | 213 (79) |
| Diabetes mellitus | 190 (70) |
| Hemoglobin $A_{1C}$ (%) of diabetic patients | 8.0 ± 2.1 |
| Asymptomatic bacteriuria | 63 (23) |
| Urinary tract infection | 97 (36) |
| Urosepsis | 111 (41) |
| Bacterial characteristic | |
| Phylogenetic group | |
| A | 31 (11) |
| B1 | 43 (16) |
| B2 | 136 (50) |
| D | 61 (23) |
| Antimicrobial resistance | |
| Ampicillin | 210 (77) |
| Gentamicin | 89 (33) |
| Cefazolin | 80 (30) |
| Second-generation cephalosporins | 59 (22) |
| Third-generation cephalosporins | 56 (21) |
| Fourth-generation cephalosporins | 31 (11) |
| Fluoroquinolones | 86 (32) |

Data are presented as mean ± standard deviation or number (percentage).

**Table 2** Host and bacterial characteristics of *Escherichia coli* isolates in relation to diabetes mellitus

| | Diabetes mellitus (−) ($n = 81$) | Diabetes mellitus (+) ($n = 190$) | *p* value |
|---|---|---|---|
| Host characteristic | | | |
| ABU/UTI/urosepsis | 23/29/29 | 40/68/82 | 0.356 |
| Age (y) | 66 ± 17 | 69 ± 12 | 0.188 |
| Sex (female) | 65 (80) | 148 (78) | 0.747 |
| Bacterial characteristic | | | |
| Phylogenetic group | | | 0.855 |
| A | 8 (10) | 23 (12) | |
| B1 | 15 (19) | 28 (15) | |
| B2 | 40 (49) | 96 (51) | |
| D | 18 (22) | 43 (23) | |
| K1 capsule, *neuA* | 24 (30) | 37 (19) | 0.081 |
| Adhesin | | | |
| *papG I* | 0 | 0 | — |
| *papG II* | 34 (42) | 57 (30) | 0.068 |
| *papG III* | 6 (7) | 22 (12) | 0.386 |
| *fimH* | 76 (94) | 183 (96) | 0.351 |
| *sfa* | 3 (4) | 12 (6) | 0.564 |
| *foc* | 3 (4) | 12 (6) | 0.564 |
| *afa* | 25 (31) | 100 (53) | 0.001 |
| *iha* | 31 (38) | 68 (36) | 0.783 |
| Toxin | | | |
| *hlyA* | 16 (20) | 35 (18) | 0.865 |
| *cnf1* | 10 (12) | 28 (15) | 0.704 |
| Siderophore | | | |
| *iroN* | 34 (42) | 74 (39) | 0.685 |
| *iutA* | 56 (69) | 125 (66) | 0.673 |
| Miscellaneous | | | |
| *ompT* | 67 (83) | 144 (76) | 0.263 |
| *usp* | 47 (58) | 100 (53) | 0.428 |

Data are presented as mean ± standard deviation or number (percentage).
ABU = asymptomatic bacteriuria; UTI = urinary tract infection.

**Table 3** Host and bacterial characteristics of 190 *Escherichia coli* isolates in diabetic patients

| | ABU ($n = 40$) | UTI ($n = 68$) | Urosepsis ($n = 82$) | $p$ value |
|---|---|---|---|---|
| Host characteristic | | | | |
| Age (y) | 70 ± 9 | 71 ± 13 | 66 ± 12 | 0.070 |
| Sex (female) | 34 (85) | 56 (82) | 58 (71) | 0.111 |
| $HbA_{1C}$ (%) | 7.5 ± 1.5 | 7.7 ± 2.0 | 8.5 ± 2.3 | 0.013 |
| Bacterial characteristic | | | | |
| Phylogenetic group | | | | 0.121 |
| A | 6 (15) | 12 (18) | 5 (6) | |
| B1 | 7 (18) | 10 (15) | 11 (13) | |
| B2 | 18 (45) | 37 (54) | 41 (50) | |
| D | 9 (23) | 9 (13) | 25 (30) | |
| K1 capsule, *neuA* | 5 (13) | 9 (13) | 23 (28) | 0.034 |
| Adhesin | | | | |
| *papG I* | 0 | 0 | 0 | — |
| *papG II* | 4 (10) | 13 (19) | 40 (49) | <0.0001 |
| *papG III* | 4 (10) | 6 (9) | 12 (15) | 0.509 |
| *fimH* | 39 (98) | 63 (93) | 81 (99) | 0.126 |
| *sfa* | 3 (8) | 2 (3) | 7 (9) | 0.352 |
| *foc* | 0 | 7 (10) | 5 (6) | 0.104 |
| *afa* | 11 (28) | 30 (44) | 59 (72) | <0.0001 |
| *iha* | 13 (33) | 22 (32) | 33 (40) | 0.536 |
| Toxin | | | | |
| *hlyA* | 2 (5) | 14 (21) | 19 (23) | 0.044 |
| *cnf1* | 3 (8) | 11 (16) | 14 (17) | 0.344 |
| Siderophore | | | | |
| *iroN* | 14 (35) | 27 (40) | 33 (40) | 0.845 |
| *iutA* | 24 (60) | 45 (66) | 56 (68) | 0.661 |
| Miscellaneous | | | | |
| *ompT* | 29 (73) | 48 (71) | 67 (82) | 0.246 |
| *usp* | 17 (43) | 40 (59) | 43 (52) | 0.260 |

Data are presented as mean ± standard deviation or number (percentage).
ABU = asymptomatic bacteriuria; $HbA_{1C}$ = glycated hemoglobin; UTI = urinary tract infection.

**Table 4** Host and bacterial characteristics of *Escherichia coli* isolates in 81 nondiabetic patients

| | ABU ($n = 23$) | UTI ($n = 29$) | Urosepsis ($n = 29$) | $p$ value |
|---|---|---|---|---|
| Host characteristic | | | | |
| Age (y) | 63 ± 19 | 64 ± 20 | 72 ± 14 | 0.199 |
| Sex (female) | 20 (87) | 22 (76) | 23 (79) | 0.600 |
| Bacterial characteristic | | | | |
| Phylogenetic group | | | | 0.466 |
| A | 2 (9) | 4 (14) | 2 (7) | |
| B1 | 6 (26) | 7 (24) | 2 (7) | |
| B2 | 10 (43) | 12 (41) | 18 (62) | |
| D | 5 (22) | 6 (21) | 7 (24) | |
| K1 capsule, *neuA* | 4 (17) | 7 (24) | 13 (45) | 0.071 |
| Adhesin | | | | |
| *papG I* | 0 | 0 | 0 | — |
| *papG II* | 5 (22) | 9 (26) | 20 (69) | 0.0009 |
| *papG III* | 4 (17) | 1 (3) | 1 (3) | 0.097 |
| *fimH* | 21 (91) | 27 (93) | 28 (97) | 0.722 |
| *sfa* | 2 (9) | 0 | 1 (3) | 0.256 |
| *foc* | 0 | 3 (10) | 0 | 0.061 |
| *afa* | 1 (4) | 6 (21) | 18 (62) | <0.0001 |
| *iha* | 6 (26) | 9 (31) | 16 (55) | 0.061 |
| Toxin | | | | |
| *hlyA* | 4 (17) | 4 (14) | 8 (28) | 0.396 |
| *cnf1* | 4 (17) | 3 (10) | 3 (10) | 0.685 |
| Siderophore | | | | |
| *iroN* | 6 (26) | 16 (55) | 12 (41) | 0.107 |
| *iutA* | 13 (57) | 20 (69) | 23 (79) | 0.210 |
| Miscellaneous | | | | |
| *ompT* | 15 (65) | 26 (90) | 26 (90) | 0.032 |
| *usp* | 12 (52) | 17 (59) | 18 (62) | 0.770 |

Data are presented as mean ± standard deviation or number (percentage).
ABU = asymptomatic bacteriuria; UTI = urinary tract infection.

that $HbA_{1C}$ [odds ratio (OR) per unit change: 1.3, 95% confidence interval (CI): 1.1–1.6, $p = 0.0059$), *papG II* (OR: 5.8, 95% CI: 2.4–14.2, $p = 0.0001$), and *afa* (OR: 6.5, 95% CI: 3.1–13.7, $p < 0.0001$] were associated with *E. coli* urosepsis in diabetic patients. The results of host and bacterial characteristics of *E. coli* isolates in 81 nondiabetic patients in relation to ABU, UTI and urosepsis are shown in Table 4. Virulence factor genes with *papG II, afa and ompT* were more common in the urosepsis isolates, whereas they were relatively low in the ABU isolates.

The prevalence of antimicrobial resistance of *E. coli* isolates to second- and third-generation cephalosporins was more common in the diabetic group compared to that in the nondiabetic group. There was a trend towards decline in antimicrobial resistance to cefazolin, second- and third-generation cephalosporins, and fluoroquinolones associated with the increased severity of *E. coli*-related infection. The lowest rate of antimicrobial resistance of *E. coli* isolates was in the urosepsis subgroup (Table 5). There was no significant difference in antimicrobial resistance among the three groups in the nondiabetic patients (Table 5).

## Discussion

This study addressed the bacterial characteristics and glycemic control in diabetic patients with *E. coli* infections arising in the urinary tract. Poorer glycemic control contributed to development of urosepsis. In diabetic patients with urosepsis, the corresponding *E. coli* isolates were more virulent but less resistant to antibiotics than those from diabetic patients with ABU or UTI. Bacterial characteristics including *papG II* and *afa* genes were important virulence factors for development of *E. coli* urosepsis in diabetic patients.

It is well known that diabetic patients are immunocompromised and have an increased risk for different infections. Glycemic control is an important outcome indicator for diabetic patients with infection.[9,10] Investigations regarding bacterial characteristics and glycemic

**Table 5** Antimicrobial resistance of urinary-tract-related *Escherichia coli* isolates

| | Diabetes mellitus (−) ($n = 81$) | Diabetes mellitus (+) ($n = 190$) | $p$ value |
|---|---|---|---|
| Ampicillin | 57 (70) | 153 (81) | 0.081 |
| Gentamicin | 26 (32) | 63 (33) | 0.889 |
| Cefazolin | 22 (27) | 58 (31) | 0.663 |
| Second-generation cephalosporins | 11 (14) | 48 (25) | 0.037 |
| Third-generation cephalosporins | 10 (12) | 46 (24) | 0.033 |
| Fourth-generation cephalosporins | 12 (15) | 19 (10) | 0.298 |
| Fluoroquinolones | 20 (25) | 66 (35) | 0.118 |
| Diabetes group ($n = 190$) | ABU ($n = 40$) | UTI ($n = 68$) | Urosepsis ($n = 82$) | $p$ value |
| Ampicillin | 33 (83) | 59 (87) | 61 (74) | 0.153 |
| Gentamicin | 17 (43) | 25 (37) | 21 (26) | 0.130 |
| Cefazolin | 17 (43) | 25 (37) | 16 (20) | 0.013 |
| Second-generation cephalosporins | 14 (35) | 22 (32) | 12 (15) | 0.013 |
| Third-generation cephalosporins | 13 (33) | 21 (31) | 12 (15) | 0.027 |
| Fourth-generation cephalosporins | 4 (10) | 11 (16) | 4 (5) | 0.072 |
| Fluoroquinolones | 20 (50) | 29 (43) | 17 (21) | 0.001 |
| Non-diabetes group ($n = 81$) | ABU ($n = 23$) | UTI ($n = 29$) | Urosepsis ($n = 29$) | $p$ value |
| Ampicillin | 16 (70) | 22 (76) | 19 (66) | 0.686 |
| Gentamicin | 7 (30) | 10 (34) | 9 (31) | 0.942 |
| Cefazolin | 6 (26) | 5 (17) | 11 (38) | 0.206 |
| Second-generation cephalosporins | 5 (22) | 4 (14) | 2 (7) | 0.300 |
| Third-generation cephalosporins | 5 (22) | 4 (14) | 1 (3) | 0.132 |
| Fourth-generation cephalosporins | 5 (22) | 5 (17) | 2 (7) | 0.294 |
| Fluoroquinolones | 8 (35) | 8 (28) | 4 (14) | 0.198 |

Data are presented as mean ± standard deviation or number (percentage).
ABU = asymptomatic bacteriuria; UTI = urinary tract infection.

control in *E. coli*-related infections arising in the urinary tract have been scarce. $HbA_{1C}$ level as indicator of glycemic control reported in many studies was measured following admission or diagnosis of infection, which is difficult to understand the glycemic control prior to the development of infection. The present study included 190 diabetic patients with available $HbA_{1C}$ values within 3 months before collection of *E. coli* isolates, related to colonization or infection of the urinary tract. This study demonstrated that diabetic patients with urosepsis had the highest $HbA_{1C}$ values compared to that in the ABU and UTI groups. Besides, $HbA_{1C}$ value was an independent determinant for occurrence of urosepsis. These results emphasized an important role of glycemic control in the development of *E. coli* urosepsis in diabetic patients.

There are few data concerning the bacterial characteristics in diabetic patients with *E. coli* bacteremia. Previous studies have shown that the distribution of bacterial virulence factors depends on the primary source of *E. coli* bacteremia, and greater prevalence of most virulence characteristics contributes to the occurrence of *E. coli* bacteremia.[1,11] However, several studies have revealed no significant difference in bacterial determinants between patients with and without *E. coli* bacteremia.[12–14] The present study demonstrated a similar bacterial virulence profile in diabetic and nondiabetic patients. *E. coli* isolates from urosepsis exhibited a significantly greater prevalence of *neuA*, *papG II*, *afa* and *hlyA* genes than nonurosepsis isolates in diabetic patients. Using multivariate logic regression analysis, we demonstrated that *papG II and afa* genes, but not *neuA* and *hlyA* genes, were important determinants for *E. coli* urosepsis in diabetic patients. The present study suggests that more bacterial virulence traits may be necessary for development of *E. coli* urosepsis in diabetic patients, and that *papG II* and *afa* genes are the important bacterial virulence factors.

Meiland et al have reported lower antimicrobial resistance rates in *E. coli* isolated from urine of diabetic women than those from urine samples of the general female population.[15] Bonadio et al have found that *E. coli* isolates are resistant at similar rates to ampicillin, cotrimoxazole, ciprofloxacin and nitrofurantoin in both diabetic and nondiabetic patients.[16] They have concluded that diabetes mellitus *per se* does not seem to influence the susceptibility patterns of uropathogens to antimicrobials.[16] With very few exceptions, there have been no differences observed in the antimicrobial resistance profiles between diabetic and nondiabetic groups.[17] The present study showed a similar antimicrobial resistance profile between diabetic and nondiabetic patients, except for a higher resistance rate to the second- and third-generation cephalosporins in the diabetic group. The lowest rate of resistance to cefazolin, second- and third-generation cephalosporins, and fluoroquinolones was found in the urosepsis-related *E. coli* isolates derived from diabetic patients. These data do not allow us to infer causality between antimicrobial resistance and different *E. coli* infections. Compared to diabetic patients with asymptomatic bacteriuria or UTI without bacteremia, diabetic patients with urosepsis might have received antimicrobial agents with stronger potency, higher

dose, and/or longer duration to eradicate the *E. coli* from the bloodstream. The probability of antimicrobial-resistant E. coli strains remaining in the urinary tract of diabetic patients with urosepsis is lower than that in diabetic patients with ABU or UTI.

The main limitation of this study was its retrospective inclusion of diabetic patients with $HbA_{1C}$ examined within 3 months before collection of *E. coli* strains, which may have affected the distribution of bacterial sources, virulence characteristics, and antimicrobial resistance profiles of *E. coli* isolates. In addition, diabetes and glycemic control were the main host factors investigated for association with the bacterial characteristics and *E. coli* infections. The role of other important host factors, such as anatomical defects and immunodeficiency, in the development of infection could not be overlooked, although they were not included for analysis in this study because of insufficient information from chart records.

In conclusion, this study demonstrated the important roles of glycemic control and bacterial characteristics in *E. coli* infections arising in the urinary tract in diabetic patients. More virulence characteristics of *E. coli* isolates, especially those with *papG II* and *afa* genes, and poorer glycemic control were significantly associated with development of *E. coli* urosepsis in diabetic patients.

## Financial support

This work was supported in part by the National Cheng Kung University Hospital, Taiwan (NCKUH-10006001).

## Potential conflicts of interest

All authors declare no conflicts of interest.

## References

1. Wang MC, Tseng CC, Chen CY, Wu JJ, Huang JJ. The role of bacterial virulence and host factors in patients with *Escherichia coli* bacteremia who have acute cholangitis or upper urinary tract infection. *Clin Infect Dis* 2002;**35**:1161—6.
2. Muller LM, Gorter KJ, Hak E, Goudzwaard WL, Schellevis FG, Hoepelman AI, et al. Increased risk of common infections in patients with type 1 and type 2 diabetes mellitus. *Clin Infect Dis* 2005;**41**:281—8.
3. Kofteridis DP, Papadimitraki E, Mantadakis E, Maraki S, Papadakis JA, Tzifa G, et al. Effect of diabetes mellitus on the clinical and microbiological features of hospitalized elderly patients with acute pyelonephritis. *J Am Geriatr Soc* 2009;**57**: 2125—8.
4. Peleg AY, Weerarathna T, McCarthy JS, Davis TM. Common infections in diabetes: pathogenesis, management and relationship to glycaemic control. *Diabetes Metab Res Rev* 2007; **23**:3—13.
5. Bonadio M, Boldrini E, Forotti G, Matteucci E, Vigna A, Mori S, et al. Asymptomatic bacteriuria in women with diabetes: influence of metabolic control. *Clin Infect Dis* 2004;**38**:e41—5.
6. Tseng CC, Wu JJ, Wang MC, Hor LI, Ko YH, Huang JJ. Host and bacterial virulence factors predisposing to emphysematous pyelonephritis. *Am J Kidney Dis* 2005;**46**:432—9.
7. Wang MC, Tseng CC, Wu AB, Huang JJ, Sheu BS, Wu JJ. Different roles of host and bacterial factors in *Escherichia coli* extraintestinal infections. *Clin Microbiol Infect* 2009;**15**:372—9.
8. Clermont O, Bonacorsi S, Bingen E. Rapid and simple determination of the *Escherichia coli* phylogenetic group. *Appl Environ Microbiol* 2000;**66**:4555—8.
9. Gornik I, Gornik O, Gasparović V. HbA1c is outcome predictor in diabetic patients with sepsis. *Diabetes Res Clin Pract* 2007;**77**: 120—5.
10. Bertoni AG, Saydah S, Brancati FL. Diabetes and the risk of infection-related mortality in the U.S. *Diabetes Care* 2001;**24**: 1044—9.
11. Sannes MR, Kuskowski MA, Owens K, Gajewski A, Johnson JR. Virulence factor profiles and phylogenetic background of *Escherichia coli* isolates from veterans with bacteremia and uninfected control subjects. *J Infect Dis* 2004;**190**:2121—8.
12. Venier AG, Talon D, Patry I, Mercier-Girard D, Bertrand X. Patient and bacterial determinants involved in symptomatic urinary tract infection caused by *Escherichia coli* with and without bacteraemia. *Clin Microbiol Infect* 2007;**13**:196—215.
13. Bonacorsi S, Houdouin V, Mariani-Kurkdjian P, Mahjoub-Messai F, Bingen E. Comparative prevalence of virulence factors in *Escherichia coli* causing urinary tract infection in male infants with and without bacteremia. *J Clin Microbiol* 2006;**44**:1156—8.
14. Moreno E, Planells I, Prats G, Planes AM, Moreno G, Andreu A. Comparative study of *Escherichia coli* virulence determinants in strains causing urinary tract bacteremia versus strains causing pyelonephritis and other source of bacteremia. *Diagn Microbiol Infect Dis* 2005;**53**:93—9.
15. Meiland R, Geerlings SE, De Neeling AJ, Hoepelman AI. Diabetes mellitus in itself is not a risk factor for antibiotic resistance in *Escherichia coli* isolated from patients with bacteriuria. *Diabet Med* 2004;**21**:1032—4.
16. Bonadio M, Costarelli S, Morelli G, Tartaglia T. The influence of diabetes mellitus on the spectrum of uropathogens and the antimicrobial resistance in elderly adult patients with urinary tract infection. *BMC Infect Dis* 2006;**6**:54.
17. Ghenghesh KS, Elkateb E, Berbash N, Abdel Nada R, Ahmed SF, Rahouma A, et al. Uropathogens from diabetic patients in Libya: virulence factors and phylogenetic groups of *Escherichia coli* isolates. *J Med Microbiol* 2009;**58**:1006—14.