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Research article

Sex differences in aged 80 and over hospitalized patients with community-acquired UTI: A prospective observational study

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ABSTRACT

Aim: This study aimed to evaluate clinically significant sex differences that could have an effect on the choice of treatment and outcomes of urinary tract infection (UTI) in aged 80 and over hospitalized patients with community-acquired UTI.
Methods: This was a prospective study of 161 patients aged 80 and over admitted to hospital with community-acquired UTI. Epidemiological, clinical, laboratory and microbiologic variables were compared between both sexes. Multivariate analysis was performed using logistic regression to determine the variables independently associated with sex.
Results: In a population of 91 (56.52%) women and 70 (43.48%) men, aged 80 and over, we found that women were more likely to have cognitive impairment (p = 0.035) and less likely to have chronic obstructive pulmonary disease (COPD) (p = 0.006) and indwelling urinary catheter (p < 0.001) than men. Levels of creatinine were higher in men than in women (p = 0.008). Septic shock at presentation was more frequent in the male group (p = 0.043). Men had a higher rate of polymicrobial infection (p = 0.035) and *Pseudomonas aeruginosa* infection (p = 0.003). Factors independently associated with sex by multivariate analysis were septic shock, cognitive impairment, COPD and indwelling urinary catheter.
Conclusion: Men aged 80 and over with community-acquired UTI had more septic shock at admission to hospital and higher rates of indwelling urinary catheter, while women had more cognitive impairment. There were no differences in outcomes between sexes.

1. Introduction

Urinary tract infection (UTI) remains among the most common infections leading to hospital admission in older and very old adults and is a frequent cause of bacteremia and sepsis [1, 2]. UTI is much more common in women than in men due to certain anatomical and physiological characteristics, although this difference decreases with age [3]. Several conditions such as poor bladder emptying and loss of estrogens make older women even more susceptible to UTI [4], whereas prostatic obstruction is the main predisposing factor to UTI in older males [5]. Other risk factors for UTI in both older men and women include frequent urethral catheterization, perineal soiling from fecal incontinence, and several comorbidities [6, 7]. For these reasons, both asymptomatic

bacteriuria and community-acquired UTI requiring hospital admission are extremely common in older adults and even more in aged 80 and over patients [8, 9].

Sex differences in aged ≥60 years with UTI have been found in some studies. Therefore, etiologies other than *Escherichia coli*, such as *Pseudomonas aeruginosa* and *Enterococcus faecalis*, have been found more frequently in men [10]. The influence of sex on multidrug-resistant bacteria have been found to be higher in men in some studies [11, 12], while others have shown different results [13]. Health care associated UTI appear to be more common in older women [14, 15]. However, to our knowledge there are no previous studies specifically designed to analyze sex differences on aged 80 and over hospitalized patients with UTI. We have carried out a prospective study in order to know the

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influence of sex on the clinical characteristics that could have an effect on the choice of treatment and the outcomes of community-acquired UTI in patients aged 80 and over.

2. Methods

2.1. Study design and patients

A cohort prospective observational study was carried out at the Doctor Peset University Hospital, a university hospital in Valencia, Spain.

All patients aged 80 and over diagnosed with community-acquired UTI, who were consecutively admitted to an internal medicine ward, between December 2016 and December 2019, were assessed for inclusion. The diagnosis of UTI was initially made in the hospital emergency department by a first physician, and confirmed after admission by the physician in charge, based on history, physical examination, laboratory and microbiological diagnostic procedures. Patients with nosocomial UTI, negative urine culture and those who were transferred from the Intensive Care Unit (ICU) were excluded. Routine clinical care for UTI was applied without any changes in its management.

2.2. Data collection and definitions

Epidemiological, clinical, laboratory and microbiologic variables were extracted from the electronic medical record and collected by the researchers, according to a previously established data collection form [16]. The patients were followed up to a month after discharge and their prognosis and outcomes were also recorded. The flow chart of the patients eligible for the study and those finally studied during follow-up is shown in Figure 1.

Age, sex, clinical symptoms and signs and health care associated infection variables were directly gathered from anamnesis and physical examination. Comorbidities including diabetes mellitus (fasting plasma glucose values $\geq$ 126 mg/dL or glycated hemoglobin values $\geq$ 6.5 percent), cognitive impairment (clinical criteria for dementia or mild neurocognitive disorder according to their definition in the Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition [DSM-5]), chronic kidney disease (decreased glomerular filtration rate under 60 ml/min on laboratory test, estimated by CKD-EPI equation), chronic obstructive pulmonary disease (COPD, spirometry demonstrating airflow limitation by a forced expiratory volume in 1 s/forced vital capacity [FEV1/FVC] ratio less than 0.7 or less than the lower limit of normal that is incompletely reversible after the administration of an inhaled bronchodilator), connective tissue disease (history of rheumatoid arthritis, systemic lupus erythematosus, polymyalgia rheumatica, dermatomyositis/polymyositis or mixed connective tissue disease, according to their clinical criteria) and indwelling urinary catheter were registered when they were documented on the electronic medical record. Fever was considered when the patient reported that the temperature was $\geq$38 °C at home or when it was measured in the emergency department. Laboratory
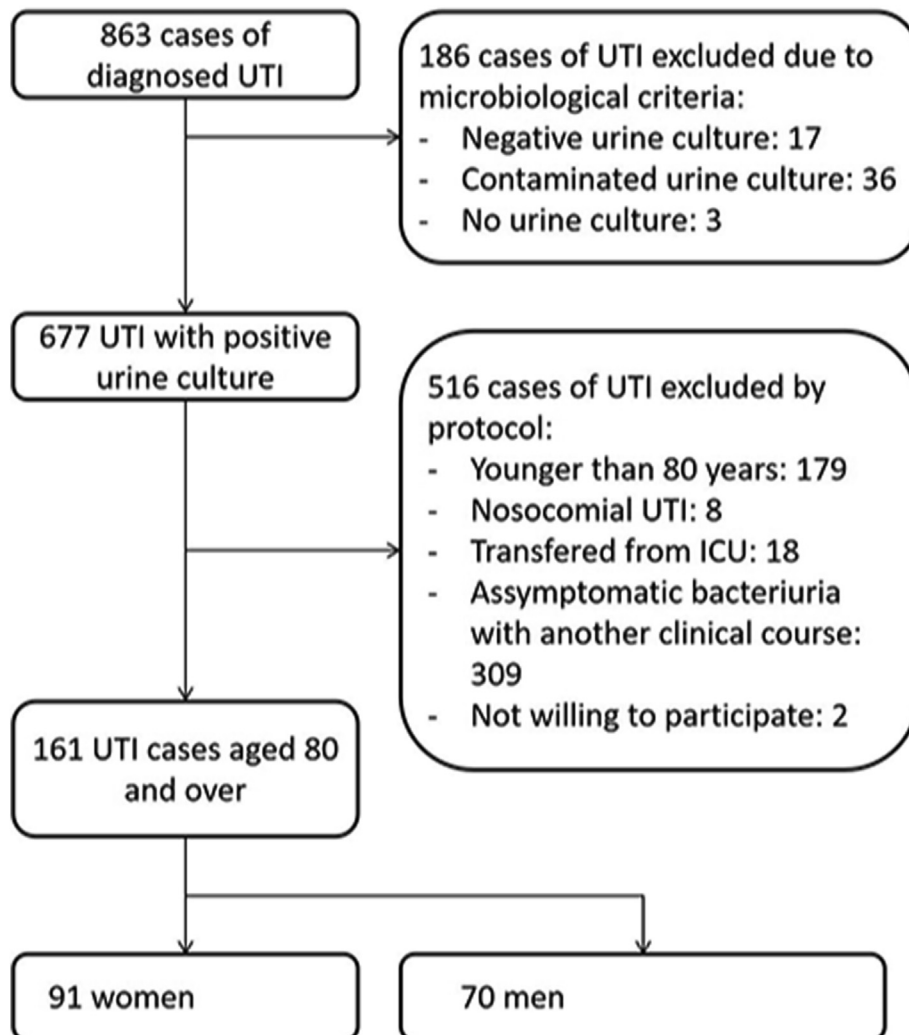

Figure 1. Flowchart of 161 cases of community-acquired urinary tract infection. ICU, intensive care unit; UTI, urinary tract infection.

Table 1. Epidemiological and clinical characteristics and outcomes of patients according to sex.

	All (n = 161)	Women (n = 91)	Men (n = 70)	P-value
Age in years, median [IQR]	87 [83–90]	87 [80–94]	85.5 [80–91.5]	0.328
Barthel index ≤35, n (%)	86 (53.4)	53 (58.24)	33 (47.14)	0.162
Comorbidities, n (%)				
Diabetes mellitus	62 (38.51)	35 (38.46)	27 (38.57)	0.989
Cognitive impairment	68 (42.24)	45 (49.45)	23 (32.86)	**0.035**
COPD	14 (8.70)	3 (3.30)	11 (15.71)	**0.006**
Chronic kidney disease	72 (44.72)	38 (41.76)	34 (48.57)	0.389
Connective tissue disease	7 (4.35)	3 (3.30)	4 (5.71)	0.456
Indwelling urinary catheter	42 (26.09)	9 (9.89)	33 (47.14)	**<0.001**
Charlson Comorbidity Index ≥3 points, n (%)	159 (98.8)	91 (100)	68 (97.1)	0.106
McCabe ≥2 (ultimately or rapidly fatal)	151 (93.8)	86 (94.5)	65 (92.9)	0.748
Healthcare-associated UTI, n (%)	101 (62.73)	56 (61.54)	45 (64.29)	0.721
Previous antibiotic therapy, n (%)	79 (49.1)	41 (45.1)	38 (54.3)	0.269
Previous hospitalization, n (%)	55 (34.2)	30 (32.9)	25 (35.8)	0.740
Nursing home residence, n (%)	19 (11.8)	11 (12.09)	8 (11.43)	0.899
Clinical symptoms and signs, n (%)				
Dysuria, urinary frequency and/or urgency	74 (45.96)	37 (40.66)	37 (52.86)	0.124
Fever	122 (75.78)	66 (72.53)	56 (80)	0.273
Flank pain	36 (22.36)	17 (18.68)	19 (27.14)	0.201
Costovertebral angle tenderness	25 (15.53)	14 (15.38)	11 (15.71)	0.954
Nausea and/or vomiting	4 (2.48)	2 (2.20)	2 (2.85)	0.790
Marked fatigue or malaise	10 (6.21)	6 (6.59)	4 (5.71)	0.819
Acute mental status changes	90 (55.90)	55 (60.44)	35 (50)	0.186
Macroscopic hematuria	5 (3.10)	2 (2.20)	3 (4.26)	0.198
Acute urinary retention	46 (28.57)	26 (28.57)	20 (28.57)	1.000
Vital signs				
Temperature (ºC), mean ± SD	37.19 (1.19)	37.08 (1.23)	37.34 (1.13)	0.167
Mean arterial pressure (mmHg), mean ± SD	86.41 (21.02)	88.52 (20.36)	83.68 (21.69)	0.148
Heart rate (bpm), median [IQR]	90 [77–104]	92 [65–119]	94 [67–121]	0.583
Respiratory rate (bpm), median [IQR]	16 [14–22]	20 [11–29]	16 [8–24]	0.462
Glasgow coma scale ≤14, n (%)	90 (55.9)	55 (60.4)	35 (50)	0.203
Sepsis (SOFA ≥2), n (%)	93 (57.8)	51 (56)	42 (60)	0.633
Septic shock, n (%)	28 (17.39)	11 (12.09)	17 (24.29)	**0.043**
APACHE II score, median [IQR]	14 [10–18]	14 [6–12]	17 [9–25]	0.065
Bacteremia, positive/total of blood cultures, n (%)	36/92 (39.13)	20/45 (44.44)	16/47 (34.04)	0.078
Inadequate empiric antibiotic therapy, n (%)	44 (27.33)	22 (24.18)	22 (31.43)	0.306
Length of hospital stay, median [IQR]	5 [4–8]	5 [0–10]	5 [0–10]	0.533
In-hospital mortality, n (%)	23 (14.29)	16 (17.58)	7 (10)	0.173
30-day mortality, n (%)	33 (20.50)	19 (20.88)	14 (20)	0.891

assessments consisted of a coagulation testing, complete blood count, blood chemistry test including assessment of liver and renal function and measures of electrolytes, procalcitonine and C-reactive protein. Microbiological data were obtained from urine and blood culture and susceptibility testing. They included presence of bacteremia, etiology of UTI by culture isolation, pattern of resistance of the isolated microorganisms and occurrence of polymicrobial infection. The detail microbiological procedures have been previously published [16]. Multidrug-resistant bacteria was defined as non-susceptibility to at least one agent in three or more antimicrobial categories (extended-spectrum penicillins, carbapenems, cephalosporins, aminoglycosides, and fluoroquinolones for gramnegative bacteria; and ampicillin, vancomycin, fluoroquinolones, fosfomycin and linezolid for grampositive bacteria).

Patients were classified according to their underlying diseases using a modified McCabe and Jackson's classification with the following categories: 1 (non-fatal); 2 (rapidly fatal); and 3 (ultimately fatal) [17]. The Charlson Comorbidity Index (CCI) adjusted for age was used as a measure of total comorbidity burden [18]. Functional status of the patients was ranked using the Barthel index, considering a score of ≤35 to define severe or total dependence for basic activities of daily living [19]. The

acute physiology and chronic health evaluation classification system (APACHE II) score was used to identify illness severity at admission [20]. Community onset healthcare-associated UTI (HCA-UTI) was defined by the presence of any of the following criteria: (I) hospitalization in the last 90 days, (II) previous use of antibiotics in the last 3 months, and (III) residing in a nursing home [21]. Sepsis and septic shock were defined according to the criteria of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) [22].

At the end of follow-up, inadequate empirical antimicrobial therapy (IEAT), length of stay in hospital, in-hospital mortality, and 30-day mortality were recorded. IEAT was considered as the occurrence of ineffective treatment due to absence of specific antimicrobial agents directed against the microorganism or the administration of an antimicrobial agent to which the responsible microorganism was resistant at the time the causative microorganism and its antibiotic susceptibility were known [23].

The study was approved by the Clinical Research Ethics Committee of the Doctor Peset University Hospital. Informed consent was signed by every patient or his legal representative when the patient was unable to consent. The data were anonymously analyzed according to the sex of the

patients. Treatment of data, information sheet and informed consent are in accordance under the provisions of the Declaration of Helsinki (version of Fortaleza 2013) [24].

2.3. Statistical analysis

Quantitative variables are reported as the mean ± SD and compared using Student's t-test or analysis of variance (ANOVA) when the distribution was normal. They were reported as the median and the inter-quartile range [IQR] and compared using Mann-Whitney U-test when their distribution was not normal. Qualitative variables are reported as the number and percentage and they were compared with chi square test and Fisher's exact test. Multivariate analysis was performed using logistic regression. An α significance level of ≤0.05 for a two-tailed test was considered for all tests. The statistical package SPSS version 22 from IBM for Windows was used for the statistical analysis.

3. Results

A total of 161 patients aged 80 and over with community-acquired UTI were included into the study. Ninety-one (56.52%) were women and 70 (43.48%) men. The mean age was 87 years (95% CI 83–90 years), without significant differences in age between sexes.

Baseline characteristics and outcomes according to sex are shown in Table 1 (Epidemiological and clinical characteristics and outcomes of patients according to sex), as well as comorbidities, frequency of clinical symptoms and signs, and severity scores at presentation. Women were more likely to have cognitive impairment (49.75% vs. 32.86%, p = 0.035) and less likely to have COPD (3.3% vs. 15.71%, p = 0.006) and indwelling urinary catheter (9.89% vs. 47.14%, p < 0.001) than men. There were no differences between sexes in Charlson Comorbidity Index, which was ≥3 points in 159 (98.8%) of the patients. McCabe's index was ≥2 in 151 (93.8%) patients and Barthel index was ≤35 in 86 (53.4%) patients without significant differences between sexes. Severity measured by APACHE II score was comparable in both groups. There were similar rates of sepsis in both groups, but septic shock at presentation was more frequent in the male group (12.09% vs. 24.29%, p = 0.043). Hospital mortality was 14.29% (17.58% in women and 10% in men) and 30-day mortality was 20.5% (20.88% in women and 20% in men), with no statistical differences between sexes. There was no significant difference in the length of hospital stay, with a median of 5 days in both sexes. IEAT was 27.3% (24.18% in women and 31.43% in men), without any statistically significant differences between groups.

The laboratory parameters are described in Table 2 (Laboratory data at admission according to sex). Levels of creatinine were higher in men than in women (p = 0.008). There were no significant differences in other laboratory tests.

The microbiological characteristics of UTI are shown in Table 3 (Etiology of UTI according to sex). *Escherichia coli* was the most common cause of infection in both sexes (61.5% in women and 60% in men,

respectively). Men had a higher rate of polymicrobial infection than women (6.6% vs. 17.1%, respectively; p = 0.035). A higher rate of *Pseudomonas aeruginosa* infection was found in men (3.3% in women vs 17.1% in men; p = 0.003). There was no significant association between polymicrobial infection and septic shock in men (p = 0.123).

Patients were treated with different empirical antibiotic regimens. Most of them were treated with ceftriaxone (46%), followed by carbapenems (24.2%), other beta-lactams (8.7%), quinolones (6.2%) and beta-lactams and gentamycin (3.1%). Treatment options did not influence in-hospital mortality (p 0.632) nor were there any differences between sexes (p = 0.144).

A logistic regression model was elaborated using the variables with a p-value <0.1 in the univariate analysis to identify those factors independently associated with sex. Cognitive impairment was associated with female sex (OR 0,36; p = 0.010) and COPD (OR 7,53; p = 0.006), septic

Table 3. Etiology of UTI according to sex.

	All (n = 161)	Women (n = 91)	Men (n = 70)	P-value
Escherichia coli, n (%)	98 (60.9)	56 (61.5)	42 (60)	0.843
Klebsiella spp., n (%)	29 (18.0)	19 (20.9)	10 (14.3)	0.280
Enterococcus spp., n (%)	20 (12.4)	8 (8.8)	12 (17.1)	0.177
Pseudomonas aeruginosa, n (%)	15 (9.3)	3 (3.3)	12 (17.1)	**0.003**
Proteus mirabilis, n (%)	5 (3.1)	4 (4.4)	1 (1.4)	0.282
Serratia spp., n (%)	2 (1.2)	1 (1.1)	1 (1.4)	0.851
Citrobacter spp., n (%)	2 (1.2)	1 (1.1)	1 (1.4)	0.851
Other bacteria	6 (3.7)	3 (1.9)	3 (1.9)	0.743
Candida spp., n (%)	3 (1.9)	2 (2.2)	1 (1.4)	0.720
Polymicrobial infection, n (%)	18 (11.2)	6 (6.6)	12 (17.1)	**0.035**
Multidrug-resistant bacteria, n (%)	63 (39.1)	34 (37.4)	29 (41.5)	0.860
Extended-spectrum β-lactamase producing bacteria, n (%)	16 (9.9)	11 (12.1)	5 (7.1)	0.298

Table 4. Variables independently associated with sex.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Cognitive impairment*	0.67 (0.45–0.99)	0.035	0.36 (0.16–0.78)	**0.010**
COPD**	1.96 (1.4–2.74)	0.006	7.53 (1.77–32.04)	**0.006**
Urinary catheter**	2.53 (1.85–3.45)	<0.001	9.82 (3.35–28.79)	**<0.001**
Septic shock**	1.52 (1.06–2.19)	0.043	3.13 (3.13–8.27)	**0.022**
P. aeruginosa	2.01 (1.46–2.78)	0.003	0.96 (0.16–5.71)	0.967
Polymicrobial infection	1.64 (1.12–2.41)	0.035	0.86 (0.29–4.39)	0.861

* Associated with female sex.
** Associated with male sex.

Table 2. Laboratory data at admission according to sex.

	All (n = 161)	Women (n = 91)	Men (n = 70)	P-value
Creatinine (mg/dl), (mean ± SD)	1.5 [1.1–2.4]	1.5 [1–2]	1.8 [0.4–3.2]	**0.008**
Albumin (mg/dl), (mean ± SD)	3.1 [2.7–3.4]	2.9 [2.2–3.6]	2.8 [2–3.6]	0.380
Bicarbonate (mEq/L), (mean ± SD)	24.53 (5.46)	24.96 (5.86)	24.01 (4.94)	0.299
C-reactive protein >10 mg/l, n (%)	149 (92.54)	84 (92.30)	65 (92.85)	0.895
Procalcitonine ≥0.5 ng/dL, n (%)	140 (86.9)	78 (85.7)	62 (88.6)	0.644
Lactate ≥2 mmol/L, n (%)	87 (54)	50 (54.9)	37 (52.9)	0.874
Hemoglobin (g/dL), (mean ± SD)	11.76 (2.18)	11.61 (2.23)	11.96 (2.11)	0.310
Leukocyte count (cells/μL), (mean ± SD)	12600 [8700–18350]	13100 [4100–22100]	16300 [7300–25300]	0.107
Platelet count (cells/μL), (mean ± SD)	186000 [146000–250500]	198000 [72–324000]	193000 [80750–305250]	0.853
Pyuria (cells/μL), (mean ± SD)	1054 [388–3837]	1564 [0–5612]	1298.5 [0–7413]	0.123

shock (OR 3,13; p = 0.022) and urinary catheter (OR 9,82; p < 0.001) were associated with male sex (see Table 4, Variables independently associated with sex).

4. Discussion

In this study, we found that men and women aged 80 years and older admitted to hospital with community-acquired UTI had certain differences in terms of comorbidities, clinical presentation and etiology, which may have important clinical practice implications.

In our findings UTI in women was more commonly associated with cognitive impairment than in men. This association was not unexpected, as dementia more commonly affects women [26] and cognitive impairment has been found to be an independent predictor of developing UTI among the very old in the general population [27]. Patients in our study also showed a high prevalence of severe or total dependence for basic activities of daily living, but there was no difference between sexes. Catheter-associated UTI was more than four times more common in men, similarly to other previous studies which found that male sex and older age were independent risk factors for indwelling urinary catheter, which increases the risk of UTI approximately 2–3 times [28]. The use of indwelling catheter has been associated with UTI caused by drug-resistant bacteria in some studies [12, 29]. However, as in others works [5, 30], the frequencies of multidrug-resistant bacteria or Extended-spectrum β-lactamase producing bacteria in our study were not different between sexes. *Pseudomonas aeruginosa* and polymicrobial infection were more common in men by univariate analysis and even though they were not statistically associated by multivariate analysis, probably due to the fact that indwelling urinary catheter was more common in men, we suggest considering antibiotics with activity for *Pseudomonas aeruginosa* and polymicrobial infections, at least in severe UTI in catheter-associated UTI in men.

As might be expected, the frequency of COPD was much more prevalent in men. This finding could almost certainly be attributable to the higher proportion of smokers in men. Factors associated with healthcare-associated UTI, such as previous hospitalization, use of antibiotics or nursing house residence, have been associated with longer hospitalization and higher mortality [23] and some studies have found that they are more common in women [14, 15]. However, factors associated with healthcare-associated UTI were similar in both sexes in our study. This might be due to the fact that our patients were older than those included in previous studies.

We would point out that in our study male sex was associated with septic shock, although there were not differences in severity measured by APACHE II nor in the incidence of sepsis, as well as IEAT, length of stay and mortality were similar in both sexes. This prevalence of more severe forms of infections in men has been described in a big Korean study on patients with sepsis from different sources, where it was found that organ failure was more common in men, although septic shock was similar in both sexes [31]. Furthermore, another Italian study showed that men more commonly have septic shock and younger age than women in critical care [32]. Another aspect of clinical interest is the higher percentages of infections caused by *P. aeruginosa* and polymicrobial infections in men in the univariate analysis, which are more difficult of being empirically treated. Although, these differences disappeared in the multivariate analysis, which could be explained because of their well-known association with indwelling urinary catheter that is more common in men.

The main strength of our study is its prospective design focused on a well-defined population and addressed specifically to analyze the possible differences between women and men. The study also has several limitations. Firstly, it was carried out in a single center, so our findings may be difficult to generalize to other healthcare setting or other geographic regions. Secondly, the population in our study corresponds to very old patients admitted to an internal medicine department and our findings could differ in other populations with UTI, such as nosocomial

UTI or critical care patients. All in all, our results may help the clinician to treat better very old women and men with community-acquired UTI admitted to hospital.

In this study involving patients aged 80 and over with community-acquired UTI, men had more septic shock on admission to hospital and higher rates of indwelling urinary catheter, which could account for different etiologies, while women had more cognitive impairment. However, there were no differences in outcomes between sexes.

Declarations

Author contribution statement

Ian López-Cruz; Arturo Artero: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Ana Esparcia; Manuel Madrazo: Performed the experiments; Contributed reagents, materials, analysis tools or data.

Juan Alberola: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

José María Eiros: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

[1] L.E. Nicolle, Urinary tract infections in the older adult, Clin. Geriatr. Med. 32 (3) (2016) 523–538.

[2] K.E. Rudd, S.C. Johnson, K.M. Agesa, K.A. Shackelford, D. Tsoi, D.R. Kievlan, et al., Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study, Lancet 395 (10219) (2020) 200–211.

[3] B. Foxman, Urinary tract infection syndromes. Occurrence, recurrence, bacteriology, risk factors, and disease burden, Infect. Dis. Clin. 28 (1) (2014) 1–13.

[4] N. Rodhe, S. Mölstad, L. Englund, K. Svärdsudd, Asymptomatic bacteriuria in a population of elderly residents living in a community setting: prevalence, characteristics and associated factors, Fam. Pract. 23 (3) (2006) 303–307.

[5] A. Smithson, J. Ramos, E. Niño, A. Culla, U. Pertierra, M. Friscia, et al., Characteristics of febrile urinary tract infections in older male adults, BMC Geriatr. 19 (1) (2019) 334.

[6] A. Gomila, J. Carratalà, N. Eliakim-Raz, E. Shaw, C. Tebé, M. Wolkewitz, et al., Clinical outcomes of hospitalised patients with catheter-associated urinary tract infection in countries with a high rate of multidrug-resistance: the COMBACTE-MAGNET RESCUING study, Antimicrob. Resist. Infect. Control 8 (1) (2019) 1–8.

[7] J.S. Baldassarre, D. Kaye, Special problems of urinary tract infection in the elderly, Med. Clin. 75 (2) (1991) 375–390.

[8] Z.T. Osakwe, E. Larson, J. Shang, Urinary tract infection-related hospitalization among older adults receiving home health care, Am. J. Infect. Control 47 (7) (2019) 786–792.

[9] L.E. Nicolle, K. Gupta, S.F. Bradley, R. Colgan, G.P. DeMuri, D. Drekonja, et al., Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America, Clin. Infect. Dis. 68 (2019) 1611–1615. Oxford University Press.

[10] E. Magliano, V. Grazioli, L. Deflorio, A.I. Leuci, R. Mattina, P. Romano, et al., Gender and age-dependent etiology of community-acquired urinary tract infections, Sci. World J. 2012 (2012).

[11] Y.C. Lee, C.Y. Hsiao, M.C. Hung, S.C. Hung, H.P. Wang, Y.J. Huang, et al., Bacteremic urinary tract infection caused by multidrug-resistant enterobacteriaceae

are associated with severe sepsis at admission, Med (United States) 95 (20) (2016) 1–7.

[12] M. Tumbarello, F. Raffaelli, M. Peghin, A.R. Losito, L. Chirico, G. Giuliano, et al., Characterisation and risk factor profiling of Pseudomonas aeruginosa urinary tract infections: pinpointing those likely to be caused by multidrug-resistant strains, Int. J. Antimicrob. Agents 55 (4) (2020) 105900.

[13] O. Fasugba, A. Das, G. Mnatzaganian, B.G. Mitchell, P. Collignon, A. Gardner, Incidence of single-drug resistant, multidrug-resistant and extensively drug-resistant Escherichia coli urinary tract infections: an Australian laboratory-based retrospective study, J Glob Antimicrob Resist 16 (2019) 254–259.

[14] B.G. Mitchell, J.K. Ferguson, M. Anderson, J. Sear, A. Barnett, Length of stay and mortality associated with healthcare-associated urinary tract infections: a multi-state model, J. Hosp. Infect. 93 (1) (2016) 92–99.

[15] Y.P. Tabak, A.H. Sung, G. Ye, L. Vankeepuram, V. Gupta, E. McCann, Attributable clinical and economic burden of carbapenem-non-susceptible Gram-negative infections in patients hospitalized with complicated urinary tract infections, J. Hosp. Infect. 102 (1) (2019) 37–44.

[16] A. Artero, A. Esparcia, J. Alberola, M. Madrazo, J.M. Nogueira, J.M. Eiros, Prospective cohort study of risk factors for extended-spectrum ß-lactamase-producing Escherichia coli urinary tract infections in elderly patients admitted to hospital, Int. J. Clin. Pract. 71 (9) (2017) 1–7.

[17] W.R. McCabe, G.G. Jackson, Gram-negative bacteremia: II. Clinical, laboratory, and therapeutic observations, Arch. Intern. Med. 110 (6) (1962) 856–864.

[18] M.E. Charlson, P. Pompei, K.L. Ales, C.R. MacKenzie, A new method of classifying prognostic comorbidity in longitudinal studies: development and validation, J. Chron. Dis. 40 (5) (1987) 373–383.

[19] F.I. Mahoney, D.W. Barthel, Functional evaluation: the barthel index, Md. State Med. J. 14 (1965) 61–65.

[20] W.A. Knaus, E.A. Draper, D.P. Wagner, J.E. Zimmerman, Apache II: a severity of disease classification system, Crit. Care Med. 13 (10) (1985) 818–829.

[21] N.D. Friedman, K.S. Kaye, J.E. Stout, S.A. McGarry, S.L. Trivette, J.P. Briggs, et al., Health care-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections, Ann. Intern. Med. 137 (10) (2002) 791–797.

[22] M. Singer, C.S. Deutschman, C. Seymour, M. Shankar-Hari, D. Annane, M. Bauer, et al., The third international consensus definitions for sepsis and septic shock (sepsis-3), JAMA, J. Am. Med. Assoc. 315 (8) (2016) 801–810.

[23] A.B. Gómez Belda, J. De la Fuente, L.F. Diez, J.A. Capdevila, L. Inglada, A. Arca, et al., Inadequate empirical antimicrobial treatment in older people with bacteremic urinary tract infection who reside in nursing homes: a multicenter prospective observational study, Geriatr. Gerontol. Int. 19 (11) (2019) 1112–1117.

[24] Association WM, World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects 310, JAMA - Journal of the American Medical Association. American Medical Association, 2013, pp. 2191–2194.

[26] E. Nichols, C.E.I. Szoeke, S.E. Vollset, N. Abbasi, F. Abd-Allah, J. Abdela, et al., Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Neurol. 18 (1) (2019) 88–106.

[27] M.A.A. Caljouw, W.P.J. den Elzen, H.J.M. Cools, J. Gussekloo, Predictive factors of urinary tract infections among the oldest old in the general population. A population-based prospective follow-up study, BMC Med. 9 (2011) 57.

[28] M. Adomi, M. Iwagami, T. Kawahara, S. Hamada, K. Iijima, S. Yoshie, et al., Factors associated with long-term urinary catheterisation and its impact on urinary tract infection among older people in the community: a population-based observational study in a city in Japan, BMJ Open 9 (6) (2019).

[29] S. Bischoff, T. Walter, M. Gerigk, M. Ebert, R. Vogelmann, Empiric antibiotic therapy in urinary tract infection in patients with risk factors for antibiotic resistance in a German emergency department, BMC Infect. Dis. 18 (1) (2018) 1–7.

[30] B.A. Faine, N. Mohr, P. Vakkalanka, A.S. Gao, S.Y. Liang, Validation of a clinical decision rule to identify risk factors associated with multidrug-resistant urinary pathogens in the emergency department, Ann. Pharmacother. 53 (1) (2019) 56–60.

[31] D.W. Park, B.C. Chunx, J.M. Kim, J.W. Sohn, K.R. Peck, Y.S. Kim, et al., Epidemiological and clinical characteristics of community-acquired severe sepsis and septic shock: a prospective observational study in 12 university hospitals in Korea, J. Kor. Med. Sci. 27 (11) (2012) 1308–1314.

[32] Y. Sakr, C. Elia, L. Mascia, B. Barberis, S. Cardellino, S. Livigni, et al., The influence of gender on the epidemiology of and outcome from severe sepsis, Crit. Care 17 (2) (2013).