American Journal of Infection Control 47 (2019) 1479–1483

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Factors associated with multidrug-resistant bacteria in a cohort of patients with asymptomatic bacteriuria who underwent urological surgery

Jorge A. Ramos-Castaneda MSc, PhD(c) [a,*], Alberto Ruano-Ravina PharmD, MPH, PhD [b], Diego F. Salinas MD [c], Javier Osorio-Manrique MD [d], Angela M. Segura-Cardona MSc, PhD [a], Elkin V. Lemos-Luengas MD, MSc, PhD [e]

[a] Public Health Observatory, Graduate School, Universidad CES, Medellín, Colombia
[b] Department of Preventive Medicine and Public Health, Universidad de Santiago de Compostela, España CIBER of Epidemiology and Public Health, CIBERESP, Madrid, Spain
[c] Infectious Diseases Unit, Hospital Universitario Hernando Moncaleano Perdomo, Neiva, Colombia
[d] Department of Urology, Centro Especializado de Urología, Neiva, Colombia
[e] Public Health Observatory, Universidad CES, Medellín, Colombia

Key Words:
Bacterial resistance
Urinary tract infection
Urological surgical procedures

Background: Although the factors associated to bacterial resistance in patients with asymptomatic bacteriuria (ASB) have been studied in pregnant, fertile age women, patients with spinal cord injury, and those with urogynecological disorders, nothing is known about the factors associated with multidrug-resistant (MDR) bacteria in patients with ASB and planned urological procedures. This study therefore sought to identify the sociodemographic and clinical factors associated with MDR bacteria in a cohort of patients with ASB scheduled for urological procedures.

Methods: We conducted a nested case–control study on a cohort of patients with ASB and planned urological procedures at 3 Colombian medical centers. Cases were patients with MDR bacteria and controls were patients without MDR bacteria.

Results: A total of 184 patients were included, 41.8% (n = 77) of whom presented ASB with MDR bacteria. The factors linking ASB with MDR bacteria were: advanced age (odds ratio, 1.03; 95% confidence interval, 1.01-1.06) and hospitalization within the 3-month period before surgery (odds ratio, 2.35; 95% confidence interval, 1.08-5.21).

Conclusions: Bacterial resistance is frequent among patients with ASB and planned urological procedures. Advanced age and prior hospitalization should be borne in mind for patients with planned urological procedures because they are factors associated with the presence of MDR bacteria.

Antimicrobial resistance (AMR) is considered a public health problem and a threat to humanity.[1] In developed countries, incidence of infection due to multidrug-resistant (MDR) bacteria is 131 per 100,000 population,[2] with a mortality rate of 7 patients per 100,000 every year.[2] As compared with patients infected with nonresistant bacteria, those attended for MDR bacterial infections increase health care costs by >36%.[3] It is estimated that by 2050, over 10 million persons may die as a consequence of AMR, a figure that is even higher than deaths expected from cancer and diabetes.[4]

AMR is frequent in patients with health care–associated infections,[5] pulmonary tuberculosis,[6] in community-acquired infections[7] such as pneumonia, urinary tract infections,[8] skin and soft tissue infections, as well as in patients colonized as in the case of asymptomatic bacteriuria (ASB).[9]

Although it is known that urine is not sterile and that urinary microbiota is useful for bodily functions,[10] patients with ASB are not expected to be colonized by MDR bacteria. Previous studies have indicated that

* Address correspondence to Jorge A. Ramos-Castaneda, MSc, PhD(c), Universidad CES, Graduate School, Calle 10A # 22-04, Medellin, Colombia.
E-mail address: ramos.jorge@uces.edu.co (J.A. Ramos-Castaneda).

Funding/support: The principal author (Jorge A Ramos-Castaneda) is the beneficiary of grant 677-2014 COLCIENCIAS and Departamento del Huila.

Conflicts of interest: None to report.

Author contributions: J.A.R. conceived and designed the study, acquired and analyzed the data, interpreted the findings, and wrote the manuscript. A.R.R. and E.V.L. designed the study, interpreted the findings, and wrote the manuscript. A.M.S. designed the study. D.F.S. and J.O.M. interpreted the findings and wrote the manuscript. All authors critically reviewed this report and approved the final version.

This research is part of the work conducted toward the PhD title of Jorge A. Ramos-Castañeda.

https://doi.org/10.1016/j.ajic.2019.06.005
0196-6553/

the prevalence of MDR bacteria in patients with ASB is 16%,[9] and it should be screened in pregnant women and prior to endourological procedures to determine perioperative prophylactic antibiotics.[11-13] ASB does not represent a risk or danger to patients, except in the earlier described 2 situations,[14-16] but the appearance of MDR bacteria generates concern because of the risk of such bacteria invading other tissues, generating localized and systemic infections,[17] and possibly disseminating MDR bacteria to other persons.

Bacterial resistance in patients with ASB has been studied in certain groups, including pregnant,[18] women of fertile age,[19] hospitalized patients,[20] patients with spinal cord injury,[21] and women with urogynecological disorders,[22] but not in patients with planned urological procedures. Bearing in mind that over 30% of patients scheduled for urological procedures present with ASB,[23] and that this poses a risk factor for postsurgical infectious complications, it is important to ascertain precisely which factors are associated with the MDR bacteria in patients with ASB.

The aim of this study was to identify the sociodemographic and clinical factors associated with the presence of MDR bacteria in a cohort of patients with ASB who were scheduled for urological procedures.

METHODS

Study type and study population

We conducted a nested case–control study on a cohort of patients with ASB and planned urological procedures at 3 Colombian medical centers.

Patients with planned urological procedures were consecutively recruited during April 2018 through January 2019. All patients were screened to detect ASB prior to surgery. ASB was defined as a bacterial isolate in a voided urine sample having a count of $>10^5$ (colony-forming unit/mL), assessed as being from a person who does not exhibit signs or symptoms of urinary tract infection.[24] The urological procedures included were transurethral resection of prostate (partial or radical), tumors of bladder or urethra, open prostatectomy (partial or radical), ureterolithotomy, nephrolithotomy, nephrectomy, and flexible ureterorenoscopy. We excluded all patients with urinary tract infection, immunosuppression secondary to glucocorticoid use, and hematological or solid-organ malignancies undergoing chemotherapy or radiation treatment, as well as patients aged <18 years.

A case was defined as any patient with ASB who had MDR bacteria. Multidrug-resistance was defined as nonsusceptibility to at least 1 agent in 3 or more categories of antibiotics, taking into account the intrinsic resistance of microorganisms to certain antimicrobial agents.[25] Antimicrobial categories were aminoglycoside, antipseudomonal penicillin + β-lactamase inhibitors, carbapenems, nonextended spectrum cephalosporins, extended spectrum cephalosporins, fluoroquinolones, folate pathway inhibitors, monobactams, penicillin, penicillin + β-lactamase inhibitors, phosphonic acids, and polymyxins.[25] Controls were patients with ASB due to nonresistant bacteria.

All isolates were identified by means of the microbiology laboratory's standard method. Susceptibility criteria were defined by reference to the Clinical & Laboratory Standards Institute cut-off values.[26]

Independent variables

The independent variables were sex, age, personal history of conditions such as arterial hypertension, diabetes mellitus, urological cancer, renal lithiasis, or benign prostatic hyperplasia. Data were also collected on prior manipulation of the urinary tract (surgery or endoscopic procedure) in the preceding 3 months,[13,23] antibiotic use in the preceding 3 months, type of urological intervention, microorganism isolated, and hospitalization in the preceding 3 months.

Statistical analysis

The independent variables were compared in groups with and without MDR bacteria. The χ^2 test was used to establish significant differences with the categorical variables. Age was compared using the Student t test. The odds ratios (OR) with their 95% confidence intervals (CI) were calculated for the independent variables. We fitted a logistic regression model for explanatory purposes, in which we included variables with statistical significance in the bivariate analysis, the interactions, and the confounding variables. All data analyses were performed using the R Studio 1.1.4 software package (R Core Team; R Foundation for Statistical Computing, Vienna, Austria).

Ethical considerations

The study was submitted to and approved by the Universidad CES research ethics committee (record no. 123, study 631) and by the ethics committees of the respective participating institutions. Patients' informed verbal consent was obtained for the review of clinical histories. The principal investigator entered into a confidentiality agreement with the institutions. In all cases, consent was obtained in accordance with the provisions of the latest version of the Declaration of Helsinki.

RESULTS

During the study period, 184 patients with ASB were scheduled for urological surgery; they had a mean age of 61.4 (SD 13.9) years and were mostly men (62.0%). The most frequent nonurological condition was arterial hypertension (30.98%). Benign prostatic hyperplasia (41.30%) and renal lithiasis (32.06%) were the 2 most frequent urological disorders (Table 1).

Over 40% of patients in this cohort reported some prior manipulation of the urinary tract in the last 3 months (mainly endoscopic procedures), as well as hospitalization (40.8%) or antibiotic use in the

Table 1
Demographic and clinical characteristics of the patients with asymptomatic bacteriuria (N = 184)

Characteristics	*N (%)*
City	
Neiva	162 (88.0)
Medellín	22 (11.9)
Institution	
1	22 (11.9)
2	146 (79.3)
3	16 (8.7)
Sex	
Male	114 (61.9)
Female	70 (38.0)
Age (years)	
Mean (SD)	61.43 (13.9)
Median (range interquartile)	63 (17)
Comorbidities	
Arterial hypertension	57 (30.9)
Diabetes mellitus	24 (13.0)
Urological cancer	13 (7.0)
Urolithiasis	59 (32.0)
Benign prostatic hyperplasia	76 (41.3)
History of a urological intervention	
*Previous urological intervention**	84 (45.6)
*Previous endoscopic intervention**	50 (27.1)
*Previous surgery**	34 (18.4)
Permanent bladder catheter	49 (26.6)
Intermittent bladder catheter	2 (1.0)
Ureteral stent	21 (11.4)
Hospitalization in the last 3 months	75 (40.7)
Antibiotics in the last 3 months	102 (55.4)

*In the last 3 months.

Table 2
Microbiological characteristics of the patients with asymptomatic bacteriuria (N = 184)

Microbiological characteristic	MDR bacteria N (%)	Non-MDR bacteria N (%)	N (%)
Escherichia coli	30 (42.9)	40 (57.1)	70 (38.0)
Klebsiella pneumoniae	25 (69.4)	11 (30.6)	36 (19.5)
Pseudomona aeruginosa	4 (23.5)	13 (76.5)	17 (9.2)
Enterococcus faecalis	1 (7.1)	13 (92.9)	14 (7.6)
Proteus mirabilis	3 (25.0)	9 (75.0)	12 (6.5)
Serratia marcescens	4 (44.4)	5 (55.6)	9 (4.8)
Morganella morganii	2 (40.0)	3 (60.0)	5 (2.7)
Enterobacter cloacae	1 (25.0)	3 (75.0)	4 (2.1)
Klebsiella oxytoca	1 (25.0)	3 (75.0)	4 (2.1)
Acinetobacter baumannii	2 (66.7)	1 (33.3)	3 (1.6)
Citrobacter freundii	0	3 (100.0)	3 (1.6)
Streptococcus agalactiae	0	2 (100.0)	2 (1.0)
Others[*]	4 (100.0)	0	4 (2.1)

MDR, multidrug-resistant.
[*]*Hafnia alvei, Providencia rettgeri, Pseudomona luteola, or Pseudomona putida.*

preceding 3 months (55.4%) (Table 1). In terms of use of urological devices, indwelling urinary catheter and ureteral stents were the devices most used by patients prior to urological surgery (26.6% and 11.4%, respectively) (Table 1).

A total of 41.8% (n = 77) of patients presented with MDR bacteria in this cohort, and *Escherichia coli* and *Klebsiella pneumoniae* were the microorganisms more frequently seen (57.6%) (Table 2).

The crude analysis showed that, compared with controls, cases had a higher age (OR, 1.03; 95% CI, 1.00-1.05) and registered a higher frequency of previous urological interventions (OR, 1.86; 95% CI, 1.03-3.36), particularly surgery (OR, 3.15; 95% CI, 1.45-7.05), and of hospitalization in the preceding 3 months (OR, 2.96; 95% CI, 1.61-5.46) (Table 3). In addition, there were other variables that displayed an association, although without reaching statistical significance, such as antibiotic use in the 3 months immediately preceding urological surgery (OR, 1.78; 95% CI, 0.98-3.25) (Table 3).

The multivariate logistic regression analysis showed that having previously undergone hospitalization (OR, 2.35; 95% CI, 1.08-5.21) and the advanced age (OR, 1.03; 95% CI, 1.01-1.06) were factors associated with the acquisition of MDR bacteria organism colonization in patients with ASB. Surgery and antibiotic use in the 3 months immediately preceding urological surgery was not associated with the presence of MDR bacteria (Table 4).

DISCUSSION

This study has observed that advanced age as well as hospitalization 3 months prior to surgery are factors associated with the presence of MDR bacteria in a cohort of patients with ASB and planned urological procedures. To our knowledge, this is the largest prospective study in terms of sample size conducted on patients with ASB and planned urological procedures in Latin America, and the second largest performed worldwide.

One of the factors associated with the appearance of antibiotic resistance is having recently undergone hospitalization. During hospitalization, patients are exposed to invasive devices, contact with health care MDR bacteria-colonized personnel, and risk of acquiring health care–associated infections,[27,28] factors that may trigger new acquisition of MDR bacteria organism colonization. In our study, evidence of a patient being hospitalized in the preceding 3 months was associated with the appearance of MDR bacteria. This could be because of the direct relationship that exists between hospitalization and antibiotic use, the main factor for generation of MDR bacteria, as well as the use of medications that alter the human microbiota.[29] In this respect, Pobiega et al[9] observed that previous hospitalization was associated with urinary tract infection by extended-spectrum β-lactamase-producing bacteria.

Advanced age was another factor found to be associated with multidrug resistance in patients with ASB. There are studies that have shown a direct relationship between age and antibiotic resistance[30] as result of the physiological changes that occur during adult age and increase both susceptibility to and appearance of MDR bacteria.[31]

Table 3
Demographic and clinical characteristics associated with the presence of an MDR microorganism in patients with asymptomatic bacteriuria (N = 184)

Characteristics	MDR bacteria N = 77	Non-MDR bacteria N = 107	*P*	Crude OR (95% CI)
Sex				
Male	52 (67.5)	62 (57.9)		
Female	25 (32.4)	45 (42.0)	.24	1.51 (0.82-2.78)
Age				
Mean	64.4	59.2	<.01	1.03 (1.00-1.05)
Comorbidities				
Arterial hypertension	29 (37.6)	28 (26.1)	.13	1.71 (0.91-3.20)
Diabetes mellitus	7 (9.0)	17 (15.8)	.26	0.53 (0.21-1.35)
Urological cancer	6 (7.7)	7 (6.5)	.97	1.21 (0.39-3.74)
Urolithiasis	23 (29.8)	36 (33.6)	.70	0.84 (0.45-1.58)
Benign prostatic hyperplasia	37 (48.0)	39 (36.4)	.15	1.61 (0.89-2.93)
History of a urological intervention				
Previous urological intervention[*]	42 (54.5)	42 (39.2)	.05	1.86 (1.03-3.36)
Previous endoscopic intervention[*]	20 (25.9)	30 (28.0)	.76	0.90 (0.46-1.75)
Previous surgery[*]	22 (28.5)	12 (11.2)	.003	3.15 (1.45-7.05)
Permanent bladder catheter	26 (33.7)	23 (21.4)	.09	1.86 (0.96-3.60)
Ureteral stent	9 (11.6)	12 (11.2)	1.0	1.05 (0.42-2.62)
Hospitalization in the last 3 months	43 (55.8)	32 (29.9)	<.01	2.96 (1.61-5.46)
Antibiotics in the last 3 months	49 (63.6)	53 (49.5)	.08	1.78 (0.98-3.25)
Reason for urological intervention				
Lithiasis	22 (28.5)	29 (27.1)	Reference	Reference
Urological cancer	7 (9.0)	10 (9.3)	1.00	1.03 (0.34-3.16)
Hydronephrosis	8 (10.3)	15 (14.0)	.91	1.21 (0.44-3.28)
Benign prostatic hyperplasia	31 (40.2)	39 (36.4)	.95	0.91 (0.44-1.90)
Urinary incontinence	7 (9.0)	9 (8.4)	1.00	0.93 (0.30-2.90)
Tumor	2 (2.6)	5 (4.6)	.79	1.81 (0.32-10.24)

CI, confidence interval; *MDR*, multidrug-resistant; *OR*, odds ratio.
[*]In the last 3 months.

Table 4
Associated factors with the presence of MDR bacteria in patients with asymptomatic bacteriuria (N = 184)

Associated factors	Crude OR (95% CI)	Adjusted OR (95% CI)*	*P*
Hospitalization in the last 3 months	2.96 (1.61-5.46)	2.35 (1.08-5.21)	.03
Age (years)	1.03 (1.00-1.05)	1.03 (1.01-1.06)	<.01
Previous surgery in the last 3 months	3.15 (1.45-7.05)	2.38 (0.95-5.96)	.06
Antibiotics in the last 3 months	1.78 (0.98-3.25)	0.85 (0.40-1.79)	.67

CI, confidence interval; *MDR*, multidrug-resistant; *OR*, odds ratio.
*Adjusted OR by age, previous surgery, and antibiotics in the last 3 months.

In patients with ASB, MDR bacteria are found in: pregnant women (10%-20%),[18] patients with spinal cord injury (50%),[21] hospitalized patients (16%),[9] and patients with planned urological procedures (30%).[23] In our study, over 40% of patients with ASB who were scheduled for urological surgery had MDR bacteria. This difference could be owing to overuse of antibiotics received by these patients prior to urological procedures[32] in line with the recommendations of treating ASB prior to urological surgery.[13] This factor might be increasing resistance rates.[33]

Treatment of ASB is associated with urinary tract infection by MDR bacteria.[34] It is this that has given rise to the debate about evaluating the usefulness and consequences—in terms of antibiotic resistance—of screening for and treating ASB prior to urological surgery,[23,35] particularly when one bears in mind that urine is not sterile and that its microbiota poses protective functions for the body.[22,36] Similarly, the usefulness of identifying and treating ASB has been evaluated in orthopedic surgery,[14] cardiovascular surgery,[15] neurosurgery, spinal cord injury,[37] and transplant patients,[16] with the conclusion that, rather than lowering the risk of infection, treatment of ASB actually poses a risk in terms of antibiotic resistance.

Considering that the cohort of patients with ASB displayed a high rate of bacterial resistance, it is important to assess the risk–benefit relationship of treating bacteriuria prior to urological surgery. Care must be prioritized, and other factors assessed in patients who have undergone recent hospitalization or are of advanced age because they will have a risk of developing MDR bacteria in urine and might experience postsurgical infectious complications.

This study has some limitations. Information was extracted from hospital records and may not have registered all relevant variables, such as antibiotic use, urinary tract manipulation, and hospitalization in the prior 3 months. Isolates were identified using the standard method, albeit of different clinical laboratories, because patient care depends on each individual hospital protocols. Sample size was not large enough to allow for analysis by subgroup, taking into account the type of resistance (MDR, extensively drug-resistant, or pandrug-resistant bacteria).[25] Therefore, the study was based on one of the largest sample sizes used for this specific topic. Data were collected from 3 hospitals in the same country, so that rates of ASB and MDR bacteria may not be generalizable to rates of MDR bacteria in other parts of the world. Finally, the study evaluated the presence of MDR bacteria, but it did not show the rate of resistance by each category of antibiotics.

The study's advantages include consecutive sampling, allowing for the control of selection bias that was conducted in several health centers, which serves to enhance its external validity at least at a national level. Finally, the definition and evaluation of multidrug-resistance was based on findings reported in the literature, according to microorganism's intrinsic resistance.[25]

Conclusions

Patients with ASB who have undergone urological surgery displayed a high bacterial resistance rate. Both advanced age and hospitalization within the 3 months immediately preceding the surgical procedure were found to be associated with the presence of MDR bacteria. Given the observed frequency and severity of possible postsurgical infectious complications, it would perhaps be advisable for displaying these characteristics to be screened for the presence of MDR bacteria. Even so, there is a need for more studies to evaluate other factors associated with antibiotic resistance, in which antibiotic use and the mechanism of specific resistance are clearly distinguished. It is imperative to have studies evaluating the usefulness and consequences—in terms of antibiotic resistance—of screening and treating ASB prior to urological surgery.

Acknowledgments

Jorge A Ramos-Castaneda is grateful to Clinica CES, Centro Especializado de Urologia, and Hospital Universitario Hernando Moncaleano Perdomo de Neiva.

References

1. Organización Mundial de la Salud. Estrategia mundial de la OMS para contener la resistencia a los antimicrobianos. Rev Panam Salud Pública 2001;10.
2. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis 2019;19:56-66.
3. Lemos EV, Hoz FP, Alvis N, Einarson TR, Quevedo E, Castaneda C, et al. Impact of carbapenem resistance on clinical and economic outcomes among patients with *Acinetobacter baumannii* infection in Colombia. Clin Microbiol Infect 2014;20:174-80.
4. O'Neill J. Review on antimicrobial resistance. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. Wellcome Trust and the HM Government; 2014.
5. Ramos-Castañeda JA, Ruano-Ravina A, Barbosa-Lorenzo R, Paillier-Gonzalez JE, Saldaña-Campos JC, Salinas DF, et al. Mortality due to KPC carbapenemase-producing *Klebsiella pneumoniae* infections: systematic review and meta-analysis: mortality due to KPC *Klebsiella pneumoniae* infections. J Infect 2018;76:438-48.
6. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis 2018;18:318-27.
7. Bharadwaj R, Robinson ML, Balasubramanian U, Kulkarni V, Kagal A, Raichur P, et al. Drug-resistant *Enterobacteriaceae* colonization is associated with healthcare utilization and antimicrobial use among inpatients in Pune, India. BMC Infect Dis 2018;18:504-12.
8. Leal AL, Cortés JA, Arias G, Ovalle MV, Saavedra SY, Buitrago G, et al. [Emergence of resistance to third generation cephalosporins by *Enterobacteriaceae* causing community-onset urinary tract infections in hospitals in Colombia]. Enfermedades Infecc Microbiol Clínica 2013;31:298-303.
9. Pobiega M, Wojkowska-Mach J, Chmielarczyk A, Romaniszyn D, Adamski P, Heczko PB, et al. Molecular characterization and drug resistance of *Escherichia coli* strains isolated from urine from long-term care facility residents in Cracow, Poland. Med Sci Monit 2013;19:317-26.
10. Wolfe AJ, Toh E, Shibata N, Rong R, Kenton K, FitzGerald M, et al. Evidence of uncultivated bacteria in the adult female bladder. J Clin Microbiol 2012;50:1376-83.
11. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis 2005;40:643-54.
12. Ramos JA, Salinas DF, Osorio J, Ruano-Ravina A. Antibiotic prophylaxis and its appropriate timing for urological surgical procedures in patients with asymptomatic bacteriuria: a systematic review. Arab J Urol 2016;14:234-9.
13. Bonkat G, Pickard R, Bartoletti R, Bruyère F, Geerlings SE, Wagenlehner F, et al. EAU guidelines on urological infections London (UK), European Association of Urology, 2017.
14. Sousa R, Muñoz-Mahamud E, Quayle J, Dias da Costa L, Casals C, Scott P, et al. Is asymptomatic bacteriuria a risk factor for prosthetic joint infection? Clin Infect Dis 2014;59:41-7.
15. Duarte JC, Reyes P, Bermúdez D, Alzate JP, Maldonado JD, Cortés JA. Bacteriuria is not associated with surgical site infection in patients undergoing cardiovascular surgery. Am J Infect Control 2018;46:180-5.
16. Coussement J, Abramowicz D. Should we treat asymptomatic bacteriuria after renal transplantation? Nephrol Dial Transplant 2014;29:260-2.
17. Ye C, Kumar D, Carbonneau M, Keough A, Ma M, Tandon P. Asymptomatic bacteriuria is an independent predictor of urinary tract infections in an ambulatory cirrhotic population: a prospective evaluation. Liver Int 2014;34:e39-44.
18. Tadesse S, Kahsay T, Adhanom G, Kahsu G, Legese H, Derbie A. Prevalence, antimicrobial susceptibility profile and predictors of asymptomatic bacteriuria among pregnant women in Adigrat General Hospital, Northern Ethiopia. BMC Res Notes 2018;11:740.

19. Afoakwa P, Domfeh S, Afranie B, Owusu D, Donkor S, Sakyi K, et al. Asymptomatic bacteriuria and anti-microbial susceptibility patterns among women of reproductive age. A cross-sectional study in primary care, Ghana. Med Sci 2018;6:118.
20. Khair HN, VanTassell P, Henderson JP, Warren DK, Marschall J, Program CPE. Vancomycin resistance has no influence on outcomes of enterococcal bacteriuria. J Hosp Infect 2013;85:183-8.
21. Fouts DE, Pieper R, Szpakowski S, Pohl H, Knoblach S, Suh MJ, et al. Integrated next-generation sequencing of 16S rDNA and metaproteomics differentiate the healthy urine microbiome from asymptomatic bacteriuria in neuropathic bladder associated with spinal cord injury. J Transl Med 2012;10:174.
22. Wolfe AJ, Brubaker L. Urobiome updates: advances in urinary microbiome research. Nat Rev Urol 2019;16:73-4.
23. Cai T, Verze P, Palmieri A, Gacci M, Lanzafame P, Malossini G, et al. Is preoperative assessment and treatment of asymptomatic bacteriuria necessary for reducing the risk of postoperative symptomatic urinary tract infections after urologic surgical procedures? Urology 2017;99:100-5.
24. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309-32.
25. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 2012;18:268-81.
26. Clinical & Laboratory Standards Institute: CLSI Guidelines. Available from: http://clsi.org/. Accessed December 5, 2018.
27. ALfadli M, EL-Sehsah EM, Ramadan MA. Risk factors and distribution of MDROs among patients with healthcare associated burn wound infection. Germs 2018;8:199-206.
28. Osorio J, Barreto J, Samboni CF, Cándelo LA, Álvarez LC, Benavidez S, et al. [Risk factors for acute kidney injury in patients treated with polymyxin B experience from 139 cases at a tertiary university hospital in Colombia]. Rev Chil Infectol 2017;34:7-13.
29. Keeney KM, Yurist-Doutsch S, Arrieta M-C, Finlay BB. Effects of antibiotics on human microbiota and subsequent disease. Annu Rev Microbiol 2014;68:217-35.
30. Milovanovic T, Dumic I, Veličkovic J, Lalosevic MS, Nikolic V, Palibrk I. Epidemiology and risk factors for multi-drug resistant hospital-acquired urinary tract infection in patients with liver cirrhosis: single center experience in Serbia. BMC Infect Dis 2019;19:141.
31. Erb S, Frei R, Tschudin Sutter S, Egli A, Dangel M, Bonkat G, et al. Basic patient characteristics predict antimicrobial resistance in *E. coli* from urinary tract specimens: a retrospective cohort analysis of 5246 urine samples. Swiss Med Wkly 2018;148:w14660.
32. Mossanen M, Calvert JK, Holt SK, James AC, Wright JL, Harper JD, et al. Overuse of antimicrobial prophylaxis in community practice urology. J Urol 2015;193:543-7.
33. Bausch K, Roth JA, Seifert HH, Widmer AF. Overuse of antimicrobial prophylaxis in low-risk patients undergoing transurethral resection of the prostate. Swiss Med Wkly 2018;148, w14594.
34. Cai T, Nesi G, Mazzoli S, Meacci F, Lanzafame P, Caciagli P, et al. Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. Clin Infect Dis 2015;61:1655-61.
35. Cai T, Koves B, Johansen TEB. Asymptomatic bacteriuria, to screen or not to screen–and when to treat? Curr Opin Urol 2017;27:107-11.
36. Brubaker L, Wolfe AJ. The female urinary microbiota, urinary health and common urinary disorders. Ann Transl Med 2017;5:34.
37. Chong JT, Klausner AP, Petrossian A, Byrne MD, Moore JR, Goetz LL, et al. Pre-procedural antibiotics for endoscopic urological procedures: initial experience in individuals with spinal cord injury and asymptomatic bacteriuria. J Spinal Cord Med 2015;38:187-92.