Acta Med Croatica, 73 (2019) 49-55 *Ckinical Study*

URINARY TRACT INFECTIONS IN THE ELDERLY. THE EFFECT OF REDUCING THE AGE CRITERIA IN A GERIATRIC SERVICE

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Introduction: Urinary tract infections (UTIs) are one of the most common community-acquired infections in older adults. ***Methodology:*** This was a retrospective and descriptive study carried out in a Mexican Geriatric Service from January 2013 to December 2015. Demographic characteristics of patients were recorded including age, gender, cause of disease, urine culture, microorganism identification and antibiogram. The objective of this study was to describe the situational status of microbial antibiotic resistance in the elderly after reduction of the age criteria to be treated in a geriatric service. ***Results:*** One hundred and eighty-two geriatric patients (74 males mean age 81.5±13.5 years and 108 females mean age 81.5±11.5 years) with positive urine culture for one or more microbial identification and antibiograms were included in the analysis. The most common isolations were positive for *Escherichia coli* BLEE, *Escherichia coli, Candida albicans, Enterococcus faecalis, Pseudomonas aeruginosa, Proteus vulgaris and Klebsiella pneumoniae.* After widening of the age range to enter the geriatric service (in 2015), there was a reduction in total cases of *Escherichia coli* BLEE and an increase for *Escherichia coli. Conclusion:* In our study, a growing increase of *E. coli* BLEE was recorded, however, at the same time, it was possible to confirm that the majority of cases of this bacterium showed resistance to β-lactams, cephalosporins of different generations, quinolones and sulfas, demonstrating that it is becoming a public health problem.

Key words: amikacin, carbapenems, elderly, resistance, sensitivity, urinary tract infection

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INTRODUCTION

Urinary tract infections (UTIs) are one of the most common community-acquired infections in older adults and their prevalence increases with age. As the number of elderly people tends to increase, this type of infection will increase in the future, making it imperative to improve diagnosis and treatment since aging causes alterations in the mechanisms of defense against infections (1,2).

Urinary tract infections are those infections for which ever more money is invested for their treatment since they are most prevalent in the general population, as well as in the geriatric population, and also are the most common cause of bacteremia (3). It is worth noting that the overall number of medical visits for UTIs is twice higher among women of all ages compared with men (4).

Urinary tract infections are mostly generated by gram-negative bacteria and risk factors have been described extensively, such as cardiovascular disease (CVD), cognitive and/or functional impairment, bladder catheters, and previous antimicrobial treatment (5,6). The main routes of infection are ascending, hematogenous and contiguity (7,8).

In women, the urethral pathway accounts for most of UTIs, whereas in men these infections are often complicated. It is recognized that the pathogenesis of UTIs in the elderly is associated with physiological changes caused by the aging itself (9,10).

Comorbidity is the main predisposing factor for bacteriuria in the elderly. In this line, the most frequent diseases are benign prostatic hypertrophy, cognitive impairment, diabetes mellitus, Parkinson's disease, etc. (11,12). In addition, institutionalized elderly persons are more likely to have a catheter and anatomical or functional abnormalities of urinary tract.

As this type of infection is frequent in geriatric patients, we must suspect it when there is a change in the clinical or functional situation of the elderly (acute confusional state, dehydration, falls and immobility); if the patient has a feverish syndrome, suspicion must be even higher (13,14). Notwithstanding, common symptoms of upper (chills, fever, leukocytosis, low back pain, etc.) or lower (bladder tenesmus, low abdominal pain, urinary incontinence, urinary tract dysuria, etc.) UTI have an atypical presentation in the elderly (Table 1) (5).

Table 1.
Symptoms related to urinary tract

General symptoms	Local symptoms
- Fever	- Dysuria
- Functional impairment	- Frequency of urination
- Acute confusional state	- Bladder tenesmus
- Asthenia	- Urgency to urination
- Apathy	- Incontinence
- Anorexia	- Abdominal pain
- Falls	

Another aspect to be considered in the elderly is the increased risk of infection by classically pathogenic nosocomial pathogens, probably related to repetitive antibiotic treatments (15). The objective of this study was to describe the situational status of microbial antibiotic resistance in the elderly after reduction of the age criteria to be treated in a geriatric service.

METHODS

This was a retrospective and descriptive study carried out at the Centro Médico ISSEMYM, Metepec, State of Mexico, Mexico. A review of clinical records of patients hospitalized with UTIs was performed at the Geriatric Service from January 2013 to December 2015. During the last year, the age criterion to be treated at the geriatric service was reduced from 65 to 60 years. Demographic characteristics of patients were recorded including age, gender, cause of disease, urine culture, microbial identification and antibiogram. Patients having taken antibiotics before urine testing were excluded from the study but the presence of urinary catheter was not an exclusion factor.

All urine samples were inoculated using standard procedure in culture media using specific Chromoagar for isolation of bacilli, cocci and yeast. They were incubated at 37 °C for 24 hours and after incubation, bacteria and yeasts were confirmed by Gram staining. Microbial identification was then carried out through Vitek 2 cards for fermenting and non-fermenting gram-negative bacilli, cocci and non-gram-positive spore forming bacilli and yeast and levaduriform organisms, incubated in the Vitek 2 XL (BioMérieux, France), through which antibiotic susceptibility was also performed by means of microdilution broth based cards, including the following groups of antibiotics: a) β-lactams (ampicillin, ampicillin/sulbactam, aztreonam, piperacillin/tazobactam, benzylpenicillin), b) cephalosporins (cefazolin, ceftriaxone, cefepime, ceftazidime, cefalotin, cefuroxime), c) carbapenems (ertapenem, imipenem, meropenem), d) aminoglycosides (amikacin, gentamicin, tobramycin), e) quinolones (ciprofloxacin, moxifloxacin, levofloxacin), f) glycylglycines (tigecycline), g) nitrofurantoin, h) sulfas (trimethoprim/sulfamethoxazole), i) oxazolidinone (linezolid), and j) glycopeptide (vancomycin). Resistance or sensitivity was determined in accordance with the minimum inhibitory concentration (MIC). All data were plotted and analyzed in an Excel data sheet.

RESULTS

One hundred and eighty-two geriatric patients (74 males mean age 81.5±13.5 years and 108 females mean age 81.5±11.5 years) with positive urine culture for one or more microbial identification and antibiograms were included in the analysis.

The most common isolations were positive for *Escherichia coli* BLEE, *Escherichia coli*, *Candida albicans*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Klebsiella pneumoniae* (Fig. 1).

Generally speaking, for *E. coli* BLEE there are only two options with scarce or null resistance, i.e. carbapenems and glycylglycine. Aminoglycosides offer between 40% and 50% of sensitivity. Paradoxically, when reducing the age of acceptance to the geriatric service, nitrofurantoin showed less sensitivity (Fig. 2).

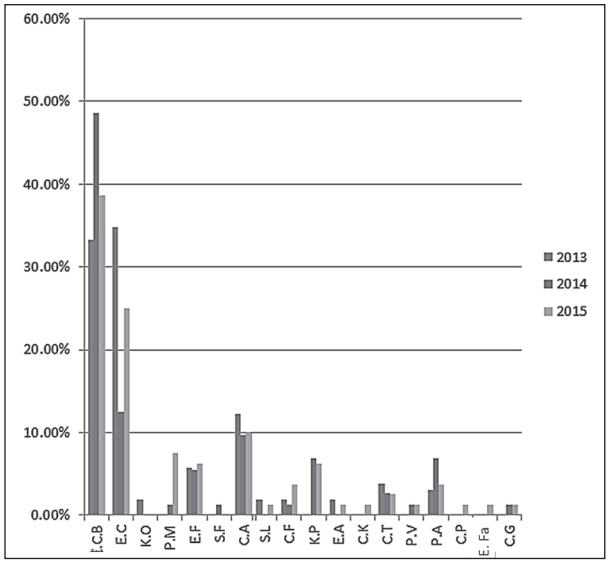

Fig. 1. *Microbiological isolations per study year.*
C.A.: Candida albicans, C.F.: Citrobacter freundii complex, C.G.: Candida glabrata, C.K.: Candida krusei, C.P.: Candida parapsilopsis, C.T.: Candida tropicalis, E.A.: Enterobacter aerogenes, E.C.: Escherichia coli, E.C.B.: Escherichia coli BLEE, E.F.: Enterococcus faecalis, E.Fa.: Enterococcus faecium, K.O.: Klebsiella oxytoca, K.P.: Klebsiella pneumoniae, P.A.: Pseudomonas aeruginosa, P.M.: Proteus mirabilis, P.V.: Proteus vulgaris, S.L.: Staphylococcus lentus.

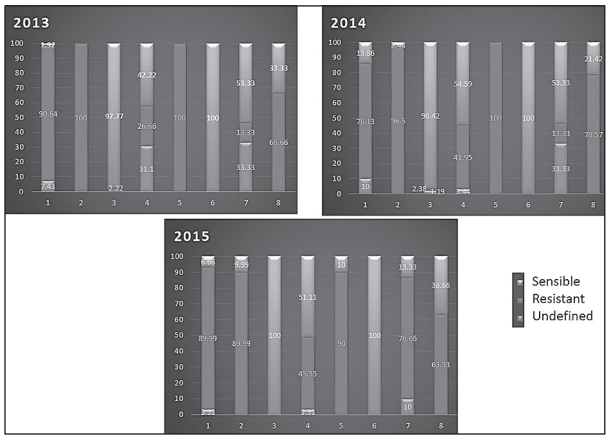

Fig. 2. *Antibiotic resistance (A) and sensitivity (B) for E. coli BLEE.*
1: β-lactams (ampicillin, ampicillin/sulbactam, aztreonam, piperacillin/tazobactam), 2: cephalosporins (cefazolin, ceftriaxone, cefepime), 3: carbapenems (ertapenem, imipenem, meropenem), 4: aminoglycosides (amikacin, gentamicin, tobramycin), 5: quinolones (ciprofloxacin, moxifloxacin), 6: glycylglycines (tigecycline), 7: nitrofurantoin, 8: sulfas (trimethoprim/sulfamethoxazole).

In the case of *Escherichia coli* (Fig. 3), the best options for sensitivity are also carbapenems and glycylglycine, with nitrofurantoin as a third alternative. Practically all groups of antibiotics showed better response when reducing the age to be treated in the geriatric service.

Enterococcus faecalis (Fig. 4) showed 100% sensitivity for glycylglycine and nitrofurantoin in this three-year survey. Linezolid had 25% resistance in the year 2013 and then was 100% effective. Vancomycin was the fourth most effective antibiotic.

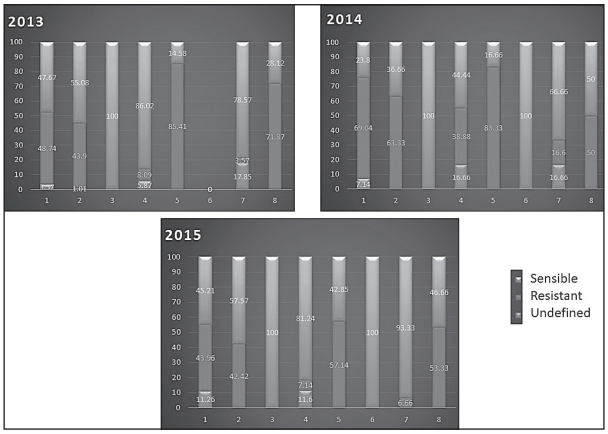

Fig. 3. *Antibiotic resistance (A) and sensitivity (B) for E. coli.*
1: β-lactams (ampicillin, ampicillin/sulbactam, aztreonam, piperacillin/tazobactam), 2: cephalosporins (cefazolin, ceftriaxone, cefepime), 3: carbapenems (ertapenem, imipenem, meropenem), 4: aminoglycosides (amikacin, gentamicin, tobramycin), 5: quinolones (ciprofloxacin, moxifloxacin), 6: glycylglycines (tigecycline), 7: nitrofurantoin, 8: sulfas (trimethoprim/sulfamethoxazole).

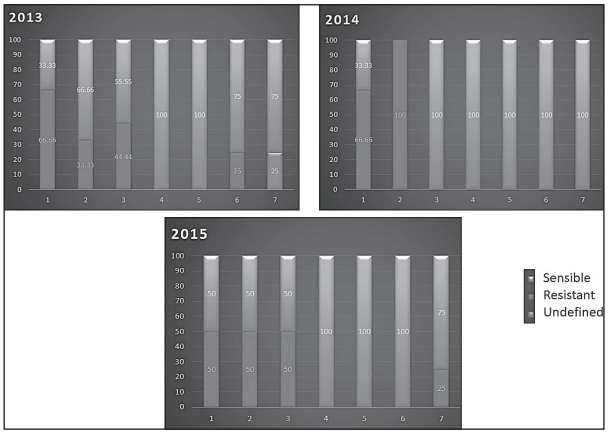

Fig. 4. *Antibiotic resistance (A) and sensitivity (B) for Enterococcus faecalis*
1: β-lactams (ampicillin, ampicillin/sulbactam, benzylpenicillin), 2: aminoglycosides (gentamicin), 3: quinolones (ciprofloxacin, moxifloxacin, levofloxacin), 4: glycylglycines (tigecycline), 5: nitrofurantoin, 6: oxazolidinone (linezolid), 7: glycopeptide (vancomycin).

When analyzing the *Pseudomonas aeruginosa* spectrum (Fig. 5), unfortunately the information was incomplete in 2015, as sulfas and glycylglycines were not tested for unknown reasons. The best option seems to be aminoglycosides and probably tigecycline taking into account the antibiogram from 2014.

Klebsiella pneumonia (Fig. 6) showed dramatic improvement in the antibiogram within the 3-year period and the elective antibiotic choice should be tigecycline followed by carbapenems and aminoglycosides.

After widening the age range to enter geriatric service (in 2015), there was a reduction in the total cases of *Escherichia coli* BLEE and an increase for *Escherichia coli*. *Candida albicans* showed no significant chang-

es. For the less common microorganisms, there was an increase that almost doubled the casuistry of the previous year (2014) for *Citrobacter freundii* complex and *Proteus mirabilis*, while a reduction was verified for *Pseudomonas aeruginosa*. The rest of the isolated agents kept the same percentages.

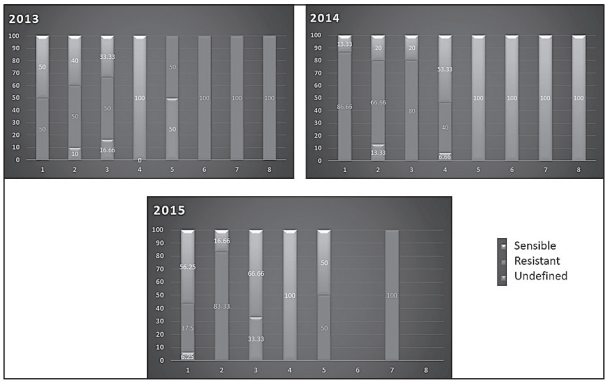

Fig. 5. *Antibiotic resistance (A) and sensitivity (B) for Pseudomonas aeruginosa*
1: β-lactams (ampicillin, ampicillin/sulbactam, aztreonam, piperacillin/tazobactam), 2: cephalosporins (cefazolin, ceftriaxone, cefepime, ceftazidime, cefotaxime), 3: carbapenems (ertapenem, imipenem, meropenem), 4: Aminoglycosides (amikacin, gentamicin, tobramycin), 5: quinolones (ciprofloxacin, moxifloxacin, levofloxacin), 6: glycylglycines (tigecycline), 7: nitrofurantoin, 8: sulfas (trimethoprim/sulfamethoxazole).

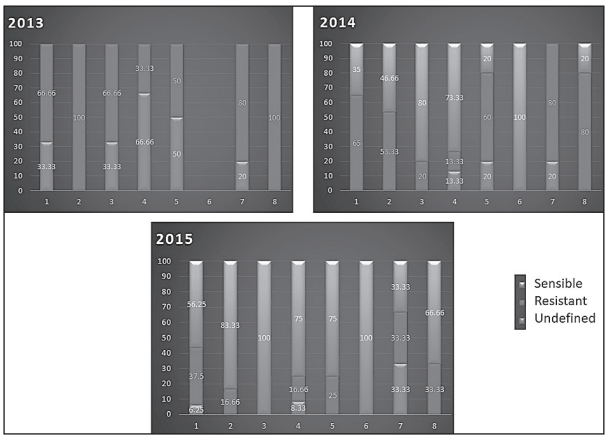

Fig. 6. *Antibiotic resistance (A) and sensitivity (B) for Klebsiella pneumoniae*
1: β-lactams (ampicillin, ampicillin/sulbactam, aztreonam, piperacillin/tazobactam), 2: cephalosporins (cefazolin, ceftriaxone, cefepime, ceftazidime, cefalotin, cefuroxime), 3: carbapenems (ertapenem, imipenem, meropenem), 4: Aminoglycosides (amikacin, gentamicin, tobramycin), 5: quinolones (ciprofloxacin, moxifloxacin, levofloxacin), 6: glycylglycines (tigecycline), 7: nitrofurantoin, 8: sulfas (trimethoprim/sulfamethoxazole).

DISCUSSION

The bacteriological differences of UTIs in the elderly are essentially based on the general characteristics of the patient, with differences attributed to gender or place of living (16,17). In a previous study in Latin America, Leoni *et al*. published the isolation and resistance rate for: a) *Escherichia coli* (67.7% of isolations): ampicillin/sulbactam (52.7%), ciprofloxacin (51.9%), trimethoprim/sulfamethoxazole (45.7%), cefotaxime (12.9%) and amikacin (3.9%), b) *Klebsiella pneumoniae* (11.97% of isolations): ciprofloxacin (60.8%), trimethoprim/sulfamethoxazole (50%), cefotaxime (47.8%) and amikacin (4.7%) and c) *Enterococcus* spp. (9.89% of isolations): ampicillin (0%), vancomycin (0%). They also isolated *Candida* spp. (3.66%), *Proteus mirabilis* (2.6%), *Staphylococcus aureus* (2.6%), *Enterobacter cloacae* (1.56%) and *Pseudomonas aeruginosa* (1.56%). There was no imipenem resistance among gram-negative organisms. The isolations were mostly monomicrobial and in female gender (18).

The goal of treating UTIs can also be disappearance of urinary symptoms but not necessarily general symptoms before sterilization of urine. This last point can only be accepted for patients who have a permanent urinary catheter, and in this case, the accuracy of catheter-associated UTIs is a preeminent action before deciding on initiating any antibiotic (19).

As demonstrated worldwide (20,21), a growing increase of resistance against *E. coli* BLEE has been found for β-lactams, cephalosporins of different generations, quinolones and sulfas, demonstrating that it is becoming a public health problem. The results of this study showed that *E. coli* BLEE was responsible for approximately 40% of UTIs in the geriatric population, followed by *E. coli*. A 100% sensitivity was reported for the cases of *E. coli* BLEE to carbapenemes and glycylcyclines, whereas the sensitivity to third-generation cephalosporins was reported to be close to 79% in 2015. Meanwhile, for *E. coli*, a 100% sensitivity was reported for aminoglycosides and carbapenemes, and third-generation cephalosporins were used, yielding results close to 93% sensitivity, however, with the use of drugs belonging to the group of quinolones, sulfas, beta-lactams and penicillins having remained below 50% during the three years of the present study.

Urinary tract infections by *Candida albicans* are frequent, reaching the third place in the elderly. *Candida albicans* was present in some cases of our study. In this respect, several studies have reported on the ascending trend of this infection (22,23). Although the use of fluconazole is still effective, its indication can be delayed when the treatment is focused only against bacteria. When resistance is corroborated, the next options including voriconazole, flucytosine, or amphotericin B are expensive for most patients.

Enterococcus faecalis is one of the bacteria that predominates in UTIs, especially in cases of elderly pa-

tients (24). However, in our study, resistance to several types of antibiotics was observed, such as aminoglycosides and quinolones, but showed good sensitivity to nitrofurantoin (with the exception of the year 2014), as well as to oxazolidinones (linezolid) and glycopeptides (vancomycin), thus being good treatment options against this kind of infection.

In contrast to the literature, in our study, isolated cases of *Enterococcus fecalis* and *Klebsiella pneumoniae* with 6% each, and *Pseudomonas* with 3% were low in frequency and the rest of UTIs corresponded to even more extraordinary cases of other agents.

In our patients, *Proteus mirabilis* was reported only in 2015, showing high sensitivity to the institutional antibiotics. On the other hand, *Pseudomonas aeruginosa* is not a pathogen associated with UTIs frequently. However, it causes great mortality in hospitalized patients because it produces bacteremia and its association with age is fatal (25). Timely diagnosis should be made to enable prompt treatment, as shown in Figure 5; this bacterium is very resistant to nitrofurantoin and sulfas (100%) and is generally resistant to multiple drugs, however, it is sensitive to aminoglycosides according to our study, so that amikacin, gentamicin or tobramycin may be given as treatment.

In general, after widening the age range to be treated in geriatric service, there was an important change in the percentages of total cases only for *E. coli* BLEE and *E. coli*. In the former case, it was accompanied by clear reduction in the resistance against quinolones and sulfas. For the latter species, the resistance reduction was observed for all the tested antibiotics with the exception of sulfas.

It is clear from this and other studies that treatment of any type of symptomatic UTI in the geriatric patient should be initiated as soon as possible. The choice of antimicrobials does not change significantly in relation to young patients, but variability in the etiology, side effects, need for dose adjustment and the existence of comorbidities must be taken into account. Some authors indicate that the goal of treatment in the elderly patient is the disappearance of symptoms rather than sterilization of the urine. Unfortunately, high resistance rates have been observed for all antimicrobials among patients aged ≥65 (20). For example, Zec *et al*. did not identify a single antibiotic with either low or moderate resistance rates; in fact, all antimicrobial agents showed resistance rates of more than 20% (ranging from 26.1% for piperacillin-tazobactam to 73.7% for ampicillin) (26). These findings are in accordance with numerous studies that also encountered high resistance rates among older age groups.

Clinicians should individualize the treatment and estimate the probabilities of resistance of a particular patient, as the first-instance treatment is a quinolone formula, but the bacteria are usually resistant, as shown in Figure 7; therefore, this treatment should be reconsidered. Nitrofurantoin can be administered as it has more than 50% effectiveness. However, one should take into account the type of microorganism. Ideally, sensitivity and resistance tests should be performed before implementing the treatment. Therefore, previous history of consumption of some antibiotics is fundamental to choosing empiric antibiotic treatment.

In elderly patients, especially those with a serious clinical situation, previously treated with antimicrobials (particularly advanced spectrum cephalosporins), or in cases in which the acquisition is related to the sanitary environment and those with recurrent UTIs, it is advisable to cover against enterococcus until the results of the cultures are available. In this sense, ampicillin may be added to the treatment or can be covered with piperacillin-tazobactam and an aminoglycoside (the latter always in a single daily dose). Regarding the duration of treatment, there are no specific recommendations for the elderly. In general, long regimens of 7 days should be used.

Finally, it is important to mention that antibiotic therapy should not be used routinely in people with asymptomatic bacteriuria and, where antibiotics are required, healthcare professionals should follow local prescribing guidelines (6). Developing countries with inequities in their national income distribution face limited resources for health care (27).

A limitation of this study was that analysis of all groups of antibiotics that might be recommended was not always available, along with the lack of implementation of confirmatory molecular tests. Notwithstanding, the microbiological profile is helpful to characterize a population with low/absent carbapenem resistance.

In general, by reducing the age criterion to be hospitalized in a geriatric service, it is expected to get, as a collateral benefit, a decrement in antibiotic resistance with unknown time to keep this behavior.

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SAŽETAK

INFEKCIJE MOKRAĆNOG SUSTAVA KOD STARIJIH OSOBA. UČINAK SMANJENJA KRITERIJA DOBI U GERIJATRIJSKOJ SLUŽBI

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Uvod: Infekcije mokraćnog sustava (IMS) su jedna od najčešćih infekcija stečenih u zajednici kod starijih odraslih osoba. ***Metodologija:*** Ovo je retrospektivna i opisna studija provedena u meksičkoj gerijatrijskoj službi od siječnja 2013. do prosinca 2015. godine. Zabilježene su demografske karakteristike pacijenata, uključujući dob, spol, uzrok bolesti, kulturu urina, identifikaciju mikroorganizama i antibiogram. ***Cilj*** ove studije bio je opisati situacijski status mikrobiološke rezistencije antibiotika kod starijih osoba nakon smanjenja dobnih kriterija za liječenje u gerijatrijskoj službi. ***Rezultati:*** U analizu su bila uključena 182 gerijatrijska pacijenta (74 muškarca prosječne dobi 81,5±13,5 godina i 108 žena prosječne dobi 81,5±11,5 godina) s pozitivnom kulturom urina za jednu ili više bakterijskih identifikacija i antibiogramima. Najzastupljenije izolacije bile su pozitivne za *Escherichia coli* BLEE, *Escherichia coli*, *Candida albicans*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Proteus vulgaris* i *Klebsiella pneumoniae.* Nakon širenja dobnog raspona za ulazak u gerijatrijsku službu (2015. godine) došlo je do smanjenja ukupnih slučajeva *Escherichia coli* BLEE i povećanja za *Escherichia coli*. ***Zaključak:*** U našem je istraživanju pronađeno sve veće povećanje *E. coli* BLEE. Istodobno je bilo moguće potvrditi da je u većini slučajeva ova bakterija pokazala otpornost na b-laktame, cefalosporine različitih generacija, kinolonske antibiotike i sulfa lijekove pokazujući da postaje problem javnog zdravstva.

Ključne riječi: amikacin, karbapenemi, starije osobe, rezistencija, osjetljivost, infekcije mokraćnog trakta