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Original Article

Antimicrobial resistance in patients with urinary tract infections and the impact on empiric therapy in Serbia

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Abstract

Introduction: Surveillance of antimicrobial resistance is essential in establishing treatment guidelines for urinary tract infections. The aim of this pilot study was to analyse resistance rates of pathogens, across different demographics and determine whether adjustments in empiric therapy should be considered for different age and gender groups.
Methodology: A 5-year retrospective study included 256 patients hospitalised, under the initial diagnosis of Fever of Unknown Origin who were then subsequently diagnosed with a urinary tract infection at the Clinic for Infectious and Tropical Diseases, Clinical Centre of Serbia. Patients were evaluated using demographic, clinical, and antimicrobial resistance data with appropriate statistical analysis including ANOVA significance testing, univariate, and multivariate analysis.
Results: Resistance rates were above the threshold of 20% for the majority of the antimicrobials tested, the only exception being carbapenems. Amikacin, cefepime, and norfloxacin were agents that could be effectively used as empiric therapy in younger adults with resistance rates of 4.2, 8.0, and 10.0%, respectively. Moderate resistance rates of 17.4% for amikacin and 19.1% for cefepime were observed in the age group 35-64 years. High resistance rates were observed for all antimicrobials among patients 65 years and over. Among male patients, resistance rates to most antimicrobials were high. In female patients, amikacin and cefepime had resistance rates less than 20%. Younger age presented as a negative risk factor for infection by a multi-drug resistant pathogen.
Conclusion: Age and gender demonstrated to be significant factors for determining proper empiric therapy; large-scale studies from Serbia are needed to solidify these findings.

Key words: antimicrobial resistance; antibiotic use; bacterial infections; multidrug resistance; epidemiology.

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Introduction

Antimicrobial resistance has become one of the greatest issues in healthcare today [1]. Increased prescription and consumption of antimicrobial agents are perhaps the most influential factors which led to the emergence and spread of resistance [2]. Unfortunately, uncontrolled and unmonitored spread of resistance has left limited options for effective treatment [1]. Due to the fact that identification of a pathogen often takes at least a few days, and patients usually require immediate therapy, guidelines regarding empiric treatment should be carefully created on the grounds of local epidemiology and surveillance data. Evidence-based guidelines would undoubtedly lead to marked reductions in treatment costs [3], duration of average length of hospital stay (ALOS) [4], and — most importantly — provide better patient outcomes.

Urinary tract infections (UTIs) are one of the most prevailing microbial diseases, with more than 7 million physician visits annually in the US [5]. In Europe, 9% of all prescribed antibiotics are used to treat UTIs [6]. They present in various forms, from uncomplicated cystitis and pyelonephritis to the more dangerous, and possibly life-threatening, urosepsis. Reports from various European countries and the US have indicated that UTIs are among the most frequent reasons for medical consultation and hospitalisation [7], which illustrates the burden of UTIs in medical practice.

In the current era of high antibiotic resistance, the spectrum of effective empiric therapy is slowly becoming narrowed and hence, it is essential to investigate which factors are significant in determining the precise empiric therapy in order to salvage current therapeutic strategies. Among the numerous factors which have been established as significant for the development of antimicrobial resistance, gender and age are now emerging to be important when determining empiric therapy. However, in Serbia studies investigating the role of age and gender are non-existent; studies that have been published regarding UTIs in the country were oriented towards resistance of hospital-acquired (HA) infections [8] and resistance of pathogens in the paediatric population [9,10].

The primary goal of this pilot study was to analyse antimicrobial resistance rates among patients hospitalised with complicated UTI, irrespective of etiology, within a 5-year period in a tertiary care facility. Additionally, we investigated whether age and gender had a significant impact on the presence of Multidrug resistant (MDR) infection. Factors, which induced a longer duration of hospital stay, were also assessed.

Methodology

We conducted a retrospective study in August 2015 at the Department of Clinical Pharmacotherapy, Clinic for Infectious and Tropical Diseases, Clinical Centre of Serbia, Belgrade. Between January 1, 2010 and August 1, 2015, a total of 278 patients were admitted under the presumptive diagnosis of UTI.

The majority of the patients were initially hospitalised under the diagnosis of Fever of Unknown Origin (FUO), and as a result those included in the study were subsequently diagnosed with any one of the four urinary tract syndromes: cystitis, prostatitis, pyelonephritis and urosepsis. Cystitis was defined as the presence of dysuria, frequency, urgency, without axillary fever (< 37.5C); prostatitis as an acute febrile episode with lower back or perineal tenderness with urinary frequency or dysuria and possible acute urinary retention; pyelonephritis was recognized as the presence of fever and spontaneous or provoked lumbar tenderness; and urosepsis was defined as the presence of sepsis criteria with a positive urine or blood culture for a uropathogen with no other infection source [11]. All cases were considered as complicated UTIs.

Patients excluded from this study were those who did not exhibit clear diagnostic criteria for UTI [5] and patients under 18 years of age.

Demographic and clinical data including presence of risk factors and comorbidities, was collected. Descriptive statistics were used to summarise patient characteristics, profile of microbes isolated, and antimicrobial resistance. All patients were categorized into three age groups: 18-34 years, 35-64 years, and 65 years and over. Urine cultures were considered positive if there was monomicrobial growth of $\geq 10^5$ CFU/ml, while polymicrobial infection was diagnosed if two species exhibited growth of $\geq 10^5$ CFU/ml on urine culture. More than two species on culture was considered as contamination and was excluded from analysis. ANOVA testing was performed in order to evaluate whether patient age and gender, presence of certain risk factors: antibiotic consumption 90 days prior to admission, UTI within 1 year, non-UTI infection on admission, immunosuppression, diabetes mellitus (DM), recent or present catheterisation, and existence of underlying malignancy [15], along with, pathogen responsible for infection and change in antimicrobial therapy, contributed to a prolonged ALOS.

Antimicrobial susceptibility testing was performed by the Kirby-Bauer disk diffusion method, according to Clinical and Laboratory Standards Institute (CLSI) guidelines [12]. Intermediate and resistant strains were categorized as resistant. We classified resistance rates into three groups: low (<10%), moderate (10-20%), and high (>20%) [13]. We used the European Centre for Disease Prevention and Control (ECDC) definitions of Multidrug resistant (MDR) bacteria [14], which state that a pathogen is defined as MDR if it is resistant to ≥ 1 drug from ≥ 3 groups of antimicrobial agents. The following antimicrobial groups were analysed: aminoglycosides**,** antipseudomonal penicillins, carbapenems, non-extended and extended spectrum cephalosporins, fluoroquinolones, folate pathway inhibitors, glycopeptides, glycylcyclines, penicillins, penicillins with beta lactamase inhibitors, and phenicols.

We investigated whether there were correlations between the presence of MDR strains and different age groups and catheterisation using univariate and multivariate analysis. A level of significance $p < 0.05$ in the univariate analysis was included in the multivariate analysis, in order to establish independent predictors for MDR.

The Ethics committee of the Clinical Centre of Serbia, in accordance with the Declaration of Helsinki, approved this study.

Results

Of the 278 admitted patients, 256 were included in the study. From these patients, a total of 145 positive urine cultures were found, with 178 isolated organisms. The most commonly isolated species were *Escherichia coli* (n = 65, 36.5%), followed by *Enterococcus faecalis* (n = 41, 23.0%) and *Klebsiella spp.* (n = 23, 12.9%). Additional species included *Proteus mirabilis* (n = 16, 8.9%), *Pseudomonas aeruginosa* (n = 13, 7.3%), and coagulase-negative staphylococci (n = 10, 5.6%). *Providentia retgerri* and *Staphylococcus aureus* were each isolated twice (1.1%) (Table 1). Polymicrobial infection was detected in 30 patients (20.7%). Patients with negative urine culture (n = 111), were diagnosed with UTI on clinical grounds, based on typical symptomatology, and presence of leukocytes and bacteria in urinalysis. Sterile cultures were most likely the result of recent antibiotic use.

Of the total 256 patients, almost half were between 35-64 years old (n = 120, 46.9%), while 77 patients were 65 years and over (31.1%), and 59 (23.0%) were between 18-34 years old (Table 2). Females were slightly more prevalent (n = 157, 61.3%).

On admission, the majority of the patients had some risk factor for developing a UTI (n = 191, 74.6%). More than half of our patients consumed antibiotics 90 days prior to admission (n = 142, 60.5%). Of the remaining risk factors, the most prevalent were: concomitant non-UTI coinfection at the time of admission (n = 77, 30.1%), UTI within the last year (n = 57, 22.3%), and presence of nephrolithiasis (n = 22, 8.6%).

The ALOS was 18.86 ± 9.4 days. The factors which significantly correlated with an increased ALOS were: age over 65 years (n = 77, 30.1%, p=0.004), positive urine culture (n = 145, 57%, p = 0.021), UTI due to *Klebsiella spp.* (n = 23, 12.9%, p = 0.005), and change of therapy during hospitalisation (n = 23, 9%, p = 0.003). Intrahospital development of *Clostridium difficile* infection expectedly increased the ALOS in our patients (n = 7, 2.7 %, p < 0.001).

Overall antimicrobial resistance to commonly used antimicrobial agents was evaluated and further examined across different age and gender groups (Table 3). Of the antimicrobial agents tested, resistance rates to penicillins – amoxicillin, ampicillin, and amoxicillin-clavulanic acid – were high across all age groups (range 22.7-73.7%) and genders (range 55.6-68.0%). Resistance rates to piperacillin-tazobactam were moderate in the age group 18-34 years (17.4%), and high (range 23.0-36.4%) across all other age and gender groups. Resistance rates to the cephalosporin group of antimicrobials were low for ceftriaxone and cefepime (7.7% and 8.0%, respectively) within the age group 18-34 years, while resistance to cefuroxime was moderate (17.4%) within the same age group. Moderate resistance in the age group 35-64 was observed only against cefepime (19.1%), while resistance to all cephalosporins was high within the age group 65 years and over (range 28.6-35.3%). Of the aminoglycoside antibiotics, low resistance to amikacin was detected within the age group 18-34 years (4.2%) and moderate within the age group 35-64 years (17.4%). Gentamicin resistance, on the other hand, was high across all age groups (range 20.8-33.3%). Resistance rates to fluoroquinolones were moderate for norfloxacin and ofloxacin (10.0 and 13.0%, respectively) within the age group 18-34 years, while all fluoroquinolones, including ciprofloxacin, showed high resistance rates across all other age groups (range 23.1-52.6%). Resistance to trimethoprim-sulfamethoxazole was high across all age and gender groups (range 31.8-56.3%).

Resistance to carbapenems – meropenem and imipenem – across all age groups and genders was low (range 4.0-8.5%), except in the group 65 years and over, where resistance rates were moderate (15.0 and 17.1%, respectively).

Table 1. Isolated uropathogens from 145 positive urine cultures (n=178)

Uropathogens	N	%
Escherichia coli	65	36.5
Enterococcus faecalis	41	23
Klebsiella spp	23	12.9
Proteus mirabilis	16	8.9
Pseudomonas aeruginosa	13	7.3
Coagulase-negative staphylococci	10	5.6
Providentia retgerri	2	1.1
Staphylococcus aureus	2	1.1
Proteus vulgaris	1	0.6
Morganella morganii	1	0.6
Acinetobacter baumanii	1	0.6
Beta hemolytic group B streptococcus	1	0.6
Enterocbacter cloacae	1	0.6
Enterococcus faecium	1	0.6
Total	**178**	**100**

Table 2. Association of variables with prolonged duration of hospital stay

Patient characteristics (N=256)	**ALOS 18.86 ± 9.4 days**			
	Present (%)	**Yes (days)**	**No (days)**	***P* value[a]**
Gender and Age groups				
Gender (Female)	157 (61,3)	18.80	18.96	0.897
18-34 years	59 (23,0)	17.51	19.27	0.222
35-64 years	120 (46,9)	17.88	19.74	0.114
≥65 years	77 (30,1)	**21.44**	17.75	**0.004**
Risk factors and Comorbidities				
Antibiotic consumption*	156 (60,9)	19.16	18.40	0.529
Hypertension	85 (33.2)	18.31	19.14	0.504
Non-UTI infection	77 (30,1)	**21.69**	17.65	**0.001**
Previous UTI	57 (22,3)	19.09	18.80	0.947
Diabetes Mellitus	25 (9.8)	18.92	18.86	0.975
Catheterisation	16 (6,3)	19.13	18.85	0.909
Immunosuppression	13 (5,1)	**24.00**	18.59	**0.043**
Presence of malignancy	12 (4,6)	20,42	18.79	0.558
Benign Prostatic Hyperplasia	11 (4,3)	17.91	18.91	0.731
Uropathogens and Therapy				
Positive urine culture	145 (57,0)	**20.53**	16.65	**0.001**
Escherichia coli	65 (36,5)	22.18	19.21	0.088
Enterococcus faecalis	41 (23,0)	18.62	20.70	0.325
Klebsiella spp	23 (12,9)	**26.50**	19.38	**0.005**
Clostridium difficle infection	7 (2,7)	**40.29**	18.26	< **0.001**
Change in therapy	23 (9.0)	**24.43**	18.31	**0.003**
Polymicrobial infection	30 (20,7)	22.60	19.91	0.213

ANOVA analysis used, ALOS: average length of stay, UTI: urinary tract Infection, **statistically significant**. *(90 days prior to admission).

Table 3. Antimicrobial resistance rates, and their distribution among different age and gender groups

	Antimicrobial Agents													
	N	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**
Age groups in years	**AMX**		**AMP**		**AM-CL**		**PIP-TZ**		**CFTX**		**CEPH**		**CEFU**	
18-34 (n=59)	26	50.0	28	53.6	22	22.7	23	**17.4**	26	**7.7**	22	27.3	23	**17.4**
35-64 (n=120)	39	56.4	46	65.2	39	41.0	46	26.1	47	31.9	45	31.1	39	35.9
≥65 (n=77)	30	66.7	38	73.7	29	55.2	38	26.1	40	32.5	34	35.3	32	31.3
Gender														
Males (n=99)	27	55.6	35	57.1	25	44.0	33	36.4	34	38.2	29	34.5	27	33.3
Females (n=157)	68	58.8	77	68.8	65	40.0	74	23.0	79	21.5	72	30.6	67	28.4
Total (n=256)	95	57.9	112	65.2	90	41.1	107	27.1	113	26.5	101	31.7	94	29.8
	N	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**
Age groups in years	**CEFP**		**AMI**		**GEN**		**CIP**		**OFL**		**NOR**		**LEVO**	
18-34 (n=59)	25	**8.0**	24	**4.2**	24	20.8	12	33.3	23	**13.0**	20	**10.0**	2	50.0
35-64 (n=120)	47	**19.1**	46	**17.4**	41	31.7	35	34.3	32	40.6	26	23.1	5	40.0
≥65 (n=77)	42	28.6	40	27.5	36	33.3	37	43.2	19	52.6	20	40.0	14	57.1
Gender														
Males (n=99)	35	28.6	33	30.3	27	40.7	33	51.5	22	50.0	15	40.0	8	75.0
Females (n=157)	79	**16.5**	77	**13.0**	74	25.7	51	29.4	52	28.8	51	**19.6**	13	38.5
Total (n=256)	114	20.2	110	**18.2**	101	29.7	84	38.1	74	35.1	66	24.2	21	52.4
	N	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**	**N**	**R (%)**
Age groups in years	**TMP-SMX**		**MER**		**IMI**		**NIF**		**VAN**		**TIG**		**CAM**	
18-34 (n=59)	22	31.8	25	**4.0**	25	**4.0**	5	40.0	9	**11.1**	3	**0.00**	4	**0.00**
35-64 (n=120)	39	51.3	47	**8.5**	47	**4.3**	10	30.0	13	30.8	7	**14.3**	6	50.0
≥65 (n=77)	32	56.3	40	**15.0**	41	**17.1**	12	33.3	13	23.1	5	40.0	3	**0.00**
Gender														
Males (n=99)	27	55.6	34	**14.7**	35	**14.3**	10	20.0	12	0.00	5	20.0	2	0.00
Females (n=157)	66	45.5	78	**7.7**	78	**6.4**	17	41.2	23	34.8	10	20.0	11	27.3
Total (n=256)	93	48.4	112	**9.8**	3	**8.8**	27	33.3	35	22.9	15	20.0	13	23.1

N: number of isolates tested, R (%): percentage of resistant isolates, **<20% resistance rate,** *AMX*, amoxicillin; *AMP*, ampicillin; *AM-CL*, amoxicillin-clavulanic acid; *PIP-TZ*, piperacillin-tazobactam; *CFTX*, ceftriaxone; *CEPH*, cephalexin; *CEFU*, cefuroxime; *CEFP*, cefepime; *AMI*, amikacin; *GEN*, gentamicin; *CIP*, ciprofloxacin; *OFL*, ofloxacin; *NOR*, norfloxacin; *LEVO*, levofloxacin; *TMP-SMX*, trimethoprim-sulfamethoxazole; *MER*, meropenem; *IMI*, imipenem; *NIF*, nitrofurantoin; *VAN*, vancomycin; *TIG*, tigecycline, *CAM*, chloramphenicol.

In female patients, amikacin, norfloxacin, and cephalexin were the only antimicrobials with moderate resistance rates (13.0, 16.5, and 19.6%, respectively). In male patients, however, resistance to all antimicrobial agents was high (range 28.6-57.1%). A total of 8 Vancomycin-resistant pathogens were isolated, all from female patients, and included *Enterococcus fecalis*, *Enterococcus faecium*, and *Providentia retgerri* (n = 6, n = 1, n = 1, respectively).

Total resistance rates showed that apart from carbapenems — meropenem (14.7%) and imipenem (14.3%) — amikacin was the only antimicrobial agent with a moderate resistance rate (18.2%).

Of the total 178 isolated pathogens, 119 were eligible to be classified as either MDR or non-MDR. The remaining 59 isolated organisms could not be analysed because antimicrobial susceptibility testing did not yield enough data necessary for MDR classification according to ECDC definitions, and were therefore excluded. Correlations between age and gender and the presence of multidrug resistance were established by using proper statistical analysis (Table 4). In our study, only the age group 18-34 years presented as a negative factor for the presence of MDR infection (OR 0.232, CI 0.081-0.664, $p < 0.006$). On the other hand, there was a significant correlation between the presence of a MDR pathogen and patients aged 65 years and over (OR 2.773, CI 1.277-6.021, $p < 0.01$). The age group 18-34 years was established as a negative predictor (OR 0.284, CI 0.095-0.849, $p < 0.024$) for a UTI caused by a MDR strain. There were 16 catherised patients, with 11 positive urine cultures. Of these, 9 pathogens were found to be MDR: *Pseudomonas aeruginosa* (n=2), *Acinetobacter baumanii* (*n*=1), Coagulase-negative staphylococci (n = 1), *Enterococcus faecalis* (n = 1), *Escherichia coli* (n = 1), *Klebsiella spp* (n = 1), *Proteus mirabilis* (n = 1), *Providentia retgerri* (n = 1). Thus, catheterisation was also analyzed in univariate (OR 15.525, CI 1.897-127.082, $p < 0.011$) and multivariate analysis, and was found to be a statistically significant positive predictor for MDR infection (OR 9.223, CI 1.073-79.292, $p < 0.043$).

Discussion

E. coli is still the pathogen responsible for the majority of UTIs, yet our results are supported by the data from other recent studies, which indicate that its overall isolation rate is decreasing [16-19]. Furthermore, our results support the rising incidence rates of *Enterococcus* and *Klebsiella* [1,20], which are increasingly turning into MDR strains, and more commonly cause complicated UTIs [1,21].

Almost 10% of our patients required a change in therapy, which significantly prolonged their hospital stay. Improper empiric therapy has been established as a significant factor for the prolongation of hospital stay [4]; guidelines regarding empiric therapy for UTIs need to be adjusted according to local epidemiological data in order to provide optimal patient care. When compared to our results, ALOS in other European countries is significantly lower (Sweden 5.3 days, Germany 6.2 days, the United Kingdom 9.3 days) [22], strengthening the fact that, surveillance of resistance rates and implementation of appropriate empiric therapy is essential in reducing the ALOS in Serbia.

Successful treatment of UTIs mandates the use of effective antimicrobials. Guidelines state that if resistance to an antimicrobial agent exceeds the 20% threshold, it should no longer be recommended for empiric therapy [5,13,23]. Resistance rates among different age groups were observed to increase as the age of the patient increased, which supports claims from other studies [24-27]. Pathogens isolated from patients within the age group 18-34 years showed low rates of resistance to several antimicrobial agents (<10%), most notably to amikacin (4.2%), ceftriaxone (7.7%), cefepime (8.0%), and norfloxacin (10.0%),

Table 4. Univariate and multivariate analysis of age and gender, and the development of Multidrug Resistant infection.

				Statistical analysis			
		Isolates (n=119)		Univariate		Multivariate	
Characteristics (MDR Isolates)	**Total cohort (N)**	**MDR - positive**	**MDR - negative**	**OR (95% CI)**	***P* (sig)**	***P* value**	**OR (95% CI)**
Gender (Male)	99	17	23	1.086 (0.502-2.347)	0.835		
18-34	59	5	23	0.232 (0.081-0.664)	**0.006**	**0.024**	0.284 (0.095-0.849)
35-64	120	20	30	0.92 (0.438-1.929)	0.824		
≥65 years	77	24	18	2.773 (1.277-6.021)	**0.01**		

MDR: Multidrug Resistant, OR: odds ratio, CI: confidence interval, **statistically significant**.

which implies that these agents should be used as first-line therapy for this age group in our population. Studies have reported variable resistance rates to these drugs across different regions ranging from less than 10% to more than 80% [20,28], which further illustrates the importance of determining local susceptibility rates to antimicrobials.

Conversely, there was not a single antimicrobial agent with a low resistance rate in the age group 35-64 years; only two agents exhibited moderate resistance (10-20%), namely amikacin (17.4%) and cefepime (19.1%). Finally, for patients over the age of 65, we 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% (ranged from 26.1% for piperacillin-tazobactam to 73.7% for ampicillin). According to our results, not one agent could be declared fit for empiric use in elderly patients. Our findings are in accordance with numerous studies which also encountered high resistance rates among older age groups [24-27].

MDR strains can be difficult to treat and almost always require the use of potent antimicrobial agents. Treatment guidelines provide alternative regimens in the presence of certain risk factors, such as catheterisation or prior UTI, due to the higher probability for infection by a resistant organism [5,23]. Although catheterisation proved to be a positive predictor for MDR infection in our study, due to the very small number of isolates used in our analysis (number of catheterised patients = 16, MDR = 9), no conclusions can be made at this time and larger studies are required to investigate this association further. We did, however, additionally discover that age also affects the presence of resistant pathogens, both positively and negatively. Our results, therefore, indicate that empiric therapy should be adjusted for different age groups as well, which is becoming a major topic of research [7].

We observed significant differences in antimicrobial resistance rates between genders as well. For female patients, three drugs exhibited resistance rates below 20%, and could therefore be considered as empiric therapy: amikacin (13.0%), cefepime (16.5%), and norfloxacin (19.6%). Microbes isolated from male patients had high resistance rates (> 20%) to all antibiotics bringing into question whether empiric therapy should be the same for both genders [7,29]. Results from different studies confirm our findings that resistance rates were higher in male patients than in female [27,30]. In fact, certain studies imply that empiric therapy for genders should be established through gender-stratified surveillance studies [30].

Overall resistance rates in the total sample were less than 20% to only three antimicrobials: amikacin, meropenem, and imipenem. Given the fact that carbapenems are reserved antibiotics, we can suggest that amikacin should be used as a first-line agent in empiric therapy. These findings contradict the majority of existing treatment guidelines, which suggest trimethoprim-sulfamethoxazole and ciprofloxacin as first-line agents for treating different forms of UTIs [5,13,23]. In our study however, overall resistance rates to these drugs were 48.4% and 38.1%, respectively. There are more studies demonstrating high resistance rates to both agents [23,28,31-34], which together with our findings, question the position of trimethoprim-sulfamethoxazole and ciprofloxacin as first-line therapy for UTIs. Furthermore, neither gentamicin nor cephalosporins — including cefepime, ceftriaxone, cefuroxime, and cephalexin — could be used as empiric therapy in Serbia [5,16,26] due to high resistance rates observed in this study: 29.7% for gentamicin, and 20.2%, 26.5%, 29.8%, and 31.7% for the cephalosporins respectively. Pathogens isolated from neighbouring countries confirm our findings, with resistance rates to these drugs reaching more than 50% in some [35].

Our study exhibited certain limitations. The number of patients included in our study is not sufficient for the obtained data to be generalized to all forms of UTI, as we could not evaluate our patients from the aspect of the acquisition of infection (community acquired, hospital acquired, or health-care associated). Future surveillance studies will make this a priority. Furthermore, age and gender-dependent etiology was not analysed, which has shown to be important in determining optimal empiric therapy [36]. Data regarding the use of specific antimicrobials prior to hospitalisation was incomplete and, therefore, could not be used to identify correlations between the consumption of specific antimicrobials and the presence of MDR strains as has been established as significant by other studies [37]. In spite of our best efforts at standardization, due to a lack of financial and technical support, there were inconsistencies in microbial susceptibility testing. Single antibiotics or single groups of antibiotics were at times solely tested, and this led to an inability to classify all MDR pathogens. Finally, data regarding the route of administration of therapy was not available for all patients and was, as a result, omitted from our study.

Conclusion

This pilot study confirmed that there is an urgent need for evaluation of the true extent of antimicrobial resistance of uropathogens in Serbia. Resistance rates suggest a narrow spectrum of empiric therapy, and indicate different approaches in empiric therapy across age groups and gender could be implemented. Having in mind the global spread of antimicrobial resistance, Serbia needs to initiate active surveillance and define proper empiric therapy based on the obtained data. These steps will not only aid in controlling the spread of antimicrobial resistance and the development of MDR strains, but also reduce the length of hospital stay and improve patient care.

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