Women's experiences with antibiotic use in urinary tract infections: Insights from the patient's perspective

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Abstract

From patients' perspective, the use of antibiotics to treat urinary tract infections (UTIs) in Serbia is unexplored, and therefore the aim of this study is to examine antibiotic use among these patients. An online cross-sectional study using snowball sampling was conducted during the winter of 2020/21 using a validated *Google Docs* questionnaire. The study included 236 female

patients with a mean age of 34.9 ± 14.2 years. Most of the patients perceived UTI symptoms as severe (62.3%) and disruptive for their daily routines (51.3%). The majority of the patients (77.1%) used antibiotics by doctors' prescriptions. Other patients used antibiotics on their own and their selection. Self-treatment with antibiotics was associated with perceived symptom severity (p=0.006) and residence (p=0.017). In total, 17 different antibiotics were reported as being used for UTI treatment and the most frequent were fluoroquinolones (30.3%), cephalosporins (21.2%), and sulfonamides (15.7%). The highest consistency with national and European guidelines in doctors' decisions on antibiotic therapy was observed for treating UTIs in pregnant women (80.0%). These findings emphasize the need for education of healthcare professionals and clinical practice improvement in making rational antibiotic prescribing decisions.

Introduction

In 2022, Serbia was a country with a high prevalence of antibiotic use with 76.8% of the patients using antibiotics, compared to less than 50% in European Union countries (1). Furthermore, a significant rate of irrational antibiotic use has been observed, primarily through self-medication (2). This contributes to Serbia being classified among the European countries with high levels of antimicrobial resistance (3). The increasing resistance of uropathogenic bacteria to treatment poses a significant public health concern (4). One of the primary drivers of irrational antibiotic use is urinary tract infections (UTIs), with prevalence rates reaching up to 70% (5).

Urinary tract infections are no longer considered a uniform pathology with a one-size-fits-all treatment approach. Instead, bridging the gap between standard treatment guidelines and individual patient preferences is essential (6). Studies have shown a high rate of inadequate empirical treatment for UTIs, which is associated with increased morbidity and mortality (7–10).

According to national and European guidelines, UTIs are treated with antibiotics. For uncomplicated UTIs, empiric antibiotic therapy based on symptoms is recommended, without waiting for laboratory results. First-line antibiotics in these cases include fosfomycin, nitrofurantoin, and pivmecillinam. In regions where *Escherichia coli* resistance is below 20%, trimethoprim and cotrimoxazole are also considered first-line options. Recurrent UTIs are managed similarly to uncomplicated ones. If the patient has any risk factors for a complicated course, the choice of antibiotic differs. In general, complicated UTIs are treated with fluoroquinolones such as ciprofloxacin or levofloxacin. In pregnant women, first-choice antibiotics include amoxicillin (either alone or in combination with clavulanic acid), nitrofurantoin, cephalexin, cefpodoxime, fosfomycin, and cotrimoxazole (11, 12).

Urinary tract infections, especially complicated ones, should be treated based on the results of antimicrobial susceptibility testing (AST) to ensure optimal therapeutic outcomes. First-line empirical therapy should be adjusted promptly once AST data become available. Targeted antimicrobial therapy plays a crucial role in minimizing inappropriate antibiotic use and in mitigating the development of antimicrobial resistance (13, 14).

Beta-lactam antibiotics, including amoxicillin/clavulanic acid, cefuroxime, ceftibuten, and cefixime, are not recommended as first-line treatments for uncomplicated cystitis and should only be used when alternative antibiotics are unavailable. This recommendation is based on their limited efficacy, high incidence of side effects, and negative environmental impact. Aminopenicillins, such as ampicillin and amoxicillin, are no longer suitable for the empirical treatment of uncomplicated cystitis due to the high resistance rates of *E. coli*. Similarly, fluoroquinolones should be reserved as a last therapeutic option due to their severe adverse effects (11, 12).

Key factors influencing healthcare professionals' selection of empirical antibiotic therapy for UTIs include the antibacterial spectrum, local resistance patterns,

comorbidities (e.g., renal or hepatic impairment), history of drug allergies, prior antibiotic exposure, antibiotic safety profile, and urinary antibiotic concentrations (11, 12).

In Serbia, limited data are available on antibiotic use for UTI treatment, particularly from patients' perspective. Therefore, this study aims to examine antibiotic use among patients with UTI symptoms.

Methodology

A quantitative, non-experimental, online cross-sectional study was conducted in Serbia using a *Google Docs* questionnaire during the winter of 2020/21. A validated questionnaire served as a data collection instrument, and participants were recruited using the snowball sampling technique.

Instrument

Given the absence of questionnaires on patient reported UTI treatment at the time of the study, the development of a new instrument was required. The questionnaire was developed and validated following a narrative review of the relevant literature, and subsequently refined through focus group discussions. In the first phase of development (narrative literature review), a thematic framework was established and initial questions were formulated. During the second phase (focus group interview and expert panel), the content of the questionnaire was further revised. Several questions were reformulated or removed, and additional questions were added. The third phase (pretesting) aimed to evaluate the clarity and appropriateness of the formulated questions. The cognitive interview methodology was used in this phase. Based on the feedback received, the final version of the questionnaire was developed and validated, with particular attention paid to ensuring both face and content validity. The final version consisted of 29 questions divided into six domains (15).

This study was part of a larger project. For this study, we used unpublished data focusing specifically on responses related to basic demographic information and antibiotic use. The basic demographic variables included age, gender, place of residence, level of education, employment status, economic status, and health characteristics. Questions on antibiotic use assessed the specific antibiotic last used for UTI treatment and how it was obtained (with or without a doctor's prescription). The data on the antibiotics used were provided by the respondents themselves. The respondents also had the option to report the use of multiple antibiotics.

Target Population

The target population was comprised of adult female citizens of the Republic of Serbia. Inclusion criteria for participation in the study were: being an adult woman residing in the Republic of Serbia, voluntary consent to participate, the presence of UTI symptoms in the last year, and the use of antibiotics for UTI treatment.

Only responses of the patients who provided accurate and precise antibiotic names were included in the analysis. The patients' data that were incomplete or incorrect were excluded from the statistical processing.

Data Collection

The survey instrument was distributed electronically and made available on social media platforms. Both random sampling and the snowball sampling technique were employed for participant recruitment.

All collected data were password-protected to prevent unauthorized access and stored on the server of the University of Belgrade – Faculty of Pharmacy. Only a researcher had access to the original dataset. The data were collected and stored in a way that ensured respondent anonymity.

Data analysis

The collected data about antibiotic use were later compared with two guidelines: the global guideline of the European Association of Urology (EAU) Guidelines for the Treatment of UTIs (11), and the national guideline for Good Clinical Practice for the Prevention and Treatment of Uncomplicated UTIs (12).

The statistical analysis of the quantitative data was performed using IBM SPSS Statistics (SPSS v.18; SPSS Inc., Chicago, IL, USA). The descriptive and inferential statistical tests were used for data analysis. The chi-square test was used to compare categorical data distributions between groups. A significance level of $p < 0.05$ was considered statistically significant in all analyses.

Ethical Approval

The study was approved by the Ethics Committee for Biomedical Research of the Faculty of Pharmacy, University of Belgrade (Decision No. 2203/2).

Results

The study included 236 female patients, most of whom lived in urban areas, held a university degree, and were employed (Table 1). In most cases, patients perceived their symptoms as severe (62.3%) and disruptive to daily activities (51.3%). Following the onset of symptoms, the patients were advised on their therapy by a doctor (55.1%), pharmacist (18.2%), or family and friends (15.3%). There was a small proportion of patients who didn't ask anyone for the treatment advice (11.4%).

Table I   The basic characteristics of the patients

Tabela I   Osnovne karakteristike pacijenata

All patients (N)	236
Age, Mean (SD), Range	34.9 (14.2), 18 – 81
Gender, n (%)	
Male	0 (0.0)
Female	236 (100.0)
Residency, n (%)	
Urban	186 (78.8)
Rural	50 (21.2)
Education level, n (%)	
Primary school	4 (1.7)
Secondary school	71 (30.1)
High school	16 (6.8)
University	96 (40.7)
Postgraduate	49 (20.8)
Employment status, n (%)	
Employed	118 (50.0)
Retired	12 (5.1)
Unemployed	38 (16.1)
Student	68 (28.8)
Comorbidities, n (%)	
Yes	59 (25.0)
No	177 (75.0)

Most of the patients (36.4%) experienced three or more recurrences of UTIs, followed by two (29.2%) and one (29.7%) in the last year, while 4.7% could not remember the number of UTI episodes. Overall, 23.7% of patients reported hematuria, whereas 17.4% experienced fever during UTIs.

Antibiotics were most commonly prescribed by a doctor (n=182, 77.1%), while the remaining cases involved self-medication, with patients obtaining antibiotics from a pharmacy without prior medical consultation.

Self-medication was significantly associated with perceived symptom severity (17.0% among those with severe symptoms vs. 32.6% among those who did not perceive symptoms as serious, Chi = 7.623, p=0.006) and place of residence (19.9% in urban vs. 36.0% in rural areas, Chi = 5.720, p=0.017) (Figure 1).

90,0%
80,0%
70,0%
60,0%
50,0%
40,0%
30,0%
20,0%
10,0%
0,0%

80.1%   *
64.0%
19.9%   36.0%
83.0%   *
67.4%
17.0%   32.6%

Urban   Rural   Symptoms are serious   Symptoms are not serious

■ Doctor's prescription

■ Without a doctor's prescription
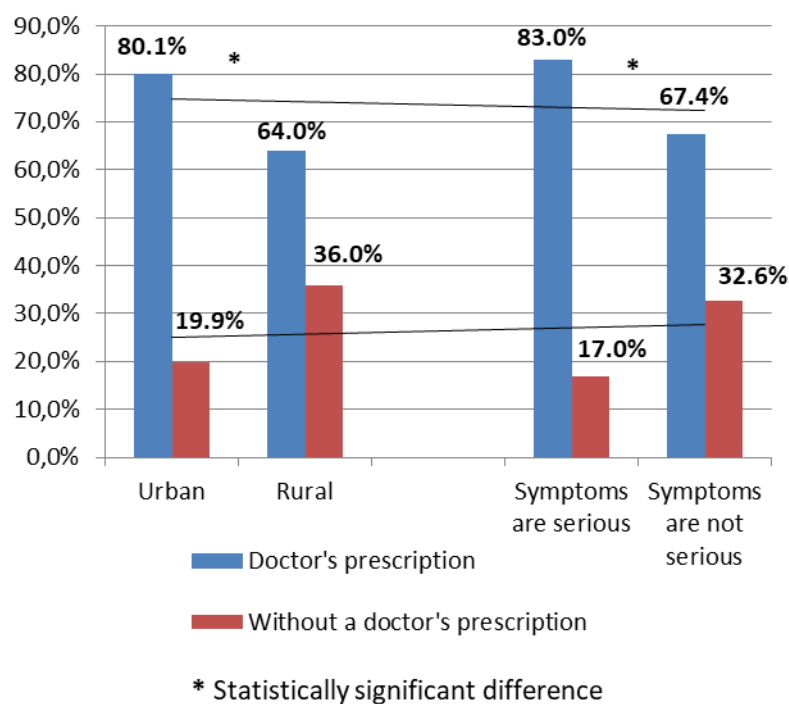
* Statistically significant difference

Figure 1. Antibiotic Prescription and Self-Medication Patterns in UTI Treatment: Association with Symptom Severity and Residence

Slika 1.   Propisivanje antibiotika i obrasci samolečenja kod urinarnih infekcija: povezanost sa težinom simptoma i mestom stanovanja

Of the 236 patients, five reported using a drug that could not be classified as an antibiotic, while 47 were unable to recall the name of the antibiotic they had taken. These patients were excluded from further analysis. A total of 184 patients reported using 17 different antibiotics, with fluoroquinolones being the most commonly used (n = 60), followed by cephalosporins (n = 42) and sulfonamides (n = 31). Aminopenicillins were reported by 25 patients (Figure 2). Some of the participants (n = 14, 7.6%) reported taking two antibiotics at the same time. Ciprofloxacin was the most frequently used antibiotic in combination therapy, most often administered together with fosfomycin (in three cases). More details are presented in Table II.
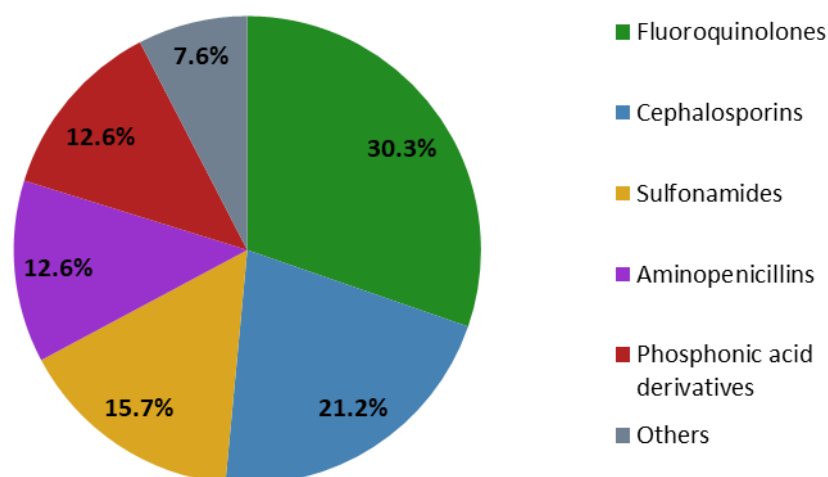
Figure 2. **Most commonly used antibiotic classes in UTI therapy, according to patient reports**

Slika 2. **Najčešće primenjivane klase antibiotika u terapiji urinarnih infekcija, prema navodima pacijenata**

Table II Summary of antibiotics reported by patients for UTI treatment

Tabela II Pregled antibiotika koje su pacijenti prijavili za lečenje urinarnih infekcija

Antibiotic	Total (n=184)	Used by a doctor's prescription	Used without a doctor's prescription
		n (%)	
Ciprofloxacin	44 (23.9)	38 (20.6)	6 (3.3)
Cotrimoxazole	31 (16.8)	22 (11.9)	9 (4.9)
Cephalexin	31 (16.8)	21 (11.4)	10 (5.4)
Fosfomycin	25 (13.6)	17 (9.2)	8 (4.4)
Amoxicillin + clavulanic acid	21 (11.4)	19 (10.3)	2 (1.1)
Cefixime	10 (5.4)	9 (4.9)	1 (0.5)
Norfloxacin	8 (4.3)	6 (3.2)	2 (1.1)
Levofloxacin	8 (4.3)	6 (3.2)	2 (1.1)
Pipemidine acid	6 (3.2)	0 (0.0)	6 (3.2)
Ampicillin	4 (2.2)	3 (1.6)	1 (0.5)
Nitrofurantoin	3 (1.6)	3 (1.6)	0 (0.0)
Doxycycline	2 (1.1)	2 (1.1)	0 (0.0)
Azithromycin	1 (0.5)	1 (0.5)	0 (0.0)
Nitroxoline	1 (0.5)	1 (0.5)	0 (0.0)
Cefpodoxime	1 (0.5)	1 (0.5)	0 (0.0)
Midecamycin	1 (0.5)	1 (0.5)	0 (0.0)
Clindamycin	1 (0.5)	0 (0.0)	1 (0.5)

Among patients with three or more UTI recurrences in the last year (n=86), the most frequently used antibiotics were ciprofloxacin (n=17), cotrimoxazole (n=14), and fosfomycin (n=9), followed by amoxicillin/clavulanic acid (n=8), cephalexin (n=6), levofloxacin (n=4), cefixime (n=4), pipemidic acid (n=4), ampicillin (n=2), norfloxacin (n=1), nitroxoline (n=1), and cefpodoxime (n=1). Seven patients reported using two antibiotics concurrently, including ciprofloxacin combined with fosfomycin (n=2), cefixime (n=2), or amoxicillin/clavulanic acid (n=1), cotrimoxazole with amoxicillin/clavulanic acid (n=1), and cephalexin with levofloxacin (n=1). Twenty-two patients did not specify the antibiotic used.

Patients who reported complications such as blood in the urine (n=56) also reported using ciprofloxacin (n=13) and cephalexin (n=9), followed by fosfomycin (n=8), cotrimoxazole (n=6), amoxicillin/clavulanic acid (n=5), levofloxacin (n=3), cefixime (n=3), nitrofurantoin (n=2) and, norfloxacin (1). Four patients reported using two antibiotics simultaneously, including ciprofloxacin combined with fosfomycin, amoxicillin/clavulanic acid, or nitrofurantoin, as well as norfloxacin combined with fosfomycin. Ten patients did not specify the antibiotic used, and eleven reported obtaining antibiotics from a pharmacist without a prescription.

Among patients with fever (n=41), the most frequently used antibiotics were ciprofloxacin (n=8) and cotrimoxazole (n=5), followed by amoxicillin/clavulanic acid (n=5), fosfomycin (n=5), cephalexin (n=3), levofloxacin (n=3), cefixime (1), and doxycycline (n=1). Five patients reported concurrent antibiotic use, including ciprofloxacin with fosfomycin, amoxicillin/clavulanic acid, or cefixime, and levofloxacin with fosfomycin or cephalexin. Twelve patients did not specify the antibiotic used, and four reported receiving antibiotics from a pharmacist without a prescription.

Twelve of the antibiotic users were pregnant women. Three of them reported using cephalexin or amoxicillin, two used fosfomycin, one used ciprofloxacin and one used doxycycline. Four pregnant women reported obtaining antibiotics from pharmacists without a prescription, specifically amoxicillin/clavulanic acid, cephalexin, fosfomycin, and ciprofloxacin.

The analysis of the consistent use of national and European guidelines revealed the highest consistency rates among pregnant women (80.0%). Conversely, the lowest consistency with guidelines was observed in patients with systemic symptoms, such as hematuria (26.5%) and fever (19.3%). Among the patients with recurrent UTIs, 34.8% used first-line antibiotics, 66.7% received alternative treatments, and 8.7% used antibiotics not listed in the guidelines.

Discussion

The results reveal considerable variation in the use of antibiotics for treating UTIs, along with a significant deviation from current European and national treatment guidelines. However, it remains uncertain whether these variations stem from differences in clinical presentations, regional bacterial susceptibility, or other factors. Unjustified

variations in antibiotic use could lead to unnecessary resource consumption, prolonged recovery, increased risk of adverse events, and the promotion of antimicrobial resistance, especially when broad-spectrum antibiotics are involved (16).

The high and irrational use of antibiotics in Serbia, as confirmed by this study, remains a significant public health concern. Among patients who used antibiotics, 22.9% did so without a doctor's prescription. This finding aligns with previous research showing that nearly half of Serbian patients had self-medicated with antibiotics at least once, with a quarter doing so during their last infection. Cystitis was among the top five conditions for which antibiotics were used in self-medication (2).

Ciprofloxacin, a second-generation fluoroquinolone, was the most commonly used antibiotic for UTIs in this study, based on patient reported data. However, according to EAU guidelines, fluoroquinolones should only be used as a last resort due to their potential adverse effects, which may lead patients to discontinue treatment or seek alternative therapies (11, 17). Cephalosporins were also widely used, despite EAU recommendations against their empirical use due to the risk of ecological collateral damage and the development of multidrug-resistant strains (11, 18, 19).

A significant finding of this study was the use of pipemidic acid, an antibiotic withdrawn from the Serbian market in 2019 following European Medicines Agency recommendations (20). Despite its broad-spectrum activity, pipemidic acid has poor solubility, a short elimination half-life, and significant adverse effects, which led to its withdrawal from clinical use (21, 22). The presence of this antibiotic in treatments reported by the patients raises concerns regarding drug availability, regulatory oversight, and potential gaps in enforcement. Further investigation is needed to determine whether patients obtained this medication from residual stockpiles or through illegal distribution channels. These findings point to possible irregularities in the Serbian antibiotic market and underscore the need for enhanced surveillance and stricter regulatory controls.

The practice of using antibiotics as a self-medication, not prescribed/recommended by the doctor, has also been reported in other countries, particularly for UTIs (23). This study found that self-medication was associated with the perceived severity of symptoms, suggesting that individuals who consider their symptoms to be mild may undervalue medical consultation, increasing their risk of inadequate treatment. Additionally, rural residents had higher self-medication rates than urban populations, likely due to limited access to healthcare and information (24, 25).

These findings emphasize the urgent need for targeted interventions, particularly in rural areas and among individuals who underestimate the severity of their symptoms. Raising awareness about the risks of self-medication and inappropriate antibiotic use, along with improving access to healthcare, is essential for mitigating antimicrobial resistance and enhancing overall patient care (26).

Of the five most commonly used antibiotics in this study, based on patient self-reports, only two (cotrimoxazole and fosfomycin) are recommended as first-line treatment in national and European guidelines. The use of fluoroquinolones is of concern

since European regulations restrict their prescription due to serious, long-term side effects. These antibiotics are usually only recommended when other options are ineffective, which was not the case in our sample (27). This misuse of fluoroquinolones reflects a broader trend in Serbia, similar to other countries where fluoroquinolone prescribing has not significantly decreased (28). Similarly, beta-lactam antibiotics, including aminopenicillins, are not recommended as first-line agents due to high *E. coli* resistance rates and a greater risk of side effects, yet they were used by 12.6% of patients (29, 30).

Other studies have reported varying levels of conformity to antibiotic guidelines for UTI treatment, ranging from 23.8% in Wales to 66.7% in the Netherlands. In Wales, trimethoprim was the most commonly prescribed antibiotic (76.5%), fosfomycin in Spain (75.9%), and nitrofurantoin in the Netherlands (79.7%). In England, trimethoprim and nitrofurantoin were prescribed to 46.1% and 48.7% of patients, respectively, while in Spain, the prescription rate for amoxicillin/clavulanic was 9.7% and for ciprofloxacin 9.2% (31).

A significant 7.6% of the patients used two antibiotics simultaneously, which suggests potential misuse, possibly due to inappropriate healthcare professional recommendations or self-medication. Notably, 19.9% of the patients did not know which antibiotic they had used, indicating a lack of patient knowledge and awareness regarding the proper antibiotic use.

Furthermore, patients who had experienced more than three episodes of UTI symptoms in the previous year reported using antibiotics that were more often aligned with national and European guidelines. Their repeated experience of UTI symptoms may have contributed to a better understanding of the condition and its management, potentially influencing the types of antibiotics they were prescribed or chose to use. The pattern of antibiotic use indicates a tendency toward first-line recommended therapies, such as cotrimoxazole and fosfomycin, among those with more frequent prior episodes. Previous therapeutic experiences may have raised their awareness of the importance of appropriate antibiotic use, leading to a preference for first-line treatments over broad-spectrum or less recommended options. Overall, repeated experience with UTI may foster a more rational approach to antibiotic use that is more closely aligned with evidence-based recommendations.

The use of antibiotics with high resistance rates, such as beta-lactams, remains a significant concern. Additionally, using combination therapies in some cases may increase the risk of side effects and further promote resistance (32). In a previous study, the overall resistance rates to trimethoprim-sulfamethoxazole and ciprofloxacin were reported to be 48.4% and 38.1%, respectively. High levels of resistance were also observed for gentamicin (29.7%) and for cephalosporins, including cefepime (20.2%), ceftriaxone (26.5%), cefuroxime (29.8%), and cephalexin (31.7%). Resistance rates below 20% were only observed for three antimicrobials: amikacin (18.2%), meropenem (9.8%), and imipenem (8.8%) (33). Similarly, a study conducted at the Clinical Center Niš reported increased *E. coli* resistance to ceftriaxone and ciprofloxacin

from 12% and 16%, respectively, in 2011 to 38% for both antibiotics in 2014 (34). Further evidence of high antimicrobial resistance in *E. coli* was provided by a study conducted at the Center for Microbiology of the Institute of Public Health Kragujevac during 2020–2021. This study found the lowest resistance rates for amikacin (4.0%) and fosfomycin (6.2%), while the highest resistance rates were observed for ciprofloxacin (35.5%), cephalexin (24.5%), and gentamicin (20.7%) (35).

In patients with complicated infections, the pattern of antibiotic use was similar. Despite EAU guidelines recommending fluoroquinolones for mild to moderate symptoms (11), patients with hematuria reported using ciprofloxacin and cephalexin, while those with fever often used ciprofloxacin and cotrimoxazole, sometimes in combination.

Pregnant women showed relatively good adherence to guidelines, although there were deviations, such as the use of ciprofloxacin and doxycycline, which are not recommended during pregnancy (36, 37). The fact that four pregnant women obtained antibiotics from pharmacists without prescriptions highlights a significant issue with irrational and risky antibiotic use during pregnancy.

Strengths and Limitations

To the best of our knowledge, this is the first study in Serbia to investigate antibiotic use among female patients with UTI symptoms, with an additional strength as the results present self-medication of patients with antibiotics.

However, the study is subject to some limitations, including recall bias, as certain questions in the questionnaire pertain to the previous year. Additionally, no further analysis was conducted based on clinical diagnoses, and there is a risk of misinterpretation due to different treatment recommendations for different types of UTI.

Conclusion

These findings underscore the importance of standardizing clinical practices and enhancing the education of both healthcare professionals and patients regarding the rational use of antibiotics in UTI treatment, especially given the growing concern of antimicrobial resistance. Future interventions should focus on promoting adherence to first-line antibiotic recommendations and raising awareness about the potential risks of inappropriate antibiotic use.

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Declaration of Competing Interest

The authors declare that they have no conflicts of interest to disclose, including financial, personal or other relationships.

Author contributions

AJ: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing –original draft; MD: Conceptualization, Methodology, Investigation, Data curation, Writing – editing; IT: Conceptualization, Methodology, Investigation, Data curation, Writing – editing; BV: Methodology, Investigation, Eriting – editing; DP: Methodology, Investigation, Writing – editing; RVR: Investigation, Writing – editing; MO: Investigation, Writing – editing; AK: Investigation, Writing – editing; PDž: Investigation, Writing – editing; DK: Conceptualization, Methodology, Investigation, Data curation, Supervision, Project administration, Writing – editing. All authors were responsible for critically revising this work for important intellectual content. All authors are accountable for all aspects of this work.

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Iskustva žena sa upotrebom antibiotika kod urinarnih infekcija: Uvidi iz perspektive pacijentkinja

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Kratak sadržaj

Upotreba antibiotika u lečenju infekcija urinarnog trakta (IUT) u Srbiji je nedovoljno istražena, posebno iz ugla pacijenata, te je cilj studije da se ispita upotreba antibiotika kod ovih pacijenata. Sprovedena je onlajn studija preseka tokom zime 2020/21. godine, korišćenjem validiranog *Google Docs* upitnika i tehnike snežne grudve. Studija je obuhvatila 236 pacijenta ženskog pola, prosečne starosti 34,9 ± 14,2 godina. Većina pacijenata smatrala je simptome ozbiljnim (62,3%), i da simptomi ometaju njihove svakodnevne aktivnosti (51,3%). Većina pacijenata (77,1%) je koristila antibiotike propisane na lekarski recept. Ostali pacijenti su koristili antibiotike samostalno, po sopstvenom izboru. Samolečenje antibioticima je bilo povezano sa

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percepcijom ozbiljnosti simptoma (p=0,006) i prebivalištem (p=0,017). Pacijenti su prijavili upotrebu 17 različitih antibiotika za lečenje IUT, od kojih su najzastupljeniji bili fluorohinoloni (30,3%), cefalosporini (21,2%) i sulfonamidi (15,7%). Najveća usklađenost primene antibiotika sa nacionalnim i evropskim smernicama uočena je kod trudnica (80,0%). Rezultati istraživanja ističu potrebu za edukacijom zdravstvenih profesionalaca i unapređenju kliničke prakse u donošenju odluka o racionalnom propisivanju antibiotika.

Ključne reči: upotreba antibiotika, izveštaj pacijenta, samolečenje, pridržavanje smernica