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Prevalence study on the use of antibiotics in a tertiary healthcare facility

Studija prevalencije o upotrebi antibiotika u ustanovi zdravstvene zaštite tercijarnog nivoa

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Abstract

Background/Aim. Prevalence studies, also known as cross-sectional studies, offer an effective approach for gathering high-quality data on particular health concerns. The aim of the study was to analyze the utilization of antimicrobial medications (AM) in a tertiary healthcare institution. **Methods.** A prevalence study on AM use was performed at the University Clinical Center Kragujevac, Serbia, in early November 2022. This research was conducted as part of the Fifth National Research Initiative and employed the standardized methodology established by the European Center for Disease Prevention and Control (ECDC). Data was collected on all patients admitted to the ward before 8 a.m. **Results.** Among the 567 patients included in the study, 246 received at least one AM, yielding a prevalence rate of 43.4% (95% confidence interval: 39.3–47.6). The most common indications for AM use were community-acquired infections (54.9%), followed by healthcare-associated infections (19.1%), surgical prophylaxis (20.7%), and medical prophylaxis (3.7%). Parenteral administration was the most common route for AM administration (89.6%). In 97.6% of cases, the rationale for the drug application was documented in the patient's medical records. Third-generation cephalosporins were the most frequently utilized antimicrobial group, comprising 17.9% of usage, followed by carbapenems at 12.7%, glycopeptides also at 12.7%, and fluoroquinolones at 11.8%. According to the Access-Watch-Reserve (AWaRe) classification, antibiotics under supervision were prescribed most frequently (66.4%), followed by first-choice antibiotics (28.1%), with reserve antibiotics comprising 5.5%. **Conclusion.** The implementation of measures to regulate the use of AM is required to retain the efficacy of these medications in the future.

Key words:
anti-bacterial agents; serbia; tertiary healthcare.

Apstrakt

Uvod/Cilj. Studije prevalencije, poznate i kao studije preseka, nude efikasan način prikupljanja visokokvalitetnih podataka o određenim zdravstvenim problemima. Cilj rada bio je da se analiza upotreba antimikrobnih lekova (AML) u ustanovi zdravstvene zaštite tercijarnog nivoa. **Metode.** Studija prevalencije o upotrebi AML sprovedena je u Univerzitetskom kliničkom centru Kragujevac, Srbija, početkom novembra 2022. godine. Ovo istraživanje sprovedeno je u okviru Pete nacionalne studije, i korišćena je standardizovana metodologija Evropskog centra za prevenciju i kontrolu bolesti (*European Center for Disease Prevention and Control* – ECDC). Prikupljeni su podaci o svim pacijentima primljenim na odeljenje pre 8 časova ujutru. **Rezultati**. Od 567 pacijenata uključenih u studiju, njih 246 primalo je najmanje jedan AML, što čini prevalenciju od 43,4% (95% interval poverenja 39,3–47,6). Najćešće idikacije za primenu AML bile su vanbolničke infekcije (54,9%), bolničke infekcije (19,1%), hirurška profilaksa (20,7%) i medicinska profilaksa (3,7%). Parenteralna primena predstavljala je najčešći put za aplikaciju AML (89,6%). U 97,6% slučajeva, razlozi za primenu leka dokumentovani su u medicinskom kartonu pacijenta. Cefalosporini treće generacije bili su najčešće korišćena antimikrobna grupa, sa 17,9% upotrebe, zatim karbapenemi sa 12,7%, glikopeptidi takođe sa 12,7% i

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fluorohinoloni sa 11,8% upotrebe. Prema *Access-Watch-Reserve* (AWaRe) klasifikaciji, najučestalije su propisivani antibiotici pod nadzorom (66,4%), potom antibiotici prvog izbora (28,1%), dok su rezervni antibiotici činili 5,5%. **Zaključak.** Neophodno je uvođenje mera za kontrolisanje upotrebe AML kako bi se očuvala efikasnost ovih lekova u budućnosti.

Ključne reči:
antibiotici; srbija; zdravstvena zaštita, tercijarna.

Introduction

Effective antimicrobial medication (AM) is essential in modern medicine for fighting bacterial infections. Nonetheless, data from nearly every part of the world show that microbes are becoming increasingly resistant to antibiotics, indicating that resistance is evolving into a serious health and socioeconomic problem [1]. If the warnings from the scientific community about the overuse and misuse of antibiotics are ignored, the overall burden of antimicrobial resistance is predicted to increase even further in the coming years. Despite a plethora of ongoing studies, no new AMs are anticipated any time soon; hence, greater efforts are required to maintain the sensitivity of existing medications [2].

Monitoring antibiotic use at the hospital, regional, and national levels is crucial, as it offers significant insights for the development of health policies and the implementation of control measures for antibiotic utilization. These studies serve as valuable and cost-effective instruments for monitoring antibiotic consumption, facilitating the collection of detailed and reliable information. In Europe, prevalence studies of healthcare-associated infections (HAIs) and antibiotic use are periodically conducted using standardized methodologies from the European Center for Disease Prevention and Control (ECDC), facilitating cross-country data comparisons. The ECDC study [3], conducted between 2011 and 2012 in European Union/European Economic Area (EU/EEA) countries, indicated that the average prevalence of patients receiving at least one prescribed AM was 35.0% (with country-specific rates ranging from 21.4% to 54.7%). The subsequent ECDC study, conducted from 2016 to 2017, reported a prevalence of 32.9% (with country-specific rates ranging from 16.0% to 55.6%) [4]. Despite being a non-EU member, the Republic of Serbia was invited to participate in this second study. It revealed a prevalence of patients with at least one prescribed AM at 41.3% [95% confidence interval (CI): 40.5–42.1]. The Republic of Serbia, in conjunction with Southern and Eastern European nations, has consistently ranked among the highest in Europe for antimicrobial consumption and bacterial resistance levels across all examined species. The Ministry of Health established a National Clinical Practice Guideline for Rational Antibiotic Use to tackle this issue [5]. This guideline offers healthcare professionals clear guidance on selecting appropriate therapeutic approaches in daily practice, optimizing antibiotic use, and reducing resistance rates.

This study aims to analyze the utilization of AMs in a tertiary healthcare institution and identify the risk factors influencing their use.

Methods

This prevalence study was conducted at the University Clinical Center Kragujevac, Serbia, during the first week of November 2022 as part of the Fifth National and Third European Point Prevalence Study on HAIs and antimicrobial use. The methodology of the ECDC [6] was implemented in the investigation. The research in Serbia was coordinated by a Working Group of the Ministry of Health and the Institute of Public Health of Serbia "Dr. Milan Jovanović Batut", which was specifically established. The Working Group operated through the appropriate institutions and public health centers. Hospitals participated voluntarily in the investigation. Our hospital, which is a tertiary healthcare institution with a total of 1,118 hospital beds, including 97 beds in intensive care units, was one of the participants.

The study adhered to the established methodology, encompassing all hospital departments and all patients admitted before 8:00 a.m. on the day of the study who remained hospitalized at the time of data collection. Emergency departments were excluded, except for those where patients are monitored for more than 24 hrs. Additionally, patients treated in day hospitals, those receiving one-day therapy or surgery on the study day, as well as individuals seen in outpatient clinics, emergency departments, or outpatient dialysis units, were also excluded. Data for each department and its hospitalized patients were required to be collected within a single day.

The research team, comprising physicians and medical technicians from the hospital and the pertinent public health institute, completed two days of theoretical and practical training before initiating the study. Surveyors gathered the requisite data by examining patient records and engaging in direct communication with physicians in the departments.

The collected data were inserted into two epidemiological questionnaires. The initial questionnaire gathered data regarding the department, which encompassed the department type, the bed count, and the number of patients admitted on the study date. In the second questionnaire, the patients were asked about sociodemographic information as well as specifics about their current hospitalization, such as the severity of their illness based on the McCabe score, the use of invasive procedures (such as surgery, central venous catheter, urinary catheter, or intubation), and their antimicrobial use. Antibiotic data were collected exclusively for patients receiving at least one antimicrobial during the study, except for surgical prophylaxis, where administration occurred up to 24 hrs prior to the study documentation.

Each antimicrobial drug was assigned to the fifth Anatomical-Therapeutic-Chemical (ATC) Classification level, along with details regarding the method of administration, indication [community-acquired infections (CAIs), acute HAIs, surgical or medical prophylaxes], diagnosis, documentation of the reason for drug use, initiation of therapy, and daily dosage. The duration of antibiotic use for surgical prophylaxis was also documented (one dose, one day, or multiple days).

The study included the following antimicrobials according to the fifth ATC level classification: J01 (antibiotics for systemic use), J02 (antimycotics for systemic use), A07AA (intestinal anti-infectives), P01AB (nitroimidazole derivatives – antiprotozoals), D01BA (antifungals for systemic use), and J04AB02 (rifampicin). Antiviral agents and antituberculous drugs were excluded unless utilized for the treatment of mycobacteriosis other than tuberculosis. All observed antibiotics were further categorized according to the Access-Watch-Reserve (AWaRe) classification [7] into first-choice antibiotics (Access), controlled antibiotics (Watch), and reserve antibiotics (Reserve).

To classify an infection as an active HAI, the established HAI criteria must be fulfilled, with signs and symptoms evident on the study date, or the patient must be undergoing treatment for the infection. Symptoms of infection must manifest after the third day of admission unless the patient was re-admitted to the hospital within 48 hrs. There were exceptions to these criteria for surgical site infections, infections caused by *Clostridioides* (*C.*) *difficile*, and infections associated with medical devices.

All collected data were systematically coded and stored in a database. SPSS 22.0 for Windows was used to analyze the data. A Chi-square test was used to determine the statistical significance of the variables. A separate test, univariate logistic regression, was also performed. The dependent variable was group membership (patients who received at least one prescribed antibiotic vs. patients who received no antibiotic), while all other factors were independent. All factors that showed statistically significant variations between groups were included in the multivariate logistic regression model. Before applying this multivariate technique, its assumptions were checked to see if they were satisfied (binary outcome, independence of observations, no multicollinearity, no extreme outliers, and a sufficient sample size). The quality of the regression models was checked by the Hosmer and Lemeshow test, Cox and Snell R-squared, and Nagelkerke R-squared. The results were considered statistically significant if the probability of the null hypothesis was 0.05 or below.

The prevalence of patients with AM was calculated, using patients receiving at least one antimicrobial at the time of the study as the unit of observation. The denominator comprised all patients treated at the hospital departments during the same period of antimicrobial drug usage. Patients receiving multiple antimicrobials were counted only once. Prevalences were calculated, accompanied by their 95% CI, which were determined using the Clopper-Pearson exact method for proportions and STATA version 18.0.

This study adhered to the ECDC methodology, which did not necessitate approval from the Institutional Ethics Committee. This ongoing practice, which has not been sufficiently regulated in the past, must undergo future changes to ensure the protection of patients and their data through the work of the Ethics Committees.

Results

The study sample comprised 567 patients, with 292 (51.5%) of them identified as male. The age of all patients was 51.4 ± 25.5 years (range: 0–93 years, median: 60.0), and the length of hospitalization was 10.1 ± 13.4 days (range: 0–116 days, median: 5.0). The majority of patients were admitted to surgical departments [212 (37.4%)] and internal medicine departments [154 (27.2%)]. This was followed by the intensive care unit [85 (15.0%)], gynecology and obstetrics [31 (5.5%)], pediatrics [21 (3.7%)], neonatology [9 (1.6%)], and other mixed departments [45 (7.9%)] (data not shown).

Out of the overall patient cohort, 246 received at least one AM, yielding a prevalence of 43.4% (95% CI: 39.3–47.6). The basic characteristics of the patients, categorized by whether they received AM, are presented in Table 1. A statistically significant difference was observed between the group receiving antibiotics and the group not receiving any in terms of patient age, length of hospital stay, the assessment of the patients' condition according to the McCrabe score, and the department in which they were hospitalized ($p < 0.05$). Patients who received AM more often had a fatal disease (24.0%) compared to those who did not receive AM (15.6%). The majority of patients with AM received treatment in surgical departments (39.4%), whereas most patients in the non-antibiotic group were treated in internal medicine departments (41.1%). Patients who received AM were significantly more likely to undergo medical procedures during their current hospitalization compared to those who did not. Specifically, they had higher rates of surgical intervention (32.6% vs. 15.6%), central venous catheter placement (13.4% vs. 3.7%), urinary catheterization (45.1% vs. 15.0%), and intubation (11.4% vs. 1.9%). Moreover, individuals who received at least one antimicrobial agent during the trial exhibited a statistically significantly higher incidence of HAIs (19.1%) compared to those who did not receive AM.

Approximately 74.0% of patients who received antimicrobial therapy did so for therapeutic purposes, with 54.9% treated for CAIs and 19.1% for HAIs. Surgical prophylaxis was the rationale for antibiotic use in 20.7% of patients, whereas 3.7% took it for medical prophylaxis (Table 2). Concerning the duration of surgical prophylaxis, 14 (27.5%) patients (prevalence: 2.5; 95% CI: 1.4–4.1) were administered a single dose of antibiotic, 10 (19.6%) patients (prevalence: 1.8; 95% CI: 0.8–3.2) underwent prophylaxis for one day, whereas over half of the patients [27 (52.9%)] (prevalence: 4.8; 95% CI: 3.2–6.9) received antibiotics for more than one day (data not shown).

Table 1

Distribution of patients based on the use of antimicrobial agents at the University Clinical Center Kragujevac in the first week of November 2022

Characteristics	Patients with AM (n = 246)	Patients without AM (n = 321)	χ^2 test	*p*
Male gender	132 (53.7)	160 (49.8)	0.811	0.368
Age groups (years)				
< 1	23 (9.3)	20 (6.2)		
1–14	15 (6.1)	16 (5.0)		
15–24	9 (3.7)	15 (4.7)	19.831	0.001
25–64	80 (32.5)	161 (50.2)		
≥ 65	119 (48.4)	109 (34.0)		
Length of hospital stay (days)				
1–3	76 (30.9)	140 (43.6)		
4–7	64 (26.0)	51 (15.9)		
8–14	62 (25.2)	54 (16.8)	20.656	< 0.001
15–29	29 (11.8)	44 (13.7)		
≥ 30	15 (6.1)	32 (10.0)		
McCabe score				
non-fatal disease	150 (61.0)	213 (66.4)		
fatal disease	59 (24.0)	50 (15.6)	9.727	0.021
rapidly fatal disease	28 (11.4)	52 (16.2)		
[1] unknown	9 (3.7)	6 (1.9)		
Department				
internal medicine	80 (32.5)	132 (41.1)		
surgery	97 (39.4)	79 (24.6)		
intensive care units	23 (9.3)	15 (4.7)	55.378	< 0.001
gynecology with obstetrics	13 (5.3)	28 (8.7)		
pediatrics	32 (13.0)	23 (7.2)		
other departments	1 (0.4)	44 (13.7)		
Surgical intervention				
none	166 (67.5)	271 (84.4)		
NHSH	55 (22.4)	33 (10.3)	22.730	< 0.001
non-NHSH	25 (10.2)	17 (5.3)		
Central venous catheter	33 (13.4)	12 (3.7)	17.847	< 0.001
Urinary catheter	111 (45.1)	48 (15.0)	62.817	< 0.001
Intubation	28 (11.4)	6 (1.9)	22.359	< 0.001
Healthcare-associated infection	47 (19.1)	1 (0.3)	63.43	< 0.001

AM – antimicrobial medication; NHSH – National Health Surveillance Network.
Values are given as numbers (percentages).
***Note*: [1] The questionnaire in the research trial used the option “unknown” for some data.**

Table 2

Prevalence of antimicrobial agent use by indication and route of administration at the University Clinical Center Kragujevac in the first week of November 2022

Variable	Patients	Prevalence (95% CI)
Total	246 (100)	43.4 (39.3–47.6)
Therapy		
community-acquired infections	135 (54.9)	24.2 (20.7–27.9)
healthcare-associated infection	47 (19.1)	8.5 (6.3–11.1)
total	182 (74.0)	32.5 (28.6–36.5)
Prophylaxis		
surgical	51 (20.7)	9.0 (6.8–11.7)
medical	9 (3.7)	1.6 (0.7–3.0)
[1] unknown	4 (1.6)	0.7 (0.2–1.8)
Route of administration		
parenteral	225 (89.6)	39.7 (35.6–43.8)
oral	25 (10.0)	4.4 (2.9–6.4)
[1] unknown	1 (0.4)	0.2 (0.0–1.0)
Reason for use noted		
yes	240 (97.6)	42.3 (38.2–46.5)

CI – confidence interval.
Values are given as numbers (percentages) or mean values (minimum–maximum).
***Note*: [1] The questionnaire in the research trial used the option “unknown” for some data.**

Parenteral administration constituted 89.6% of therapies for administering AM, whilst the oral route was utilized in 10.0% of therapies. The rationale for using AM was frequently recorded in the patient's medical documentation (97.6%) (Table 2).

Among the 246 individuals receiving AM, a total of 346 medications were administered, resulting in an average of 1.4 AM *per* patient. In the treatment of CAIs, categorized by anatomical localization, the most commonly prescribed antimicrobial agents were for respiratory tract infections (20.2%), urinary tract infections (15.3%), and clinical sepsis (14.6%). In the treatment of HAIs, the most commonly recommended medications were for respiratory tract infections (32.1%), surgical site infections (21.8%), and urinary tract infections (16.7%) (Table 3).

Antibacterial drugs for systemic use (ATC group J01) constituted the predominant category of AMs utilized (99.0%). The most commonly used AM group was third-generation cephalosporins (17.9%), followed by carbapenems (12.7%), glycopeptides (12.7%), and fluoroquinolones (11.8%). Among the antimicrobials prescribed for treating CAIs, the most frequently utilized were third-generation cephalosporins (22.2%), fluoroquinolones (14.6%), and carbapenems (12.6%). In contrast, for the

Table 3

Indications for the use of antimicrobial agents and prescribed classes of antibiotics, and antibiotics according to ATC 5th level classification

Variable	Therapy of infections n = 276 (79.8%)		Infection prophylaxis n = 66 (19.1%)		[1] Unknown n = 4 (1.1%)	Total n = 346 (100%)
	community-acquired infections n = 198 (71.7%)	healthcare-associated infection n = 78 (28.3%)	surgical prophylaxis n = 55 (83.3%)	medical prophylaxis n = 11 (16.7%)		
Indications						
surgical site infections	21 (10.6)	17 (21.8)	44 (80.0)	0 (0.0)	0 (0.0)	82 (23.7)
respiratory infections	49 (24.7)	25 (32.1)	0 (0.0)	0 (0.0)	0 (0.0)	74 (21.4)
urinary tract infections	40 (20.2)	13 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	53 (15.3)
clinical sepsis	29 (14.6)	10 (12.8)	0 (0.0)	0 (0.0)	0 (0.0)	39 (11.3)
cellulitis, wound, deep soft tissue infections	28 (14.1)	3 (3.8)	1 (1.8)	0 (0.0)	0 (0.0)	32 (9.2)
gastrointestinal infections	5 (2.5)	5 (6.4)	0 (0.0)	2 (18.2)	0 (0.0)	12 (3.5)
ear, nose, and throat infections	10 (5.1)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	11(3.2)
gynecology and obstetrics	2 (1.0)	0 (0.0)	8 (14.5)	1 (9.1)	0 (0.0)	11(3.2)
laboratory-confirmed bacteremia	3 (1.5)	4 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)	7 (2.0)
febrile neutropenia	4 (2.0)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	5 (1.4)
intra-abdominal sepsis	4 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.2)
septic arthritis/osteomyelitis	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
other/[1] unknown	3 (1.5)	0 (0.0)	2 (3.6)	6 (54.5)	4 (100.0)	15 (4.3)
Antibiotics						
penicillins with extended spectrum and combinations, including beta-lactamase inhibitors	9 (4.5)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	10 (2.9)
beta-lactam sensitive penicillins	3 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.9)
first-generation cephalosporins	4 (2.0)	0 (0.0)	20 (36.4)	1 (9.1)	0 (0.0)	25 (7.2)
second-generation cephalosporins	3 (1.5)	0 (0.0)	8 (14.5)	0 (0.0)	1(25.0)	12 (3.5)
third-generation cephalosporins	44 (22.2)	8 (10.0)	7 (12.7)	3 (27.3)	0 (0.0)	62 (17.9)
fourth-generation cephalosporins	6 (3.0)	7 (9.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (3.8)
carbapenems	25 (12.6)	14 (17.9)	4 (7.3)	1 (9.1)	0 (0.0)	44 (12.7)
macrolides	9 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (2.6)
aminoglycosides	18 (9.1)	7 (9.0)	4 (7.3)	1 (9.1)	2 (50.0)	32 (9.2)
fluoroquinolones	20 (14.6)	5 (6.4)	5 (9.1)	1 (9.1)	1 (25.0)	41 (11.8)
glycopeptides	19 (9.6)	20 (25.6)	4 (7.3)	1 (9.1)	0 (0.0)	44 (12.7)
imidazole derivatives	13 (6.6)	7 (9.0)	3 (5.5)	0 (0.0)	0 (0.0)	23 (6.6)
colistin	4 (2.0)	6 (7.7)	0 (0.0)	1 (9.1)	0 (0.0)	11 (3.2)
antimycotics	1 (0.5)	2 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.9)
sulfamethoxazole and trimethoprim	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
clindamycin	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.6)
tetracyclines	2 (1.0)	2 (2.6)	0 (0.0)	1 (9.1)	0 (0.0)	5 (1.4)
others	6 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.7)

ATC – Anatomical Therapeutic Chemical.
Values are given as numbers (percentages).
***Note*: [1] The questionnaire in the research trial used the option "unknown" for some data.**

treatment of HAIs, the predominant agents were glycopeptides (25.6%) and carbapenems (17.9%). Over one-third of the drugs (36.4%) administered for surgical prophylaxis were first-generation cephalosporins (Table 3).

The predominant category of prescribed antimicrobials, as *per* the AWaRe categorization, was the Watch group, comprising 66.4%, followed by Access at 28.1%, and Reserve antibiotics at 5.5%. Furthermore, antibiotics were predominantly administered for both therapeutic and preventive objectives (Figure 1).

In multivariate logistic regression, the dependent variable was the use or absence of AM. All characteristics that were significant according to univariate logistic regression were included as independent variables. The results of multivariate logistic regression are shown in Table 4. Multivariate logistic regression identified the following independent risk factors for the use of AM: surgical intervention (OR = 1.501; 95% CI: 1.126–2.002; p = 0.006), placement of a urinary catheter (OR = 4.186; 95% CI: 2.562–6.841; p = 0.000), and presence of HAIs (OR = 60.239; 95% CI: 7.988–454.256; p = 0.000). The final binary logistic regression model demonstrated a satisfactory fit to the data: Hosmer and Lemeshow's test was 7.113 (p = 0.525), Cox and Snell's R-square was 0.251, and Nagelkerke's R-square was 0.370.

Discussion

Bacterial resistance to antibiotics poses a significant worldwide health challenge and endangers public health, as it affects treatment outcomes and escalates healthcare costs [8]. Since it is directly correlated with the use of AM, research of this type is a prerequisite for identifying targets and taking measures for their rational application.

The demographic structure of the patients included in this study shows that our results are consistent with the results of research at the national level [9]. Although men were more often represented in the group of patients who received AM, the difference was not statistically significant. Our results are similar to those from other studies [9, 10]. The findings indicate that the patient's age, length of hospital

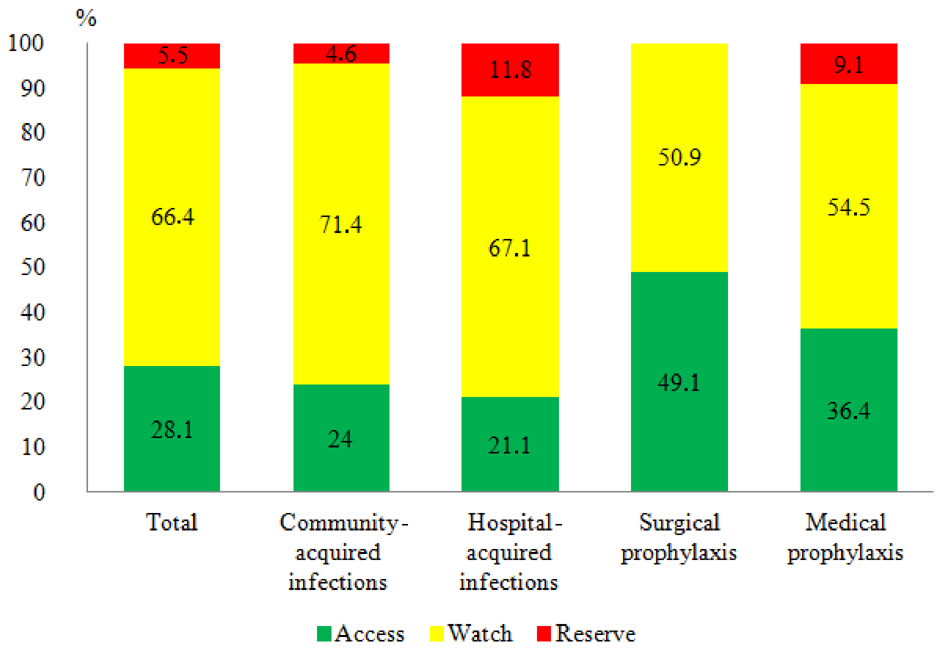

Fig. 1 – Antibiotic use according to the Access-Watch-Reserve classification.

Table 4

Multivariate logistic regression analysis for using antimicrobial agents

Variable	OR	95% CI lower	95% CI upper	p
Age groups (years)	0.839	0.702	1.003	0.054
Length of hospital stay (days)	0.866	0.745	1.008	0.063
McCabe score	0.909	0.692	1.195	0.495
Department	0.998	0.893	1.116	0.979
Surgical intervention	1.501	1.126	2.002	0.006
Central venous catheter	0.922	0.378	2.253	0.859
Urinary catheter	4.186	2.562	6.841	0.000
Intubation	0.587	0.184	1.872	0.368
Healthcare-associated infection	60.239	7.988	454.256	0.000

OR – odds ratio; CI – confidence interval.

stay, and severity of illness (as measured by the McCabe score) were statistically significantly associated with more frequent use of AM. A longer hospital stay increases the likelihood that patients will acquire multiresistant nosocomial strains of various microorganisms. This can lead to the development of HAIs, which means that AM needs to be used. Additionally, various diagnostic and therapeutic methods, including surgery, vascular and urinary catheters, or intubation, are required. The processing of our study results indicated only the statistical association between the use of AM and these procedures.

In our study, 43.4% of patients received at least one antimicrobial agent (95% CI: 39.3–47.6), indicating that approximately one in two patients were treated with antibiotics during hospitalization. This prevalence exceeds that reported in the Third European study [11], which found that 35.5% of patients had received at least one antibiotic (with country-specific rates ranging from 20.8% to 56.5%). Following adjustments for the number of occupied hospital beds by country, the overall prevalence was estimated at 32.4% (95% CI: 29.7–35.1). This implies that 390,957 patients receive antibiotics daily in hospitals across the EU/EEA [11]. Studies conducted using the same methodology in various European countries reported comparable rates – for instance, Italy showed a prevalence of 42.1% (95% CI: 41.3–43.0) [12]. In contrast, Switzerland reported a notably lower prevalence of 27.6% (95% CI: 25.9–29.4) [13]. In certain regions of the world, there is a lower prevalence of antibiotic use. For instance, Li et al. [14] report a prevalence of 28.2% in Chinese hospitals, while Frenette et al. [15] indicate a prevalence of 34.0% in Canada.

The prevalence observed in our study is also slightly lower than that reported in the Fifth National Study [9], which found a rate of 44.8% (95% CI: 43.9–45.6). This means that 5,065 (95% CI: 4,765–5,369) patients receive at least one antibiotic every day in hospitals across the Republic of Serbia. The variability in prevalence rates among hospitals can be attributed to the distinct characteristics of individual institutions, such as the treatment of specific patient populations (e.g., surgical or pediatric patients), variations in medical practices, and differences in antimicrobial prescribing practices and the frequency of HAIs.

In this study, 74.0% of the patients received AM for medical reasons. Among these, 54.9% received antibiotics to address CAIs, whereas 19.5% utilized them for the treatment of HAIs. Other studies also indicate that infection treatment is the predominant reason for antibiotic administration in hospital settings [9, 14]. The elevated rate of antibiotic prescriptions for CAIs may be attributed to the demographic characteristics of these patients, who are typically older and often present with multiple comorbidities or compromised immune systems. They may have also received treatment for an infection prior to hospital admission. When all outpatient treatment options have been exhausted, patients are admitted to the hospital for continued care and antibiotic therapy requiring multiple daily parenteral administrations. Our study found that nearly 20% of patients were administered antibiotics for the treatment of HAIs. This indicates that healthcare workers must adhere more rigorously to infection prevention and control measures to reduce the reliance on antibiotics, which is essential in the strategy to prevent unnecessary antibiotic use.

The application of antimicrobial agents in surgical prophylaxis involves administering a single dose of an effective agent before surgery to minimize the risk of postoperative infections. In our study, 20.7% of patients received antimicrobial agents for surgical prophylaxis. However, it is significant that over half of the patients (52.9%) received these agents for more than one day without a clear indication. Nonetheless, this finding is relatively promising, given that a study conducted in Serbia five years earlier reported that over 70% of patients received surgical prophylaxis for more than one day [16]. Similar results have been reported in a related study [13]. Surgical prophylaxis must encompass the preoperative period, with a single dose of AM administered 60–120 min before the procedure, typically providing adequate protection against potential infection, barring instances of substantial blood loss or extended surgery. The rationale for extending surgical prophylaxis beyond one day is typically not substantiated [17]. The obtained result should be prioritized within our hospital to initiate measures that limit unnecessary prolongation of surgical prophylaxis, thereby enhancing the management of antimicrobial use in this patient population.

Contemporary antimicrobial administration practices favor oral routes over parenteral ones due to their reduced trauma to patients and lower treatment costs. Our study identified the parenteral route for antibiotic administration as the predominant choice (89.6%), aligning with findings from other researchers who report similar dominance in pediatric (93.3%) and adult patients (96.4%) [18]. Future efforts should prioritize transitioning to oral AM when the patient's condition allows.

A notable practice in our hospital is the thorough documentation of the reasons for prescribing AM in the patient's medical records (97.6%), a finding not observed in another similar study [18]. Documenting the rationale for initiating antibiotics enables all physicians involved in patient care to consistently review and assess the appropriateness of their use or duration.

Our study found that most of the AMs used to treat CAIs were prescribed for respiratory tract infections (24.7%), urinary tract infections (20.2%), and clinical sepsis (14.6%), which aligns with expectations. In the treatment of HAIs, the predominant indications for prescribing antibiotics were respiratory tract infections (32.1%), surgical site infections (21.8%), and urinary tract infections (16.7%). This distribution aligns with trends observed in other hospitals, although the ranking may differ.

In the management of CAIs, third-generation cephalosporins (22.2%), fluoroquinolones (14.6%), and carbapenems (12.6%) were the most commonly used antibiotics. In contrast, for HAIs, glycopeptides (25.6%) and carbapenems (17.9%) were the predominant antibiotics employed, indicating a reliance on broad-spectrum agents. This pattern of antibiotic use may be associated with the emergence and dissemination of *C. difficile* and other multidrug-resistant bacteria linked with healthcare within our hospital. The prevalence of AM use in our hospital differs from that reported in hospitals across other European countries. Plachouras et al. [19], in their analysis of data from the Second study on AM use in European countries, reported that the most commonly prescribed antibiotics belonged to the penicillin combinations group, which includes beta-lactamase inhibitors (J01CR). Recent findings from the Third European Antibiotic Use Prevalence Study [11] indicate that other beta-lactam antibiotics (J01D) were the most frequently used, accounting for 35.6% of total antibiotic consumption. Among these, third-generation cephalosporins were the most prevalent (44.4%), followed by carbapenems (19.0%), second-generation cephalosporins (17.5%), first-generation cephalosporins (16.7%), and fourth-generation cephalosporins (1.4%). This study indicates that penicillins (J01C) represent the second most frequently utilized class of antibiotics, comprising 30.0%. Furthermore, combinations of penicillins, which include beta-lactamase inhibitors (J01CR), constitute 71.8% of total penicillin usage. A study on antimicrobial use in Greece [20] found that the most prescribed agents were penicillin combinations with beta-lactamase inhibitors (16.2%), followed by second-generation cephalosporins (10.9%), glycopeptides (9.4%), fluoroquinolones (9.2%), and carbapenems (8.3%). Sevin et al. [21] reported that in French hospitals, amoxicillin-clavulanic acid (27.6%) was the most frequently prescribed antibiotic for hospital-acquired pneumonia. For urinary tract infections, the most commonly prescribed antibiotics were ofloxacin (13.9%), amoxicillin (13.6%), and amoxicillin-clavulanic acid. In Italy, penicillin combinations, which include beta-lactamase inhibitors, were prescribed most frequently at a rate of 35.0% [22]. The utilization rates of these antibiotics in German hospitals were nearly identical, with 33.2% for the first category, followed by third-generation cephalosporins at 9.5% and second-generation cephalosporins at 9.1% [23]. The extensive use of broad-spectrum antibiotics necessitates a reevaluation of their indications and the implementation of more stringent management programs that address the risks of antimicrobial resistance and prioritize patient safety. A crucial component of an effective strategy to combat increasing resistance is the appropriate use and stringent regulation of broad-spectrum antimicrobials [24].

This study reveals that first-generation cephalosporins constituted 36.4% of the antimicrobial agents used in surgical prophylaxis, whereas second-generation cephalosporins represented 14.5%, and third-generation cephalosporins accounted for 12.7%. Cefazolin, a first-generation cephalosporin, is the preferred agent for providing sufficient coverage against the majority of pathogens responsible for postoperative infections. It rarely causes allergic reactions or side effects, achieves sufficient tissue concentrations, and is cost-effective, making it the optimal choice for prophylaxis in most surgical procedures [17].

According to the AWaRe classification, the majority of prescribed antibiotics belonged to the Watch group (66.4%), while the Access group accounted for less than one-third of all prescriptions (28.1%), and the Reserve group accounted for 5.5%. Comparable findings were reported in a recent study [12], where 71.8% of prescribed antibiotics were categorized as Watch, 19.6% as Access, and 8.6% as Reserve antibiotics. The AWaRe classification for measuring antibiotic consumption offers significant insights into the quality of antibiotic utilization in a specific context. The World Health Organization recommends that by 2023, at least 60% of all antibiotics nationally prescribed fall within the Access group. This group includes narrow-spectrum antibiotics that have a low potential for resistance and a favorable safety profile. In contrast, antibiotics in the Watch and Reserve groups are intended for the treatment of severe clinical manifestations or infections caused by pathogens resistant to other antibiotics, with the aim of mitigating the increasing issue of antibiotic resistance [25]. The data suggest that policymakers regarding antibiotic use in our hospital will encounter considerable challenges in the near future.

In the evaluation of risk factors associated with AM usage, univariate analysis indicated significance for various demographic characteristics and medical procedures during current hospitalizations. However, multivariate analysis identified three specific risk factors: surgical intervention, placement of a urinary catheter, and the presence of HAIs. These established risk factors are linked to the incidence of HAI, suggesting that these patients are likely to have increased exposure to various AM. Available studies indicate an association between secondary healthcare facilities and a potential risk factor for AM, attributed to insufficient diagnostic or interventional resources, along with antibiotic stewardship programs [20, 26].

A limitation of this study primarily arises from its design as a prevalence study, which involved data collection on a single day, potentially compromising the representativeness of the findings. Incidence studies yield more reliable data; however, they are time-consuming, resource-intensive, and consequently costlier. Additionally, our hospital, as a tertiary-level healthcare facility, manages more complex cases of patients, thereby enhancing the probability of AM utilization. Despite certain limitations, the data obtained provide valuable insights into AM use and can serve as a baseline indicator for managing their application.

Conclusion

This prevalence study provided valuable information on antimicrobial medication consumption in a tertiary-level healthcare facility. The high prevalence highlights the need for implementing antibiotic stewardship measures to maintain the long-term effectiveness of antimicrobial medication and ensure our ability to treat infections in the future. Healthcare workers must collaborate closely with policymakers at all levels of the healthcare system to promote the rational and responsible use of antibiotics and help combat antimicrobial resistance.

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