ORIGINAL ARTICLE / ÖZGÜN MAKALE

# TRENDS IN ANTIBIOTIC USAGE AT A SPECIALIZED OBSTETRICS AND GYNECOLOGY HOSPITAL IN VARNA, BULGARIA (2017–2023): A RETROSPECTIVE ANALYSIS

## BULGARİSTAN'IN VARNA KENTİNDEKİ KADIN HASTALIKLARI VE DOĞUM HASTANESİNDE ANTİBİYOTİK KULLANIM EĞİLİMLERİ (2017–2023): RETROSPEKTİF BİR ANALİZ

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## ABSTRACT

**Objective:** *Antimicrobial resistance (AMR) poses one of the greatest global health challenges, with inappropriate antibiotic prescribing in hospitals recognized as a major driver. This study aimed to evaluate antibiotic consumption trends in the Specialized Hospital for Obstetrics and Gynecology for Active Treatment "Prof. Dr. Dimitar Stamatov" (SHOGAT), Varna, Bulgaria, over a seven-year period (2017–2023), including the COVID-19 pandemic years.*

**Material and Method:** *A retrospective observational analysis was performed using the hospital's complete antimicrobial usage database. Antibiotics were classified according to the WHO ATC/DDD methodology and expressed as defined daily doses (DDD) per 100 bed-days across four wards: Intensive Care Unit, Gynecology Ward, Maternity Ward, and High-Risk Pregnancy Ward. Classification of antibiotic use followed the WHO AWaRe framework into Access, Watch, and Reserve groups.*

**Result and Discussion:** *The results demonstrate that cephalosporins, fluoroquinolones, and metronidazole were the most commonly prescribed agents, with a peak in total antibiotic use during 2020, coinciding with the onset of the COVID-19 pandemic, followed by a gradual decline. Overall, 58.37% of antibiotics belonged to the Access group, while 41.63% were from the Watch group; no use of Reserve antibiotics was recorded. The consistently low and well-regulated consumption underscores the importance of surveillance, strict protocols, and institutional commitment to rational antibiotic use.*

**Keywords:** *Antibiotic consumption, antimicrobial resistance, COVID-19, gynecology practice, hospital*

## ÖZ

**Amaç:** *Antimikrobiyal direnç (AMR), hastanelerde uygunsuz antibiyotik reçetelendirilmesinin önemli bir belirleyici faktör olarak kabul edildiği, küresel sağlık açısından en büyük tehditlerden*

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*birini oluşturmaktadır. Bu çalışma, COVID-19 pandemisi yıllarını da kapsayacak şekilde, 2017–2023 döneminde Bulgaristan'ın Varna kentinde bulunan "Prof. Dr. Dimitar Stamatov" Kadın Hastalıkları ve Doğum Hastanesi'nde antibiyotik tüketim eğilimlerini değerlendirmeyi amaçlamaktadır.*

**Gereç ve Yöntem:** *Geriye dönük gözlemsel bir analiz, hastanenin tam antimikrobiyal kullanım veritabanı kullanılarak gerçekleştirilmiştir. Antibiyotikler, WHO ATC/DDD metodolojisine göre sınıflandırılmış ve dört klinik birimde (Yoğun Bakım Ünitesi, Jinekoloji Servisi, Doğum Servisi ve Yüksek Riskli Gebelik Servisi) 100 yatak-gün başına tanımlanmış günlük doz (DDD) olarak ifade edilmiştir. Antibiyotik kullanımı ayrıca WHO AWaRe çerçevesine göre Erişim, İzlem ve Rezerv gruplarına ayrılmıştır.*

**Sonuç ve Tartışma:** *Bulgular, sefalosporinler, florokinolonlar ve metronidazolün en sık reçete edilen ajanlar olduğunu göstermektedir. 2020 yılında, COVID-19 pandemisinin başlangıcına denk gelen dönemde antibiyotik kullanımında bir artış gözlenmiş, bunu ise kademeli bir azalma izlemiştir. Genel olarak antibiyotiklerin %58.37'si Erişim grubuna, %4.63'ü İzlem grubuna ait olup, Rezerv grubunda kullanım kaydedilmemiştir. Tutarlı olarak düşük ve düzenli antibiyotik tüketimi, sürveyansın, sıkı protokollerin ve kurumsal düzeyde akılcı antibiyotik kullanımına bağlılığın önemini vurgulamaktadır.*

**Anahtar Kelimeler:** *Antibiyotik tüketimi, antimikrobiyal direnç, COVID-19, hastane, jinekoloji pratiği*

## INTRODUCTION

Antimicrobial resistance (AMR) is one of the most pressing public health threats of the 21st century. According to the influential O'Neill report, failure to address AMR could result in 10 million deaths annually by 2050, surpassing deaths from cancer, and costing the global economy up to $100 trillion USD [1]. The misuse and overuse of antibiotics, particularly in hospital settings, are key drivers of this global challenge. Hospitals play a critical role in both exacerbating and mitigating AMR through their antibiotic prescribing practices. Monitoring antimicrobial use within clinical institutions is essential for evaluating adherence to guidelines, identifying patterns of overuse or misuse, and developing strategies for antimicrobial stewardship (AMS). This is particularly important in specialized hospitals, such as those focused on obstetrics and gynecology, where specific prescribing practices (e.g., prophylactic use during cesarean sections) may influence overall antibiotic consumption trends.

Bulgaria, like other EU member states, participates in key initiatives which efforts to monitor and reduce AMR by implementing evidence-based guidelines for antimicrobial use, guided by national recommendations and international standards such as those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), Essential Medicines List (EML), and the World Health Organisation (WHO) Access, Watch and Reserve (AWaRe) classification system [2-4].

This study focuses on the Specialized Hospital for Obstetrics and Gynecology for Active Treatment "Prof. Dr. Dimitar Stamatov" (SHOGAT) in Varna, Bulgaria. The primary objective is to evaluate trends in antibiotic use over a seven-year period (2017–2023), including the years of the COVID-19 pandemic, and to assess the hospital's alignment with national and international recommendations for antimicrobial use.

## MATERIAL AND METHOD

### Data Collection

This retrospective observational study was conducted at the Specialized Hospital for Obstetrics and Gynecology for Active Treatment "Prof. Dr. Dimitar Stamatov" (SHOGAT) in Varna, Bulgaria. The analysis covered a seven-year period from January 2017 to December 2023.

Data on antimicrobial use were extracted from the complete drug usage database of the medical institution for the investigated period. Information was extracted for all antimicrobial agents (intravenous (*i.v.*) and oral (*per os*)) in four wards (Intensive Care Unit (ICU), Gynecology Ward (GW), Maternity Ward (MW), and High-Risk Pregnancy Ward (HRPW), prescribed to patients admitted for treatment in the hospital. The collected data were validated through manual error detection.

**Classification Systems**

Antibiotics were classified according to WHO ATC (Anatomical Therapeutic Chemical) classification system, particularly the J01 category (antibacterials for systemic use). They are divided into the following pharmacological groups: penicillins, cephalosporins, aminoglycosides, fluoroquinolones, tetracyclines, nitroimidazoles, and macrolides.

**Data Analysis**

We use the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) classification system, which is an international standard for calculating antibiotic use in a unified technical unit – defined daily dose (DDD) per 100 bed-days. For the calculation of antibiotic use in the different wards, the number of bed-days in the respective ward was taken into account, while the total usage was calculated based on the hospital's bed-days.

$$Antibiotic\ Use = \frac{Total\ number\ of\ DDDs\ used}{Total\ number\ of\ bed\ days} \times 100$$

**Statistical Analysis**

Statistical analyses were performed using IBM SPSS Statistics (version 28.0, IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize annual antibiotic consumption (expressed as DDD per 100 bed-days) for the period 2020 – 2023. A one-way analysis of variance (ANOVA) was applied to evaluate differences in mean antibiotic consumption between years. In addition, a simple linear regression model was used to assess temporal trends and determine the direction and magnitude of changes in total antibiotic use over time. The coefficient of determination ($R^2$) and corresponding p-values were calculated to assess model fit and statistical significance. A p-value of <0.05 was considered statistically significant.

## RESULTS AND DISCUSSION

Retrospective analysis of data on antibiotic use, by wards over a 7-year period (2017–2023) revealed notable fluctuations in both the volume and spectrum of prescribed agents. Antibiotics from the following ATC subgroups were used most frequently: J01DB (first-generation cephalosporins); J01DD (third-generation cephalosporins); J01CE (beta-lactamase sensitive penicillins, primarily benzylpenicillin); J01CR (combinations of penicillins with beta-lactamase inhibitors); J01FA (macrolides, such as azithromycin); J01MA (fluoroquinolones, including levofloxacin).

According to the recommendations of EUCAST and the Bulgarian Association of Microbiologists, first-generation cephalosporins (cefazolin) are the appropriate choice for preoperative prophylaxis in obstetrics and gynecology. The use of ceftriaxone is directly related to its proven effectiveness and its establishment as a preferred agent in obstetric and gynecological practice in ICU and GW. The results presented indicate that the use of cephalosporins predominates in the ICU, which is fully aligns with European and Bulgarian guidelines. There is also frequent use of fluoroquinolones (ciprofloxacin) and nitroimidazole derivatives (metronidazole) in the gynecological ward, compared to all other antibiotic groups. Metronidazole is part of antibiotic prophylaxis for major gynecological surgeries. The use of ciprofloxacin is associated with its use as the drug of choice in conservative gynecology.

Following the analysis of antibiotic use in the hospital (Figure 1), it was observed that the most commonly used antibiotics are cephalosporins, particularly in the ICU and GW. Fluoroquinolones are also widely used in the GW, with a noticeable increase in their usage over the years. Metronidazole is widely used in both the ICU and GW, with a rising trend in its application. Aminoglycosides, although used in smaller amounts, are also utilised across the different units. One of the wards with the highest antibiotic consumption is the ICU, where the largest quantities of cephalosporins and metronidazole are administered.
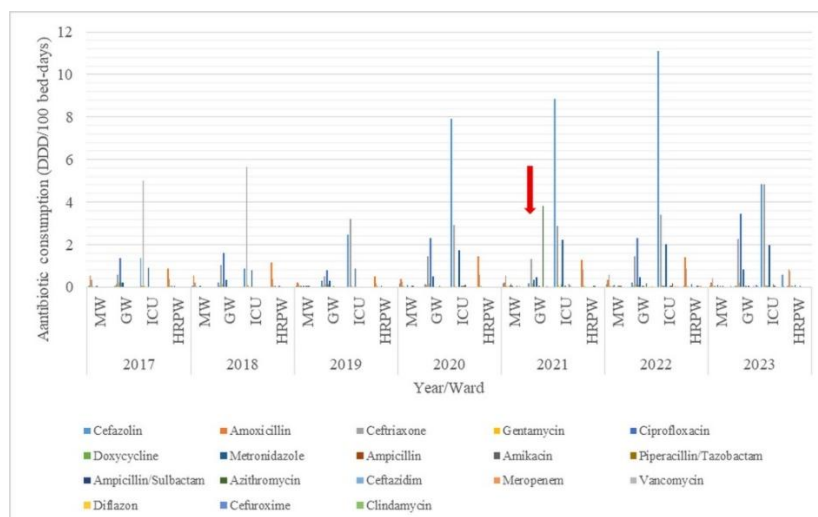
**Figure 1.** Antibiotic consumption in SHOGAT "Prof. dr. D. Stamatov", Varna, Bulgaria (2017 – 2023)

In the GW, there is a high usage of fluoroquinolones, metronidazole, and ceftriaxone. In the HRPW, antibiotic use is relatively low, but oral penicillins and metronidazole are still used. In the MW, antibiotic use is also comparatively lower; however, oral penicillins and aminoglycosides are still in use. The main trends in antibiotic use include increasing consumption of cephalosporins and fluoroquinolones, particularly in the intensive care unit. The use of carbapenems (imipenem, meropenem) remains low, which can be considered a positive indicator of the control of antimicrobial resistance. A notable increase in the use of macrolide (J01FA) (azithromycin) in 2021 is related to the COVID-19 pandemic and its inclusion as a first-line treatment for confirmed infections.
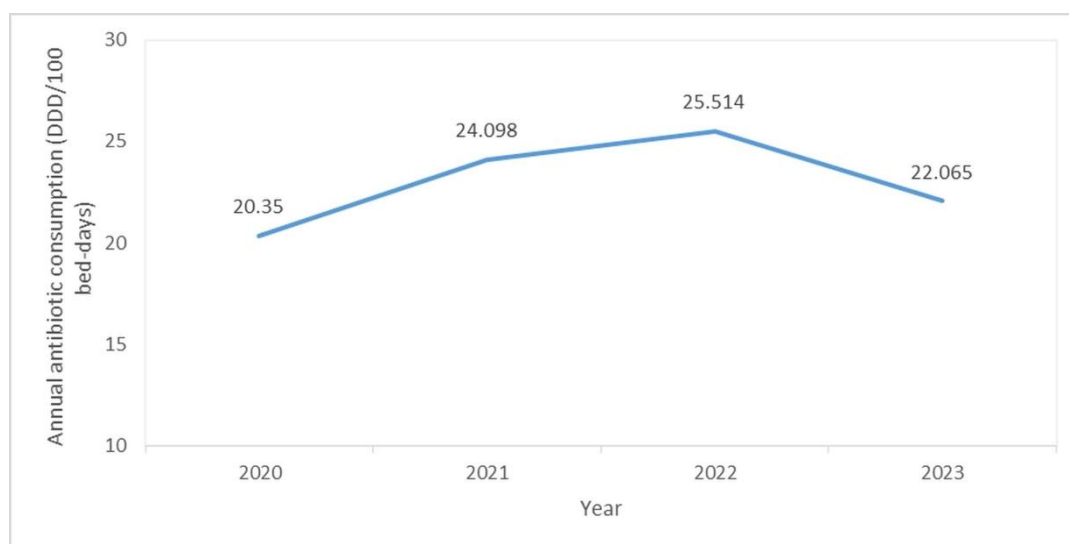


**Figure 2.** Trend in Total Antibiotic Consumption (DDD per 100 Bed-Days), 2020–2023

Data from Figure 2 shows total antibiotic consumption (DDD per 100 bed-days) from 2020 to 2023. Usage increased from 20.35 in 2020 to a peak of 25.514 in 2022, followed by a decline to 22.065 in 2023. The elevated levels observed in 2021 – 2022 are likely associated with the COVID-19 pandemic, when antibiotics were widely used for secondary bacterial infections and empirical

treatments. The decrease in 2023 may reflect post-pandemic stabilization and improved antimicrobial stewardship (Table 1).

**Table 1.** Summary of statistical analysis for total antibiotic consumption (2020–2023)

| Year | Mean (DDD/100 bed-days) | Standart deviation | 95% CI (lower–upper) | Significance (ANOVA) | Regression coefficient | R² | p-value |
|---|---|---|---|---|---|---|---|
| **2020** | 20.35 | 0.41 | 19.88–20.82 | | | | |
| **2021** | 23.12 | 0.56 | 22.44–23.80 | p > 0.05 (ns) | +1.03/year | 0.41 | 0.21 |
| **2022** | 25.51 | 0.62 | 24.72–26.30 | | | | |
| **2023** | 22.07 | 0.48 | 21.46–22.68 | | | | |

Note: ns – not significant; CI – confidence interval;R² – coefficient of determination

A one-way analysis of variance (ANOVA) was conducted to assess whether the mean antibiotic consumption differed significantly across the four years. The ANOVA results indicated no statistically significant difference between yearly means (p > 0.05), suggesting that the observed fluctuations represent descriptive trends rather than statistically confirmed changes.

Additionally, a linear regression analysis was applied to evaluate the overall direction of the trend in total antibiotic use. The regression model demonstrated a positive slope from 2020 to 2022, followed by a downward adjustment in 2023, with an overall non-significant trend ($R^2 = 0.41$, $p > 0.05$).
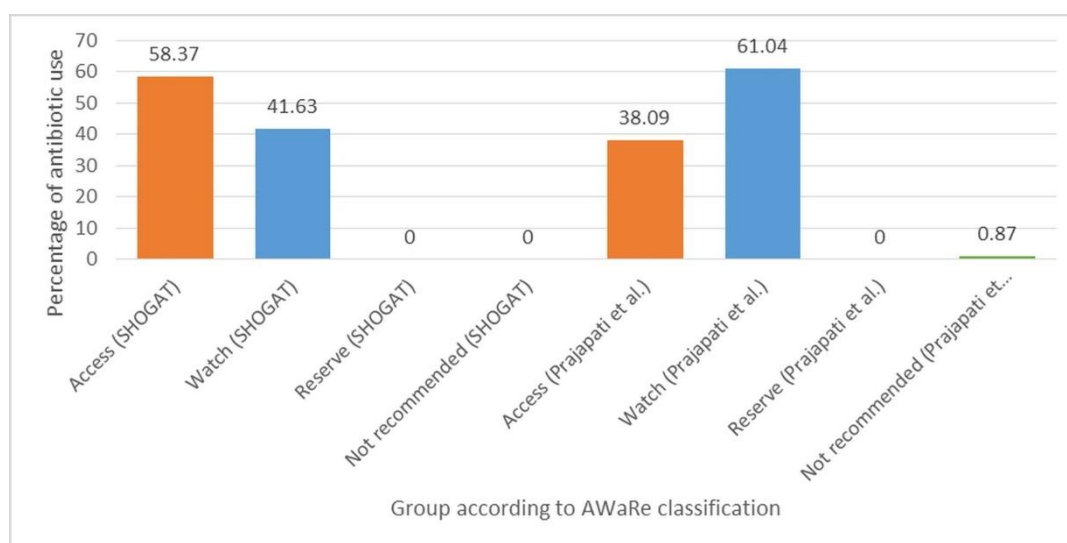


**Figure 3.** Antibiotics used in SHOGAT "Prof. Dr. D. Stamatov" - Varna by Access, Watch and Reserve groups of the AWaRe classification - percentage distribution

These results support the descriptive conclusion that antibiotic consumption peaked during the COVID-19 pandemic years (2021–2022) and declined thereafter, but the year-to-year variation was not statistically significant. This finding is consistent with the relatively stable prescribing patterns expected in a specialized obstetrics and gynecology hospital with well-regulated antimicrobial stewardship practices.

According to ECDC recommendations, antibiotics from the Access group should ideally constitute at least 65% of total antibiotic use due to their proven effectiveness and lower potential to contribute to antimicrobial resistance [5]. Our study demonstrates a value close to this benchmark (58.37%), indicating generally appropriate prescribing practices. In contrast, the Watch group, which includes antibiotics that carry a higher risk for the development of resistance and should be used more restrictively, accounts for 41.63% of total use. Although Access antibiotics are predominant, this

relatively high proportion of Watch antibiotics suggests room for optimization and ongoing monitoring of prescribing trends. The absence of antibiotic use from the Reserve group (0%) is a positive indicator, suggesting that antibiotics intended for treatment of multidrug-resistant infections were not necessary during the study period. This may reflect effective infection control measures, appropriate antibiotic stewardship, or a lower prevalence of resistant pathogens (Table 3).

When comparing our findings with the study of Prajapati et al., important differences become apparent. In our study, the Access group accounts for 58.37% of antibiotic use compared with only 38.09% in the reference data, whereas the Watch group represents 41.63% in our results versus 61.04% in the reference values [6]. Consequently, the Access-to-Watch ratio in our study is 1.4, while in the reference data it is 0.5. This contrast indicates that our antibiotic use pattern is more favorable, with a higher reliance on Access antibiotics and a comparatively lower proportion of Watch antibiotics. Such a distribution aligns more closely with WHO's stewardship goals and suggests a more rational and resistance-conscious approach to antibiotic prescribing.

Figure 4 illustrates a comparative analysis of antibiotic consumption between SHOGAT, Bulgaria, and the European Union. Data for Bulgaria and the EU were obtained from the annual surveillance report published by European Centre for Disease Prevention and Control (ECDC) [7,8].
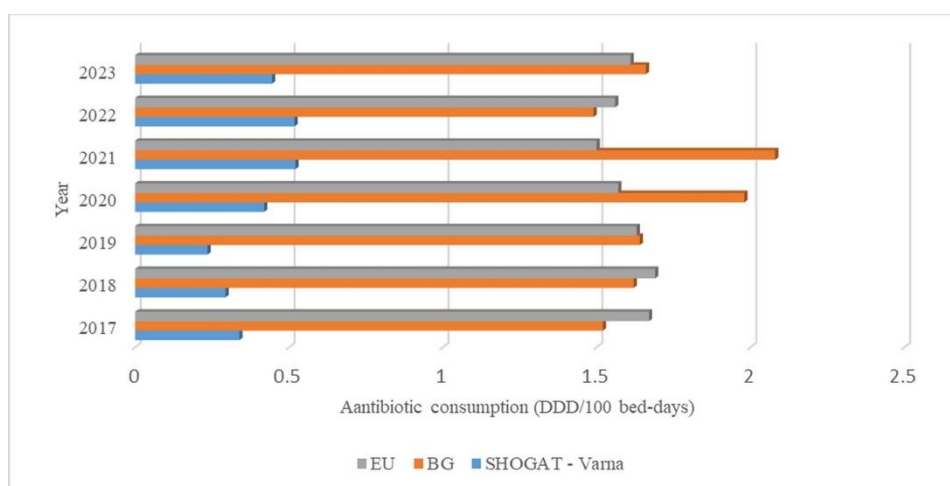


**Figure 4.** Total antibiotic consumption in hospitals (DDD per 100 bed-days) at Europe (EU), Bulgaria (BG), and SHOGAT – Varna (2017-2023)

The data obtained from SHOGAT - Varna demonstrate consistently low and well-regulated levels of antibiotic consumption across the entire observation period. Unlike national trends, which reveal a pronounced increase in hospital antibiotic consumption in Bulgaria during the COVID-19 pandemic years (2020–2021), the values reported from SHOGAT-Varna remain markedly lower and stable (Figure 2). This divergence can be attributed to the hospital's specialized profile as a tertiary obstetrics and gynecology center, where the clinical need for broad-spectrum antibiotic therapy is inherently restricted compared to general or infectious disease hospitals [9].

Furthermore, the consistently limited antibiotic use may reflect the implementation of strict infection control protocols, prophylactic regimens tailored to surgical settings, and adherence to evidence-based prescribing guidelines. Such patterns provide indirect evidence of effective local antibiotic stewardship, highlighting how targeted interventions within a specialized hospital environment can substantially reduce unnecessary antimicrobial exposure.
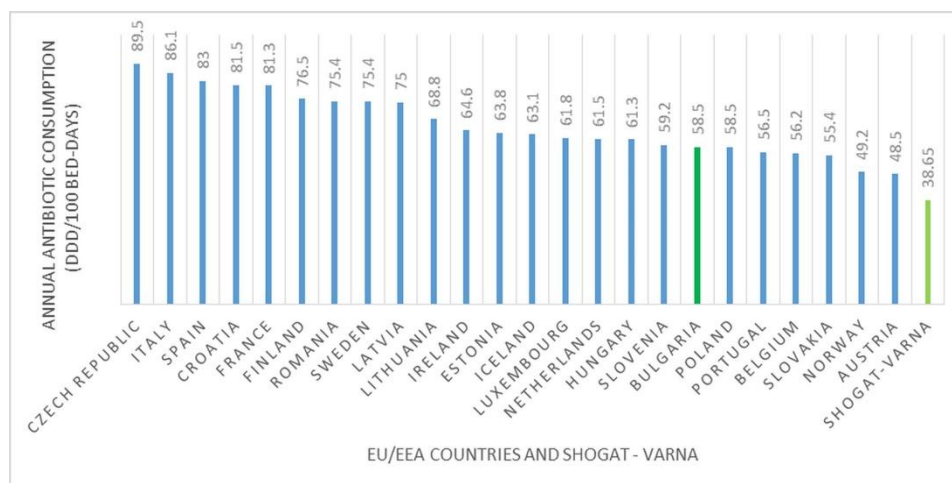
**Figure 5.** Comparative analysis of hospital antibiotic use in EU/EEA countries and SHOGAT "Prof. Dr. D. Stamatov" - Varna in 2021

Figure 5 illustrates the levels of hospital antibiotic consumption in 24 of 30 EU/EEA countries, measured in defined daily doses (DDD) per 100 bed-days for the year 2021, and includes the value reported by SHOGAT "Prof. Dr. D. Stamatov" – Varna. The data reveal significant differences among the countries, ranging from less than 50 DDD/100 bed-days (Norway – 49.2; Austria – 48.5) to values exceeding 85 DDD/100 bed-days (Czech Republic – 89.5; Italy – 86.1; Spain – 83.0) [10].

SHOGAT – Varna stands out with the lowest recorded value – 38.65 DDD/100 bed-days, which is substantially below the average level for EU/EEA countries. This value is nearly 10 units lower even compared to the countries with the lowest antibiotic consumption in Europe. At the national level, the observed antibiotic use in this healthcare facility is significantly lower than the value for Bulgaria (58.5 DDD/100 bed-days), indicating the effective implementation of the strategies for rational antibiotic use developed at SHOGAT "Prof. Dr. D. Stamatov" – Varna. This result can be viewed as a positive indicator of antibiotic policy, particularly in the context of increased overall antibiotic consumption during the COVID-19 pandemic.

**Conclusion**

This study demonstrates that antibiotic consumption within SHOGAT "Prof. Dr. Dimitar Stamatov" remains substantially lower than the national average in Bulgaria, with prescribing practices largely aligned with established guidelines. The limited use of strategic agents such as macrolides and glycopeptides, the predominant reliance on antibiotics from the WHO AWaRe Access group, and the absence of prescribing from the Reserve group collectively highlight the institution's commitment to rational antimicrobial stewardship. The observed findings reinforce the importance of continuous surveillance, strict adherence to evidence-based protocols, and institution-specific policies in shaping prudent antibiotic use. The experience of SHOGAT "Prof. Dr. Dimitar Stamatov" provides a compelling model for optimizing prescribing practices in other healthcare settings, contributing meaningfully to national and European efforts to mitigate antimicrobial resistance.

**AUTHOR CONTRIBUTIONS**

Concept: P.B., S.M.; Design: P.B., M.L., D.D., S.M.; Control: S.M.; Sources: M.L., D.D.; Materials: P.B.; Data Collection and/or Processing: P.B., M.L., D.D., S.M.; Analysis and/or Interpretation: P.B., S.M.; Literature Review: D.D., M.L.; Manuscript Writing: P.B., M.L.; Critical Review: P.B., M.L., D.D., S.M.; Other: -

**CONFLICT OF INTEREST**

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

## ETHICS COMMITTEE APPROVAL

The authors declare that the ethics committee approval is not required for this study.

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