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Comparison of Total Antibiotic Consumption of European Union Countries and Türkiye in the Period 2010-2021: Rational Drug Use and the Effects of the Pandemic

Avrupa Birliği Ülkeleri ve Türkiye'nin 2010-2021 Dönemi Toplam Antibiyotik Tüketiminin Karşılaştırılması: Akılcı İlaç Kullanımı ve Pandeminin Etkileri

Murat KAVRUK¹(iD), Samet UÇAK¹(iD), Burcu SAPMAZ²(iD), Canan Çiçek DEMİR³(iD), Ali Doğan DURSUN⁴(iD)

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ABSTRACT

Introduction: Many initiatives are being implemented worldwide to reduce antibiotic consumption; however, the comparative analysis of these initiatives and their effectiveness in the face of large-scale variables such as pandemics are not thoroughly examined. In this regard, this study aims to analyze the total antibiotic consumption trends in the ATC group J01 in Türkiye and European countries, explore the differences between countries, and investigate the impact of the recent pandemic on changes in antibiotic consumption data

Materials and Methods: ATC group J01 total antibiotic consumption (hospital + community) data of Türkiye and 19 European countries between 2010 and 2021 were concatenated and compared. Data from the European Centre for Disease Prevention and Control (ECDC) and the Turkish Medicines and Medical Devices Agency (TITCK) were used for the study. Antibiotic consumption data was represented in terms of defined daily dose (DDD) per 1000 patients per day.

Results: Despite having the highest antibiotic consumption during the period in focus, Türkiye showed a statistically significant (p= 0.05) decrease with antibiotic consumption data of 41.43 defined daily doses (DDD) per 1000 patients per day between 2010-2015 and 32.24 DDD per 1000 patients per day between 2016-2021. In 2021, when the COVID-19 pandemic was in effect, antibiotic consumption in Europe dropped to 14.91 defined daily doses (DDD) per 1000 patients per day, the lowest level between 2010 and 2021, while in Türkiye it dropped to 24.39 defined daily doses (DDD) per 1000 patients per day recorded in 2020 and increased to 26.97 defined daily doses (DDD) per 1000 patients per day recorded in 2021.

Conclusion: Rational drug use practices were effective in reducing antibiotic consumption in Türkiye. However, the trend was disrupted with the 2021 consumption data, indicating a deviation from the previous progress. In contrast, European countries displayed variations in antibiotic consumption levels, but overall, they experienced a decrease in consumption during the COVID-19 pandemic.

Key Words: Antibiotic consumption; Türkiye; ECDC; Defined daily dose; COVID-19

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¹ Deparment of Medical Biology, İstanbul Aydın University Faculty of Medicine, İstanbul, Türkiye

² Department of Medical Microbiology, İstanbul Aydın University Faculty of Medicine, İstanbul, Türkiye

³ Department of Internal Medicine, Atılım University Faculty of Medicine, Ankara, Türkiye

⁴ Department of Medical Physiology, Atılım University Faculty of Medicine, Ankara, Türkiye

ÖZ

Avrupa Birliği Ülkeleri ve Türkiye'nin 2010-2021 Dönemi Toplam Antibiyotik Tüketiminin Karşılaştırılması: Akılcı İlaç Kullanımı ve Pandeminin Etkileri

Murat KAVRUK¹, Samet UÇAK¹, Burcu SAPMAZ², Canan Çiçek DEMİR³, Ali Doğan DURSUN⁴

Giriş: Antibiyotik tüketimini düşürmek adına dünya genelinde pek çok uygulama yapılmaktadır fakat bu uygulamaların karşılaştırmalı analizi ve pandemi gibi geniş çaplı değişkenler karşısındaki durumu yeterince analiz edilmemektedir. Bu kapsamda; Türkiye ve Avrupa ülkelerinin ATC grubu J01 toplam antibiyotik tüketim eğilimleri ve ülkeler arasındaki farklılıklar incelenmiş olup son dönemde yaşanan pandeminin antibiyotik tüketim verilerindeki değişime etkisi sorgulanmıştır.

Materyal ve Metod: Türkiye ve 19 Avrupa ülkesinin 2010-2021 yılları arasındaki ATC grubu J01 toplam antibiyotik tüketimi (hastane + toplum) verileri birleştirilerek karşılaştırıldı. Çalışma için Avrupa Hastalık Önleme ve Kontrol Merkezi (ECDC) ve Türkiye İlaç ve Tıbbi Cihaz Kurumu (TICKK) verileri kullanılmıştır. Antibiyotik tüketim verileri, günlük 1000 hasta başına tanımlanmış günlük doz (DDD) cinsinden temsil edildi.

Bulgular: Türkiye, odaklanılan dönemde en yüksek antibiyotik tüketimine sahip olmasına rağmen 2010-2015 tarihleri arasında 41.43 günlük 1000 hasta başına tanımlanmış günlük doz (DDD) ve 2016-2021 tarihleri arasında 32.24 günlük 1000 hasta başına tanımlanmış günlük doz (DDD) antibiyotik tüketim verisi ile istatistiksel olarak (p= 0.05) anlamlı bir düşüş gösterdi. COVID-19 pandemisinin etkili olduğu 2021 yılında Avrupa'da, çalışmaya konu olan 2010-2021 yılları arasındaki en düşük düzeyi olan 14.91 günlük 1000 hasta başına tanımlanmış günlük doz (DDD)'a gerilerken Türkiye'de 2020 yılındaki kaydedilen 24.39 günlük 1000 hasta başına tanımlanmış günlük doz (DDD) seviyesine düşen antibiyotik tüketimi, 2021 yılında 26.97 günlük 1000 hasta başına tanımlanmış günlük doz (DDD) seviyesine yükseldi.

Sonuç: Akılcı ilaç kullanımı uygulamaları, Türkiye için antibiyotik tüketimini azaltmada etkili olmakla birlikte, 2021 tüketim verileri ile trendin bozulduğu gözlemlenmiştir. Avrupa ülkeleri antibiyotik tüketim miktarlarında farklılık gösterse de toplamda COVID-19 pandemisi ile azalan bir tüketim durumuna girdiği tespit edilmiştir.

Anahtar Kelimeler: Antibiyotik kullanımı; Türkiye; ECDC; Tanımlanmış günlük doz; COVID-19

INTRODUCTION

Antibiotics are drugs that are used in the treatment of bacterial infectious diseases and are of significant importance for human health. They are used extensively due to their usefulness in the treatment of infections and surgical operations. This poses both a burden on health systems and a new health risk with the emergence of antibiotic-resistant bacterial strains from overuse and misuse of antibiotics^[1]. In 2019, antimicrobial resistance was declared by World Health Organization (WHO) as one of the top 10 global public health threats^[2]. For this reason, countries are putting regulations in effect regarding antibiotic use. For example, with the rational drug use practices launched in Türkiye in 2003, the use of antibiotics in terms of quality and quantity has been closely monitored. This led to the "National Action Plan for Rational

Use of Medicines 2014-2017" being published and concrete steps have been taken towards the use of antibiotics $^{[3]}$.

Rational drug use was first proposed by the World Health Organization in 1985. In 1996, the first pilot implementation was started at the educational level in Türkiye $^{[4]}$. As a result of the implementation of the Action Plan on Rational Use of Medicines covering the years 2014-2017, positive progress has been made throughout the country, including antibiotics $^{[3]}$. There are valuable reviews in the literature on the rational drug use process, causes, and rational antibiotic use $^{[4-6]}$.

Tracking and reporting of antibiotic consumption in Europe is an old institutional practice whose results were first analyzed in $2001^{[7]}$. From the antibiotic consumption data of the European Union and European Economic Area, consumption trends and changes were summarized for

¹ İstanbul Aydın Üniversitesi Tıp Fakültesi, Tıbbi Biyoloji Anabilim Dalı, İstanbul, Türkiye

² İstanbul Aydın Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, İstanbul, Türkiye

³ Atılım Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Ankara, Türkiye

⁴ Atılım Üniversitesi Tıp Fakültesi, Tıbbi Fizyoloji Anabilim Dalı, Ankara, Türkiye

1997-2009 and 1997-2017^[8,9]. There are also studies investigating antibiotic consumption in the OECD (Organization for Economic Cooperation and Development) countries and other parts of the world^[10,11]. All these studies were performed during the pre-pandemic period and focused on presenting current situations. The approach in this study can be summarized as follows:

- The statistical effect of the decisions and laws of the countries on the use of antibiotics
- The antibiotic use performance of Türkiye compared to the European Union countries and,
- The analysis of the preliminary data during and after the pandemic.

In this context, antibiotics consumption data of Türkiye and nineteen European Union countries between the years 2010-2021 were examined comparatively.

MATERIALS and METHODS

Source, Quality, and Quantity of the Dataset

The dataset examined in this study was primarily based on the "Antimicrobial Consumption-

Annual Epidemiological Report for 2021 of the European Union" published by the European Center for Disease Prevention and Control^[12]. 29 countries [Twenty-nine European Union (EU)] Member States and two European Economic Area (EEA) countries (Iceland and Norway) reported data on antimicrobial consumption. Since the EU data is cumulative, the antibiotic consumption data between the years 2010 to 2021 could be considered for most of the countries. There were two challenges in constructing the database; acquiring the data for all of the years for each country and verifying that the data represents the total consumption (not only hospital or community usage of antibiotics). Based on the availability and completeness of data for the period in question, 19 out of 29 countries were selected for the missing 2010 data of Greece and Lithuania^[13]. Antibiotic consumption data of Türkiye for these 12 years was obtained from published information from the Turkish Medicines and Medical Devices Agency^[14]. The countries whose data was used were geographically shown in Figure 1 below and listed in Table 1 in the following section.

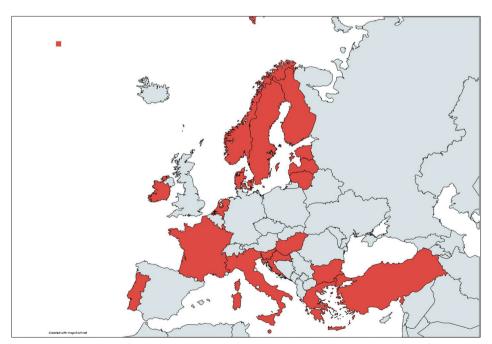


Figure 1. Geographical distribution of 20 countries (shown in red) that are the subject of this study. This area represented 42% (313 million) of the European population. Created by MapChart (mapchart.net).

Table 1. Consumption of antibacterials (ATC group J01) in total (community and hospital sector), Türkiye
and 19 EU/EEA countries, 2010–2021, expressed as DDD per 1000 inhabitants per day

Country	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Bulgaria	16.80	17.96	17.11	18.33	19.63	19.83	18.96	20.19	20.84	20.40	22.43	23.93
Croatia	18.63	18.10	19.90	19.09	19.28	19.63	18.62	18.48	18.70	18.70	15.58	18.06
Denmark	17.48	18.25	17.30	17.48	17.11	17.46	16.95	16.18	15.50	15.24	14.21	14.34
Estonia	11.30	12.32	12.15	11.95	11.86	12.08	11.93	11.55	11.74	11.75	10.43	10.05
Finland	19.71	21.49	20.62	19.54	19.10	18.10	17.40	15.69	15.43	14.64	11.88	11.28
France	24.92	24.99	25.64	25.79	24.81	25.47	25.55	24.62	24.64	24.43	19.74	20.95
Greece	34.44	32.28	29.72	29.66	30.90	33.05	32.97	34.08	33.99	33.95	27.99	23.41
Hungary	14.79	14.84	14.06	14.41	15.11	15.77	14.37	14.52	14.81	14.40	11.21	11.91
Ireland	18.87	20.71	20.95	21.57	20.93	22.92	21.95	20.85	22.34	22.69	18.48	17.73
Italy	24.73	24.95	24.49	25.05	24.35	24.12	23.50	20.79	21.28	21.57	18.32	17.45
Latvia	12.28	12.74	12.82	13.20	12.48	12.99	12.81	13.87	13.34	13.83	11.83	11.59
Lithuania	14.26	15.33	15.13	16.95	14.99	15.68	16.50	16.57	16.23	16.02	14.08	13.62
Luxembourg	25.02	25.11	24.91	24.90	23.16	23.40	22.88	22.44	22.03	21.09	16.08	15.86
Malta	19.70	21.22	20.46	21.83	21.64	20.89	20.54	22.20	19.86	20.36	16.32	15.54
Netherlands	10.85	10.90	10.86	10.37	10.19	10.28	10.04	9.72	9.68	9.43	8.49	8.29
Norway	16.73	17.46	17.85	17.11	16.83	16.72	16.16	15.66	15.19	14.82	13.83	13.91
Portugal	19.83	20.50	19.99	17.53	17.95	18.71	18.93	18.24	19.01	19.24	15.10	15.22
Slovenia	13.28	13.30	13.12	13.23	12.99	13.28	12.90	13.04	13.10	12.94	10.11	10.11
Sweden	15.18	15.39	15.25	14.22	13.95	13.50	13.20	12.75	12.41	11.79	10.33	10.09
Türkiye	39.70	42.28	42.30	42.40	40.40	41.50	41.50	36.40	30.96	33.20	24.39	26.97

All antibiotic usage data throughout the study is expressed in terms of the Anatomical Therapeutic Chemical (ATC) classification system for the allocation of antimicrobials and Defined Daily Doses (DDDs) per 1000 inhabitants per day, as defined by the World Health Organization Drug Statistics Methodology Collaboration Center^[15,16]. The Defined Daily Dose (DDD) is the assumed average daily maintenance dose of a drug used for its main indication in adults. This unit of measurement allows for the statistical comparison of different antibiotics.

The total antibiotics consumption data for each country were made up of the following antibiotic subgroups: tetracyclines (J01A), penicillins (J01C), other beta-lactams (J01D), sulfonamides and trimethoprim (J01E), macrolides, lincosamides and streptogramins (J01F), and quinolones (J01M) and other antibiotics in total (J01X). However, due to the unavailability/inaccessibility of consumption data for the anti-

mycotics (J02), antifungals (D01B), and antivirals (J05) for systemic use, these groups could not be included in the study.

Statistical Analysis Conducted on Dataset

Concatenation, tabulation, graphical resentation, and forecast analysis of data were performed using Microsoft Excel 2021 software. Forecast analysis was conducted by using the existing time-based data and the AAA version of the Exponential Smoothing (ETS) algorithm to forecast future values. Frequency and descriptive statistics were used with mean, standard deviation, minimum and maximum values. Analysis of variance (ANOVA) test was performed to reveal the impact of change in Defined Daily Doses (DDD) per 1000 inhabitants per day for each country between the 2010-2015 and 2016-2021 periods. For all these tests, p< 0.05 was considered statistically significant. These procedures were processed in SPSS version 22.0 for Windows.

RESULTS

Since the antibiotic consumption data for the countries were antibiotic subgroup-specific, the first step conducted was the concatenation of antibiotic consumption data for each country on an annual basis. The final dataset is given in Table 1. A detailed inspection of the annual consumption data revealed that Türkiye and Greece had the highest antibiotic consumption nationwide, while the Netherlands had the lowest consumption value.

Considering the discrepancy antibiotic consumption between Türkiye and many other countries, as well as the variation in Türkive's data, further analysis was conducted to examine the trend over the years. Figure 2 illustrates this analysis, showing a consistent decline in Türkiye's total antibiotic consumption from 2010 to 2021. This decline became more prominent starting in 2017 when the annual data fell below the average line for the 2010-2021 period, indicated by the green dots. However, when comparing the annual data (represented by red columns) with the average consumption of EU countries (represented by blue columns) for each specific year, it is evident that Türkiye's antibiotic consumption remains high in comparison to the EU.

After the implementation of a program in Türkiye, the use of antibiotics without a prescription was banned in 2015. As a result, there was a noticeable decrease in the subsequent years in the use of antibiotics, which accounted for 35% of prescriptions issued by family physicians^[17]. This result is a concrete output of the Rational Antibiotic Use Program initiated by the Ministry of Health in 2003. From this perspective, we questioned whether there is a significant difference in the total antibiotic consumption of Türkiye concerning this change in the national strategy. Thus, by taking the year 2015 as a milestone, our study focused on the statistical analysis of the antibiotic consumption data of two six-year periods of 2010-2015 and 2016-2021. these periods into account, we analyzed 19 other countries from the EU. Firstly, we compared the average total antibacterial consumption of each country for two six-year periods. We measured the change in consumption amounts as a percentage. As depicted in Figure 3, it is evident

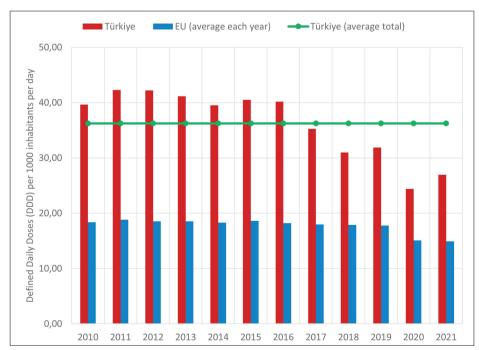


Figure 2. Consumption trend of J01 group antibacterials for Türkiye (red columns), average of EU countries for each year (blue columns), and average of Türkiye between 2010 and 2021 (green dotted line), expressed as DDD per 1000 inhabitants per day.

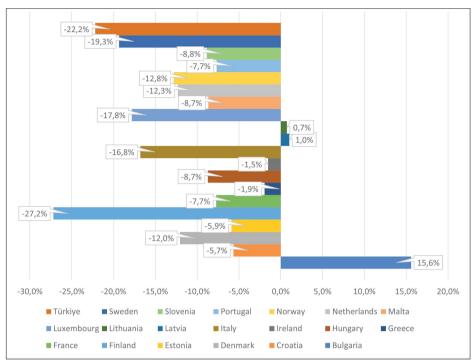


Figure 3. Antibiotic consumption difference between the 2010-2015 and 2016-2021 periods in terms of direction and percentage of change for each country as a subject of study.

that nearly all EU countries, including Türkiye, exhibited a decrease in antibiotic consumption (DDD per 1000 inhabitants per day) from 2016 to 2021 compared to the period of 2010-2015. In terms of decreasing antibiotic consumption, Finland ranks first (27.2% decrease), followed by Türkiye (22.2%) and Sweden (19.3%). This trend was reversed with the exception of data from Bulgaria with a 15.6% increase in antibiotic consumption followed by small increases in Lithuania (0.7%) and Latvia (1.0%).

The changes in antibiotic consumption between the two time periods were further validated using an ANOVA analysis of the data. The results, presented in Table 2, indicate that several countries (highlighted in bold and italics) experienced statistically significant changes in antibiotic consumption, with a 95% confidence level. It should be noted that only Bulgaria showed an increase in antibiotic consumption, while other countries demonstrated a decrease. Therefore, it can be concluded that out of the 20 countries included in this study, including Türkiye, eight countries were able to consistently reduce antibiotic consumption despite the challenges posed by antimicrobial resistance and the burden on the healthcare system.

Based on the data in Table 1, Figure 4 presents the annual J01 group antibiotic consumption values of three countries with the highest antibiotic consumption, three countries with the lowest antibiotic consumption, and Bulgaria, which stands out as being different in the opposite direction. Türkiye, having the highest antibiotic consumption in Europe, shows a downward trend starting in 2017. This trend allowed Türkiye to reach a lower annual antibiotic consumption value than Greece in 2020 for the first time, despite Greece being ranked second in terms of highest consumption. In 2021, the ranking was once again reversed, with Greece surpassing Türkiye in terms of annual antibiotic consumption. Additionally, France, which typically ranks third in terms of average antibiotic consumption, was replaced by Bulgaria during the pandemic every year. As depicted in the figure, the three countries with the lowest antibiotic consumption also experienced a decrease in consumption due to the pandemic, and this decrease continued in 2021.

Table 2. Consumption of antibacterial (ATC group J01) in the community and hospital sector, Türkiye and 19 EU/EEA countries, 2010–2021, expressed as DDD per 1000 inhabitants per day

Country	2010-2015	2016-2021	Change	P value
Bulgaria	18.28	21.13	(+)	0.009
Croatia	19.10	18.02	(-)	0.085
Denmark	17.51	15.40	(-)	0.001
Estonia	11.94	11.24	(-)	0.076
Finland	19.76	14.38	(-)	0.001
France	25.27	23.32	(-)	0.075
Greece	31.67	31.06	(-)	0.763
Hungary	14.83	13.54	(-)	0.086
Ireland	20.99	20.67	(-)	0.761
Italy	24.62	20.49	(-)	0.001
Latvia	12.75	12.88	(+)	0.768
Lithuania	15.39	15.50	(+)	0.864
Luxembourg	24.42	20.06	(-)	0.010
Malta	20.96	19.14	(-)	0.134
Netherlands	10.58	9.27	(-)	0.002
Norway	17.12	14.93	(-)	0.000
Portugal	19.09	17.62	(-)	0.147
Slovenia	13.20	12.03	(-)	0.085
Sweden	14.58	11.76	(-)	0.001
Türkiye	41.43	32.24	(-)	0.005

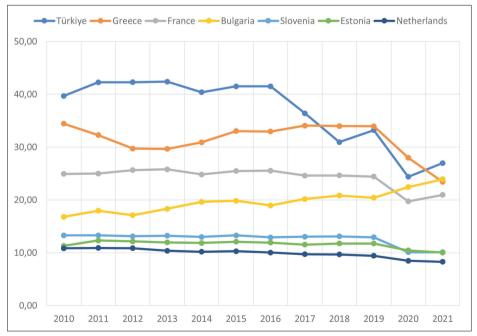


Figure 4. Annual J01 group antibiotic consumption data of the three lowest (Netherlands, Estonia, Slovenia), three highest (Türkiye, Greece, France) countries, and Bulgaria having an opposite trend than other EU countries.

Country	2018	2019	2020	2021	Graph	Country	2018	2019	2020	2021	Graph
Bulgaria	20,84	20,40	22,43	23,93	- 1	Latvia	13,34	13,83	11,83	11,59	
Croatia	18,70	18,70	15,58	18,06		Lithuania	16,23	16,02	14,08	13,62	
Denmark	15,50	15,24	14,21	14,34		Luxembourg	22,03	21,09	16,08	15,86	
Estonia	11,74	11,75	10,43	10,05		Malta	19,86	20,36	16,32	15,54	
Finland	15,43	14,64	11,88	11,28		Netherlands	9,68	9,43	8,49	8,29	
France	24,64	24,43	19,74	20,95		Norway	15,19	14,82	13,83	13,91	
Greece	33,99	33,95	27,99	23,41		Portugal	19,01	19,24	15,10	15,22	
Hungary	14,81	14,40	11,21	11,91	II	Slovenia	13,10	12,94	10,11	10,11	
Ireland	22,34	22,69	18,48	17,73		Sweden	12,41	11,79	10,33	10,09	
Italy	21,28	21,57	18,32	17,45	11.	Türkiye	30,96	33,20	24,39	26,97	

Figure 5. Total consumption of J01 group antibiotics in two years of pre-pandemic and pandemic periods. The highest number of consumption amounts were represented as red columns for each country.

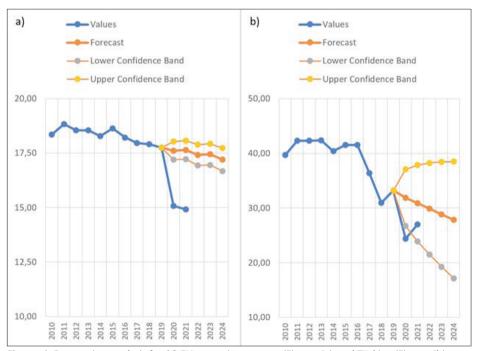


Figure 6. Forecasting analysis for 19 EU countries average (Figure 6a) and Türkiye (Figure 6b).

Antibiotic Consumption During COVID-19 Pandemic

Officially starting at the end of 2019, the COVID-19 pandemic, caused by SARS-CoV-2, altered the structure and functioning of nearly every system worldwide. Interestingly but understandably, the total antibiotic consumption in the population, encompassing both the community and hospital sectors, was negatively affected in

Europe. Physical distancing measures and the widespread closure of social areas effectively curtailed the spread of conventional infectious diseases, thereby establishing their own recurring seasonal and annual pandemics. According to a report by the European Centre for Disease Prevention and Control (ECDC), there was a notable increase of over 15% in total antibiotic consumption among humans between 2019 and

 $2020^{[18]}$ Based on this finding, an analysis was conducted for each country using the fouryear dataset, with 2018 and 2019 considered as the pre-pandemic period and 2020-2021 as the pandemic period. The change in antibiotic consumption during these years is summarized in Figure 5. Except for Bulgaria, which notably adopted a distinct strategy in combating the coronavirus, the countries examined in this study exhibited a decrease in nationwide antibiotic consumption. However, there was a shift in this trend for some countries in 2021. Croatia nearly returned to its pre-pandemic antibiotic consumption levels, while Türkiye, France, and Hungary followed Croatia in this upward trend.

To understand this shift in antibiotic consumption amounts and its significance, a forecasting analysis was conducted using data from the average of 19 EU countries (Figure 6a) and Türkiye (Figure 6b). The forecasting analysis began in 2019, and a five-year forecast was made based on historical data from the previous 10 years, with a 95% confidence level and an assumption of non-pandemic conditions. Comparing the "forecasted" 2020 and 2021 antibiotic consumption data with the "real" data from the same years, it was found that the decrease in antibiotic consumption in Europe is statistically significant based on the data at hand. However, while Türkiye experienced a decrease in antibiotic consumption during the period of mass closure in 2020 and showed a significant shift in trend, the data from the consecutive year, 2021, brought consumption levels back within the confidence interval.

DISCUSSION

The analysis demonstrated that Türkiye still had the highest consumption of ATC group J01 antibiotics compared to Europe. This indicates the positive impact of Rational Drug Use practices implemented in Türkiye. Türkiye and Greece were identified as having the highest nationwide antibiotic consumption, while the Netherlands had the lowest consumption among the countries examined in this study. Starting from 2017, Türkiye's total antibiotic consumption fell below its 12-year average, and in 2020, it swapped its position with Greece to become the second-highest

consumer of antibiotics throughout Europe. This 22% decrease in antibiotic consumption during the second six-year period can be attributed directly to the nationwide rational antibiotic use program. Considering the economic status of the eight countries listed in Table 2 that achieved similar reductions in antibiotic consumption, the effectiveness of Türkiye's legislation, strategies, and implementation became evident.

According to the World Health Organization (WHO) and as demonstrated numerically in this study, there was a decrease in total antibiotic consumption during the COVID-19 pandemic. Almost all European countries examined in this study, except Bulgaria, experienced a decrease in antibiotic consumption. However, for some countries, including Türkiye, the positive impact of the COVID-19 pandemic on antibiotic consumption did not last long. It is interesting to observe that Bulgaria's antibiotic consumption strategy during the COVID-19 challenge was opposite to the general trend in Europe. The analysis of the effects of COVID-19 and post-pandemic consumption attitudes presented in this study provides preliminary insights into the variations in antibiotic consumption in the post-pandemic era. This finding serves as a pioneering study in understanding whether the impact of COVID-19 on antibiotic consumption will be sustainable and permanent. Further studies and discussions will be conducted to analyze the different responses obtained from future data.

Rational antibiotic use practices, implemented and monitored by the Department of Rational Drug Use of the Turkish Medicines and Medical Devices Agency, demonstrated a statistically significant impact on total antibiotic utilization in the five years preceding the pandemic. This study indicates the need for strategies aimed at sustaining the decreased levels of antibiotic use in the post-pandemic era, which poses a new challenge for countries, including Türkiye. Irrespective of the World Health Organization's or national authorities' declaration regarding the end of the pandemic, it is foreseeable that the virus will cause seasonal outbreaks similar to influenza during specific times of the year. Consequently, practices leading to

misuse, such as misdiagnosing viral illnesses, opportunistic infections resulting from weakened immune systems, and the prescription of broad-spectrum antibiotics, will resurface in the healthcare system during the process of normalization. Therefore, the research team recommends conducting a more comprehensive investigation of sub-antibiotic groups in European countries, the OECD, or Türkiye. The decline in antibiotic usage observed during the pandemic presents a temporary opportunity to address a pressing issue faced by humanity, namely antibiotic resistance. Performing a meta-analysis on drug optimization and the use of broad-spectrum antibiotics has the potential to generate a scientific undertaking that would be well-received by society, serving as a continuation of this study.

ETHICS COMMITTEE APPROVAL

Ethics committee approval is not needed for this article due to the study's nature.

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: All of authors

Analysis/Interpretation: All of authors

Data Collection or Processing: All of authors

Writing: All of authors

Review and Correction: All of authors

Final Approval: All of authors

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Address for Correspondence/Yazışma Adresi

Dr. Murat KAVRUK

Department of Medical Biology, İstanbul Aydın University Faculty of Medicine,

İstanbul-Türkiye

E-posta: muratkavruk@aydin.edu.tr