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Analysis of the National Antifungal Consumption Data of Turkey During 2013-2019

Türkiye'nin 2013-2019 Yılları Ulusal Antifungal Tüketim Verilerinin Analizi

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Abstract

Introduction: Monitoring antimicrobial consumption is important to encourage the prudent use of antifungal drugs and to minimize antifungal selective pressure. There is limited data on the national consumption of systemic antifungals in Turkey. This study aimed to investigate the antifungal consumption data of Turkey in ambulatory care and inpatients during 2013-2019 and to compare the consumption data of systemic antifungals in Turkey to that of European countries in 2019.

Materials and Methods: Data were obtained retrospectively from the records of the Medicines and Medical Devices Agency of Turkey. The consumption of systemic antifungals according to the Anatomical Therapeutic Chemical (ATC) was calculated using the ATC/Defined Daily Dose (DDD) methodology. In addition, the systemic antifungals consumption data of European countries in 2019 according to eCDC was obtained and compared with that of Turkey obtained in this study expressed in [Defined Inhabitant Dose (DID) - DDD per 1000 inhabitants daily].

Results: Terbinafine (overall median DID: 0.5288), itraconazole (DID: 0.1648), and fluconazole (DID: 0.1068) were the most consumed agents in the outpatient setting. Azoles (DID: 0.0291) were the most commonly consumed agent in inpatients setting, followed by amphotericin-B (DID: 0.0173) and echinocandins (DID: 0.0051). Total antifungal consumption in Turkey was 1.52 DID for outpatients and 0.08 DID for inpatients in 2019.

Conclusion: To the best of our knowledge, this study reported the national antifungal consumption data of Turkey for the first time. Antifungals use among outpatients in Turkey showed a decreasing trend from 2016 to 2019 compared to consumption between 2013 and 2016. However, Turkey is still one of the leading antifungal consumers among European countries, especially in ambulatory care.

Keywords: Systemic antifungals, antifungal consumption, national data, outpatients, inpatients, Turkey

Öz

Giriş: Antimikrobiyal tüketimin izlenmesi, antifungal ilaçların ihtiyatlı kullanımını teşvik etmek ve antifungal seçici baskıyı en aza indirmek için önemlidir. Türkiye'de sistemik antifungallerin ulusal tüketim verilerine ilişkin sınırlı veri mevcuttur. 2013-2019 yılları arasında ayakta ve yatan hastalarda Türkiye'nin antifungal tüketim verilerinin araştırılması amaçlanmaktadır. İkincil amaç ise 2019 yılı Türkiye'deki sistemik antifungallerin tüketim verilerinin Avrupa ülkeleri ile karşılaştırılmasıdır.

Gereç ve Yöntem: Veriler Türkiye İlaç ve Tıbbi Cihaz Kurumu kayıtlarından geriye dönük olarak elde edilmiştir. Sistemik antifungallerin tüketimi "Anatomical Therapeutic Chemical"- Anatomik, Terapötik ve Kimyasal sınıflandırma sistemi / "Defined Daily Dose"- Günlük Tanımlanmış Doz (ATC/

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Öz

DDD) metodolojisi kullanılarak hesaplanmıştır. Ayrıca, Avrupa ülkelerinin 2019 yılı sistemik antifungal tüketim verileri eCDC web sitesinden elede edilmiş ve çalışmamızdaki Türkiye verileri ile karşılaştırılarak ["Defined Inhabitant Dose" (DID) - DDD / 1000 kişi başına günlük doz] olarak sunulmuştur.
Bulgular: Terbinafin (medyan DID: 0.5288), itrakonazol (DID: 0.1648) ve flukonazol (DID: 0.1068) ayaktan tedavide en çok tüketilen ajanlardır. Azoller (DID: 0.0291) yatan hastalarda en sık tüketilen ajanlar olup bunu amfoterisin-B (DID: 0.0173) ve ekinokandinler (DID: 0.0051) izlemektedir. Türkiye'de 2019 yılında toplam antifungal tüketimi ayaktan hastalar için 1,52 DID ve yatan hastalar için 0,08 DID olarak saptanmıştır.
Sonuç: Bildiğimiz kadarıyla Türkiye'nin ulusal antifungal tüketim verileri ilk kez bu çalışmada rapor edilmektedir. Türkiye'de 2016-19 yılları arasında ayaktan tedavi gören hastalarda antifungal kullanımı, 2013-16 yılları arasındaki tüketime göre azalma eğilimi göstermektedir. Bununla birlikte, Türkiye özellikle ayaktan antifungal tedavi konusunda Avrupa ülkeleri arasında önde gelen tüketicilerden biri olmaya devam etmektedir.
Anahtar Kelimeler: Sistemik antifungaller, antifungal tüketimi, ulusal veriler, ayaktan hasta, yatan hasta, Türkiye

Introduction

The widespread use of broad spectrum antifungals results in selection pressure on causative agents and can lead to an increasing number of resistant pathogens. Consumption of antifungals affects the distribution of fungal species and reduces the sensitivity of target pathogens. The monitoring of antifungal consumption trends is essential to minimize antifungal selective pressure and should be applied both locally and nationally. In addition, local knowledge on the use of antifungals is crucial to strategy setting and allows us to implement the necessary measures to support the appropriate use of antifungals[1].

Recently, opportunistic fungal infections have been increasing with the increase in the immunocompromised patient population[2]. In addition, empirical treatment in high-risk patients, as demonstrated by the high prescription rate of antifungal drugs in intensive care units (ICU) and hematology-oncology units, significantly increases consumption. Treatment options are expanding with the introduction of new and different antifungal classes (polyenes, azoles, echinocandins, and flucytosine).

In Turkey, there is a need to provide nationwide reference data (for comparison) by evaluating systemic antifungal consumption patterns in both ambulatory and hospital care sectors. Available published data are often limited to the hospital sector or a specific hospital unit such as the ICU[3,4]. In this study, nationwide antifungal consumption data was investigated in the community and inpatients during 2013-2019 in Turkey.

Materials and Methods

Ethical approval for this retrospective descriptive study was obtained from the Ethics Committee of the Ankara City Hospital (protocol no: E-21-1664, date: 17.03.2021).

Methodology Used for the Comparisons of Systemic Antifungals

Antifungal drugs are classified according to the internationally accepted Anatomical Therapeutic Chemical (ATC) coding system standardized by the World Health Organization (WHO)[5]. Comparisons can be made between regions and countries using the WHO "Anatomical Therapeutic Chemical" and "Daily Defined Dose" (ATC/DDD) methodology. It is possible to have a standard and acceptable comparison by excluding the differences such as dose and duration of consumed drugs using this method[6]. The consumption data for 2013-2019 is presented as DDD/1000 inhabitants per day ["Defined Inhabitant Dose" (DID) based on the ATC/DDD index is applied].

The consumption data of the following systemic antifungals were calculated by the Turkish Medicines and Medical Devices Agency in the present study: terbinafine (D01BA02), posaconazole (J02AC04), voriconazole (J02AC03), itraconazole (J02AC02), fluconazole (J02AC01), ketoconazole (J02AB02), conventional and liposomal amphotericin B (J02AA01), caspofungin (J02AX04), micafungin (J02AX05), and anidulafungin (J02AX06). Sales data used in the calculation was obtained from the Pharmaceutical Track and Trace System. While the sales data to the pharmacy were used in the calculation for outpatients, the sales data to the hospital were used in the calculation for inpatients. Information about the country's population for the relevant years was obtained from the data published by the Turkish Statistical Institute[7]. In addition, the number of refugees under temporary protection in Turkey was included in the calculation by taking the data of the Ministry of Interior Directorate General of Migration Management.

A detailed list containing information about antimycotic agents consumed in Turkey (unit amount, amount in box or package, pharmaceutical form, and route of administration) was created. Then, the DDD, which is used by WHO in the standardization of the comparison of the comsumption of different drugs and determined for the main indication in adults for each product, was obtained[8]. The daily dose defined for each product per package was calculated (DDD per package=[unit power × package size]/DDD), and the obtained value was multiplied by the number of antimycotics sold in the relevant year to obtain the number of DDD sold in the year. Then, the obtained result was divided by the mid-year population and the number of days

assessed and multiplied by 1000 to calculate the final measure unit of DDD/daily dose per 1000 person (DID). Outpatient and hospital-based consumption data of antimycotics were obtained by summing the DDD value per 1000 people per day obtained for each drug.

Additionally, consumption data of systemic antifungals of European countries in 2019 according to eCDC[9] were obtained and compared with that of Turkey obtained in this study, expressed in DID.

Statistical Analysis

IBM Statistical Package for the Social Sciences Statistics version 22 program was used for statistical analysis. Mann-Whitney U analysis was used in comparison of antifungal agents between inpatients and outpatients. Friedman's variance analysis was used to determine the changes in antifungal use in inpatients and outpatients by years. Wilcoxon Signed-Rank analysis was used for pairwise comparisons by years.

Results

National Antifungal Consumption Data During 2013-2019

The annual antifungal consumption data of Turkey was calculated as DID for inpatients and outpatients. Changes in total consumption and per antifungal drug by years were analyzed. DID-based antifungal consumption trends over the years are shown in Figure 1. The consumption data for each systemic antifungal (J02) and (D01B) by years on the basis of DID for outpatients and inpatients in addition to median DID level of antifungal consumption (OAC) are summarized in Table 1. When the OAC was evaluated, terbinafine was the most consumed agent (overall median DID: 0.5288) in Turkey, which was commonly used by outpatients, followed by itraconazole and fluconazole with an overall median DID of 0.1648 and 0.1068, respectively. The overall azole consumption in 2013 and 2019 were similar in ambulatory care (DID: 0.5498 vs 0.5488). However, it increased in hospitalized patients (DID: 0.0248 vs 0.0423, 70.6% increase). Friedman's variance analyses revealed that median OAC and antifungal consumption in hospitalized patients changed significantly over the years (p=0.0038 and p=0.002, respectively) (Table 1). Wilcoxon Signed-Rank Pairwise analysis was performed to determine the differences in antifungals consumption between years, and the results are presented in Table 2. Consumption data of systemic antifungals of European countries in 2019 according to eCDC[9] and that of Turkey obtained in this study and expressed in DID are summarized in Table 3.

National Inpatient Data: Analysis Results of Hospital-based Antifungal Consumption

The DID level of antifungals for inpatients showed an upward trend in annual consumption data except for 2018 (Figure 1). Friedman's variance analyses revealed that the median annual systemic antifungal consumption of inpatients changed significantly (p=0.002) by 50% between 2013 (0.002 DID) and 2019 (0.003 DID) (Table 1). When the OAC was evaluated, the most commonly consumed antifungals were azoles, followed by amphotericin B and echinocandins, respectively.

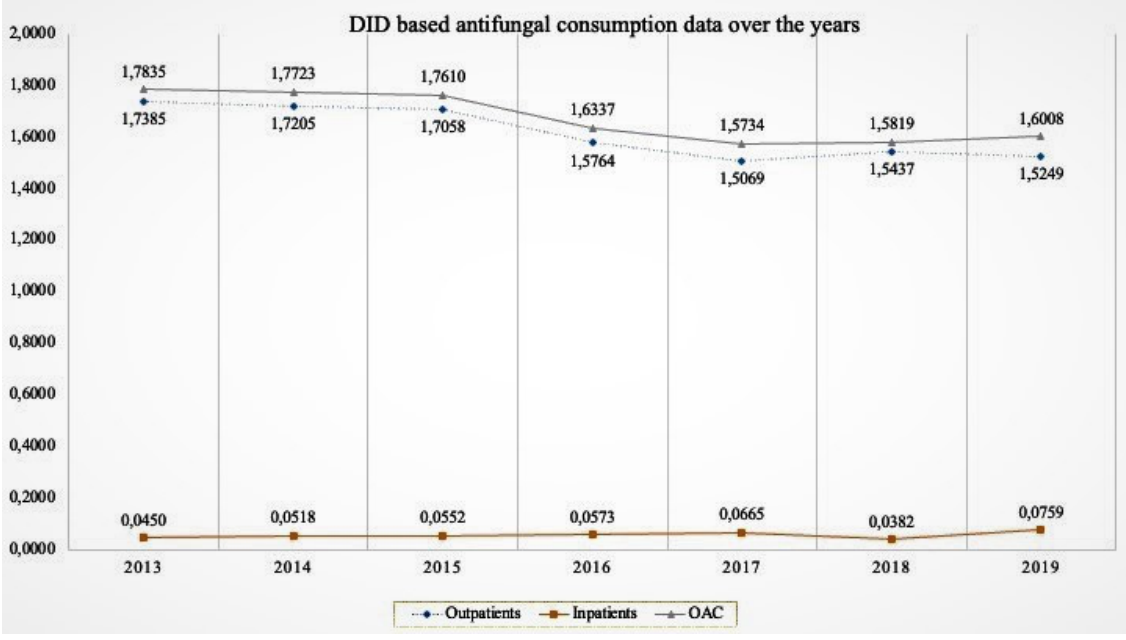


Figure 1. DID-based antifungal consumption trend over the years
DID: Defined Inhabitant Dose

Table 1. DID-based annual consumption of systemic antifungals (J02) and (D01B) in ambulatory care and hospitalized patients during 2013-2019

		Terbinafin	Amphotericin B	Ketoconazole	Fluconazole	Itraconazole	Voriconazole	Posaconazole	Caspofungin	Micafungin	Anidulafungin	Median
OAC (median DID)	2013	0,5944	0,0078	0,0146	0,0939	0,1732	0,0034	0,0021	0,0017	0,0000	0,0005	0,0021
	2014	0,6001	0,0084	0,0014	0,1005	0,1677	0,0043	0,0012	0,0017	0,0000	0,0007	0,0021
	2015	0,5937	0,0089	0,0000	0,1022	0,1671	0,0050	0,0012	0,0016	0,0000	0,0009	0,0015
	2016	0,5288	0,0093	0,0014	0,1068	0,1604	0,0056	0,0015	0,0017	0,0001	0,0013	0,0021
	2017	0,4897	0,0103	0,0014	0,1105	0,1613	0,0056	0,0043	0,0014	0,0007	0,0017	0,0030
	2018	0,5007	0,0067	0,0004	0,1076	0,1648	0,0054	0,0034	0,0008	0,0006	0,0007	0,0014
	2019	0,4883	0,0123	0,0012	0,1231	0,1611	0,0068	0,0034	0,0019	0,0011	0,0014	0,0028
	Median	0,5288	0,0089	0,0014	0,1068	0,1648	0,0054	0,0021	0,0017	0,0001	0,0009	**0,0038**
	2013-2019	-17,9	57,3	-92,1	31,1	-7,0	98,2	59,3	10,5		147,7	33,3
	X^2	10,714	5,143	11,786	8,786	3,643	8,571	11,143	8,357	11,297	4,500	10,236
	p	0,098	0,526	0,067	0,186	0,725	0,199	0,084	0,213	0,080	0,609	0,115
Inpatients (DID)	2013	0,0019	0,0140	0,0001	0,0191	0,0004	0,0031	0,0021	0,0033	0,0000	0,0011	0,0020
	2014	0,0060	0,0158	0,0000	0,0201	0,0004	0,0034	0,0012	0,0034	0,0000	0,0014	0,0024
	2015	0,0048	0,0173	0,0000	0,0228	0,0005	0,0037	0,0012	0,0031	0,0000	0,0017	0,0024
	2016	0,0009	0,0186	0,0000	0,0253	0,0005	0,0045	0,0016	0,0032	0,0002	0,0026	0,0021
	2017	0,0009	0,0205	0,0000	0,0287	0,0006	0,0042	0,0042	0,0027	0,0013	0,0034	0,0030
	2018	0,0003	0,0133	0,0000	0,0152	0,0003	0,0029	0,0022	0,0015	0,0011	0,0014	0,0014
	2019	0,0007	0,0242	0,0000	0,0334	0,0005	0,0055	0,0029	0,0037	0,0021	0,0027	0,0028
	Median	0,0009	0,0173	0,0000	0,0228	0,0005	0,0037	0,0021	0,0032	0,0002	0,0017	0,0019
	2013-2019	-61,2	73,5	-96,5	75,0	36,5	77,8	38,3	12,5		154,5	40,4
	X^2											21,471
	p											*0,002*
Outpatients (DID)	2013	1,1870	0,0016	0,0292	0,1687	0,3460	0,0038	0,0021	0,0001	0,0000	0,0000	0,0029
	2014	1,1943	0,0010	0,0027	0,1810	0,3350	0,0053	0,0012	0,0000	0,0000	0,0001	0,0019
	2015	1,1826	0,0004	0,0000	0,1816	0,3336	0,0063	0,0012	0,0001	0,0000	0,0000	0,0008
	2016	1,0567	0,0001	0,0027	0,1883	0,3203	0,0066	0,0015	0,0001	0,0000	0,0000	0,0021
	2017	0,9785	0,0001	0,0027	0,1923	0,3221	0,0069	0,0043	0,0000	0,0000	0,0000	0,0035
	2018	1,0010	0,0000	0,0008	0,2000	0,3294	0,0080	0,0045	0,0000	0,0000	0,0000	0,0027
	2019	0,9758	0,0003	0,0023	0,2128	0,3218	0,0081	0,0038	0,0000	0,0000	0,0000	0,0031
	Median	1,0567	0,0003	0,0027	0,1883	0,3294	0,0066	0,0021	0,0000	0,0000	0,0000	0,0024
	2013-2019	-17,8	-84,0	-92,1	26,2	-7,0	114,8	80,2	-57,3		-65,6	4,0
	X^2											1,664
	p											0,948

Friedman's variance analysis was used.

DID: Defined Inhabitant Dose, OAC: Overall antifungal consumption

Table 2. Wilcoxon Signed-Rank Pairwise analysis of antifungal consumption

OAC	2013	2014	2015	2016	2017	2018	Inpatients	2013	2014	2015	2016	2017	2018
2014	0.376						**2014**	0.059					
2015	0.940	0.970					**2015**	0.139	0.386				
2016	0.911	0.391	0.232				**2016**	0.169	0.139	0.114			
2017	0.550	0.455	0.296	0.093			**2017**	***0.047***	0.139	0.114	0.074		
2018	0.247	0.167	0.313	0.351	0.279		**2018**	0.203	0.093	0.114	0.059	***0.005***	
2019	0.351	0.263	0.191	***0.028***	0.502	***0.025***	**2019**	***0.028***	0.059	0.074	***0.022***	0.333	***0.005***

OAC: Overall antifungal consumption

Table 3. Consumption data of systemic antifungals in outpatients and the hospitalized patients expressed in DID in 2019 according to eCDC[9]

		Terbinafine	Amphotericin B	Ketoconazole	Fluconazole	Itraconazole	Voriconazole	Others	Total
Inpatients (DID)	France	<0.01	0.13	0.00	0.04	<0.01	<0.01	0.03	0.21
	Denmark	<0.01	0.02	<0.01	0.12	<0.01	0.01	0.04	0.20
	Italy	<0.01	0.01	<0.01	0.06	<0.01	0.01	0.03	0.13
	Greece	<0.01	0.03	<0.01	0.04	<0.01	<0.01	0.05	0.12
	Portugal	<0.01	0.03	<0.01	0.05	<0.01	0.01	0.02	0.12
	Crotia	<0.01	0.02	<0.01	0.05	<0.01	<0.01	0.01	0.10
	Belgium	<0.01	<0.01	0.00	0.05	<0.01	<0.01	0.01	0.09
	Turkey*	0.00	0.02	0.00	0.03	0.00	0.01	0.01	0.08
	Luxembourg	0.00	<0.01	0.00	0.04	<0.01	0.01	<0.01	0.07
	Finland	0.01	<0.01	<0.01	0.03	<0.01	<0.01	0.01	0.07
	Sweden	<0.01	<0.01	0.00	0.03	<0.01	<0.01	0.01	0.06
	Romania	<0.01	0.00	0.00	0.05	<0.01	<0.01	<0.01	0.06
	Norway	<0.01	<0.01	<0.01	0.03	<0.01	<0.01	0.01	0.05
	Hungary	<0.01	<0.01	0.00	0.02	<0.01	<0.01	<0.01	0.04
	Bulgaria	<0.01	0.00	0.00	0.03	<0.01	<0.01	<0.01	0.03
Outpatients (DID)	Belgium	1.78	0.00	0.00	0.67	0.49	<0.01	<0.01	2.96
	Greece	0.26	<0.01	0.00	1.20	0.62	<0.01	<0.01	2.09
	Portugal	1.41	0.00	0.00	0.27	0.28	0.00	0.00	1.96
	Finland	1.57	<0.01	0.00	0.22	0.09	<0.01	<0.01	1.89
	Turkey*	0.98	0.00	0.00	0.21	0.32	0.01	0.00	1.52
	Denmark	1.13	<0.01	0.00	0.28	0.08	<0.01	<0.01	1.48
	Luxembourg	0.37	0.00	0.00	0.55	0.54	0.00	0.00	1.45
	Norway	1.18	<0.01	<0.01	0.15	<0.01	<0.01	<0.01	1.36
	France	0.92	0.00	0.00	0.22	0.04	0.01	<0.01	1.19
	Hungary	0.74	0.00	0.00	0.21	0.11	<0.01	<0.01	1.06
	Romania	0.23	0.00	0.00	0.38	0.20	<0.01	<0.01	0.82
	Sweden	0.56	<0.01	0.00	0.21	0.02	<0.01	0.01	0.81
	Bulgaria	0.28	0.00	0.00	0.38	0.14	<0.01	0.00	0.79
	Italy	0.13	<0.01	<0.01	0.40	0.25	<0.01	<0.01	0.78
	Crotia	0.19	0.00	0.00	0.09	0.13	0.00	0.00	0.41

*Turkey data was obtained from the present study on the bases of the records of the Republic of Turkey Ministry of Health, Medicines and Medical Devices Agency.

DID: Defined Inhabitant Dose

Fluconazole was the most used antifungal agent in hospitalized patients during the study period and constituted approximately 44% of the total antifungal consumption among inpatients, with an overall median DID of 0.0228 (Table 1). Amphotericin B was the second one with an overall median DID of 0.0173. Fluconazole and amphotericin B consumptions showed an upward trend over the years except for 2018, and the change ratio between 2013 and 2019 reached 75% and 73.5%, respectively. Voriconazole is another commonly consumed antifungal agent with a median DID of 0.0037, and its consumption increased by 77.8% in 2019 when compared to 2013. Caspofungin was detected as the most used echinocandin with a median DID of 0.0032. However, the consumption of anidulafungin increased the most among echinocandins with a 154.5% increased ratio in 2019 compared to 2013.

National Outpatient Data: Analysis Results of Ambulatory Antifungal Consumption

The consumption data of systemic antifungals according to years are presented in Table 1. Friedman's variance analysis revealed no significant differences between years. Terbinafine was the most consumed antifungal agent with a rate of 66.6% in ambulatory care, followed by itraconazole (20.8%) and fluconazole (11.9%). The overall median DID level of outpatients was found at 1.0567 for terbinafine, 0.3294 for itraconazole, and 0.1883 for fluconazole. When the consumption data of 2019 was compared to 2013, voriconazole reached the highest increase in ratio of 114.8%, followed by posaconazole with a ratio of 80.2%. In contrast, it was detected that ketoconazole consumption decreased with a ratio of 92.1% (Table 1). Antifungal consumption data in ambulatory care and hospitalized patients were shown in Figure 2A and 2B. OAC for each antifungal was shown in Figure 2C. The percentage of OAC between outpatients and inpatients was shown in Figure 3.

Discussion

Systemic antifungal consumption varies across different countries[10]. Several factors have an impact on the amount of use and choices of antifungals such as healthcare policies, reimbursement conditions, frequency of potential patient population (eg. immunosuppressive and intensive care patients in need of antifungal therapy), and the knowledge of the physicians on the guidelines for antifungals. There is limited data on national antifungal consumption in our country. DID is the internationally suggested surveillance measure that provides an opportunity to compare data between countries. To the best of our knowledge, this is the first time that the use of antifungals nationwide has been reported and compared with the consumption in other European countries.

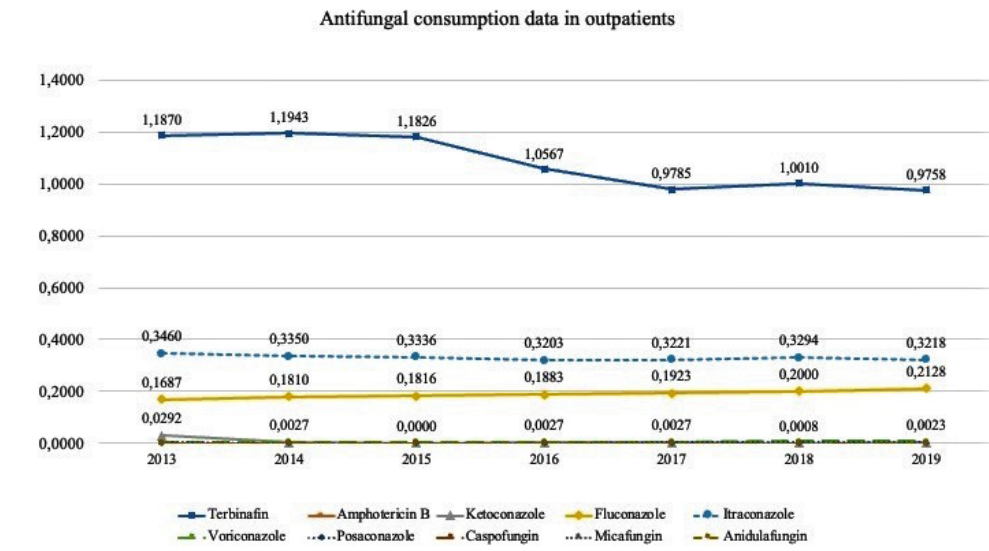
In 2019, OAC reached a DID level of 1.60 in Turkey, most of which (95%, with the 1.52 DID for 2019) constitute outpatient antifungal consumption. European antifungal surveillance data revealed that the outpatient systemic antifungal consumption represented 90-97% of overall consumption (Denmark: 90.5%; Hungary: 97%)[10]. In line with this data, outpatient systemic antifungal usage constitutes 95% of the OAC in Turkey with a DID of 1.52 for 2019.

Belgium was reported as the highest antifungal consumer for outpatients in 2009 with the highest DID level (3.24 DID), whereas Romania was the lowest consumer with a DID of 0.38[9,11]. Goemaere et al.[2] reported a significant decrease in systemic antifungal utilization by hospitalized patients in Belgium between 2003 and 2016 (25%) and showed a downward trend in average azole consumption in outpatients between 2010 and 2016 (from 1.455 DID to 1.250 DID, $p<0.005$). However, it still remains one of the biggest consumers among European countries in 2019. In contrast, Bulgaria was the lowest antifungal consumer for inpatients, with a DID level of 0.03, and Croatia was the lowest consumer with a DID of 0.41 for outpatients, as reported previously[9,10]. The DID level of antifungals for ambulatory patients in Turkey (ranged between 1.52 and 1.74 DID for the 2013-2019 period) was lower than that of many of the European countries[11]. When the distribution of utilized antifungal agents was evaluated, terbinafine was the most frequently used agent in ambulatory care and accounted for 66.6% of outpatient antifungal consumption, followed by itraconazole and fluconazole with ratios of 20.8% and 11.9%, respectively. Itraconazole and fluconazole account for the majority of azole consumption in outpatients in Turkey, similar to the previously reported national data of Belgium[2].

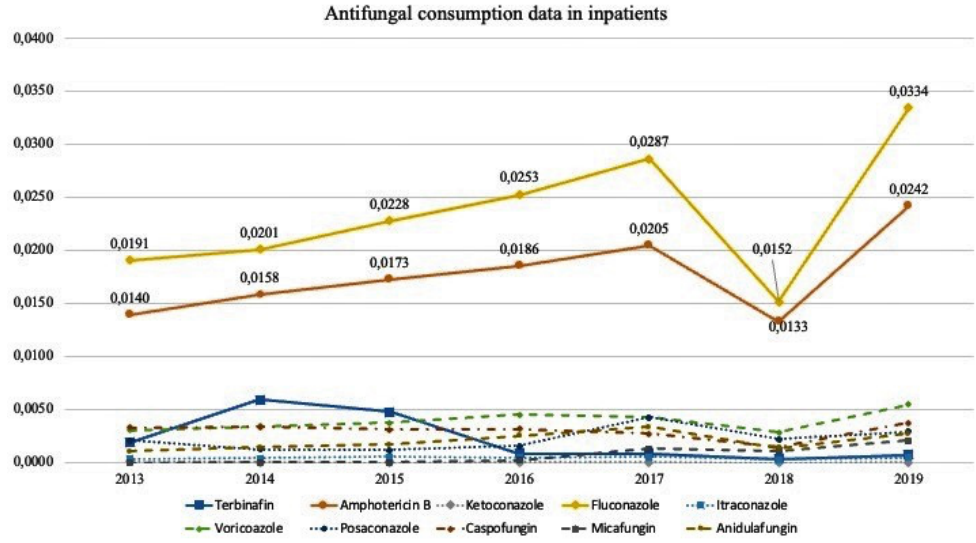
When the eCDC antifungal consumption data was evaluated, terbinafine constituted the most utilized agent in the majority of European countries in line with previous reports[9,11]. However, fluconazole was the most consumed agent among outpatients in Greece (57.4%), Italy (51.3%), Bulgaria (48.1%), Romania (46.3%), and Luxembourg (37.9%) in 2019[9]. In contrast, itraconazole was reported to be the most consumed product previously, with ratios of 52.3%, 47.8%, and 44.5% in Luxembourg, Croatia, and Italy, respectively, according to the data of the ESAC project that was conducted in 2010[10].

France and Denmark were the highest antifungal consumers in hospitalized patients among European countries in 2019 according to analysis of eCDC data[9]. Antifungal consumption in hospitalized patients showed an upward trend and had a significant increase in DID, which reached 0.076 in 2019 in Turkey. Fluconazole was detected as the most consumed agent in hospitals in Turkey, similar to European countries other than France[9]. This finding is in line with the previous studies that reported fluconazole as the most consumed antifungal agent in hospitals, with a ratio of 70-80%[12].

A)



B)



C)

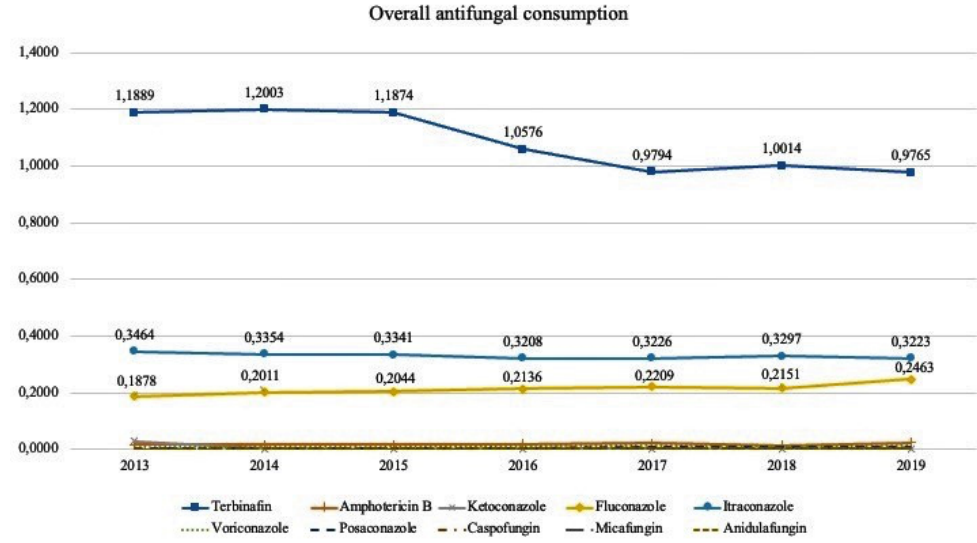
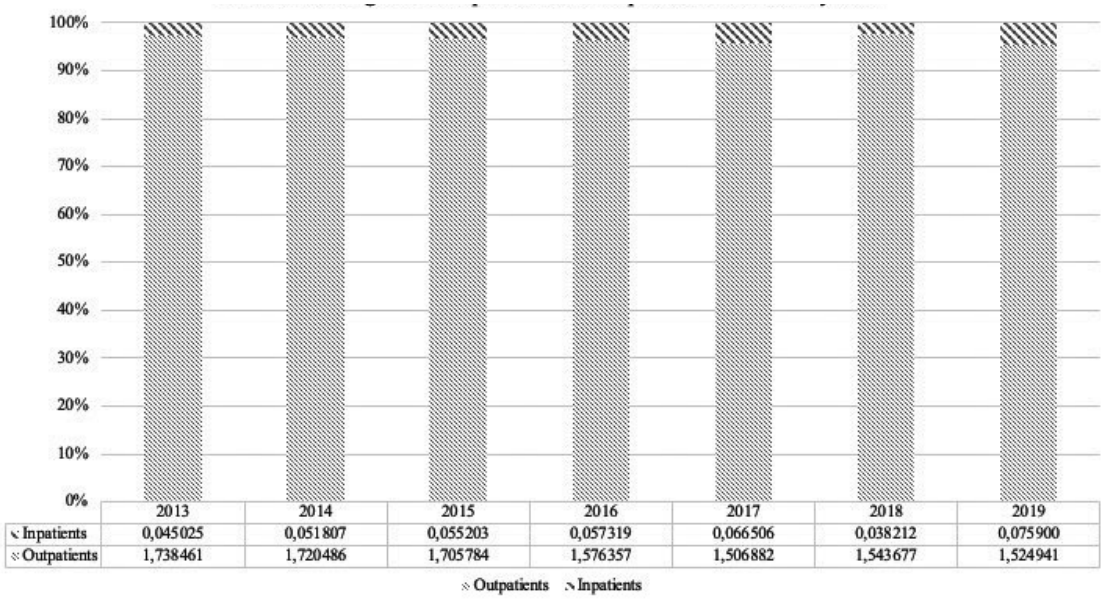


Figure 2. A) Antifungal consumption data in ambulatory care, B) Antifungal consumption data in hospitalized patients, C) Total antifungal consumption



	2013	2014	2015	2016	2017	2018	2019
Inpatients	0,045025	0,051807	0,055203	0,057319	0,066506	0,038212	0,075900
Outpatients	1,738461	1,720486	1,705784	1,576357	1,506882	1,543677	1,524941

Figure 3. Overall antifungal consumption data in hospitals and ambulatory care

Amphotericin B was the second most commonly used agent in hospitalized patients in Turkey and the most consumed antifungal agent in French hospitals in 2019[9].

Regarding antifungal consumption data over the years in our study, the most striking data was the downward trend in OAC, which was driven by outpatient antifungal utilization. Recently, there has been a remarkable decrease in the consumption of ketoconazole and terbinafine, with ratios of 92.1% and 17.9%, respectively.

In recent years, many postgraduate trainings have been organized by the Ministry of Health and Expert Associations on the rational use of antimicrobial drugs in Turkey. It was thought that these training had an effect on reducing the consumption of drugs.

Study Limitations

The strengths of the present study are as follows:

- This is the first study presenting national data on the basis of antifungal consumption in both ambulatory care and inpatients in Turkey.

- Data are comparable between countries because of the use of standard methodology as DID.

- In addition, that gives the opportunity to evaluate the efficacy of national antimicrobial stewardship programs.

- This study provides an opportunity to generate data that can be used as reference data for Turkey.

On the other hand, there are some limitations to our study. First, our study did not have detailed data on the basis of antifungal consumption in ICUs and non-ICUs. Besides, there is a lack of data on the proportion of consumed antifungals by specific units that provide care for immunosuppressed patients, such as oncology and hematology. However, these were not the main objectives of this study.

Conclusion

As a result, our study revealed that outpatient antifungal consumption accounts for the majority of antifungals utilization. Although a downward trend has been observed in recent years, Turkey is still one of the leading consumers among European countries, especially in ambulatory care. Antimicrobial stewardship programs should be re-evaluated to decrease antifungal consumption.

Further studies are needed to evaluate the differences in antifungal consumption between the ICUs, hematology clinics, and wards.

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Ethics

Ethics Committee Approval: Ethical approval for this retrospective descriptive study was obtained from the Ethics Committee of the Ankara City Hospital (protocol no: E-21-1664, date: 17.03.2021).

Informed Consent: Retrospective descriptive study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.B., O.K., Design: A.B., M.A., F.İ., O.K., Data Collection or Processing: A.B., M.A., F.İ., Analysis or Interpretation: A.B., M.A., F.İ., O.K., Literature Search: A.B., Writing: A.B., M.A., F.İ., O.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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