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Original Research

COVID-19 pandemics and antibiotics use in the University Clinical Centre of Kosova

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Abstract

Background: One profoundly consequential facet of Kosovo healthcare pertains to antimicrobial drug consumption. The absence of specific guidelines for antimicrobial usage in the context of COVID-19 resulted in a notable upswing in antibiotic consumption across the country. This surge in antibiotic usage is particularly disconcerting within hospital settings, where the risk of antibiotic-resistant infections becomes significantly more pronounced. **Objectives:** To address this concern, this paper endeavors to undertake a comprehensive analysis of antibiotic consumption within hospital facilities over the years 2020, 2021, and 2022. This analysis will juxtapose antibiotic consumption during these years against the general population and preceding years. **Results:** The findings from the clinical center reveal a substantial upsurge in the consumption of most antibiotics during 2021, followed by a subsequent decline in 2022. However, a wealth of data underscores the notable utilization of ceftriaxone, exhibiting an annual increase of 32%, and imipenem, showing an annual increase of 47%. Similar upward trends were observed with other antibiotics in this research following the consumption in the first year of the COVID-19 pandemic. **Conclusion:** Preserving patient safety and promoting rational antibiotic use necessitates heightened monitoring and strengthening antimicrobial stewardship initiatives. Moreover, antimicrobial stewardship measures must be enhanced and consistently maintained to ensure the prudent utilization of antibiotics throughout the pandemic.

Keywords: antimicrobial consumption; antimicrobial resistance; university clinical centre of kosova

INTRODUCTION

The development and spread of multidrug-resistant microbes and the lack of funding for discovering new antibiotics compromise the efficacy of many modern medications and pose severe risks to global public health.[1-3] In many regions of the world, the danger of the start and spread of antimicrobial resistance (AMR) has increased due to the abuse and misuse of antibiotics. Drug-resistant disease mortality will rise from 700,000 to 10 million annually as AMR continues to rise, with costs expected to reach $100 trillion globally by 2050.[4-5]

One of the leading causes of AMR is believed to be the overuse and misuse of antibiotics.[6-8] Antibiotic utilization must be monitored and optimized to stop or minimize the emergence of AMR.[9] AMR's effects on providing routine and emergency medical services in hospitals have been thoroughly documented. The pandemic has impacted how health awareness campaigns, preventive healthcare, and the identification and continuous management of chronic diseases are carried out.[10]

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The Ministry of Health of Kosova oversees the supply of essential medicines in Kosovo. This supply chain operates following approved lists, with the Clinical and University Hospital Service of Kosovo actively managing the contracting and distribution of these crucial medical products. However, managing the procurement and distribution of essential medicines poses distinct challenges, primarily centered around securing adequate funding to meet the diverse healthcare requirements.

The Ministry of Health of the Republic of Kosova approved the 7th update of the National Essential Medicines List (NEML) in May 2023, according to the model of essential medicines of the WHO.

The essential medicines list is organized into various subgroups based on pharmacological classes, and among these subgroups is the category of antimicrobial medicines. This antimicrobial subgroup is further subdivided using the WHO's Aware classification model. The purpose of this classification system is to support the creation of resources for antibiotic stewardship at local, national, and global levels while also addressing the critical issue of antimicrobial resistance.[11]

To facilitate the responsible utilization of antibiotics and combat the growing problem of antimicrobial resistance, the World Health Organization (WHO) has introduced the Access, Watch, Reserve (Aware) classification for antibiotics, categorizing antibiotics into distinct groups, highlighting the significance of their judicious and appropriate usage.[11] The same classification was adopted in Kosovo's essential medicines list in 2019 in the 6th update and 2023 in the 7th update of the NEML.

One particularly significant aspect of Kosovo healthcare is the

consumption of antimicrobial drugs. Notably, there has been a notable shift in the consumption patterns of these drugs over the years. Antimicrobial consumption is monitored in Kosovo since 2012 when the WHO included Kosovo as part of AMC (Antimicrobial Consumption) Network. Since then, Kosovo has not just analyzed obtained results from overall consumption (Community and hospital) but also compared with other AMR network members but as well other European countries. In 2012, the consumption of antimicrobial drugs in Kosovo stood at 26 defined daily doses per 1,000 inhabitants (DID).[12]

Following the publication of initial results and the identification of primary issues in 2012-2013, a comprehensive and systematic endeavor was initiated from the Intersectoral group for containment of antimicrobial resistance from MoH of Kosovo. This effort yielded concrete results in the enhancement and reduction of antimicrobial consumption across Kosovo. By 2017, as reported by the World Health Organization (WHO), this figure had decreased to 19 DID. This decline reflects the dedicated efforts of various stakeholders, starting from inter-sectoral groups to combat antimicrobial resistance and implementing a strategy and an action plan to address this issue.[13] This sustained progress persisted until the advent of the Covid-19 pandemic, when the consumption not only in community but also in hospital level of antimicrobials that are listed in essential medicines in Kosovo was increased significantly.

Specific antibiotics, including carbapenems, macrolides, and lincosamides, have increased significantly due to the coronavirus disease of 2019 (COVID-19). Additionally, research has shown that local and national hospitals used more Watch antibiotics during the COVID-19 pandemic.[14-15] The usual causes of this rise are increased admissions to the intensive care unit (ICU) and more extended hospital stays for COVID-19 patients. As a result, there aren't enough beds available to care for these crucial patients. The problem of bacterial co-infection leads to the potential misuse of antimicrobials.[16] This pattern was inspired by influenza, which has a high rate of co-infections (58%).[17] According to the latter, many antibiotics given to COVID-19 patients may have been unneeded and wrongly suggested.[18] Adverse drug reactions may be the reason, including a higher likelihood of antibiotic resistance.[19]

Concerns regarding the pandemic's potential impact on the developing AMR hazard have already been voiced by several academics.[20] The World Health Organization (WHO) and several experts advise against starting antibiotic treatment for COVID-19 cases that are suspected or confirmed to be mild and against prescribing antibiotics for moderate COVID-19 (unless laboratory results confirm clinical suspicion of bacterial infection) or in critically ill patients.[21] Implementing antimicrobial stewardship programs, which have worsened due to the ongoing pandemic, is problematic in many low- and middle-income countries, including Kosovo. No research has been conducted in Kosovo to evaluate the use of antibiotics among COVID-19 hospital patients.

However, the emergence of the COVID-19 pandemic introduced a new challenge. The absence of specific guidelines for antimicrobial use in the context of COVID-19 led to increased antibiotic consumption throughout the country. This surge in antibiotic usage is particularly concerning within hospital settings, where the risk of antibiotic-resistant infections becomes more pronounced. Reports from the Agency for Medicinal Products and Medical Devices (AKPPM) and the Clinical and University Hospital of Kosovo (UCCK) suggest that this increase in consumption could potentially reach alarming levels.

This paper aims to comprehensively analyze antibiotic consumption within hospital facilities in 2020, 2021, and 2022. This analysis will compare antibiotic consumption during these years with the general population and previous years. By doing so, we hope to gain insights into the evolving trends in antibiotic usage within healthcare institutions and identify potential areas for intervention and improvement. This research is crucial in the ongoing effort to safeguard public health and ensure the responsible use of antibiotics in Kosovo.

MATERIALS AND METHODS

Data was collected by retrieving information from three primary sources: the Central Pharmacy of the University Clinical Center of Kosovo through the SMSF (System for managing pharmaceutical inventories), the annual reports of the hospitals service of Kosova and the Barnatari -electronic system of Kosovo Medicines Agency.

We focused on gathering data on the antibiotics supplied in the infectious diseases and pulmonology clinics for the three years covering 2020, 2021, and 2022. From a group of antibiotics available, we selected a subset for our analysis, which included widely used antibiotics such as ceftriaxone, imipenem, levofloxacin, piperacillin tazobactam, azithromycin, and vancomycin.

The medicines are classified as per WHO ATC system and drug utilization indicator DDD/100 Bed days is used to express results for the three years in each clinic.

To gain a comprehensive understanding of the trends in antibiotic imports and their utilization within these specific clinics, we also collected import data for antibiotics in the same years from the Kosovo Medicines Agency (KMA). This information was acquired through the Barnatari system, an electronic database maintained by the KMA.

Data collection

Information on antibiotic utilization in 2020, 2021, and 2022 was extracted from the pharmacy information system maintained by both University Clinical Center of Kosovo (UCCK) and the Kosovo Medicines Agency (KMA). This dataset exclusively encompassed the usage of antibiotics among inpatients within healthcare facilities.

A thorough validation process was undertaken to ensure the accuracy and reliability of the data, which included a thorough examination of any potential errors. Subsequently, the appropriate dosages for each antibiotic were determined

through careful analysis.

Our study encompassed a diverse range of participants, encompassing individuals across all age groups and genders, irrespective of the presence or absence of comorbidities. It's essential to emphasize that no patient-specific identities or personally identifying information were included in any of the datasets utilized in our research, preserving the confidentiality and privacy of all individuals involved.

RESULTS

In the year 2020, the utilization of ceftriaxone in infectious disease clinics amounted to 34,885 doses – 0.85 DDD/100BD, with an additional 16,100 doses (0.39 DDD/100BD) administered in pulmonology clinics. Comparatively, in 2021, there was a notable increase of 32.2% in overall ceftriaxone usage, reaching 43,200 doses (1.22 DDD/100BD) in infectious disease clinics and 32,000 doses (0.9 DDD/100BD) in pulmonology clinics. However, in 2022, there was a decline in ceftriaxone usage by 14.3% compared to 2020 and a substantial 41.9% decrease compared to 2021, with 25,200 doses (0.85 DDD/100BD) used in infectious disease clinics and 18,500 doses (0.65 DDD/100BD) in pulmonology clinics. Among all antibiotics under investigation, imipenem exhibited the highest usage. In 2020, imipenem was administered 10,910 times (0.13 DDD/100BD) in infectious disease clinics and 5,827 (0.07 DDD/100BD) times in pulmonology clinics. In contrast, in 2021, there was a substantial increase of 47.17% in imipenem usage, with 14,722 doses (0.20 DDD/100BD) administered in infectious disease clinics and 17,296 (0.24 DDD/100BD) in pulmonology clinics.

However, in the following year (2022), imipenem usage decreased significantly to 8,238 doses (0.14 DDD/100BD) in infectious disease clinics and 8,930 doses (0.15 DDD/100BD) in pulmonology clinics. Levofloxacin's total consumption in infectious disease clinics was 1,520 (0.07 DDD/100BD) in 2020, 3,246 (0.18 DDD/100BD) in 2021, and 3,440 (0.24 DDD/100BD) in 2022. In contrast, pulmonology exhibited higher levofloxacin usage, with 3,900 doses (0.19 DDD/100BD) in 2020, 5,621 (0.31 DDD/100BD) in 2021, and 4,780 (0.33 DDD/100BD) in 2022. Another antibiotic, piperacillin tazobactam (P+T), was also examined. In 2020, P+T was administered 2,994 times (0.042 DDD/100B) in infectious disease clinics and only 90 times (0.001 DDD/100BD) in pulmonology. Subsequently, P+T usage increased significantly by 65.9% in infectious disease clinics (8,778 doses – 0.14 DDD/100B) and 91.7% in pulmonology (1,090 doses – 0.018 DDD/100BD) the following year. However, compared to 2021, there was a decline in P+T usage of 69% in infectious disease clinics (2,705 doses – 0.054 DDD/100BD) and a substantial 78.6% decrease in pulmonology (233 doses – 0.005 DDD/100BD). Vancomycin usage in infectious disease clinics exhibited a continuous increase. In 2020, 2,850 doses (0.035 DDD/100BD) were administered, 5,100 (0.072 DDD/100BD) in 2021, and 7,752 (0.136 DDD/100BD) in 2022. In pulmonology, vancomycin usage was 2,200 doses (0.027 DDD/100BD) in 2020, 2,900 doses (0.072 DDD/100BD) in 2021, and 1,240 doses (0.022 DDD/100BD) in 2022. Azithromycin showed different usage patterns in infectious disease clinics in 2020 (3,501 doses – 0.17 DDD/100BD), 2021 (120 doses – 0.007 DDD/100BD), and 2022 (300 doses – 0.021 DDD/100BD). Conversely, pulmonology exhibited different patterns, with 798 doses (0.039 DDD/100BD) in 2020, 771 doses (0.044 DDD/100BD) in 2021, and 990 doses (0.07 DDD/100BD) in 2022. The distribution of hospital antibiotic consumption is detailed in Table 1, and an overview of the overall distribution by year in supplied and DDD/100 BD for antibiotics in infectious disease clinics and pulmonology are illustrated in Figure 1 and Figure 2

Data on antibiotic imports for the same years were obtained from the Kosovo Medicines Agency (KMA) through the Barnatari system, the KMA's electronic database. Trends in ceftriaxone import revealed 690,864 doses in 2020, followed by a 7.9% increase in 2021 (749,947 doses) and a significant

Table 1. Antibiotics supplied doses and DDD?100 BD in Infectious disease clinics and pulmonology clinics in University Clinical Center of Kosovo (UCCK)

Antimicrobial agent	Clinic	2020		2021		2022	
		Supplied doses	DDD/100 BD	Supplied doses	DDD/100 BD	Supplied doses	DDD/100 BD
Ceftriaxone 1000	Infective	34885	0.854	43200	1.225	25200	0.885
	Pulmonology	16100	0.394	32000	0.907	18500	0.650
Imipenem 500	Infective	10910	0.134	14722	0.209	8238	0.145
	Pulmonology	5827	0.071	17296	0.245	8930	0.157
Levofloxacin 500	Infective	1520	0.074	3246	0.184	3440	0.242
	Pulmonology	3900	0.191	5621	0.319	4780	0.336
Piperacillin + Tazobactam 4000	Infective	2994	0.042	8778	0.142	2705	0.054
	Pulmonology	90	0.001	1090	0.018	233	0.005
Vancomycin 500	Infective	2850	0.035	5100	0.072	7752	0.136
	Pulmonology	2200	0.027	2900	0.041	1240	0.022
Azithromycin 500	Infective	3501	0.172	120	0.007	300	0.021
	Pulmonology	798	0.039	771	0.044	990	0.070

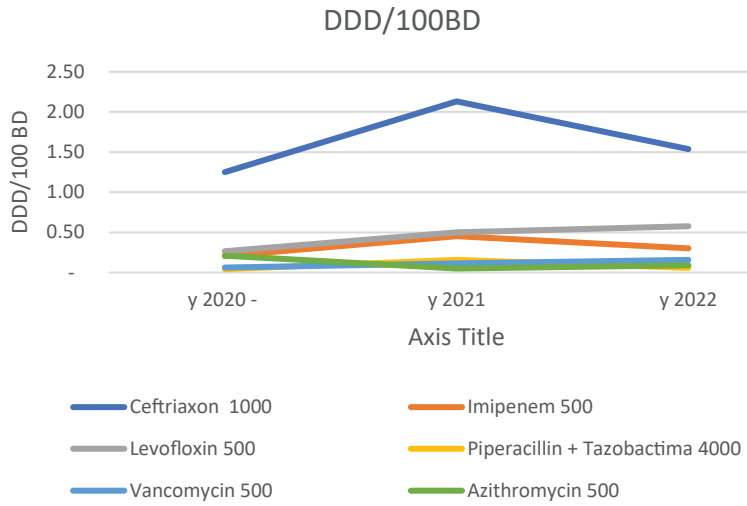

Figure 1. Utilization in DDD/100 BD of antimicrobials in years (y) infectious disease clinic and pulmonology clinic of UCCK

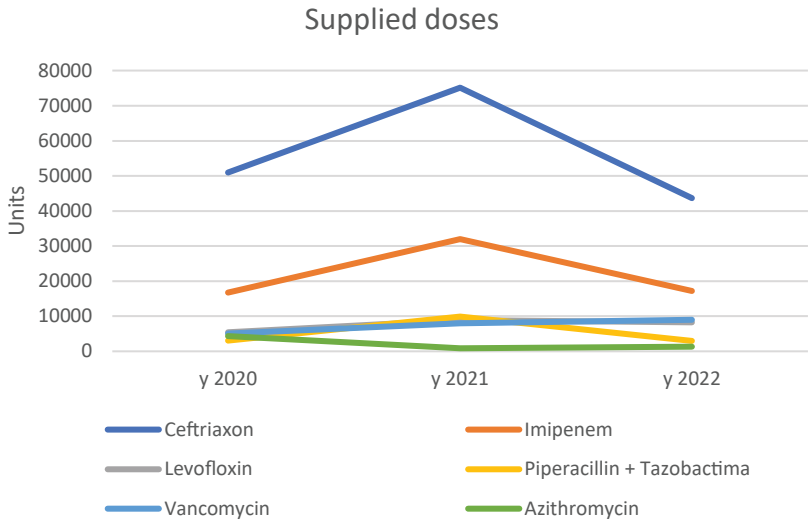

Figure 2. Distribution in antibiotic doses supplied in years (y) infectious disease clinic and pulmonology clinic of UCCK

33% increase in 2022 (1,029,995 doses). Imipenem imports were 95,780 doses in 2020, increasing to 239,810 doses in the following year (a 60% increase) but declining to 70,864 doses in 2022. Levofloxacin imports were 145,067 doses in 2020, more than doubling to 337,525 doses in 2021, and then experiencing a significant drop to 96,583 doses in 2022. Piperacillin tazobactam (P+T) imports totaled 16,250 doses in 2020, increasing by 43% to 28,500 doses in 2021 and decreasing to 12,450 doses in 2022. Vancomycin imports were 62,100 doses in 2020, increasing to 126,404 doses in 2021 (a 50.9% increase) and the remaining 62,650 doses in 2022. In contrast, azithromycin imports exhibited a different pattern. In 2021, imports were 451,376 doses, which decreased by 39% in 2021 (274,804 doses) and declined by 53% in 2022 (211,881 doses).

The antibiotic import data is presented in Table 2.

Table 2. Supplied doses of antibiotic imported in Kosovo

	year 2020	year 2021	year 2022
Ceftriaxone	69864	749947	1029995
Imipenem	95780	239810	70864
Levofloxacin	145067	337525	96583
Piperacilin+Tazobactam	16250	28500	12450
Vancomycin	62100	126404	62650
Azithromycin	451376	274804	211881

DISCUSSION

AMR's global health crisis and the COVID-19 pandemic are both happening at the same time. AMR infections cause mortality, which places a high financial cost on society.[22-24] Depending on the severe symptoms, COVID-19-infected people may need to

be admitted to the ICU. Severe comorbidities may necessitate ventilator support.[23,25]

The current study highlights the impact of the COVID-19 pandemic on antibiotic use by infectious clinics and pulmonology. As far as we know, this is the first study comparing the consumption and imports of antibiotics during the COVID-19 pandemic in Kosovo. The findings showed a rise in azithromycin use in 2020, like other research showing a rise in azithromycin use during the COVID-19 pandemic, particularly when combined with hydroxychloroquine.[26-28] The reason could be because doctors have previously used azithromycin to treat respiratory infections or because COVID-19 is commonly treated with azithromycin outside of the approved indications in other countries. A previous study in Singapore reported on this extensive use and discovered comparable patterns in increased azithromycin intake.[29] Reduced viral multiplication, suppression of entrance into host cells, and a potential immunomodulating effect are only a few of azithromycin's in vitro antiviral actions.[26-30] It has been shown that azithromycin is beneficial for people with chronic obstructive pulmonary disease.[31] Azithromycin was not found to reduce the incidence of later hospital readmissions or fatalities, so previous studies do not support its use in treating patients with mild to moderate COVID-19.[32] According to Timothy et al., adding azithromycin to standard care treatment did not improve the risk of subsequent hospital admission or death or the time to hospital admission in patients with clinically diagnosed mild-to-moderate COVID-19 who were handled without hospital admission.[33]

In contrast to 2020 and 2021, there was a decline in ceftriaxone use in 2022. The rise in other antibiotics, like Vancomycin, may be accountable for this decline in utilization. According to other studies, the utilization of third and fourth generation cephalosporins has improved incrementally.[34-38] Racial disparities, variances in the most prevalent illnesses, and the emergence of resistance in individuals who have received treatment could all be factors in this.

Levofloxacin usage has increased, according to the current study. Other studies have observed a slight rise in the use of levofloxacin. Levofloxacin is a fluoroquinolone utilized for empirical therapy rather than a single, focused antimicrobial therapy against pathogenic microorganisms.[37-38]

In this study, there was also an increase in the usage of specific antibiotics during the COVID-19 pandemic period. For example, the use of imipenem, vancomycin, and piperacilin+tazobactam. These findings are consistent with other studies.[26-28]

The current study revealed that the utilization of selected antimicrobials in infectious clinics and pulmonology increased in 2021 compared to 2020. The increases for ceftriaxone were 32.2%, followed by imipenem at 47.8%, levofloxacin at 38.9%, P+T at 68.8%, and vancomycin at 36.9%, respectively. However, in the following year, 2022, there was a decline in the use of ceftriaxone, imipenem, levofloxacin, and P+T compared to 2021 (41.9%, 46.4%, 7.3%, and 70.2%, respectively). On the other hand, vancomycin showed an increase in 2022 compared to 2021 (11%). Interestingly, azithromycin usage declined compared to 2020 in 2021 (79.3%) and 2022 (70%).

Furthermore, our study revealed changes in the imports of antibiotics in the mentioned years. Ceftriaxone imports increased by 9.3% and 33% in 2021 and 2022 compared to 2020. Imipenem imports increased by 60% in 2021 and then declined by 26% in 2022 compared to 2020. Levofloxacin was imported 57% more in 2021 than in 2020 but declined by 34% in 2022 compared to 2020 imports. P+T marked a 43% higher import in 2021 compared to 2020 but declined by 23% in 2022 compared to 2020. Vancomycin increased 51.1% in 2021 and 0.9% in 2022 compared to imports in 2020. As with azithromycin usage, the imports followed a different pattern than the others. In the year 2021, there was a 39% decline, followed by a 53% decline in 2022, compared with azithromycin imports in 2020.

The COVID-19 pandemic may have seen an increase in antimicrobial use due to several factors, including initial misdiagnosis of the infection, hospital overcrowding, a shortage of physicians with the necessary expertise, a decline in the antimicrobial stewardship team's activity, and a lack of initial therapeutic protocols. This highlights how crucial antimicrobial stewardship is to maximizing antibiotic use in hospitals, especially in urgent cases like the COVID-19 epidemic.[23-25] Encouragement of local guideline implementation, prompt de-escalation, or discontinuation of therapy when clinical signs of an unconfirmed bacterial co-infection are identified are all strategies to maximize the rational use of antibiotics. Correct antibiotic selection based on the results of microbiological tests is another strategy. Additionally, while closely monitoring potential drug interactions or toxicity, antibiotic treatment duration should follow local norms to maximize antibiotic use throughout the COVID-19 pandemic's future stage.[23,25]The intake of antibiotics increased during COVID-19, according to the authors.[39]

Antimicrobial stewardship programs must include the measurement of antibiotic consumption because it enables us to advance good clinical usage of antibiotics. The impact of changes on the use of some broad-spectrum antibiotics requires a more thorough examination of the spread of antimicrobial resistance. Our research has some limitations.

Due to the study's hospital-based setting, it was challenging to control potential confounding variables such as patient case mix and illness kind. There is a need for additional patient-level research. Additionally, only one hospital was used to conduct this investigation. It is necessary to conduct a multi-site study to comprehend better how the COVID-19 pandemic has affected the use of antibiotics.

CONCLUSIONS

This study's results helped assess how imports into Kosovo during COVID-19 and antimicrobial use at the UCCK changed. The significant increase of use of antibiotics in 2021 due to COVID-19 is not supported scientifically. Although in 2022 there was a decline of antibiotic use in hospital setting, there

is still overuse of ceftriaxone and other antimicrobial agents.

This study suggests that more efforts are required to monitor and enhance antimicrobial stewardship initiatives to preserve patient safety and appropriate antibiotic use. Additionally, antimicrobial stewardship must be improved and maintained to ensure the prudent use of antibiotics throughout the pandemic.

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References

1. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, et al. Antibiotic resistance: a rundown of a global crisis. Infect Drug Resist 2018;11:1645-58. https://doi.org/10.2147/idr.s173867
2. Aldeyab M, López-Lozano J-M, Gould IM. Global antibiotics use and resistance. In Babar Z-U-D, editor. Global Pharmaceutical Policy. Palgrave Macmillan. 2020;331-344.
3. El-Sheshtawy HS, Mahdy HM, Sofy AR, Sofy MR. Production of biosurfactant by Bacillus megaterium and its correlation with lipid peroxidation of Lactuca sativa. Egyptian Journal of Petroleum. 2022;31:1-6.
4. Piddock LJV. Reflecting on the final report of the O'Neill review on antimicrobial resistance. Lancet Infect Dis. 2016;16(7):767-8. https://doi.org/10.1016/s1473-3099(16)30127-x
5. Razzaque M. Implement antimicrobial stewardship to reduce antimicrobial drug resistance. Expert Rev Anti Infect Ther. 2020;19:559-62.
6. Jirjees FJ, Al-Obaidi HJ, Sartaj M, Conlon-Bingham G, Farren D, Scott MG, et al. Antibiotic use and resistance in hospitals: time-series analysis strategy for determining and prioritizing interventions. Hospital Pharmacy Europe. 2020;7:13-19.
7. Hayajneh WA, Al-Azzam S, Yusef D, Lattyak WJ, Lattyak EA, Gould I, et al. Identification of thresholds in relationships between specific antibiotic use and carbapenem-resistant Acinetobacter baumannii (CRAb) incidence rates in hospitalized patients in Jordan. J Antimicrob Chemother. 2021;76:524-30. https://doi.org/10.1093/jac/dkaa463
8. Conlon-Bingham GM, Aldeyab M, Scott M, Kearney MP, Farren D, Gilmore F, et al. Effects of antibiotic cycling policy on the incidence of healthcare-associated MRSA and Clostridioides difficile infection in secondary healthcare settings. Emerging Infect Dis. 2019;25(1):52-62. https://doi.org/10.3201/eid2501.180111
9. Organization WH (2015) Report of the 6th meeting of the WHO advisory group on integrated surveillance of antimicrobial resistance with AGISAR 5-year strategic framework to support the implementation of the global action plan on antimicrobial resistance (2015-2019), 10-12 June 2015, Seoul, Republic of Korea.
10. Halcomb E, McInnes S, Williams A, Ashley C, James S, Fernandez R, et al. The experiences of primary healthcare nurses during the COVID-19 pandemic in Australia. J Nurs Scholarsh. 2020;52(2):553-63. https://doi.org/10.1111/jnu.12589
11. WHO (2023) World Health Organization Model list of Essential Medicines 23rd. Geneva Switzerland.
12. Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, et al. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infectious Diseases. 2014;14(5):381-7. https://doi.org/10.1016/s1473-3099(14)70071-4
13. MSH. Plani strategjik i rezistencës antimikrobike. Accessed online on 20.09.2023. 2019. Available from: https://msh.rks-gov.net/Documents/Index/271
14. Al-Azzam S, Mhaidat NM, Banat HA, Alfaour M, Ahmad DS, Muller A, et al. An assessment of the impact of coronavirus disease (COVID-19) pandemic on national antimicrobial consumption in Jordan. Antibiotics. 2021;10:690. https://doi.org/10.3390/antibiotics10060690
15. Ul Mustafa Z, Salman M, Aldeyab M, Kow CS, Hasan SS. Antimicrobial consumption among hospitalized patients with COVID-19 in Pakistan. SN Compr Clin Med. 2021;3:1691-5. https://doi.org/10.1007/s42399-021-00966-5
16. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. https://doi.org/10.1001/jama.2020.1585
17. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect. 2020;81:266-75. https://doi.org/10.1016/j.jinf.2020.05.046
18. Mahmoudi H. Bacterial co-infections and antibiotic resistance in patients with COVID-19. GMS Hyg Infect Control. 2020;15:Doc35. https://doi.org/10.3205/dgkh000370
19. Bhimraj A, Morgan RL, Shumaker AH, Lavergne V, Baden L, Cheng VC-C, et al. () Infectious Diseases Society of America guidelines on the treatment and management of patients with coronavirus disease 2019 (COVID-19). Clin Infect Dis. 2020: ciaa478.
20. Hsu J. How COVID-19 is accelerating the threat of antimicrobial resistance. BMJ: 2020;369:m1983. https://doi.org/10.1136/bmj.m1983

www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

21. Baclic DCV, Murthy S, Emeriaud G, Money D, Yeung T, Poliquin G, et al. Clinical management of patients with COVID-19 – 2nd Interim guidance. 2020. Available: https://canadiancriticalcare.org/resources/Documents/AMMI-CCCS-PHAC-clinical-guidance-Aug21-EN-FINAL.pdf Accessed: 8 November 2022.
22. Brogan DM, Mossialos E. A critical analysis of the review on antimicrobial resistance report and the infectious disease financing facility. Global health. 2016;12:1-7. https://doi.org/10.1186/s12992-016-0147-y
23. Khor WP, Olaoye O, D'Arcy N, Krockow EM, Elshenawy RA, Rutter V, et al. The need for ongoing antimicrobial stewardship during the COVID-19 pandemic and actionable recommendations. Antibiotics. 2020;9(12):904. https://doi.org/10.3390/antibiotics9120904
24. Sofy MR, Mancy AG, Alnaggar AEAM, Refaey EE, Mohamed HI, Elnosary ME, et al. A polishing the harmful effects of broad bean mottle virus infecting broad bean plants by enhancing the immunity using different potassium concentrations. Notulae Botanicae Horti Agrobotanici Cluj-Napoca. 2022;50:12654.
25. Alanio A, Dellière S, Fodil S, Bretagne S, Mégarbane B. Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. Lancet Respir Med. 2020;8:e48-e49. https://doi.org/10.1016/s2213-2600(20)30237-x
26. Arshad S, Kilgore P, Chaudhry ZS, Jacobsen G, Wang DD, Huitsing K, et al. Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19. International Journal of Infectious Diseases. 2020;97:396-403. https://doi.org/10.1016/j.ijid.2020.06.099
27. King LM, Lovegrove MC, Shehab N, Tsay S, Budnitz DS, Geller AI, et al. Trends in US outpatient antibiotic prescriptions during the coronavirus disease 2019 pandemic. Clin Infect Dis. 2021;73(3):e652-e660. https://doi.org/10.1093/cid/ciaa1896
28. De Lusignan S, Joy M, Sherlock J, Tripathy M, van Hecke O, Gbinigie O, et al. Principle trial demonstrates scope for in-pandemic primary care antibiotic stewardship improvement. medRxiv. 2021;5(5):21250902. https://doi.org/10.3399/bjgpo.2021.0087
29. Liew Y, Lee WHL, Tan L, Kwa ALH, Thien SY, Cherng BPZ, et al. Antimicrobial stewardship programme: a vital resource for hospitals during the global coronavirus disease 2019 (COVID-19) outbreak. Int J Antimicrob Agents. 2020;56:106145. https://doi.org/10.1016/j.ijantimicag.2020.106145
30. Tran DH, Sugamata R, Hirose T, Suzuki S, Noguchi Y, Sugawara A, et al. Azithromycin, a 15-membered macrolide antibiotic, inhibits influenza A(H1N1)pdm09 virus infection by interfering with virus internalization process. J Antibiot. 2019;72(10):759-768. https://doi.org/10.1038/s41429-019-0204-x
31. Gibson PG, Yang IA, Upham JW, Reynolds PN, Hodge S, James AL, et al. Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomized, double-blind, placebo-controlled trial. Lancet. 2017;390(10095):659-68. https://doi.org/10.1016/s0140-6736(17)31281-3
32. Hinks TSC, Cureton L, Knight R, Wang A, Cane JL, Barber VS, et al. Azithromycin versus standard care in patients with mild-to-moderate COVID-19 (ATOMIC2): an open-label, randomized trial. Lancet Respir Med. 2021;9(10):1130-40. https://doi.org/10.1016/s2213-2600(21)00263-0
33. Hinks TSC, Cureton L, Knight R, Wang A, Cane JL, Barber VS, et al. Azithromycin versus standard care in patients with mild-to-moderate COVID-19 (ATOMIC2): an open-label, randomized trial. Lancet Respir Med. 2021;9(10):1130-40. https://doi.org/10.1016/s2213-2600(21)00263-0
34. Badawy IH, Hmed AA, Sofy MR, Al-Mokadem AZ. Alleviation of cadmium and nickel toxicity and phyto-stimulation of tomato plant by endophytic Micrococcus luteus and Enterobacter cloacae. Plants. 2022;11(15):2018. https://doi.org/10.3390/plants11152018
35. Grau S, Echeverria-Esnal D, Gómez-Zorrilla S, Navarrete-Rouco ME, Masclans JR, Espona M, et al. Evolution of antimicrobial consumption during the first wave of COVID-19 pandemic. Antibiotics. 2021;10(2):132. https://doi.org/10.3390/antibiotics10020132
36. HamİDİ AA, Yilmaz Ş. Antibiotic consumption in the hospital during COVID-19 pandemic, distribution of bacterial agents and antimicrobial resistance: a single-centre study. Journal of Surgery and Medicine. 2021;5:124-7.
37. Fouda HM, Sofy MR. Effect of biological synthesis of nanoparticles from Penicillium chrysogenum and traditional salt and chemical zinc nanoparticles on canola plant oil productivity and metabolic activity. Egyptian Journal of Chemistry. 2022;65:1-2.
38. Gonzalez-Zorn B. Antibiotic use in the COVID-19 crisis in Spain. Clin Microbiol Infect. 2021;27(4):646-647. https://doi.org/10.1016/j.cmi.2020.09.055
39. Castro-Lopes A, Correia S, Leal C, Resende I, Soares P, Azevedo A, et al. Increase of antimicrobial consumption in a tertiary care hospital during the first phase of the COVID-19 pandemic. Antibiotics. 2021;10(7):778. https://doi.org/10.3390/antibiotics10070778