ORIGINAL RESEARCH ARTICLE

Comparison of the Consumption of Expensive Antibiotics Based on Stewardship Guidelines Before, During, and After the Coronavirus Pandemic in Urmia in the Years 2019-2024

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Abstract

Background Using antibiotics thoughtfully not only protects patients from the risks of unnecessary treatment but also helps preserve the effectiveness of these medications by slowing the spread of antimicrobial resistance. Stewardship is an organized strategy to monitor the rational use of antibiotics, reduce drug resistance, and improve clinical outcomes. It is designed based on evidence-based guidelines and can help manage antibiotic use by providing guidance on rational antibiotic prescribing, educating physicians, limiting use, managing antibiotic prescribing software, and rotating antibiotics. This study aimed to compare the consumption of costly antibiotics based on stewardship guidelines before, during, and after the coronavirus pandemic.

Methods This descriptive comparative study was conducted at Shahid Motahari Educational and Medical Center in Urmia. Data on the consumption of expensive and inexpensive antibiotics were extracted from the hospital's HIS system, in accordance with the Ministry of Health's Stewardship Guidelines and the DOT criteria, during the period 2019-2024. Then, the percentage of consumption of costly antibiotics was calculated and compared according to the Ministry of Health Stewardship Guidelines. Finally, the data were analyzed using SPSS version 20 using repeated-measures ANOVA, and Bonferroni post-hoc test.

Results The results of comparing the three time periods showed that the use of antibiotics significantly increased during the COVID-19 period with significant changes compared to the pre-pandemic period ($p < 0.001$, mean = 4879.56). However, antibiotic use in the post-COVID-19 period significantly decreased compared during the COVID-19 ($p < 0.001$, mean = - 3604.46), although it remained higher than the pre-pandemic level ($p < 0.081$, mean = - 1275.10).

Conclusion The findings of this study emphasize the need to optimize antibiotic use and implement an antibiotic stewardship program to reduce side effects, costs, and drug resistance.

Keywords Antibiotics, Antimicrobial Stewardship, Covid-19, Pandemic

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1 Introduction

The SARS-CoV-2 coronavirus was first identified in Wuhan, China, when 41 cases of unexplained pneumonia were reported in December 2019. This virus is an enveloped, single-stranded RNA betacoronavirus belonging to the subgenus Sarbecovirus of the Coronaviridae family.[1] This global infectious disease presents unique complexities with multiple dimensions and consequences. Individuals exposed to the virus not only experienced physical complications but also faced extensive psychological impacts.[2] The pandemic exerted profound adverse effects on physical, mental, social, and economic health across society, even among those who were not infected, making daily life extremely challenging.[3]

Although there is no strong evidence supporting a specific drug for the treatment of COVID-19,[3] pharmacological interventions have remained a central component of therapy.[4] However, this does not imply that the use of medications in any form necessarily yields positive outcomes. Drugs, like a double-edged sword, can be both beneficial and harmful to health.[5]

Similar to other medications, antibiotics are associated with significant adverse effects, occurring in nearly 20% of hospitalized patients receiving them.[6] Previous studies have indicated a rising trend in bacterial resistance to commonly used antibiotics, likely due to their inappropriate or excessive use, highlighting the necessity of avoiding unjustified antibiotic prescriptions whenever possible.[7] Research further shows that antibiotics are prescribed to approximately 60% of hospitalized patients, of which 20–50% are unnecessary or inappropriate.[8,9]

Patients who receive unnecessary antibiotics are exposed to adverse drug effects without deriving any therapeutic benefit.[10] Moreover, the inappropriate use of antibiotics leads to antimicrobial resistance, a serious threat to public health. Misuse of antibiotics may also negatively impact patients who have never received them through the spread of resistant organisms.[11] The major consequences of improper antibiotic use include adverse drug reactions, prolonged hospitalization and increased costs, higher morbidity and mortality, elevated risk of secondary infections, and, most critically, the emergence of multidrug-resistant organisms.[12] Therefore, the rational and appropriate use of available antibiotics is essential to preserve their therapeutic value in modern medicine.[13]

Optimizing antibiotic use is crucial for effective infection management, protecting patients from the harms of unnecessary exposure, and combating drug resistance. Antibiotic stewardship programs can assist clinicians in improving prescribing practices, thereby enhancing clinical outcomes and minimizing harms and complications associated with irrational antibiotic use.[14] Accordingly, antibiotic stewardship systems represent one of the key strategies for rationalizing antibiotic prescribing in hospitals, with various studies demonstrating their impact in reducing microbial resistance and healthcare costs. Nonetheless, even in the United States, such programs are implemented in only a limited number of pediatric hospitals.[15,16]

Various strategies have been implemented to manage antibiotic use to reduce adverse effects and healthcare costs. One strategy is the Antimicrobial Stewardship Strategy, also known as the rational prescribing of antibiotics which was first introduced globally in 1996.[17] It was officially implemented in Iranian hospitals in 2017, with special emphasis on the unique conditions of these drugs.[18] The main approaches to antibiotic stewardship include providing evidence-based prescribing guidelines and physician education, restricting the use of certain antibiotics to approval by infectious disease specialists, reviewing physicians' orders with subsequent feedback, and implementing software-based prescribing management and antibiotic rotation policies. Each of these methods may be applied individually or in combination with others.[19] The stewardship strategy enhances the effectiveness of infection treatment while reducing treatment failures, the negative consequences of antibiotic resistance, hospital expenses, and length of stay.[20,21] Accordingly, the main objectives of these programs are to improve the quality of patient care and to stabilize or decrease microbial resistance rates.[18]

Antibiotic stewardship programs generally fall into two categories. The first includes educational strategies, such as presenting guidelines and instructions to assist physicians in appropriate antibiotic prescribing. The second consists of restrictive strategies, where prescribing certain antibiotics is not permitted without specific conditions or requires prior approval. In such cases, an antibiotic prescription form must be completed within a defined time frame.[22]

Several studies have confirmed the positive outcomes of implementing antibiotic stewardship programs in hospitals.[23] For instance, Elligsen et al. demonstrated a 23% reduction in antimicrobial drug use, along with improved sensitivity to meropenem.[24] Similarly, Rimawi et al. reported that implementation of stewardship programs not only reduced the consumption of broad-spectrum antibiotics but also decreased the duration of mechanical ventilation and length of stay in intensive care units.[25] It has been reported that successful implementation of these programs in hospitals requires educational initiatives, continuous monitoring of indicators and periodic outcomes, adequate feedback to clinical staff, and the involvement of a multidisciplinary team including infectious disease specialists, pharmacists, clinical microbiologists, epidemiologists, and representatives of infection control committees.[25]

Rationalizing drug use has always been a key objective of pharmaceutical policy-making. According to the World Health Organization, achieving rational drug use requires prescribing medications with proven therapeutic effectiveness that can meet the clinical needs of patients in a specific geographic setting with the lowest possible adverse effects and costs. Careful consideration of drug dosage and duration of therapy is equally important. Despite efforts to curb inappropriate antibiotic use, treatment costs related to antibiotics have continued to rise, particularly in developing countries. Moreover, the increasing prevalence of antibiotic-resistant strains and the reduced effectiveness of existing drugs have placed a substantial burden on healthcare systems. Since resistance has been most pronounced in countries with the highest antibiotic consumption, the adoption of new, more effective policies to curb excessive antibiotic use is urgently needed.

Accordingly, the present study was conducted with the aim of comparing the consumption of high-cost antibiotics based on stewardship guidelines before, during, and after the COVID-19 pandemic in Motahari Children's Hospital, Urmia.

2 Methods

This research was a descriptive, retrospective chart review conducted to compare the consumption of high-cost antibiotics based on stewardship guidelines before, during, and after the COVID-19 pandemic in Shahid Motahari Pediatric Specialty Hospital, Urmia. The study covered the period from October 2019 to March 2024 and utilized patient records available in the hospital's HIS system.

The study population included all hospitalized patients during this timeframe. The sample was selected through purposive census sampling and included all cases with at least one record of high-cost antibiotic use. antibiotics: Vancomycin, Liposomal Amphotericin B, Imipenem, Meropenem, Teicoplanin, Caspofungin, Colistin, Linezolid, or Voriconazole. Records that contained only low-cost antibiotics or had incomplete information were excluded from the study.

In total, 147,160 hospitalization records were available, of which 125,230 met the inclusion criteria.

Following approval of the study by the University Research Council and acquisition of the Ethics Code from the Ethics Committee, (IR.IAU.URMIA.REC.1401.142), the researcher, after obtaining an official introduction letter, referred to Motahari Pediatric Specialty Hospital in Urmia. In coordination with the HIS system administrator, data on antibiotic consumption, including both high-cost and low-cost antibiotics, were extracted for the period 2019–2024, corresponding to the pre-COVID-19, during-COVID-19, and post-COVID-19 phases.

Data collection was carried out using the standard checklist issued by the Ministry of Health, into which the extracted information was recorded. Data were analyzed based on the Days of Therapy (DOT) criterion.

The study variables included the use or non-use of high-cost antibiotics and the number of their prescriptions during the pre-pandemic, pandemic, and post-pandemic periods.

For data analysis, SPSS version 20 was used. A repeated-measures ANOVA was used for statistical testing. Before the main analysis, the assumptions of the test were examined using the Kolmogorov–Smirnov test and Mauchly's test of sphericity, both of which confirmed that the assumptions were met. Bonferroni post-hoc tests was used to compare differences on antibiotic consumption between three times points. A significance level of $p < 0.05$ was considered.

3 Results

The results showed that the most frequently used antibiotic before the COVID-19 pandemic was Meropenem 500 mg. , during the pandemic and post-pandemic was Meropenem 1 g as shown in Table 1.

Multivariate tests indicated a significant effect of the time factor. With an effect size of 0.774, there was a statistically significant difference in the consumption of the specified antibiotics across the three time periods—before, during, and after COVID-19 ($p = 0.001$). To further investigate the differences between the time points, Bonferroni post hoc tests were applied (Table 2). Comparison of the three time periods using the Bonferroni post hoc test revealed that antibiotic consumption before the COVID-19 pandemic differed significantly from consumption during the pandemic ($p < 0.001$). Similarly, consumption during the pandemic differed significantly from the post-pandemic period. Although antibiotic use after the pandemic increased compared to the pre-pandemic period, this difference was not statistically significant.

Antibiotic consumption increased markedly during the pandemic compared to the pre-pandemic period (Mean ± SD = 4879.56 ± 848.29; $p < 0.001$). Consumption decreased in the post-pandemic period compared to the pandemic period (Mean ± SD = 3604.46 ± 607.23; $p < 0.001$), although it remained higher than the pre-pandemic period (Mean ± SD = 1275.10 ± 500.09; $p > 0.081$) (Table 3).

Table 1 Frequency of high-cost antibiotic use across three time periods (before, during, and after covid-19)

Antibiotic name	Form & dose	Before COVID-19	During COVID-19	After COVID-19
Amphotericin-B Liposomal	50 mg Vial	3311	9131	3434
Caspofungin	50 mg/10 ml Vial	2453	5301	1737
Colistin	1,000,000 µAmp	2194	7584	4151
Teicoplanin 400	400 mg Vial	1930	4410	2259
Teicoplanin 200	200 mg Vial	1649	3328	991
Linezolid	600 mg/300 ml Vial	955	6848	4535
Imipenem	500 mg Vial	3691	10023	4965
Meropenem 1	1 gr Vial	954	12652	6233
Meropenem 500	500 mg Vial	4236	11105	5487
Vancomycin	500 mg Vial	953	1781	2689
Voriconazole	200 mg Vial	2997	6098	3789
Voriconazole	200 mg Tab	2717	8335	3073

Table 2 Repeated measures results for antibiotic consumption across three time periods (before, during, and after COVID-19)

Effect		P-value	F	Hypothesis df	Error df	Significance	Partial Eta Squared
Time	Pillai's trace	0.774	17/16	2/000	10/000	0/001	0.774
	Wilks' lambda	0.226	17/16	2/000	10/000	0/001	0.774
	Hotelling's trace	3.432	17/16	2/000	10/000	0/001	0.774
	Roy's largest root	3.432	17/16	2/000	10/000	0/001	0.774

Table 3 Bonferroni post hoc test results for antibiotic consumption across three time periods

Effect		Mean difference	Standard error	P-value
Before the COVID-19 pandemic	During the COVID-19 pandemic	-4879.56	848.29	< 0.001
	After the COVID-19 pandemic	-1275.10	500.09	< 0.081
During the COVID-19 pandemic	Before the COVID-19 pandemic	4879.56	848.29	< 0.001
	After the COVID-19 pandemic	3604.46	607.23	< 0.001
After the COVID-19 pandemic	Before the COVID-19 pandemic	1275.10	500.09	0.081
	During the COVID-19 pandemic	-3604.46	607.23	< 0.001

Post hoc test: Bonferroni correction

4 Discussion

This study aimed to compare the use of high-cost antibiotics based on stewardship guidelines before, during, and after the COVID-19 pandemic at Shahid Motahari Educational and Therapeutic Center in Urmia during 2019–2024.

The results indicated that antibiotic consumption increased significantly during the pandemic compared to the pre-pandemic period. In the post-pandemic period, antibiotic use decreased relative to the pandemic period, although it remained higher than the pre-pandemic level. These results are consistent with the findings of Heydargoy and Fukushige et al.[26,27] Specifically, a systematic review demonstrated that antibiotic consumption increased excessively during the pandemic in several countries, including Australia, Canada, and Japan, while stewardship programs were disrupted.[26] Similarly, a cross-sectional descriptive study found that approximately 21% of individuals used antibiotics during the COVID-19 outbreak, with 20% reporting that quarantine and fear of visiting healthcare centers led them to self-medicate. These observations suggest that fear of COVID-19 infection influenced healthcare-seeking behavior, promoted self-medication, increased inappropriate antibiotic use, and ultimately contributed to the antibiotic resistance crisis.[27] This finding may help explain the apparent discrepancy between the statistical data and researchers' expectations. Given the viral nature of COVID-19 and strict adherence to infection control protocols during the pandemic, it might have been expected that high-cost antibiotic use would decrease compared to the pre-pandemic period. Overall, the results of this study emphasize the necessity of optimizing antibiotic use and implementing antibiotic stewardship programs to reduce adverse effects, healthcare costs, and antimicrobial resistance.

Consistent with the present study, a study by Langford et al. entitled "Bacterial Coinfection and Secondary Infection in Patients with COVID-19" reported that during the COVID-19 outbreak, the impact of bacterial coinfections on viral respiratory infections increased. However, the prevalence, incidence, and characteristics of bacterial coinfections in COVID-19 patients remain poorly understood.[28] Identifying these infections can help prevent mortality and morbidity, reduce unnecessary antibiotic use, curb the spread of antimicrobial resistance, decrease treatment costs, and shorten hospital stays.[29]

Evidence suggests that COVID-19 can weaken the immune system, causing a significant reduction in lymphocyte counts. Lymphopenia is commonly observed in most patients during and after infection. One study found that lymphocyte levels can reliably predict COVID-19 severity.[30] Liu et al., examining the relationship between lymphopenia and COVID-19 severity among 115 patients, found a significant association between lymphopenia and disease severity.[31] These findings suggest that immunocompromised individuals are more susceptible to bacterial and viral infections, which, in turn, may contribute to increased antibiotic use.

During the COVID-19 pandemic, due to the high mortality and morbidity associated with the disease, as well as the severe clinical presentations requiring admission to intensive care units, mechanical ventilation remained a cornerstone of critical care.[32] Furthermore, immunosuppression in ICU patients increased their vulnerability to hospital-acquired infections, including ventilator-associated pneumonia, lung abscesses, and severe bacterial pneumonias. Patients requiring prolonged mechanical ventilation were at particularly high risk of nosocomial infections. Extended hospital stays facilitated the accumulation and proliferation of resistant bacteria within the hospital environment, thereby contributing to increased use of high-cost antibiotics and the escalation of antimicrobial resistance.

Additionally, the results of this study indicated that Meropenem was the most frequently used antibiotic across all three time periods—before, during, and after the COVID-19 pandemic. Findings from a study by Elsafi et al. similarly showed a significant increase in Meropenem use during the early months of the pandemic in Saudi Arabia compared to the pre-pandemic period. However, in subsequent waves of COVID-19, its use declined due to stewardship programs and other preventive measures, such as physical distancing, proper hand hygiene, and face masks, which helped prevent secondary bacterial infections.[33]

Meropenem is a potent carbapenem-class antibiotic used to treat serious bacterial infections. It acts by disrupting bacterial cell wall synthesis, leading to the destruction of a wide spectrum of bacteria, and is often reserved for severe infections when other antibiotics are ineffective. Its pharmacodynamics include strong bactericidal activity against both Gram-positive and Gram-negative bacteria. However, Meropenem carries a risk of serious allergic reactions, including anaphylaxis, and may also increase the risk of seizures.[34] Similarly, a study by Malik and Mundra. reported that during the COVID-19 pandemic, the most commonly used antibiotics, regardless of disease severity, were Ciprofloxacin and Azithromycin.[35]

Limitations of this study included incomplete clinical records, inaccurate entry of patient information and medications in the hospital HIS system, and the lack of assessment of patient-specific factors, such as demographic characteristics, disease severity, or underlying conditions, that may have influenced antibiotic use. Additionally, since this research was conducted in a single pediatric hospital, data from other hospitals were unavailable, preventing broader comparisons.

5 Conclusion

The findings of this study indicate that the consumption of high-cost antibiotics increased significantly during the COVID-19 pandemic compared to the pre-pandemic period. In the post-pandemic period, antibiotic use remained higher than the pre-pandemic level but decreased compared to the pandemic period. Across all three time periods, Meropenem was the most frequently used antibiotic. Based on these findings and considering the adverse effects of antibiotics, particularly high-cost antibiotics such as Meropenem, it is recommended that healthcare system administrators implement measures to ensure hospitals monitor antibiotic use closely. This includes strict oversight by hospital infection control committees, adherence to sterilization protocols, and regular infection surveillance. Medical professionals prescribing antibiotics must be made aware of the Antibiotic Stewardship Guidelines. Prioritizing preventive measures over the use of high-cost antibiotics can reduce hospital stays, lower the incidence of drug-resistant infections, and decrease financial burdens on patients and the healthcare system.

Declarations

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Artificial Intelligence Disclosure
The authors confirm that no artificial intelligence (AI) tools were used in the preparation of this manuscript.

Authors' Contributions
All authors contributed to the initial idea generation, study design, data collection, and manuscript drafting. All authors have read and approved the final version of the manuscript and declare no disagreement over its contents.

Availability of Data and Materials
The data and materials used in this study are available from the corresponding author upon reasonable request.

Conflict of Interest
The authors declare no conflicts of interest in the preparation of this study.

Consent for Publication
Not applicable.

Ethical Considerations
This study was derived from a research project approved by Islamic Azad University, Urmia Branch, under the Code of Ethics IR.IAU.URMIA.REC.1401.142.

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