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RESEARCH ARTICLE

Evaluation of Antibiotics Used in COVID-19 Patients in West of Iran: A Descriptive Study

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Abstract:

Introduction:

In coronavirus disease (COVID-19), antibiotics are frequently prescribed to treat bacterial co-infections. Moreover, antibiotics are one of the pre-eminent essential drugs utilized in treatment. However, due to their high cost and association with resistance, their consumption pattern is important to be considered. In this regard, the first step is to optimize the use of these drugs.

Objective:

Regarding limited data on assessing the pandemic effect on antibiotics used in Iran, this study aimed to describe the evaluation of antibiotics used in COVID-19 patients during the COVID-19 pandemic in West Iran.

Materials and Methods:

A total of 350 COVID-19 patients were enrolled in hospitals, and their characteristics, such as age, sex, ward, beginning and conclusion dates, organization intervals, dose, and the type of antibiotic utilized, were assessed. It was found that 180 COVID-19 patients received systemic antibiotics. Antibiotic administration was analyzed based on a Defined Daily Dose (DDD)/100-bed days (expended per 100-bed occupied days).

Results:

A total of 180 (51.43%) of the COVID-19 patients received antimicrobials, comparable to 219.62 DDD/100-bed days. Moreover, 85% of the antimicrobials were infused, and 15% were oral. Among the wards, the highest rate was in the infectious and intensive care unit (ICU) wards and the lowest in the obstetrics and gynecology wards.

Conclusion:

The use of antibiotics in patients with COVID-19 was assessed as very high, which should be reviewed in terms of the association between misuse of antibiotics and the emergence of resistance.

Keywords: Coronavirus disease, COVID-19, DDD/100 bed days, Antibiotics administration, Defined daily dose, Intensive care unit.

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1. INTRODUCTION

COVID-19 is currently the latest challenge and a threat to all human beings worldwide. The coronavirus was recognized by the international community in December, 2020. In a short time, it became a widespread pandemic worldwide [1 - 4].

Severe acute respiratory syndrome coronavirus 2 (SARS-

CoV-2) is a highly pathogenic and transmissible virus; this virus is spread mainly through droplets in the air and close contact with infected persons [4, 5]. The clinical symptoms of SARS-CoV-2 infected patients range from mild non-specific symptoms to severe pneumonia with organ dysfunction. The clinical symptoms of COVID-19 caused by the new SARS-CoV-2 are age-related [4, 6].

Bacterial co-infections are frequently determined in viral respiratory tract infections, such as influenza, and are a critical cause of dismalness and mortality. Therefore, convenient determination and antibacterial treatment are essential [4, 7].

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The recurrence, frequency, and understanding of bacterial co-infection in patients contaminated with SARS-CoV-2 are not clear; in these basic circumstances, this is a crucial knowledge gap [6, 8, 9]. In spite of the fact that antimicrobials are incapable of treating COVID-19, doctors endorse them for patients with suspected or archived COVID-19 for an assortment of reasons [10].

New information shows that using too many antibiotics during the COVID-19 outbreak could be dangerous because it might lead to bacteria that are resistant to many different types of antibiotics [11]. Using antibiotics too much and not in the right way can cause more problems like making the medicine not work well, getting worse infections, staying in the hospital longer, and making healthcare more expensive [12, 13]. Moreover, antibiotic resistance is a big problem for humans. It makes it difficult to fight against different infections and can be dangerous for our health [14].

There is a need to know more about how to fight against antibiotic resistance. Hospitals should have a group called Infection Control Committee to help people in this regard. It should be responsible for evaluating how many and what kind of antibiotics are used. Moreover, it should monitor how common germs spread and become resistant [15].

In order to determine the effectiveness of antibiotics, we must employ identical methods in order to assess and contrast their outcomes. We can do this by using a system called anatomical therapeutic chemical (ATC) to classify drugs and a way to measure how much of the drug is being used based on WHO recommendations. However, more research is needed to understand how antibiotics are used to treat infections in people with COVID-19. Researchers studied patients with COVID-19 at a hospital in Alimoradian Nahavand. The hospital helps patients who have COVID-19 with or without other health problems.

Regarding limited data on assessing the pandemic effect on antibiotics used in Iran, this study aimed to evaluate antibiotics used by COVID-19 patients during the COVID-19 pandemic in West Iran.

2. MATERIALS AND METHODS

This cross-sectional descriptive study was conducted on COVID-19 patients referred to Ayatollah Alimoradian Hospital in the city of Nahavand from December, 2021 to March, 2022.

2.1. The Selection Conditions of Patients Studied

Consolidation criteria for this consideration were based on

an overview that each suspected COVID-19 patient completed treatment after additional testing for lactate dehydrogenase (LDH), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) at the Ayatollah Alimoradian Hospital Medical Center in Nahavand, Hamadan.

All information was recorded by the Laboratory Information System (LIS). Patients with suspected COVID-19 illness had a real-time PCR test negative. Sampling was carried out utilizing the persistent purposive testing methodology, in which all COVID-19 patients who came and met examination criteria concurring with the goals were included until the required number of subjects was selected for data examination [4].

Data of all patients from clinic wards, including age, sex, inpatient ward, systemic antimicrobial utilized or used on occasions, sort of anti-microbial, estimations, interim between measurements and term of treatment, were removed.

Since the dosage utilized for each anti-microbial depends on the kind of antimicrobial, the estimation of each anti-microbial has to be measured in association with standard measurement. Utilization of the unrefined values of each antimicrobial for comparison with other antimicrobials and the estimation of common antimicrobial utilization were previously improper [16]. Therefore, the DDD system is prescribed by the WHO. To decide DDD, the normal upkeep dosage of the sedate is considered in an adult all through the course of the malady [16, 17].

Antimicrobial Consumption Index (ACI) (DDDs / 100-bed days) is utilized to indicate the DDD of the pharmaceutical consumed per 100 beds involved in the study [16, 17]:

$$\text{DDDs/ 100-bed days} = \frac{\text{Total dose in mg during study period} \times 100}{\text{DDD of drug} \times \text{study duration (days)} \times \text{bed strength} \times \text{Average bed occupancy rate}}$$

$$\text{DDD} = \frac{\text{Number of items issued} \times \text{amount of drug per item (mg)}}{\text{WHO recommended DDD of drug}}$$

For this data, information on the diverse wards counting (bed occupancy rate, number of beds per day, number of beds involved, *etc.*) was obtained from the Hospital Statistics Center at the specified time, and ACI for each anti-microbial and descriptive statistics (frequency, mean, *etc.*) was calculated utilizing SPSS v 22 software.

3. RESULTS

In this study, 350 patients were hospitalized, of which 180 (51.43%) received antibiotics, and their information was collected and analysed. Among them, 45.56% were females, and 54.44% were males (Table 1).

Table 1. Demographic information of COVID-19 hospitalized patients with antibiotics.

Variable	Total	Percentage (%)
Gender	-	-
Male	98	54.44
Female	82	45.56
Age	-	-
18-25	5	2.78
26-35	20	11.12

(Table 1) contd....

Variable	Total	Percentage (%)
36-45	25	13.9
46-55	16	8.88
56-65	46	25.55
≥ 65	68	37.77

Table 2. Analysis of antibiotic use based on ATC DDD/ 100-bed days in COVID-19 patients.

-	Antibiotic	ATC code*	Route of Administration	DDD WHO Standard	DDD/ 100 Bed Days
1	Ciprofloxacin	J01MA02	Oral	1	48.38
2	Vancomycin	J01XA01	Parenteral	2	70.18
3	Imipenem	J01DH51	Parenteral	2	64.33
4	Ceftriaxone	J01DD04	Parenteral	2	36.73

Note: * WHO Collaborating Centre for Drug Statistics Methodology Norwegian Institute of Public Health (Postboks 222 Skøyen 0213 Oslo Norway).

Table 3. Dosage of antibiotics by wards in the hospital in terms of DDD/100-bed days.

Hospital Ward	DDD/100 Bed-days* Ceftriaxone	DDD/100 Bed-days Ciprofloxacin	DDD/100 Bed-days Vancomycin	DDD/100 Bed-days Imipenem	Total
Surgery ward	6.10	8.08	8.12	9.10	31.40
ICU	8.16	10.90	13.10	17.16	49.32
Internal ward	7.5	12.10	15.20	10.08	44.88
Obstetrics and Gynecology ward	5.89	4.43	8.67	7.89	26.88
Infectious	9.08	12.87	25.09	20.10	67.14
Total	36.73	48.38	70.18	64.33	219.62

Note: * DDD per 100-bed days: The DDDs per 100-bed days may be applied when drug use by inpatients is considered.

3.1. Analysis of Antibiotic Use based on ATC DDD/100-bed day's Method

During the period from December, 2021 to March 2022, it was found that 180 patients received antimicrobials. The antimicrobials were then categorized based on the ATC code prescribed by WHO, so 4 groups of antimicrobials were obtained. The results of the calculation of the DDD as per WHO's standard are given in Table 2.

During the study, DDD/100-bed days of diverse types of antibiotics were calculated as 219.62 DDD/100-bed days in Ayatollah Alimoradian Hospital, 15% of which were orally and 85% injectable. Considering the assessment of the recurrence of antimicrobial utilization in hospitals, the most elevated rate of antimicrobial utilization had a place in infectious, intensive care units and internal wards sequentially. In the infectious and ICU wards, vancomycin and imipenem, and in the internal ward, ciprofloxacin and ceftriaxone were the most frequently used antimicrobials (Table 3).

4. DISCUSSION

This study assessed the utilization of antibiotics in COVID-19 patients in the Alimoradian Hospital during the COVID-19 outbreak from December, 2021, to March, 2022, in Nahavand. From the start of COVID-19 until the present, all patients confirmed positive for COVID-19 illness have had to be conceded to government-funded workplaces. Hence, we were able to consolidate all restorative records of COVID-19 patients. It allowed us to perform a comprehensive examination of the prevalence of antimicrobial utilization and the choice of

antimicrobial given to COVID-19 patients with suspected bacterial co-infection.

The difference in number and reality that males are more sensitive than females in COVID-19 cases may be due to the closeness of comorbidities and diverse high-risk behaviors, such as male smoking [18, 19].

It has been reported that the expression of Angiotensin-Converting Enzyme 2 (ACE2) is higher in males than in females due to different sex hormones; therefore, males are more likely to suffer from COVID-19 and have poorer clinical outcomes due to a strong association between ACE2 and COVID-19. However, other studies found that upregulation of ACE2 in COVID-19 can protect organs from injury [20]. It has been observed that the risk of COVID-19 is higher in people aged ≥ 65 years old (37.77%), which is an early elderly category. Elderly patients are at a more prominent risk of disintegration due to changes in the body's physiology and the presence of comorbidities. Older people have typical resistance that reduces with age, affecting the natural and versatile resistant frameworks to control viral diseases, making them susceptible to contamination [21]. They are additionally more vulnerable to the unfavorable impacts of drugs utilized to treat comorbidities [22].

In radiology finding, it has been found that COVID-19 is frequently characterized by pneumonia, making it difficult to recognize between bacterial or viral causes, so clinicians carry out anti-microbial treatment.

In this study, 189 (51.43%) patients received antibiotic

therapy. Antibiotic therapy is generally not recommended for patients with COVID-19 unless bacterial pneumonia has been proven. Caution should be exercised when administering antibiotics to COVID-19 patients as they may be overused, thus leading to the rise of multidrug-resistant bacteria [12].

In the study by Wenjuan Cong *et al.*, the rate of antibiotic use in patients with COVID-19 without clinical justification was 51.5%, which was similar to the use of antibiotics in the patients in this study [1,23, 24]. In another study by Nadhirah Mohamad *et al.*, the prevalence of antibiotic use was 17.1%, and 5.5% of them were prescribed two or more types of antibiotics [25].

Langford *et al.* reported in a meta-analysis study involving a large population of COVID-19 patients in UK hospitals that 75% of hospitalized COVID-19 patients received antibiotics, although only 8% had bacterial co-infection [26].

Nevertheless, the global scenario is the empirical use of antibiotics in patients with COVID-19. Studies have shown that among patients with COVID-19 who were systematically taking antibiotics, about 90% of patients were prescribed empirically [27 - 29]. This could exacerbate the already serious problem of antibiotic resistance.

Our results showed that the antibiotics vancomycin, imipenem, ciprofloxacin, and ceftriaxone were the most commonly prescribed in patients with COVID-19. Moreover, in the study by Nadhirah Mohamad *et al.*, the foremost frequent antimicrobials endorsed were amoxicillin/clavulanic acid, ceftriaxone, piperacillin/tazobactam, azithromycin, and meropenem [25].

The utilization was low in this study (36.73%), while in studies conducted by Molla *et al.* and Goncalves *et al.*, ceftriaxone was the second most common antimicrobial utilized among COVID-19 patients, where it was prescribed at a rate of nearly 54.0% [30, 31]. The difference is due to different healthcare systems, antibiotic regimens and infection control measures put in place during the pandemic. Assessment of the antimicrobials utilization quantitatively was at that point carried out utilizing the method prescribed by WHO, specifically ATC DDD/100-bed days.

The results of the calculation of DDD/100-bed days of antibiotic treatment in moderate-to-severe COVID-19 patients from December, 2021 to March, 2022 obtained a total result of 219.62 DDD/100-bed days. These data suggest prescribing empiric antibiotic therapy without microbiological evidence of infection. We have seen a significant increase in antibiotic drug use during the pandemic. On the other hand, the microbiological profile did not correspond to the frequency of consumption. Based on our findings, the age of COVID-19 patients increased had a direct relationship with the amount of antibiotic use in terms of DDD/100-bed days (P-value <0.05).

Administration of antibiotics to COVID-19 patients needs further studies as COVID-19 infection is caused by a virus and not a bacterium. This low rate of bacterial co-infections in COVID-19 patients indicates that antibiotics are not suitable for COVID-19 patients unless the patient has a proven bacterial co-infection. Due to the culture of self-medication, Iran is one of the largest consumers of antibiotics in the world, and studies

also reported that the amount of antibiotics prescribed by clinicians in COVID-19 patients is too high. The misuse of antibiotics is also a major problem worldwide [32].

Unnecessary prescriptions of antibiotics in patients with COVID-19 increase the risk of *Clostridioides difficile* infection and antimicrobial resistance [26]. The worldwide spread of antibiotic resistance has increased the need to develop new antimicrobial agents [33, 34]. Regardless of the net impact of COVID-19 on antibiotic resistance, the principles of antimicrobial stewardship should guide antibiotic management of COVID-19 patients [8]. Prospective studies are needed that assess the role of antibiotic initiation in patients with severe COVID-19 and identify appropriate parameters for safe antibiotic cessation (*e.g.*, based on imaging, clinical criteria, and/or biomarkers) [26].

CONCLUSION

This study demonstrated that the consumption of antibiotics in patients with COVID-19 was high during the epidemic of this disease. Health researchers and public health specialists need to be concerned regarding the observed rise in antibiotic use during the COVID-19 pandemic, which should be reviewed in terms of the association between the misuse of antibiotics and the emergence of resistance.

LIST OF ABBREVIATIONS

ACE2	= Angiotensin-Converting Enzyme 2
LDH	= Lactate Dehydrogenase
CRP	= C-reactive Protein
ESR	= Erythrocyte Sedimentation Rate
LIS	= Laboratory Information System
ATC	= Anatomical Therapeutic Chemical
SARS-CoV-2	= Severe Acute Respiratory Syndrome Coronavirus 2

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The project was approved by the Ethics Committee of Hamadan University of Medical Sciences with the ethics code (IR.UMSHA.REC.1399.914).

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. The study on humans was conducted in accordance with the ethical standards of the Helsinki Declaration and Good Clinical Practice.

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants of this study.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article are available within the article.

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CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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