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Pharmacotherapy of Hospitalised Patients with COVID-19 at a Tertiary Care Hospital in Nepal

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ABSTRACT

Introduction

The COVID-19 pandemic poses a major health threat with no standardized treatments for SARS-CoV-2. This study evaluates pharmacotherapy trends in COVID-19 patients during the second wave at a tertiary care facility.

Methods

A retrospective, observational, cross-sectional study was conducted in a tertiary care centre, utilising patient data from April 2021 to July 2021. The sample included 310 patients admitted with a confirmed diagnosis of COVID-19. Patients were classified based on oxygen requirement levels, and data were analysed using descriptive statistics.

Results

Of the 310 patients, 59% were male and 41% female, with a mean age of 53.37 ± 17.01 years. The average hospital stay was 10 ± 7.15 days. Most patients (66.8%) required supplemental oxygen, and 7.4% required mechanical ventilation. The majority received antibacterial therapy (307, 99.03%), with ceftriaxone being the most commonly prescribed antibiotic (73.22%). Remdesivir was the predominant antiviral, and dexamethasone was used in 88.39% of patients.

Conclusion

Antibiotic use was extensive among hospitalised COVID-19 patients, with ceftriaxone being the most common. Antiviral use was less frequent, with Remdesivir being the preferred choice. Dexamethasone played a crucial role in managing severe cases.

Keywords

Antibacterial; COVID-19; hospitalised patients; remdesivir

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INTRODUCTION

Coronavirus disease (COVID-19) has created a global health challenge like no other. Ever since its inception in Wuhan, China in the month of December, 2019; it has affected more than 200 countries with WHO declaring it a public health emergency of international concern.[1] Without exception, Nepal has also been greatly affected by the COVID-19 pandemic with more than 725,000 total reported cases more than 10,000 deaths as of 13 August 2021.[2]

One of the reason COVID-19 has posed as a big threat globally is because of its high transmission rate, lack of established therapies and standard treatment guidelines.[3,4] SARS-CoV2, also named previously as novel coronavirus (2019 nCoV), the causative agent of COVID-19, is a beta coronavirus similar to Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), based on its genomic proximity.[5,6] Currently, there are no therapeutic drugs specifically targeting SARS-CoV-2, but several treatments have shown potential, including antivirals (such as Remdesivir and Favipiravir), antimalarials (Chloroquine and Hydroxychloroquine), antiparasitic agents (Ivermectin), antibiotics (Azithromycin and Teicoplanin), as well as anti-inflammatory agents and immunomodulators (including corticosteroids, Tocilizumab, interferon-B, and convalescent plasma).[7-12]

There is a great need to determine the emerging trends of pharmacotherapy for COVID-19 cases throughout the world as it is constantly changing.

METHODS

This retrospective, observational cross-sectional study was conducted at the Department of Clinical Pharmacology at a tertiary care centre. Data collection was done between February 2022 and May 2022. We used the list of patients admitted to our centre with a diagnosis of COVID-19 during the second wave of the pandemic (from April 2021 to July 2021) as the sampling frame. The patients were categorised based on the inpatient wards where they were initially admitted.

The sample size was calculated by using following formula: $n= z^2 p (1-p)/ d^2$

Where,

n=Sample size

Z=Desired confidence level, Z value for 95% confidence limits=1.96

p=prevalence = 0.52 [13]

d= desirable error= (0.05)

Using the values, the sample size was calculated to be = $(1.96)^2 *0.52(1-0.52)/ (0.05)^2 = 383$

However, since the number of patients admitted at our centre during the above mentioned window period was finite (1600), the sample size was re-adjusted for finite population size and was found to be 310. The sampling interval was found to be 5. The first sample was selected randomly by lottery method following which every 5th patient was included in the study.

All patients admitted to our centre with a diagnosis of COVID-19 who were at least 18 years old were included in the study. However, pregnant women, patients who left the hospital against medical advice, those discharged upon their request, those transferred or referred to another centre, and those not receiving any medications were excluded from the study. The data were obtained from the medical record files (admission file, daily progress notes, CARDEX and discharge notes) from the medical record section and recorded in the proforma sheet.

Severity Level of Covid-19 based on O_2 requirement at admission where no oxygen requirement was coded as 1, Non-invasive oxygen requirement as 2 and mechanical ventilation as 3.

Thus collected data were entered in MS Excel 2019 and were analysed using SPSS version 22. Descriptive statistics were used to present the number of drugs prescribed and their frequency.

RESULTS

Among the 310 patients, 183 (59%) were male with the mean age being 53.37±17.01 and mean duration of hospital stay was 10±7.15 as shown in (Table 1).

It was seen that the majority of patients 207 (66.8%) required non-invasive (via face mask) supplemental oxygen (severity grade 2) followed by 73 (23.2%) patients not requiring any supplemental

Table 1. *Sociodemographic of the patients*

Characteristics		Number
Age	<20	6 (1.9%)
	21-59	189 (61%)
	>60	115 (37.5%)
Sex	Male	183 (59%)
	Female	127 (41%)
Province	Koshi	14 (4.5%)
	Madhesh	16 (5.2%)
	Bagmati	242 (78.1%)
	Gandaki	7 (2.3%)
	Lumbini	20 (6.5%)
	Karnali	2 (0.6%)
	Sudurpashchim	9 (2.9%)

Table 2. Total number of antibacterial agents used according to the severity of the COVID patients

Severity	Total Number of Antibacterial Used, n (%)					
	0	1	2	3	4	5
1 No oxygen requirement	2(2.78)	28 (38.89)	31 (43.06)	9 (12.50)	2 (2.78)	0 (0.00)
2 Non-invasive supplemental oxygen (via face mask)	1 (0.48)	73 (35.27)	98 (47.34)	27 (13.04)	6 (2.90)	2 (0.97)
3 -Invasive supplemental oxygen (via mechanical ventilation),	0 (0.00)	2 (8.70)	4 (17.39)	10 (43.48)	6 (26.09)	1 (4.35)
Unknown	0 (0.00)	3 (37.50)	3 (37.50)	1 (12.50)	0 (0.00)	1 (12.50)
Total	3	106	136	47	14	4

Unknown-information missing in the records

oxygen (severity grade 1) and 23 (7.4%) requiring supplemental oxygen via mechanical ventilation (severity grade 3). There were eight (2.58%) patients whose oxygen requirement at the time of admission was not clearly mentioned and was classified as of unknown severity. Most of the patients admitted with no supplemental oxygen requirement or with non-invasive supplemental oxygen (via face mask) requirement were found to be prescribed two antibacterial agents, 31(43.06%) and 98 (47.34%) respectively (Table 2) . Four (1.29%) patients were receiving up to five antimicrobial agents.

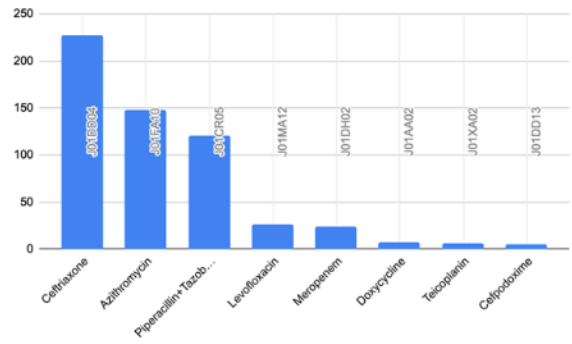

Figure 1. The top ten antibacterial agents prescribed to patients included in this study

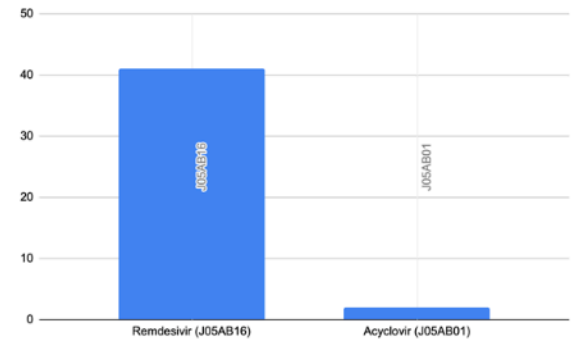

Figure 2. The proportion of antiviral agents prescribed to patients included in this study

Table 3. Other medication used in Covid-19 patients

Generic Name	ATC Code	Frequency
Dexamethasone	H02AB02	274
Pantoprazole	A02BC02	250
Enoxaparin	B01AB05	226
Paracetamol	N02BE01	114
Insulin	A10AB01	33
Codeine	R05DA04	25
Zinc	A12CB	25
Vit-C	A11GA	24

Only a small proportion of patients received an antiprotozoal agent (13, 4.19%). Similarly, the number of patients receiving any antiviral agent(s) (34, 10.97%) was also small.

Among patients admitted to the hospital for up to 15 days, the number of patients receiving five and six medicines were highest (46, 18.11%), and there were three patients who received 13 medicines. Among those staying for 16-30 days, 10 (21.74%) were prescribed eight medications. In this group, there was one patient who received 16 medicines during hospital stay. In the group of patients hospitalised for more than 30 days, three patients (30%) received five medications.

It was seen that ceftriaxone (227, 73.22%) with ATC code J01DD04 was the most common antibacterial agent prescribed to the patients included in this study. Among the antivirals, 42 patients were found to be prescribed with remdesivir (ATC code J05AB16). Similarly, metronidazole (ATC code J01XD01) was the most commonly prescribed antiprotozoal to the patients included in this study, as shown in figure 1.

Among the medicines other than antimicrobials, it was seen that most of the patients (274, 88.39%) received dexamethasone (ATC code H02AB02). Similarly, the list of ten most common other medicines used for the management of COVID-19 patients along with their ATC codes has been presented in Table 3.

DISCUSSION

Pharmacotherapy for hospitalised COVID-19 patients has evolved significantly since the early days of the pandemic. Given the limited experience in managing COVID-19, medicine availability, cost consideration, etc. prescribing patterns have varied across countries, with different antimicrobials being tried. The regimen also varied within Nepal, making it important to evaluate the prescribing patterns in COVID-19 patients. In our study, majority of patients were middle aged and male which is similar to findings of Manandhar et al. and Han et al.[14,15]

In our study, antibacterial therapy was used in 307 patients (99.03%) indicating a higher use of antibacterial with Ceftriaxone being the most commonly used antibacterial. Similar study conducted in Nepal shows the antibacterial use prevalence of 98.1%, where Cephalosporin was used in 85% of cases.[16] In contrast, Azithromycin was commonly used (87.5%) in study by Lata et al.[17] In contrast to the finding of our study, a study conducted by Han. Et. al found out that antiviral agents were most commonly prescribed to Covid-19 patients.[15] A 2020 study found 71% of hospitalised COVID-19 patients received antibacterial, despite only 1% having bacterial infections. Early reports linked 50% of COVID-19 deaths to bacterial co-infections.[18]

Study conducted from Electronic database from Mass General Brigham, US demonstrated that patients with the most severe COVID-19 (intubated or admitted to an intensive care unit) were over 3.5 times more likely to receive COVID-19 drug therapy compared to those with the least severe disease (hospitalised but not requiring supplemental oxygen).[13] In contrast, our study had increased use of medication more in patients with moderate severity (patients using non-invasive oxygen supplementation).

Remdesivir was the most commonly prescribed antivirals which is similar to the finding by Lata et al.[17] Likewise, Remdesivir was used in 21 (15.4 %) patients in study by Manandhar et al.[14] As our hospital caters the healthcare needs of patients from different socio-economic backgrounds, the affordability of the antivirals like Remdesivir could be one of the contributing factors for its less utilisation of the medicine. The need to prescribe multiple medicines in patients could have occurred due to the severity of the disease, existing co-morbidities and empirical antimicrobial therapy to prevent development of any hospital acquired infections (HAIs).

Also, Dexamethasone was the most prevalent drug used in categories other than antimicrobials, which is also evident in other studies due to evidence of lowering the risk of death among patients on mechanical ventilators and those receiving oxygen therapy.[19] The World Health Organization (WHO) and the European Medicines Agency (EMA) have also endorsed the use of dexamethasone for patients requiring oxygen or mechanical ventilation, recommending a dosage of 6 mg once daily for up to 10 days.[20] Contrast to this, the most common medicines used were vitamin C (90.4%), vitamin D (90.4%), Zinc (90.4%) and Pantoprazole (72.8%) in a study by Manandhar et al.[14]

The world has seen an information boom during the pandemic, and treatments were initiated based on poor recommendation. The fast pace of evolving evidence during a pandemic poses a challenge in prescribing dilemma among the prescribers. There is a need to establish hospital protocols with frequent revisions to maintain the rational use of medicines. There were initial recommendations for the use of corticosteroids in COVID-19 cases, which led to significant immunosuppression and ultimately exposed the patients to multiple opportunistic infections. The risk of spread of HAIs could also be a driving factor for the frequent use of antibacterial agents in the patients admitted at our centre.

Limitations of our study, including its single-centred design and small sample size, suggest that further research is needed to confirm these trends in broader settings. Therefore, our findings may not be generalizable to other settings.

CONCLUSION

Our study highlights the significant use of antibacterial in hospitalised COVID-19 patients, with ceftriaxone (ATC code: J01DD04) being the most commonly prescribed. It was seen that majority of the patients required non-invasive supplemental oxygen (severity grade two). Among them, majority were prescribed two antibacterial agents. Antiviral use, particularly remdesivir, was also prevalent, while corticosteroids like dexamethasone played a crucial role in the management. The findings underscore the need for rational prescribing practices and the development of updated hospital protocols to ensure appropriate use of medications, especially in the context of evolving evidence.

It was seen that majority of the patients required non-invasive supplemental oxygen (severity grade two). Among them, majority were prescribed two antibacterial agents.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Research concept: AM, ST. Research design: AM, PP. Literature review: AM, PP, BM, AB. Research experiment: AM, PP, AP, BM, AB. Data collection and analysis: AM, PP, AP, BM, AB, ABL, RG, RK. Statistical analysis: AM, PP, AP, AB, ABL, RG, RK, ST. Manuscript preparation: ALL

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