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Original Research Article

Drug Utilization Pattern

Drug Utilization Pattern Among COVID-19 Patients in A Tertiary Care Centre: An Observational Study

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Abstract: Drug utilization study was defined by the World Health Organization as the study of marketing, distribution, prescription, and use of drugs in a society, with special emphasis on medical, social, and economic consequences. The coronavirus disease 2019 (COVID-19) outbreak has quickly swept across the world and has been declared a Public Health Emergency of International Concern. There were 4.47 crores of COVID-19 cases in India, with 5.3 lakhs of deaths as of Dec 23, 2022. However, only a few studies evaluated the pattern of use of drugs among patients with COVID-19 in India. Hence, the current study analyzed the drug utilization pattern among COVID-19 patients at our tertiary care center (GMC/GGH) in Ongole, Andhra Pradesh, India. It is an observational, retrospective study. Case records of 100 patients coming to OP or admitted at our tertiary care center with COVID-19 from March to December 2021 were taken as the study sample. Fifty patients belonged to group A (asymptomatic and mild COVID-19 and 50 patients belonged to group B (moderate and severe COVID-19). Drug utilization pattern was assessed using the World Health Organization indicators. A total of 859 drugs were prescribed for 100 patients. Among them, 249(28.9%) were antibiotics. 219(25%) were injections. 678(78.9%) were prescribed in generic names, and 745(81%) drugs were prescribed from the national list of essential medicines of 2022. There is a significant difference in all 5 WHO indicators between groups A and B. There is a knowledge gap in many drugs used to treat COVID-19. Evidence-based pharmacotherapy for patients with COVID-19 is vital to enhance valuable healthcare resources during the pandemic. The information derived from this research work will be handed over to the stakeholders for implementing modifications wherever needed to improve clinical outcomes.

Keywords: COVID-19, Drug utilization pattern, WHO indicators, Remdesivir, Tocilizumab

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1. INTRODUCTION

The WHO (World Health Organization) defined a drug utilization study as the study of marketing, distribution, prescription, and use of drugs in a society, with special emphasis on medical, social, and economic consequences.[1] It helps identify the clinical use of drugs in various populations and its impact on the healthcare system. The coronavirus disease 2019 (COVID-19) outbreak has quickly swept across the world and has been declared a Public Health Emergency of International Concern (PHEIC)· In India, there were 4.47 crores of COVID-19 cases with 5.3 lakhs of deaths as of Dec 23, 2022.[2] Significant mortalities in COVID-19 are due to various emerging variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[3] along with inappropriate management options and a lack of preparedness to control the pandemic. The effect of the COVID-19 pandemic on the healthcare system of each country was different, based on the balance between demand and supply of services, which was linked to an ability to expand no. of hospital beds, especially in the ICU, and public health policies to contain the spread of the pandemic.[4-5] Amid the need to find effective management for COVID-19, antibiotics, antivirals, antimalarial, immunomodulatory, and corticosteroids were chosen as therapeutic measures that help decrease mortality, the need for mechanical ventilation, and other complications.[6-7] Most of the drugs proposed have a possible mechanism of action on SARS-CoV-2 or the pathology of the disease.[8-9] But most drugs didn't show enough efficacy through clinical studies, and others needed more evidence to be recommended. Even though they are used and prescribed routinely, bringing the risk of drug interactions and side effects.[10-11] Most patients show mild to moderate illness that only needs symptomatic treatment and home quarantine. But, elderly patients with underlying chronic disorders may develop severe illnesses requiring hospitalization.[12-13] Also, there were no effective treatment options to prevent the progression of the disease to severe illness. Symptomatic treatment and oxygen therapy are commonly given to hospitalized patients. Critical cases were managed using mechanical ventilation. Many drugs are repurposed as potential treatment options for COVID-19. Repurposing is a process of detecting existing drugs for novel indications. It has been the forefront clinical approach in managing the COVID-19 pandemic effectively. It is reported that more than 75% of drugs can be repurposed for novel indications. In India, various repurposed drugs like tocilizumab, dexamethasone, remdesivir, and azithromycin are recommended in managing hospitalized patients with COVID-19.[14]. As per the clinical protocol given by the ministry of health and family welfare, India, Remdesivir should be given to patients with moderate to severe COVID-19 within 1st ten days of illness only.[15] But most protocols and guidelines were not followed strictly, and various concerns regarding medication choices and safety issues exist.[16] So, it is the need of the hour to assess drug utilization patterns among COVID-19-positive patients in India. Hence, the current study aimed to assess the pattern of drug utilization among COVID-19 patients at a tertiary care center (GMC/GGH) in Ongole, Andhra Pradesh, India. To assess the drug utilization pattern occurring at a tertiary care center among COVID-19-positive patients per WHO indicators of drug utilization.

2. MATERIALS AND METHODS

It is an Observational, Retrospective study. The study is observational, as no therapy was given to any study patients as part of the study. Case records of patients coming to the outpatient unit or admitted at our tertiary care center with COVID-19 from March 2021 to December 2021 were taken as the study sample. Sample size: As per the study done by Murhekar et al.[17], the prevalence of COVID-19 among adults in India was 0.73%. Using Epi Info Software, the sample size was calculated per the population survey model: $N=Z^2PQ/E^2$, where N=sample size, Population proportion: 0.73%, Q=1-P, E-Error: 2%, Confidence level:98%. After calculation, the minimum sample size came to 99. So, we included data from 100 patients. The data of all 100 patients was complete. Patients were divided into two groups. Group A: Asymptomatic and mild COVID patients-50 in number. Group B: Moderate to severe illness patients- 50 in number

2.1. Inclusion criteria

Case records of COVID-19-positive male and female patients aged above 18 years attending OP or hospitalized in the ICU, general medicine, and pulmonology departments at our center were included.

2.2. Exclusion criteria

Case records of patients admitted with other types of pneumonia, pregnant and lactating women, and patients with incomplete data were excluded.

2.3. Study procedure

The data of patients were collected from the case sheets available in the Medical Records Department, GMC/GGH, Ongole. The severity of COVID-19 was assessed per the National Institute of Health (NIH), United States guidelines.[18] This study was conducted after getting approval from the institutional ethics committee. Data from the case sheet was entered in a case record form designed for the study and subjected to statistical analysis.

2.4. Definitions

- WHO drug prescribing indicators are as follows:[19]

1. The average number of drugs prescribed per patient
2. Percentage of drugs prescribed by generic name
3. Percentage of antibiotics prescribed
4. Percentage of injections prescribed
5. Percentage of drugs prescribed from the essential medicine list

- COVID-19 positivity was confirmed using RT PCR report
- The severity of COVID-19 was assessed as per NIH guidelines[18], which is as follows: Asymptomatic: Patients who tested positive for SARS-CoV-2 using RT-PCR test but who have no symptoms
- Mild illness: Patients with various signs or symptoms of COVID-19 but do not have dyspnoea or abnormal chest imaging.
- Moderate illness: Patients with lower respiratory infections had an oxygen saturation ≥94% on room air at sea level.
- Severe: Patients with SpO_2 <94% on room air at sea level, a respiratory rate >30 breaths/min, or lung infiltrates above 50% in the chest radiograph.

- As a part of WHO indicators, the National essential medicine list of 2022 was followed.[20]

2.5. *Ethical considerations*

Permission from the Institutional ethical committee attached to GMC/GGH, Ongole, before conducting the study. (Ref: Ethical committee registration number: ECR/1351/INST/AP/2020) We obtained written permission to use medical records from the superintendent of our hospital and the medical records section-in-charge to use data for conducting and publishing the study.

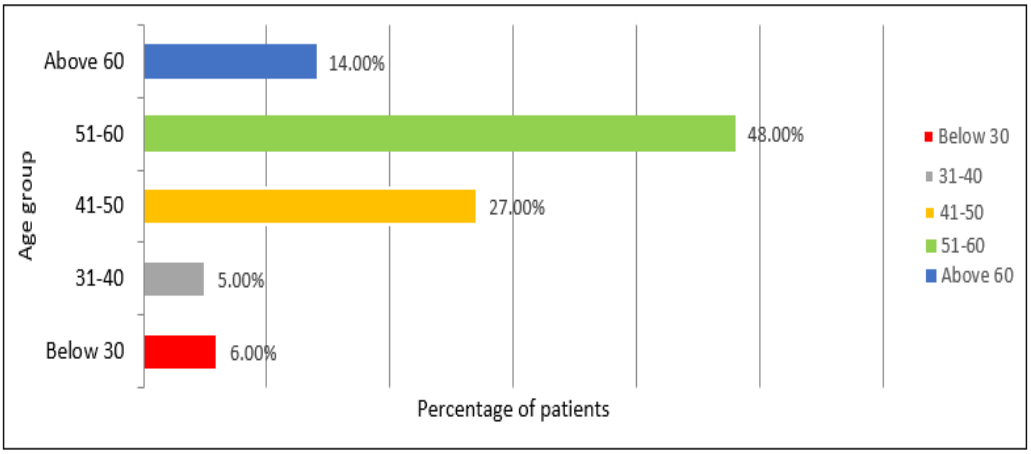
3. STATISTICAL ANALYSIS

The data collected was entered in MS Excel 2019, and analysis was carried out using Microsoft excel and statistical software called Epi info version 7.2.5 free version. First, frequencies and percentages were used. Next, comparing proportions between groups A and B was done using Z- the test. Next, numerical variables were compared using the student's T-test. Finally, a comparison between categorical variables was made using the chi-square test. A p-value less than 0.05 is considered significant.

4. RESULTS

4.1. *Age*

There is a significant difference in the mean age between groups A and B, as per the T-test (P=0.0001). The mean age of patients in group A was 38.9±2.3 years, and the mean age in group B was 47.6±2.7 years. It implies that moderate to severe COVID-19 is more common among elderly patients. Age of the patients ranged from 19 to 68 years.



Graph 1: Age distribution of patients

Graph 1 shows the age distribution of patients in the current study. Most patients (48%) were aged 51-60 years. 27% of patients were aged 41-50 years. 5% of patients were aged 31-40 years. 6% of patients were below 30 years, and 14% were above 60 years. Patients with COVID-19 who were admitted were aged above 50 years commonly.

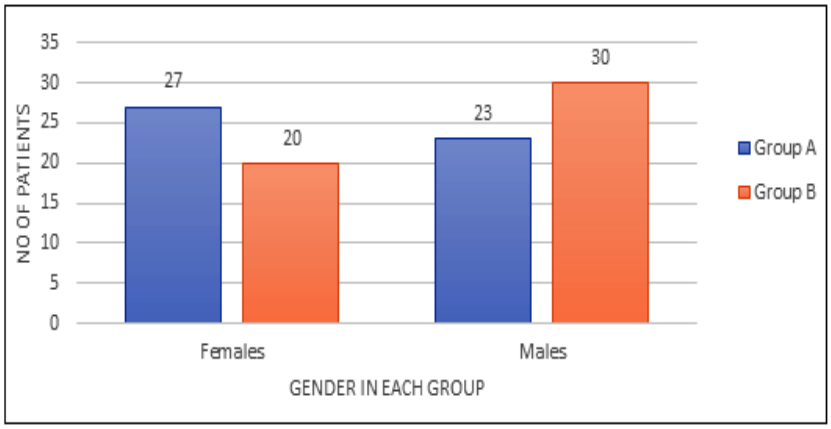
4.2. *Gender*

Overall 53% of patients were males.

Table 1: Association between Gender and Severity

Gender	Group A	Group B	Total
Females	27	20	47
Males	23	30	53
TOTAL	50	50	100
Chi-square		1.96	
P value		1.60	

Table 1 illustrates the association between gender and the severity of COVID-19. Overall, 53% of patients were males, and 47% of patients were females. Among males, 23 belonged to group A and 30 belonged to group B. Among females, 27 belonged to group A and 20 belonged to group B. There is no significant association between gender and group(P=1.6), as per the chi-square analysis.



Graph 2: Gender distribution in each group

Graph 2 illustrates the association between the gender of patients in each group in the current study. Fifty patients belonged to group A, and 50 patients belonged to group B. There were 27 females and 23 males in group A. There were 20 females and 30 males in group B. There is almost equal distribution of gender, without gender bias for comparison.

4.3. Types of drugs used by patients

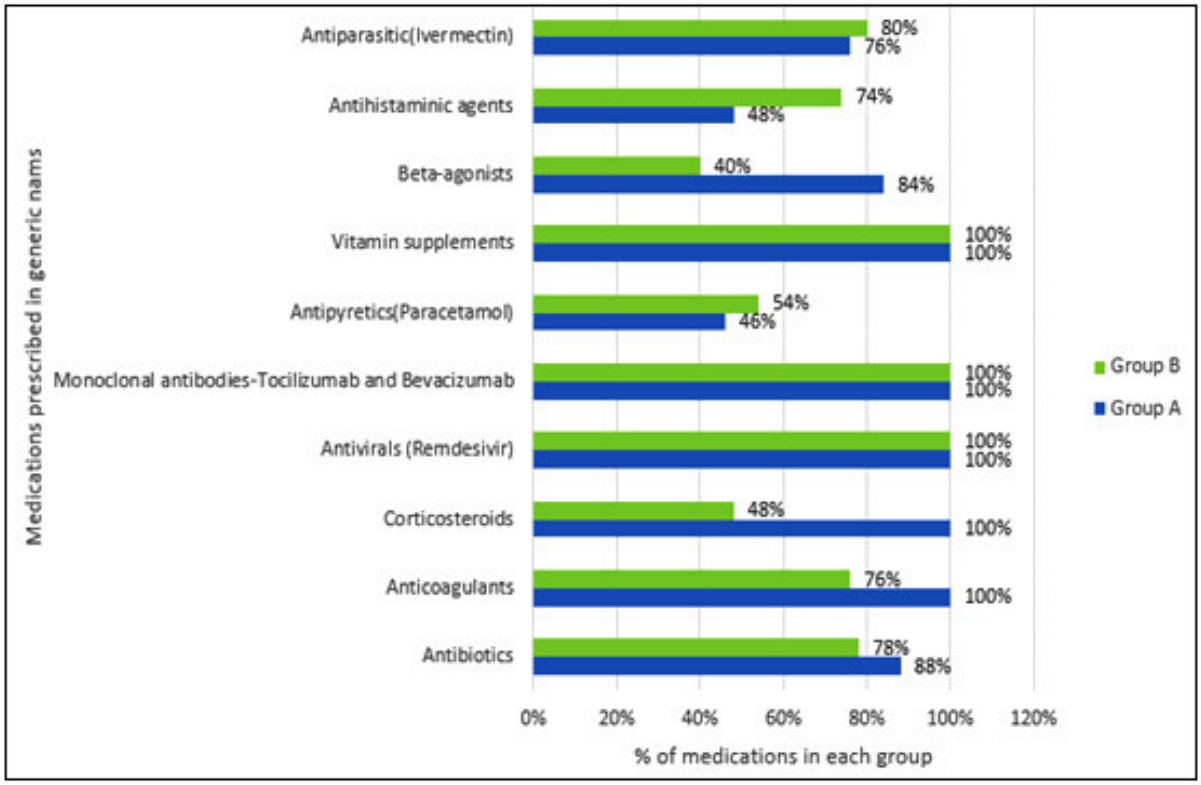
Among antibiotics, cefotaxime was most commonly used. Among anticoagulants, heparin was most commonly used. Among corticosteroids, methylprednisolone was most commonly used.

Table 2: Types of drugs used by patients in both groups

Class of drugs	Drug name	Group A(%)	Group B(%)	Total (%)
1. Antibiotics	Inj. Cefotaxime	10%	36%	23%
	Tab Cefixime	18%	26%	22%
	Tab Azithromycin	10%	12%	11%
	Tab. Doxycycline	8%	2%	5%
2. Anticoagulants and antiplatelet agents	Tab Aspirin	2%	40%	21%
	Tab Rivaroxaban	Nil	2%	1%
	Inj Heparin	Nil	54%	27%
3. Corticosteroids	Tab Methylprednisolone	2%	42%	22%
	Inj Hydrocortisone	Nil	34%	17%
	Inj. Dexamethasone	Nil	12%	6%
4. Antivirals	Inj. Remdesivir	6%	42%	24%
5. Monoclonal antibodies	Inj Tocilizumab	Nil	14%	7%
	Inj Bevacizumab	Nil	2%	1%
6. Antipyretics	Tab Paracetamol	96%	98%	97%
7. Vitamin supplements	Tab Vitamin C	100%	100%	100%
	Tab Vitamin D	100%	100%	100%
	Tab Zincovit	100%	100%	100%
8. Beta-agonists	Inj Salbutamol	4%	54%	29%
	Tab Pirfenidone	20%	4%	12%
9. Antihistaminic agents	Tab Levocetirizine	34%	42%	38%
	Tab Cetirizine	8%	20%	14%
10. Others	Tab. Ivermectin	6%	2%	4%
	Tab Hydroxychloroquine	2%	Nil	1%

Table 2 illustrates the types of drugs used by COVID-19 patients in our study. Most asymptomatic and mild COVID-19 patients (group A) used vitamin supplements and paracetamol. Most moderate to severe (group B) COVID-19 patients used anticoagulants and corticosteroids apart from paracetamol and vitamin supplements. Monoclonal antibodies weren't used by any patients in group A but by 16% of patients in group B. All patients used more than 1 drug.

4.4. *Generic name*



Graph 3: Prescription of drugs by generic names

Graph 3 illustrates prescriptions of drugs by generic names. All antivirals, monoclonal antibodies, and vitamin supplements were prescribed in their generic names to all patients in both groups. Antipyretics were rarely prescribed by their general name in both groups. 84% of drugs used by group A patients and 74% used by group B patients were prescribed in their generic name.

4.5. *Parenteral preparations(injections)*

18% of antibiotics were prescribed as injections for group A patient, and 86% were prescribed as injections for group B patients. Remdesivir, Tocilizumab, and Bevacizumab are available only as injections. None of the anticoagulants or corticosteroids is used as injectables for group A patient.

Table 3: Usage of injectables among both groups

	Injections	Group A (% of drugs)	Group B (% of drugs)
1.	Antibiotics	18%	86%
2.	Anticoagulants	0	66%
3.	Corticosteroids	0	76%
4.	Antivirals (Remdesivir)	100%	100%
5.	Monoclonal antibodies-Tocilizumab and Bevacizumab	0(not used)	100%
6.	Paracetamol	0	14%
7.	Vitamin supplements	0	0
8.	Beta-agonists	0	0
9.	Antihistaminic agents	0	0
10.	Ivermectin	0	0
11.	Others	8%	2%
	T	11%	40%

Table 3 illustrates the usage of Injectable among both groups. 18% of antibiotics were prescribed as injections for group A patient, and 86% were prescribed as injections for group B patients. Remdesivir, Tocilizumab, and Bevacizumab are available only as injections and prescribed as such. Anticoagulants or corticosteroids were not prescribed for group A patient. Vitamin supplements, beta-agonists, and antihistaminic agents; ivermectin was not prescribed as injections for any patient in both groups.

4.6. *Drugs from the National list of essential medicine list of 2022*

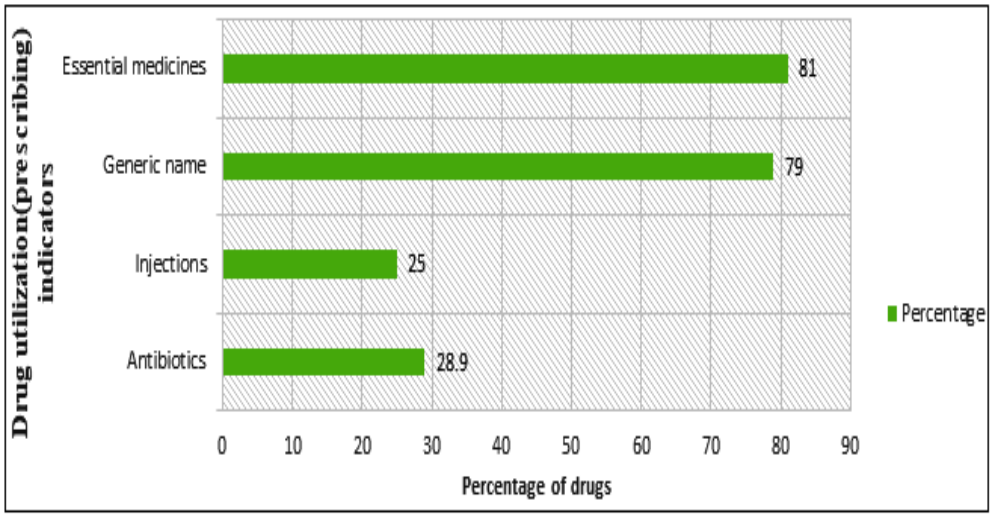
Remdesivir, Tocilizumab, Bevacizumab, levocetirizine, and Rivaroxaban drugs were not available in the essential medicine list of India 2022.

Table 4: Drugs from national list			
	National list of essential medicines	Group A (% of drugs)	Group B (% of drugs)
1.	Antibiotics	100%	100%
2.	Anticoagulants	100%	100%
3.	Corticosteroids	100%	100%
4.	Antivirals (Remdesivir)	0	0
5.	Monoclonal antibodies-Tocilizumab and Bevacizumab	NA (no one used)	0
6.	Paracetamol	100%	100%
7.	Vitamin supplements	100%	100%
8.	Beta-agonists	100%	100%
9.	Antihistaminic agents	66%	68%
10.	Others	100%	100%
	Total	85%	77%

Table 4 illustrates drugs that were prescribed from the essential medicine list. Remdesivir, Tocilizumab, Bevacizumab, Levocetirizine, and Rivaroxaban drugs were not available in the essential medicine list of India 2022. All antibiotics, corticosteroids, antipyretics, vitamin supplements, and beta-agonists were prescribed from the essential medicine list of India 2022. 66% of antihistaminic agents prescribed for group A patients and 68% for group B were available in the essential medicine list.

4.7. WHO drug utilization indicators

A total of 859 drugs were prescribed for 100 patients. Among them, 249 (28.9%) were antibiotics. 219(25%) were injections. 678(78.9%) were prescribed in generic names, and 745(81%) drugs were prescribed from the national list of essential medicines of 2022.



Graph 4: World health organisation drug utilization indicators

Graph 4 illustrates World health organization drug utilization indicators among all patients in the current study. A total of 859 drugs were prescribed for 100 patients. 81% of medications were available in the national essential medicine list of 2022. In addition, 79% of drugs were prescribed in generic names, 25% were prescribed and used as injections, and 28.9% of medications prescribed were antibiotics.

Table 5: WHO Indicators among both groups				
WHO Indicators	Group A	Group B	Z score/T value	P value
Average(Mean) Number Of Drugs Prescribed Per Patient	297 for 50 patients=5.94	562 for 50 patients=11.24	T value=12.61	< .00001
Antibiotics Among Total Drugs	65 out of 297	184 out of 562	Z score=-3.33	=00008
Drugs Prescribed In Generic Name	249 out of 297	429 out of 562	Z score=2.5	=0.01
Injections	14 out of 297	205 out of 562	Z score=-10.15	< .00001
Drugs From The National List Of Essential Medicines 2022	285 out of 297	460 out of 562	Z score=5.7	0.01

Table 5 illustrates the world health organization's drug utilization indicators. There is a significant difference in the average number of drugs prescribed per patient, antibiotic usage, drug prescription in generic name, no. of injections prescribed, and no drugs from the national list of essential medicines 2022 between the two groups. All were more in

group B patients, i.e., patients with moderate and severe COVID-19.

5. DISCUSSION

Prescriptions of 100 COVID-19-positive patients who attended our tertiary care center were analyzed to know drug utilization patterns with special emphasis on W.H.O drug utilization(prescribing) indicators in our study. Demography: Most patients (48%) were aged 51-60. 27% of patients were aged 41-50 years. Most of the patients belonged to the age group 41-60 years. 53% of patients were males. Males are slightly more than females (47%) in our study. This finding was similar to the retrospective study of Orlando V et al.[21] in which authors analyzed the data of 1532 COVID patients and found males were more commonly affected by COVID-19. Most of the patients were aged 40-59 years. A total of 897 drugs were prescribed. Most commonly prescribed include antipyretics and vitamin supplements among patients in both groups. Remdesivir was used by 24% of patients overall. Corticosteroids were used by 46% of patients overall, 74% of patients, and anticoagulants used antibiotics by 50% of patients overall in our study. The usage rate was less compared to the study of Mustafa et al.[22] COVID-19 hospitalized patients was included. Remdesivir was used by 45% of patients. Corticosteroids were used by 93.9% of patients, antibiotics by 84.9%, and anticoagulants by 60.1% of patients. The difference in usage rate was because we included asymptomatic, mild COVID-19 patients, but Mustafa et al.[22] included only hospitalized COVID-19 patients. But still, the prevalence of usage of corticosteroids was high in our study. The efficacy of corticosteroids like dexamethasone among COVID-19 patients was well defined in the RECOVERY trial[23] done in the United Kingdom using oral or injectable dexamethasone, which demonstrated decreased 28-day mortality among severe COVID-19 patients receiving ventilation and among hospitalized patients who are on non-invasive oxygen therapy but, no significant benefits were found among patients who did not need oxygen or ventilatory support. So, it is not advisable to prescribe corticosteroids for asymptomatic and mild COVID-19 patients. Among antibiotics, cefotaxime was most commonly used. Among corticosteroids, methylprednisolone was most commonly used in our study. Moderate and severe COVID-19 patients used corticosteroids and antiviral and monoclonal antibodies more than mild illness patients. In the study of Feng Sun et al.,[24] 165 COVID-19 patients were included, and the most commonly used antibiotic was Moxifloxacin. Corticosteroids were more common in the severe COVID-19 patient group than in the non-severe group, similar to our study. Antibiotics are not recommended for treating any viral infection, even COVID-19. Irrational usage of antibiotics is reported globally among patients with COVID-19, even without secondary bacterial infection. One systematic review[25] determined the use of antibiotics among patients with COVID-19 and found around 74.6% of patients with COVID-19 received antibiotics, though the prevalence of secondary bacterial infections was only 8.6%. It is necessary to start an antibiotic stewardship program at every teaching hospital to restrict the irrational usage of antibiotics and the emergence of resistance. Among anticoagulants, heparin was most commonly used. Overall usage of anticoagulants was 50% in our study, all used in prophylactic doses. Two randomized controlled trials proved the efficacy of anticoagulation therapy with heparin for COVID-19 patients. The results showed that the rate of thrombotic events decreased more with therapeutic dosing than with prophylactic dosing. Only 38.5% of patients in our study received anticoagulants in therapeutic doses.[26,27] The percentage of drugs prescribed by their generic name was 79%, and 81% were from the essential medicine list in our study. In the study by Desalegn et al.[28] at a teaching hospital, the authors used WHO drug utilization indicators. They found that 98.7% of drugs were prescribed in generic names, and 96.6% were from essential medicine lists. Only 81% of drugs were covered in the essential medicine list because Tocilizumab, Bevacizumab, and Remdesivir were not yet included in the essential medicine list of 2022, and they are reserved for only severe COVID-19 patients. There is a need to enhance generic medication prescriptions because of the cost burden on patients. Growing evidence suggests that generic drugs are equally good as branded drugs regarding bioequivalence and therapeutic equivalence.[29-32] provided all generic products should pass through quality assurance programs. Despite evidence that certain drugs like chloroquine, ivermectin, and hydroxychloroquine cause more drug-drug interactions and serious adverse effects like Q-T prolongation, raised liver enzymes, and skin rashes, with no added benefit in COVID-19, few patients were prescribed hydroxychloroquine and ivermectin in our study.[33-34] Hence, we highly recommend rational usage of drugs, i.e., using the right drug at the right doses at the right time for the right duration. There were no serious adverse effects to any of the drugs used. There was recent evidence that the prescription of drugs between men and women, by age and geographical area. We recommend future studies in this area. [35,36] Small sample size is one of the main limitations of the study. The study results can't be extrapolated to the general population, as our study was done in a single center.

6. CONCLUSION

This study is one of the few observational studies done in India to explore the drug usage pattern in patients with COVID-19. One hundred patients used a total of 897 drugs. There was a significant difference in the average no. of drugs used, no, of antibiotics used, no. of injectables used, no, of generics prescribed, and no. of drugs in the essential medicine list by asymptomatic and mild patients with moderate to severe COVID-19 patients. We provided a vital glimpse into utilization patterns of various medications routinely used to treat COVID-19. Evidence-based pharmacotherapy for patients with COVID-19 is vital to enhance valuable healthcare resources during the pandemic. The information derived from this research work will be handed over to the stakeholders for implementing the modifications wherever needed for the betterment of the patient and the community.

7. ACKNOWLEDGMENTS

We want to express my sincere thanks to Dr. Vijay Kissinger, Nodal officer of COVID-19, institutional ethics committee, and Principal and Superintendent of our college. In addition, we thank all our patients who participated in the study.

8. AUTHORS CONTRIBUTION STATEMENT

Ramya Rachamanti designed and drafted the whole study. Rajesh collected the medical records. Solomon Raju monitored the entire process. Finally, all the authors read and approved the final version of the manuscript.

9. CONFLICT OF INTEREST

Conflict of interest declared none.

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