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Drug Utilisation Study among COVID-19 Inpatients in a Tertiary Care Hospital in Eastern India

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ABSTRACT

Introduction: Coronavirus disease-2019 (COVID-19) is a global pandemic without any specific treatment to date. Drug utilisation plays a vital role in helping the health care system to understand the pattern of drug use.

Aim: To assess the prescribing trends among COVID-19 patients admitted to the hospital.

Methodology: This was a retrospective cohort study conducted at a tertiary hospital dedicated to COVID-19 patients. Patients admitted in AIIMS, Patna from March 2020 to October 2020 were analyzed for WHO core prescribing indicators and was compared with the standard WHO values.

Results: The median value of drugs prescribed was found to be 7 (IQR-6-8). The most common drugs prescribed for COVID-19 were Azithromycin (25.95%), hydroxychloroquine (23.88%) followed by paracetamol (20.17%) and Heparin (16.35%). The percentage of drugs prescribed by generic name was 77.72%. The average number of drugs from NLEM was 92.56%. Drugs were classified based on the Anatomical Therapeutic and Chemical Classification (ATC) and the majority of the drugs belonged to the J category which is the anti-infective group of drugs. The defined daily dose (DDD) /100 bed-days of azithromycin and cefixime was 5.2 and 0.092, respectively.

Conclusion: Polypharmacy being the common finding, the concept of generic prescribing was practised well. There was a lesser number of prescriptions containing drugs from the National List of Essential Medicines, and the number of prescriptions containing antibiotics and injections was following criteria. The WHO prescribing criteria were met with moderate adherence.

Key Words: Drug utilisation, COVID-19, WHO prescribing criteria, Anatomical Therapeutic Chemical Classification (ATC), Defined Daily Dose (DDD), Polypharmacy

INTRODUCTION

SARS-CoV-2 coronavirus causing Coronavirus disease 2019 originated in Wuhan, China in December 2019 and has spread rapidly across the world due to its high transmissibility and pathogenicity.[1] It was shortly declared as a Public Health Emergency of International Concern and On March 11, a global pandemic was declared.[2] Since then many drugs have been tried to treat COVID-19 infection but the effort has mostly been focused on repurposing existing medicines. The drugs that may be reused are from different pharmacological categories i.e. antimalarial, anthelmintic, anti-protozoal, anti-HIVs, anti-influenza, antineoplastics, neutralizing antibodies, immunoglobulins, and interferons.[3] These drugs have been used as a single agent or in combination, unfortunately, no medicine has yet been officially approved to treat COVID-19. The treatment guidelines for COVID-19 vary from one country to another. However, the treatment protocols across the countries are almost similar and vary very slightly and include hydroxychloroquine, chloroquine phosphate, Remedesivir, azithromycin, tocilizumab and lopinavir/ritonavir.[4] In India COVID-19 treatment guideline has been changed several times based on the latest research data. Indian Council of Medical Research (ICMR), New Delhi recommended hydroxychloroquine for prophylactic purposes in asymptomatic healthcare workers and household contacts of laboratory-confirmed patients.[5] The Government of India, Ministry of Health & Family Welfare, Directorate General of Health Services (Emergency Medical Relief (EMR) Division), recommended lopinavir/ritonavir after

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proper informed expressed consent from the patient.[6] The Government of India, Ministry of Health & Family Welfare, Directorate General of Health Services (Emergency Medical Relief (EMR) Division), recommended HCQ for mild to moderate case, low molecular weight heparin and steroid for moderate to severe case of COVID-19.[7] Spanish Society of Hospital Pharmacy recommended lopinavir/ritonavir, Remdesivir, hydroxychloroquine, chloroquine, darunavir/cobicistat, tocilizumab interferon and alfa-2B,beta-1B.[8,9] US FDA has not yet approved any drug for COVID 19 although some information regarding the drugs recommended for the treatment has been provided by the Centers for Disease Control and Prevention and includes Remdesivir, chloroquine, hydroxychloroquine, and lopinavir/ritonavir.[10] The drugs like Remdesivir, favipiravir, chloroquine phosphate, plasma, and traditional Chinese medicine was recommended by the National Health Commission of the People's Republic of China.[11] At present there is the limited number of study which summarizes the drug Utilisation in corona infected patients in a tertiary care hospital in India. Drug utilisation focus on the factors related to the prescribing, dispensing, administering, and taking of medication, and the related events including medical and non-medical determinants of drug utilisation, the effects of drug utilisation, as well as how drug utilisation relates to the beneficial or adverse effects of drug use.[12,13] Therefore this study has been designed to assess the prescribing trends among COVID-19 patients admitted to a tertiary care hospital in India. This study will be helpful to educate the prescribers, adherence towards rational drug therapy for safety and benefit to the patient.

MATERIALS AND METHODS

This retrospective observational study was carried out at All India Institute of Medical Science (AIIMS), Patna, (Bihar) India. COVID-19 patients, admitted to AIIMS Patna from March 2020 to October 2020 were included in the study. Medical Records of (n = 300) COVID-19 patients from the Medical Record Department (MRD) were evaluated for 3 months. Data were recorded on a standardized format in which information on drug utilisation among COVID-19 patients which include patient's demographic details (age, sex, duration of hospitalisation) and details of prescribed drugs (name, dose, therapeutic class, dosage form, route of administration, dosing frequency, etc.,) was retrieved from in-patient case files. Details of standard intravenous fluids, oxygen, vaccines and blood transfusion were not recorded. The prescription pattern was analysed using WHO's core prescribing indicators. Drugs are divided based on pharmacological action on the organ or system and their therapeutic and chemical properties in the anatomical therapeutic chemical (ATC) classification.[14]The World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology defines the defined daily dose (DDD) as a statistical measure of drug consumption. For grouping related drugs, it is defined in conjunction with the ATC Code drug classification system. The DDD allows for drug usage comparisons between different drugs in the same group or between different health care environments which were calculated by the following formula.[15]

DDD/ 100 bed -days =

Drug consumption in mg x 100

DDD (mg) x no. of days in study period x total no. of beds x occupancy index

The total number of beds used was 300 and the average occupancy index was 0.85. The occupancy index for every month was calculated by the Medical Records department. The occupancy index is the average monthly occupancy index for the three months of our study period.

Statistical analysis: Data were captured on Microsoft excel. The results were expressed as actual numbers, means, median (IQR) frequency (percentages) using SPSS software version 16.0., and were presented using tables.

RESULTS

Three hundred medical records of patients with confirmed COVID-19 patients were evaluated. The demographic and clinical characteristics of the patients are shown in Table 1. Of the total study population, 71.33% were male. A median number of seven medications (IQR, 6–8) were administered for the patients. Diabetes (21%) and hypertension (21%) was the most common comorbidity followed by hypothyroidism (14.28%) and hypercholesterolemia (8.4 %).

Table 1: Demographic and clinical characteristics of the patients.

Study Population	N (%)
No. of patients	300
Age, year	
<40	103(34.33%)
40-60	131(43.66%)
>60	66(22%)
Hospital stay, median IQR, days	12(11-16)
No. of drugs, median IQR	2097, 7 (6-8)
Sex	
Male	214(71.33%)
Female	86(28.66%)
ICU admission	23(7.66%)

Table 1: *(Continued)*

Study Population	N (%)
Any Comorbidities	
Diabetes	25(21%)
Hypertension	25(21%)
Diabetes + Hypertension	23(19.32%)
Hypothyroidism	17(14.28%)
Hypercholesterolemia	10(8.40%)
Asthma	5(4.20%)
Cancer	5(4.20%)
Coronary Artery Disease	4(3.36%)
Chronic Kidney Disease	3(2.52%)
Left Para Aortic Paraganglioma	1(0.84%)
Pulmonary Embolism	1(0.84%)

The analysis of drug utilisation using WHO core prescribing indicators revealed that the percentage of encounters with antibacterials and injectables was 15.63% and 11.82%, respectively. The percentage of drugs prescribed with a generic name and from the Essential Drug List of India was 77.72% and 92.56%, respectively (Table 2).

Table 2: WHO core prescribing indicators.

Core Indicators	Result(%)
The average number of drugs prescribed per encounter	6.97
Percentage of encounter with antibiotic	15.63
Percentage of encounter with injection	11.82
Percentage of drugs with the generic name	77.72
Percentage of drugs from EML	92.56

WHO: World Health Organisation, EML: Essential Medicine List

Looking at the individual drugs the most commonly prescribed drugs for COVID-19 patients include azithromycin (25.95%) hydroxychloroquine (23.88%), followed by paracetamol (20.17 %) and heparin (16.35%) from antimicrobial, analgesics, anti-inflammatory and an anticoagulant class of drugs, respectively.[Table 3]

Table 3: Medication prescribed for the COVID-19.

Drugs	No. of Patients (%)	
Azithromycin	238	25.95
Hydroxychloroquine	219	23.88
Paracetamol	185	20.17
Low Molecular weight Heparin	150	16.35

Table 3: *(Continued)*

Drugs	No. of Patients (%)	
Corticosteroid	78	8.5
Remdesivir	28	3.05
Piperacillin Tazobactum	19	2.07
Monoclonal Antibodies	3	0.32

The World Health Organization (WHO) defines polypharmacy as "the administration of many drugs at the same time or the administration of an excessive number of drugs". Polypharmacy may be defined as the administration of five or more than five drugs simultaneously which is evident in our study. [Table 4]

Table 4: Indicating degree of polypharmacy.

No. of drugs	No. of Prescriptions	(%)
2-5	68	22.66
6-7	150	50
8-10	82	27.33

Table 5 shows the Defined daily doses (DDD) by anatomical therapeutic chemical (ATC) classification codes of various drugs utilized among COVID-19 inpatients.

Table 5: Anatomic Therapeutic Chemical Classification code and DDD/100 bed-days of selected drugs.

Drug name	ATC code	DDD/100 bed-days
Vitamin C	A11GA	23.96
Azithromycin	J01FA10	5.2
Hydroxychloroquine	P01BA02	3.7
Levocetirizine	R06AE09	2.12
Pantoprazole	A02BC02	1.6
Paracetamol	N02BE01	0.52
Enoxaparin	B01AB05	0.19
Cefixime	J01DD08	0.092
Ceftriaxone	J01DD04	0.05
Levofloxacin	J01MA12	0.03

DISCUSSION

Drug Utilisation study is an important tool for ensuring quality in hospital drug use. The WHO core indicators of prescribing practice assess healthcare providers' performance in key dimensions related to drug safety. As a result, the purpose of this study was to examine the prescribing indicator that will aid in the promotion of rational drug use to improve drug safety.

The average number of drugs per encounter in our study was 6.97, which was higher than the national average. WHO recommended range is 1.6-1.8.[16] Our finding was higher than that of Hazra et al. (3.2)[17] some international studies, such as Wang et al. (3.52),[18] Bimo et al. (3.8)[19], and other Indian studies, such as Rehan et al. (2.4)[20] Tripathy et al.(2.9).[21]

The number of drugs prescribed in each encounter ranged from two to ten, with 27.33 % of encounters prescribing eight or more drugs, indicating a polypharmacy trend (Table 4). This was in line with Tripathy et al findings (30%).[21] Polypharmacy has a variety of consequences, including adverse drug reactions, drug-drug interactions, therapeutic failure, and toxicity, reduces patient compliance, unnecessary drug costs, and the risk of bacterial resistance emergence when antibiotics from different classes are prescribed to the same patient without reason.

In our study, the percentage of drugs prescribed by generic names was 77.72%, which is less when compared to the standard WHO ideal value of 100%. It was higher than the findings of Chandelkar and Rataboli's study (0.05%)[22], Rehan et al. (1.5%)[20], Tripathy et al. (68 %),[21] Hazra et al. (46.2),[17] and other international studies.[23,24]

The analysis of two common expensive modes of drug administration such as antibiotics and injections showed that the percentage of encounters with antibiotics prescribed was 15.63%, which is less than the standard range of 20-26.8 % of the WHO prescribed values. The finding of other studies conducted in India such as Hazra et al. (72.8%),[17] and Tripathy et al. (47.75 %) respectively.[21] Lower rates of antibiotic prescribing in our study due to the viral origin of COVID-19.

The percentage of encounters with injections in our study was 11.82% which was lesser than the standard range of WHO ideal value (13.4-24.1%). It was higher to the findings from Tripathy et al. (8%)[21] but very low compared to another region, South Ethiopia (38.1%)[23] and Uganda (48 %).[25]

The percentage of drugs prescribed by the NLEM in our study was 92.56%, which was lower when compared to the ideal standard value of 100%. This finding was much more to findings from studies of other parts of India such as Hazra et al. (45.71%).[17] The percentage of prescribing drugs from the essential drug list is lower in India[17] compared to other countries such as Ethiopia (99%), South Ethiopia (99.6%),[23] and Nepal (88%).[19] This difference may be due to the lack of awareness of the essential drug list. Between the mean of the estimated parameters, demographic data, it is involved in all of this, is similar to the findings in other studies.[26] Compared to studies from Dubai where the patient name was missing in 2.9%, age in 9.7%, and sex in 12%.[27] Lack of demographic indicators will lead to the source of serious medication error such as dispensing of medication to the wrong patients. The diagnosis was mentioned in 100% of prescriptions which was slightly more than other study results Shipra et al. (64.66%).[26] The doses of drugs were mentioned for 100% of the drugs which was similar to other study results such as Shipra et al. (100%).[26] Dosage form was mentioned in 100% compared to other study results Shipra et al. (98.66%).[26]Duration of treatment was mentioned in 100% compared to 92.66% in Shipra et al.[26] The DDD per 100 bed-days ranges from 23.96 to 0.03. Vitamin C was found to be the most commonly prescribed drug with DDD per 100 bed- days of 23.96 followed by antimicrobials 5.37. Among the antimicrobials, the defined daily dose (DDD) /100 bed-days of azithromycin and cefixime was 5.2 and 0.092, respectively. Our study reports the highest use of vitamin C. which plays a very important role as an immune modulator[28,29] and since this study was performed during the COVID-19 pandemic where vitamin C was used very widely and this could be the possible reason behind the highest use. The DDD per 100 bed-days of azithromycin, cefixime and ceftriaxone, levofloxacin was found to be much lesser than other studies.[30]

This study has certain limitations as it is retrospective a time-bound study with a small sample size and among COVID-19 patients. It was not possible to assess the rationality and quality of prescriptions. However, it helps to create a drug Utilisation database in a tertiary care teaching hospital of a developing country.

CONCLUSION

The WHO core prescribing indicators were met with moderate adherence. With the prevalence of polypharmacy, the concept of generic prescribing has been practised well. The prescription of NLEM drugs, antibiotics, and injections was within normal limits. Drug utilisation among covid-19 as well complied with AIIMS-Patna covid management protocol.

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Ethical Approval and informed consent: The study was approved by the Institutional Ethics Committee, AIIMS Patna (Ref. No. AIIMS/Pat/IEC/2020/647 Dated 25/01/2021). Waiver of informed consent was granted as patient details were anonymized and only medical records of hospitalized COVID-19 patients were analyzed.

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Conflict of Interest: None declared

Author's contribution: Manjhi PK analyzed data and wrote the manuscript. Singh SK wrote the introduction and Kumar R analyzed data. Priya A. and Nishi collected data from Medical Record Department. All authors read this manuscript.

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