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Pharmacotherapy for Hospitalized Patients with Covid-19: A Drug Utilization Study in a COVID-19 dedicated Unit of a Tertiary Hospital in Ghana

Charles NK Ofei-Palm[1,2*], Priscilla Ekpale[1], Evelyn Pokuaa Gyekye[1], Florence Amah Nkansah[1], Jatoe Dong[1] , Anthony Osei[1], Nicholas Adjimani[3], Augustina Koduah[4], Daniel Ankrah[1]

Abstract

The coronavirus disease 2019 (COVID-19) pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has also presented an unprecedented challenge to identify effective drugs for prevention and treatment. And in view of that, it is important to understand the determinants and patterns of pharmacological treatment over time as such knowledge helps to contextualize and understand the drivers of treatment in the management of COVID 19 patients

This was a retrospective study conducted in a COVID-19 confirmed positive hospitalized patients at a dedicated unit of a tertiary hospital A total 88.6% (47/53) had comorbidity (s). The mean age of the study participants was 47.1 ± 17.9 years. Women accounted for 58.5%, (31/53) positivity of the patients A total of 493 drugs were prescribed to manage COVID-19 symptoms and co-existent comorbidity(s) The mean medication per patient was 9.3±4.3. Per the various dosage forms, the mean per injection per patient was 2.6±1.7 whilst that of oral dosage form the median was 6±2.3 The most commonly prescribed class of drugs were Multivitamins/supplements (108, 27.1%), followed by anticoagulants (65, 16.3%), antihypertensive (64, 15.8%), antibiotics (64, 15.8%) and others (108, 15%) For the management of COVID 19 symptoms, high doses of vitamin C, Zinc and doxycycline (antimicrobial) were most prescribed whilst losartan and insulin mixtard were most frequently prescribed class of drugs for the management of COVID 19 comorbidities of hypertension and diabetes respectively.

Keywords: COVID -19; drug utilization; pharmacotherapy; Korle bu Teaching Hospital; Comorbidity(s); Ghana

Introduction

The coronavirus disease 2019 (COVID-19) pandemic was caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China, in December 2019, and has since spread worldwide [1]. It has also presented an unprecedented challenge to identify effective drugs for prevention and treatment [2]. Common COVID-19 symptoms are mild-moderate and even though infected patients with the severe acute respiratory syndrome coronavirus 2 are known to have a wide variety of clinical manifestations, only 80% of the patients infected experience only mild illness [3]. Case fatality rates (CFR) of COVID-19 have been estimated to be 5–27% globally [4, 5] especially in vulnerable populations, including older adults and patients with multiple co-morbidities such as hypertension, [6, 7].

Affiliation:

[1]Pharmacy Department, Korle Bu Teaching Hospital, Accra, Ghana

[2]Department of Medical Laboratory Technology, Accra Technical University. Accra, Ghana

[3]Pharmacy Department, Ho Teaching Hospital, Ho, Ghana

[4]School of Pharmacy, University of Ghana, Legon, Accra, Ghana

***Corresponding author:**
Charles Nii Kwade Ofei-Palm. Pharmacy Department, Korle Bu Teaching Hospital, P. O. Box 77, Korle Bu, Ghana.

Email: c.ofei-palm@kbth.gov.gh

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Several clinical trials are ongoing to provide evidence that certain drugs can have good clinical outcomes for patients hospitalized for COVID-19. However, in the management of COVID-19, patients with mild disease, supportive care has been the preferred management strategy [8] whilst pharmacological treatments with possible anti-viral effects have been primarily used for patients with moderate-to-severe disease [2].Whilst a range of medicines continue to be used off-label and are under investigation to treat COVID-19, including Remdesivir, hydroxychloroquine, azithromycin [9-11]. With COVID-19 treatment landscape is evolving, the medical community has struggled to find effective therapies to combat this novel pathogen. And in view of that, it is important to understand the determinants and patterns of pharmacological treatment over time as such knowledge helps to contextualize and understand the drivers of treatment in the management of COVID 19 patients. In Ghana, the first official cases of COVID-19 were reported on 12 March 2020. The Korle Bu Teaching Hospital became one of the designated treatment sites for COVID-19 patients whether referred to or admitted into the hospital.it created its isolation centre for the treatment of COVID 19. The Centre was known as the Fevers unit. Our aim of the study is to evaluate pharmacological treatment patterns of the COVID-19 patients admitted and identify the determinants of prescribing for COVID-19 at the isolation unit of the hospital.

Methods

This was a retrospective study conducted in a COVID-19 confirmed positive admitted at a dedicated unit (Fevers Unit) of the Korle Bu Teaching Hospital from May 2020 to August 2020 at the peak of the pandemic in Ghana using the Ministry of health's recommended data collection forms for pharmacists at all the COVID-19 centers in the country.

Data Collection Tools

To assess the characteristics of patients, a retrospective analysis of the documented medical records which included details on sociodemographic data, hospital admission data, drug utilization pattern of all laboratory-confirmed COVID-19 patients of all age groups, either gender, having comorbidity (s), date of admission, date of first COVID positive report, COVID-19 diagnosis prior to admission, diagnosis, presenting symptoms, clinical severity features, investigations chest X-Ray, ECG, biochemical examination, ophthalmic examination etc and admitted between the study period were noted and evaluated.

Also, the course during the stay in the hospital and details of any adverse drug reaction (ADR) were noted. For studying the drug utilization pattern, detailed information on drugs used including name of the drug, dosage schedule, and treatment duration were noted. The clinical outcome was assessed in terms of recovery/discharge or death.

Data Analysis

Statistical analysis was mainly descriptive using IBM SPSS Statistics (Version 21, Corp, and Armonk,NY, USA). Frequencies and percentages of various medication errors were used to describe the categorical variables. Mean and Standard deviation was used to describe continuous variables. Data from the interventions were recorded and entered into an SPSS. Data were then reviewed,evaluated, analyzed and categorized.

Ethical Approval

An administrative approval was granted by the Hospital for the research to be carried out.

Results

A total of 53 case records of lab confirmed COVID-19 positive patients were reviewed. Patients were all confirmed for COVID-19 infection positivity twice before admission. Women accounted for 58.5%, (31/53) positivity of the patients during the study period. The mean (SD) age was 47.1(17.9) years Per the age distribution, the 60+ years age group accounted for 26.4% (14/53) which is the highest followed by 40-49 age group 22.6% (12/53), then 30-39years group 18.9% (10/53). The rest of the characteristics on the various age groupings are shown in figure 1. The socio-demographic description of the study participants per employment status are as follows: non-healthcare worker (HCW); 77.3% (41/53), healthcare worker; 13.3% (7/53), and unemployed; 9.4% (5/53). The average duration of hospital stay among recovered patients was approximately 14days.Only 9.5% (5/53) patients had history of international travel. The overall case fatality rate during the study period was 1.8%.

Distribution of clinical symptoms amongst study participants

A total of 72 different clinical symptoms were recorded by the patients admitted in the unit with an average of 1.3 symptom per patient per admission. Dry cough and aches & pains accounted for 24% of total number of symptoms presented at the Centre. Dry cough was 16.75% (12/72)

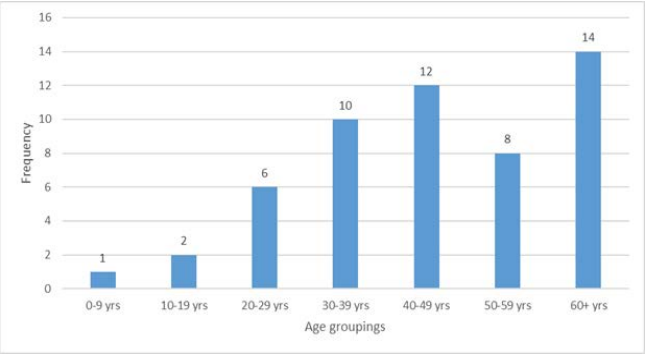

Figure 1: Age Distribution Patterns of Patients on Admission.

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and aches & pains was 16.7% (12/72) followed by tiredness 11.1% (8/72), short of breath 11.1% (8/72) and fever 9.7% (7/72). The rest of the clinical symptom(s) finding(s) among the study participants at the time of admission are shown in figure 2.

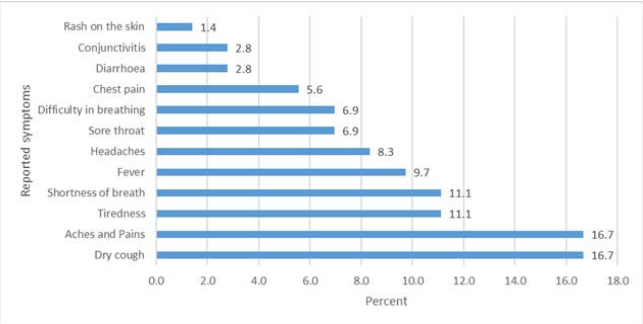

Figure 2: Distribution patterns of clinical symptoms.

Distribution of pre-existent comorbidity(s) amongst study participants

The prevalence of pre-existent comorbidity(s) amongst study participants was 88.6% (47/53) Hypertension alone 56% (30/53) was the most common underlying comorbid condition, followed by diabetes mellitus 18.7% (17/53), renal impairment 18.7% (17/53) and others.

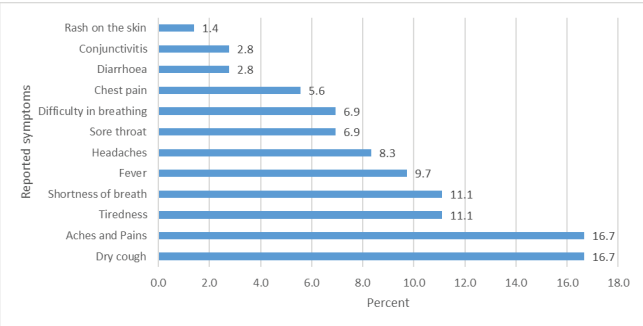

Figure 3: Distribution patterns of pre-existent comorbidity(s)

Figure 3 depicts the distribution of pre-existent comorbidity (s) among the study participants.

Temperature recordings was key in this study. In total, there were 390 temperature recordings resulting to an average of 8 temperature takings per patient on admission 71.8 % (280/390) of the temperature recordings occurred within the range of between 37ºC - 38ºC. See table 1

Drug utilization pattern amongst study participants

For the management of COVID-19 among the study participants, a total of 493 drugs were prescribed. Out of these, the COVID-19 symptoms and co-existent comorbidity(s) were managed by 398 and 95 drugs, respectively. The mean medication per patient was 9.3±4.3. Per the various dosage forms, the mean per injection per patient was 2.6±1.7 whilst that of oral dosage form the median was 6±2.3 The most commonly prescribed class of drugs were Multivitamins/ supplements (108, 27.1%), followed by anticoagulants (65, 16.3%), antihypertensives (64, 15.8%), antibiotics (64,15.8%) and others as shown in figure 4.

Management of COVID-19 symptoms

For COVID-19 symptoms, the most commonly prescribed class of drugs were multivitamins/supplements (108, 27.1%), followed by antimicrobials (63,15.8%), followed by proton pump inhibitors-PPI (25,6.3%), antipyretics (24, 6%), immunosuppressant drugs (16,4%) and others. The prescribed multivitamins/supplements and antimicrobials are detailed in figure 5 and figure 6 respectively

Dosage forms for the management of symptoms of COVID-19

Out of the total 398 drugs, 112 (28.10 %) were prescribed as injectable, 283 (71.10%) were prescribed orally with the rest 3 (0.8%) were prescribed as ophthalmic agents. Among the injectable preparations, anticoagulants mainly sc clexane/sc fragmin/heparin (65, 58%), were the most commonly prescribed agents followed by Ceftriaxone (10, 9%), Injection corticosteroids (4, 3.5%), and others. Among the oral preparations, vitamin C alone (52, 18.3%) was the most commonly prescribed drug followed by zinc or zinc containing vitamins such as zincofer/zincovite (47, 16.60%), doxycycline (34, 12%), oral proton pump inhibitors such as omeprazole/esomeprazole (15, 5.3%), oral corticosteroids mainly prednisolone/dexamethasone (12,4.25) and others.

For the management of comorbidity(s)

A total of 95 drugs were prescribed to the study participants for the management of comorbidity(s). Out of these, most commonly prescribed were antihypertensive (64, 67.3%) drugs, followed by antidiabetic drugs (63, 66.31%), proton pump inhibitors (7, 7.3%) and others.

The various antihypertensives prescribed are depicted in details in Figures 7.

Dosage forms used for managing comorbidity (s)

Out of 95 drugs prescribed, 18 (18.9%) were injectable, 73 (76.84%) were oral, 2 (2.10%) were inhalational and 2 (2.10%) were ophthalmic preparations. Among the injectable preparations insulin mixtard (8, 44.4%) was the most commonly prescribed followed by Furosemide (6, 3.33%), injection omeprazole/esomeprazole (3,16.66%) and other agents. Among the oral medications, losartan (18, 24.65 %) was the most commonly prescribed followed by amlodipine (15, 20.54%), Metoprolol (9, 12.30%), Metformin

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(9,12.30%), esomeprazole 4(5.4%) and others. In metered dose inhalers (MDIs), Seretide: -salmeterol +250 mcg of fluticasone propionate, and salbutamol inhaler were the only ones prescribed in the group accounting for (2, 2.1%) In ophthalmic medications, timolol (2, 2.1%) was the only one prescribed.

Table 1: Summary of recorded temperatures of participants.

Temperatures	Frequency	Percent
TEMPERATURES <35ºC	2	0.5
TEMPERATURES FROM 35ºC - 36ºC	108	27.7
TEMPERATURES FROM 37ºC - 38ºC	280	71.8
TOTAL	390	100.0

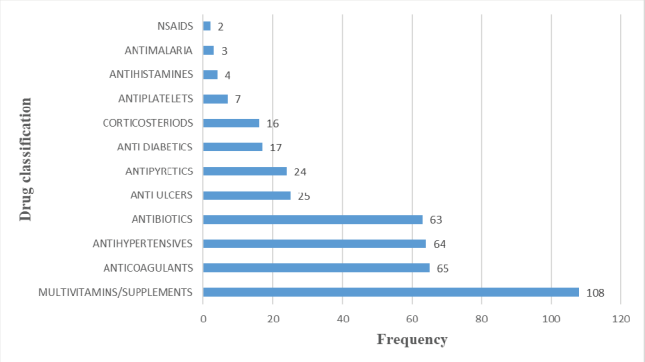

Figure 4: Drugs prescribed for the management of COVID-19 among study participants

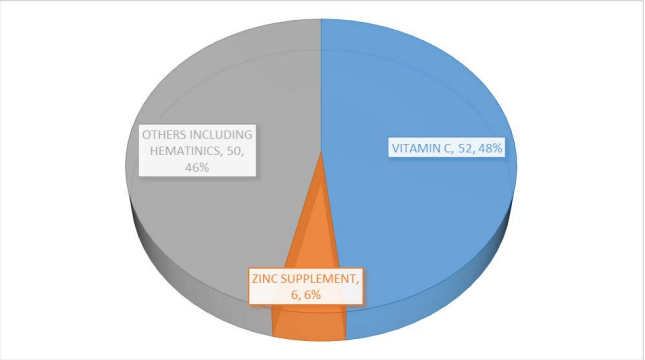

Figure 5: Description of the prescribed multivitamins/supplements

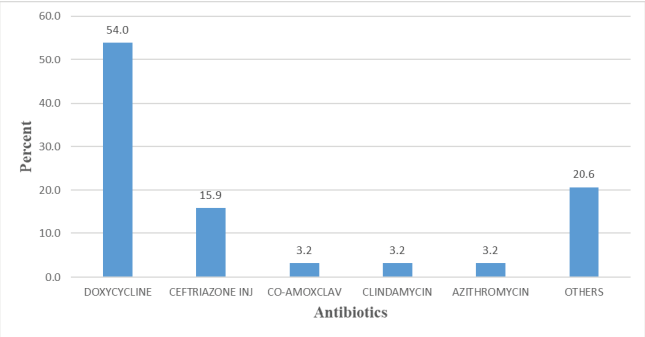

Figure 6: Different antibiotics prescribed among study participants for the management of symptoms of COVID-19.

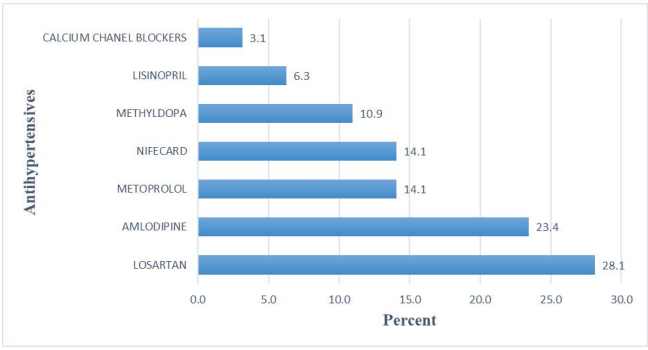

Figure 7: Different types of antihypertensive drugs prescribed to the study participants.

Discussion

Pharmacists caring for hospitalized patients with pneumonia must simultaneously provide other team members with updated, COVID-19–specific best practices and ensure consistent application of evidence-based practices, with responsibilities including optimizing medication shortages and keeping current with rapidly changing clinical information. It is also important for pharmacists to keep abreast of the unique pharmacotherapy challenges posed by COVID-19.in view of this, medicine finds itself in a very peculiar place right now. Since the onset of the coronavirus disease 2019 (COVID-19) pandemic, the medical community has struggled to find effective therapies to combat this novel pathogen. Though extensive research continues to be conducted worldwide on various aspects of COVID-19, until now research data representing the utilization of drugs among COVID-19 patients with comorbidity is very limited in Africa Sub Sahara and for that matter, Ghana. We estimate to the best of our possible knowledge, this is the first study detailing in Ghana that look at drug utilization/pharmacotherapy, clinical symptoms and comorbidities in an isolation dedicated unit of a tertiary hospital in Ghana. The mean age in this study was 47.1years, is similar to a previous study in China [12] this is much lower than the values of 49,50 and 58 reported from studies conducted in Wuhan, China the epicenter of the pandemic [13,14,15] but lower to similar studies done in COVID-19 settings in Ghana but not in tertiary hospital that recorded mean ages of 37.9years [16] and 41.9years [17] respectively. This study reported more females were males, this is contrary to the two reported studies from Ghana that had males more than females [16,17] but similar to another COVID 19 study in Ghana [18].

The COVID-19 pandemic has resulted in significant work force burdens globally. Risk of coronavirus infections among healthcare workers (HCW) was high globally during the pandemic and it was not surprising that 13.3% of infections

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in this study were from various categories of health care providers across the country. Our figure is quite low compared to other studies globally concerning HCW admitted to COVID-19 wards [19,20] but higher compared other studies [21,22]. The present study recorded the highest frequency of age group in the 60 years plus. This is not surprising since COVID -19 associated risk with age. Age is associated with increased prevalence of comorbidities, polypharmacy, cognitive impairment, dependence, and increased frailty [23]. This is also in line with other published literatures that looked increased risk of infection and complications with age [24,25]. The case fatality rate (CFR) of COVID-19 was calculated as the number of total deaths due to COVID-19 divided by the number of total confirmed COVID-19 cases multiplied by 100. CFR was investigated in our study because it may reflect disease severity, as well as the efficiency of treatment and healthcare response and strain. The present study recorded a CFR of 1.8%. This is within the average of country/territory-specific COVID-19 CFR is about 2%–3% worldwide and higher than previously reported at 0.7%–1.3% [26]. History of international travel became a key indicator for COVID -19 source during the early stages of the pandemic since COVID 19 was considered an "imported disease". In this study 9.5% (5/53) patients had history of international travel this lower than a study that was also conducted in Ghana that had 59% [16]. The low value attributed to this study is for the plausible reason that, at the time of this study, the community spread of COVID 19 has started and very fewer patients admitted were of international travels.

Higher temperature or fever is one of the key clinical symptom's characteristics of COVID -19. It is estimated that substantial number of patients will experience some level of fever. In this study, most patients had slightly high temperature. This could be because, before presentation, patients might have started antipyretic at home and continued on admission. Our results are in line with other studies that had recorded temperatures range of 37ºC - 38ºC [27]. In the present study, the prevalence of comorbidity(s) was 88.6% (47/53), higher than 25.1% recorded in a similar COVID -19 settings in Ghana [17]. The most prevalent comorbidity(s) was found to be hypertension followed by diabetes. Similarly, a retrospective study on 522 COVID-19 patients reported that the most prevalent comorbidity was hypertension followed by diabetes mellitus [28,29] and similar to the two COVID -19 studies conducted in Ghana. [16,17] this outcome corroborates the fact that hypertension is also a known risk factor for COVID-19 morbidity and mortality [30,31]. The drug utilization pattern amongst the study participants in the present study showed that drugs were prescribed for the management of COVID-19 symptoms and some were prescribed for the management of comorbidity(s). The most commonly prescribed class of drugs for the management of symptoms of COVID-19 were multivitamins: including vitamin C, Zinc or zinc containing multivitamins, followed by anticoagulants, antihypertensives and antimicrobials. Vitamin C (ascorbic acid) is a water-soluble vitamin that is thought to have beneficial effects in patients with severe and critical illnesses. It is an antioxidant and free radical scavenger that has anti-inflammatory properties, influences cellular immunity and vascular integrity, and serves as a cofactor in the generation of endogenous catecholamines [32]. In our study 98.1% (52/53) patients received vitamin C and 100% (53/53) received either zinc or multivitamins that contained higher amount/doses of zinc even though other literature indicates no benefits [33], but Ghana treatment guidelines for COVID-19 duly recommends both Zinc and Vitamin C in the management of the symptoms of COVID-19 [34].

Dry cough, short of breath, fever and tiredness which accounted for 24%, 24%, 11% and almost 10% respectively in our study is quite similar to other published literature in a COVID -19 ward in China [35, 36] and in Ghana [16,17] respectively. Antimicrobials are known to improve the symptoms of COVID 19 patients' routine empirical antibiotic therapy is not recommended for COVID-19–infected patients. However, guidelines from the Surviving Sepsis Campaign, the World Health Organization (WHO), and the Veterans Health Administration (VHA) all endorse a low threshold to evaluate and prescribe empirical antibiotic therapy for secondary bacterial pneumonia in patients with COVID-19[37] .In our study doxycycline accounted for 54% of total usage of antimicrobial and even though accounted for 98.1% (52/53) of all the patients on admission, it usage is being questioned by published literature[38] Doxycycline is often used for treating COVID-19 respiratory symptoms in the community despite an absence of evidence from clinical trials to support its use. A similar study conducted in Ghana reported no use of doxycycline [17] with the entire study period. COVID-19 has been linked with a state of hypercoagulability [39] and clinical guidelines have recommended pharmacologic prophylaxis for venous thromboembolism in all patients hospitalized for COVID-19 [40,41]. This outcome was clearly recorded in our study. Enoxaparin/fragmin/heparin use remained above 50% making it the most injectable usage throughout the study, perhaps because they serve both for thrombosis prophylaxis and thrombophilia treatment triggered by COVID-19. In our study, the most prescribed antihypertensive drug was losartan, this outcome is in line with other published literature that used and recommended losartan for the management of hypertension in COVID 19 patients [42]. Its usage is because angiotensin receptor blockers (ARBs) could be protective as they may enhance angiotensin 1–7 production consequent to reduction in angiotensin II and thus may attenuate inflammation, fibrosis, and lung injury [42]. Insulin which accounted for 44.4%, was the most prescribed antidiabetic injectable use in managing diabetics in COVID 19 patients in this study. Diabetes weakens the immune response because of

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pathological alterations in cytokine production and activation of T-cells and macrophage. Further, poor glycemic control also compromises certain aspects of immune response to a viral infection and adds to the risk of potential bacterial secondary infection in the lungs. Our results are similar to other published literature that had similar percentage usage [42].

Limitation

The limitation of this study is the small sample size. The results may not represent a larger constituency of COVID 19 management in Ghana but a significant step in providing information about drug utilization pattern in a COVID -19 settings in Ghana.

Conclusions

The most commonly prescribed class of drug at the dedicated COVID-19 Unit were: high doses of vitamin C, Zinc and doxycycline (antimicrobial) for the management of COVID 19 symptoms whilst losartan and insulin mixtard were most frequently prescribed class of drugs for the management of COVID 19 comorbidities of hypertension and diabetes respectively.

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