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Effectiveness and Safety of Combination Drug Therapy in Covid-19 patients admitted in a Designated Covid Hospital

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Abstract

Background: The corona virus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) virus has affected the whole world. Researches are on-going in search of effective and safe drugs. The first wave of the pandemic was managed with some repurposed drugs and some newer antiviral drugs. There is limited data on the effectiveness and safety of these drugs. Our study was done to determine the effectiveness and safety of drugs used as combination in COVID 19 infection.

Methods: This was a descriptive record-based study done in a tertiary care COVID hospital in Manjeri of Malappuram district in Kerala from 1st March 2020 to 30th November 2020. Demographic details, comorbidities, lab investigations, treatment measures and medications on admission till discharge, adverse effects & outcomes were taken from medical records. The severity assessment was obtained from World Health Organisation (WHO) Ordinal Scale and outcome assessment was based on the number of days taken for a 2-point step down from the WHO ordinal scale. Data were entered into Excel sheet and analysed using SPSS. The effectiveness of combination was determined using independent t test.

Results: Of the 200 patients, majority received Hydroxychloroquine (n=125) and Azithromycin(n=192). The other drugs prescribed were anticoagulants, monoclonal antibodies, steroids and convalescent plasma. All the patients in Category B had WHO ordinal scale of 3 while majority 97(59.9%) in Category C had an ordinal Scale of 4. The oxygen mask days and mean WHO 2 step down days were lower in the 45 patients who received Remdesivir with anticoagulation. The common adverse effects observed were were hematuria 17(8.5%), new onset diabetes mellitus 14(7%), diarrhoea 5(2.5%) and hypoglycemia 2(1%).

Conclusion: The majority of patients received Hydroxychloroquine and Azithromycin with or without Anticoagulants, Corticosteroids, Antiviral drugs, Monoclonal antibodies and Convalescent plasma according to severity of disease. The

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combination of Remdesivir with Anticoagulation was found to reduce the severity grade of COVID 19 infection faster compared to Anticoagulation alone and those without Remdesivir in Category C patients.

Keywords: COVID, Remdesivir, Hydroxychloroquine, WHO Ordinal Scale, Anticoagulation

INTRODUCTION

SARS-CoV-2 infection is a wide spectrum disease which encompass asymptomatic infections, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death.[1] In India, the first laboratory-confirmed case of COVID-19 was reported from Kerala on January 30, 2020.[2] The COVID-19 has resulted in the deaths of more than 68,73,477 persons worldwide as of March 16, 2023.[3]

Currently several studies have discussed the therapeutics for COVID-19, including repurposing of medications. Based on evidence on the suppression of activity, hydroxychloroquine was used along with azithromycin for the treatment.[4] Different mechanisms like blockade of viral entry into cells by inhibiting glycosylation of host receptors, immunomodulatory effects, inhibition of autophagy and lysosomal activity in host cells has led to the use of hydroxychloroquine. Azithromycin was thought to interferes with cleavage of the spike protein, preventing viral entry into host cells. [5] More antiviral drugs, anticoagulants, corticosteroids and plasma therapy were added as the treatment for the disease evolved. This study was done to determine the effectiveness and safety of combination drug therapy in COVID 19 patients admitted in a tertiary care centre which was designated as a COVID hospital during the initial year of the pandemic.

MATERIALS AND METHODS

This was a record based descriptive study done in a designated COVID hospital of Malappuram district in North Kerala after obtaining Institutional Ethics Committee Clearance. Case record files of patients >18 years of any gender, admitted in the medicine department from 1st March 2020 to 30th November 2020 and confirmed as COVID 19 positive by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) were included in the study. Pregnant ladies, lactating mothers, patients with hepatic impairment, Human Immunodeficiency Virus patients, allergy to any of the drugs included in the study and incomplete medical records were eliminated from the study. Retrospective evaluation of case sheets of all admitted patients diagnosed to have COVID19 in medicine ward was done. Patient demographics, pre-existing conditions, lab investigations, clinical measures and medications on admission till discharge, adverse events & outcomes were abstracted from medical records. The data recorded were compared across age groups (18-40, 40-60 and above 60 years), gender and patients with or without comorbidities. Data were entered into Excel sheet and analysed using SPSS. The parameter considered for monitoring outcome was WHO Ordinal Scale which is a “9 points scale- 0: no clinical or virological evidence of infection; 1: ambulatory, no activity limitation; 2: ambulatory, activity limitation; 3: hospitalized, no oxygen therapy; 4: hospitalized, oxygen mask or nasal prongs; 5: hospitalized, non-invasive mechanical ventilation (NIMV) or high-flow nasal cannula (HFNC); 6: hospitalized, intubation and invasive mechanical ventilation (IMV); 7: hospitalized, IMV + additional support such as pressors or extracardiac membranous oxygenation (ECMO); 8: death”.[6] The patients were categorized into B and C based on the guidelines released by the Ministry of Health and Family Welfare, Government of Kerala.[7] Quantitative variables were expressed as mean ± standard deviation, qualitative variables were expressed as frequencies and percentage. Independent t test was done to determine the difference in the outcome in Category B and C patients.

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Results

A total of 200 patients who were admitted in the study centre were recruited for the study. The mean age was 51.4±17.63 years with minimum age 18, maximum age 91 years. Majority were in the age group 18-40 years [73(36.5%)] followed by >60 years [65 (32.5%)] and 40-60 years [62 (31%)]. Out of the 200 patients, 136(68%) were males and 64(32%) were females. There was atleast one associated comorbidity in 116 (58%) patients which were diabetes, hypertension, dyslipidemia, ischemic heart disease, cerebrovascular accident, renal or hepatic dysfunction.

Table 1: Baseline characteristics of the patients

	Males N(%)	Females N(%)
Age in years 18-40(N=73) 40-60(N=62) >60 years(N=65)	 51(69.9) 46 (74.2) 39 (0.6)	 22 (20.1) 16 (25.8) 26 (0.4)
Associated Comorbidities (N=116)	70 (60.3)	46 (39.7)
Hypertension (N=66)	38(57.6)	28(42.4)
Diabetes Mellitus(N=85)	51(60.0)	34(40.0)
Ischemic Heart Disease(N-61)	44(72.1)	17(27.9)
Dyslipidaemia(N=17)	11(64.7)	6(35.3)
Cerebrovascular Accident(N=13)	4(30.8)	9(69.2)
Renal Disease(N=13)	9(69.2)	4(30.8)
Hepatic Disease(N=18)	11(61.1)	7(38.9)

Of the total 200 patients, 38(19%) were Category B and 162(81%) were category C. Seventy-Nine patients (39.5%) developed changes in Chest X ray of which 7 had cardiomegaly, 62 bilateral infiltrates, 4 unilateral infiltrates, 4 pleural effusion and 2 pulmonary fibrosis. The details of patients who received various antimicrobial drugs is summarised in Table 2

Table 2: Details of Antimicrobial Therapy

Drugs	Category B N(%)	Category C N(%)
Hydroxychloroquine(N=125)	30 (24)	95(76)
Lopinavir/Ritonavir(N=2)	0	2(100)
Piperacillin-Tazobactam(N=43)	1(2.3)	42(97.7)
Azithromycin(N=192)	37(19.3)	155(80.7)
Amoxicillin-Clavulanic Acid(N=6)	1(16.7)	5(83.3)
Favipiravir(N=22)	1(4.5)	21(95.5)
Remdesivir(N=47)	2(4.3)	45(93.7)

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Of the 200 patients majority received Hydroxychloroquine (HCQ) (n=125) and azithromycin(n=192) as shown in Table 2. The other drugs prescribed were anticoagulants (n=93), monoclonal antibodies (n=7), steroids(n=91) and convalescent plasma (n=32).

Table 3 summarizes the various combinations of drugs used in patients who received HCQ with other antiviral drugs like lopinavir, favipiravir and remdesivir, antibiotics like azithromycin as well as amoxicillin and clavulanic acid, anticoagulants, steroids and plasma. The table also depicts the mortality, Lactate Dehydrogenase (LDH) values, d-dimer and Ferritin at admission and at discharge. As shown in Table 3, out of the 125 patients who received hydroxychloroquine, among Category B patients, 29 received azithromycin, 1 amoxicillin + clavulanic acid, 10 steroids and 3 plasma as combinations. The antivirals and anticoagulants were given as combination along with HCQ only in the Category C patients. Out of the 24 patients who received anticoagulants with HCQ, the D-dimer was elevated in 19 patients at the time of admission and it was still elevated in 16 patients at the time of discharge.

Table 3: Combination Therapy in patients who received Hydroxychloroquine

Hydroxychloroquine	Category	Lopinavir / Ritonavir [N=2]	Favipiravir [N=1]	Remdesivir [N=12]	Azithromycin [N=121]	Amoxicillin-Clavulanic Acid[N=6]	Piperacillin-Tazobactam [N=17]	Anticoagulant [N=24]	Monoclonal Antibody [N=7}	Steroids	Plasma
Category	B	0	0	0	29 (24)	1 (16.7)	0	0	0	10 (41.7)	3(23.1)
	C	2 (100)	1 (100)	12 (100)	92 (76)	5 (83.3)	17 (100)	24 (100)	7 (100)	14 (58.3)	10 (76.9)
Mortality	Alive	1 (50)	1 (100)	12 (100)	118 (97.5)	6 (100)	14 (82.3)	21 (87.5)	7 (100)	10 (41.7)	3 (23.1)
	Dead	1 (50)	0	0	3 (2.5)	0	3 (17.6)	3 (12.5)	0	14 (58.3)	10 (76.9)
D-Dimer at admission	Normal	0	0	2 (11.8)	85 (70.2)	1 (16.7)	2 (11.8)	5 (20.8)	1 (14.3)	10 (41.7)	3 (23.1)
	Elevated	2 (100)	1 (100)	15 (88.2)	36 (29.8)	5 (83.3)	15 (88.2)	19 (79.2)	6 (85.7)	14 (58.3)	10 (76.9)
D-Dimer at discharge	Normal	1 (50)	0	5 (41.7)	96 (79.3)	2 (33.3)	6 (35.3)	8 (33.3)	3 (42.9)	14 (58.3)	5 (38.5)
	Elevated	1 (50)	1 (100)	7 (58.3)	25 (20.7)	4 (66.7)	11 (64.7)	16 (66.7)	4 (57.1)	10 (41.7)	8 (61.5)
Ferritin at admission	Normal	1 (50)	0	3 (25)	96 (79.3)	1 (16.7)	5 (29.4)	6 (25)	1 (14.3)	11 (45.8)	3 (23.1)

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	Elevated	1 (50)	1 (100)	9 (75)	25 (20.7)	5 (83.3)	12 (70.6)	18 (75)	6 (85.7)	13 (54.2)	10 (76.9)
Ferritin at Discharge	Normal	1 (50)	0	5 (41.7)	100 (82.6)	2 (33.3)	5 (29.4)	7 (29.2)	2 (28.6)	13 (54.2)	5 (38.5)
	Elevated	1 (50)	1 (100)	7 58.3%	21 (17.4)	4 (66.7)	12 (70.6)	17 (70.8)	5 (71.4)	11 (45.8)	8 (61.5)
LDH at admission	Normal	2 (100)	0	3 (25)	92 (76)	2 (33.3)	4 (23.5)	7 (29.2)	1 (14.3)	10 (41.7)	3 (23.1)
	Elevated	0	1 (100)	9 (75)	29 (24)	4 (66.7)	13 (76.5)	17 (70.8)	6 (85.7)	14 (58.3)	10 (76.9)
LDH at discharge	Normal	2 (100)	0	4 (33.3)	101 (83.5)	3 (50)	6 (35.3)	10 (41.7)	1 (14.3)	11 (45.8)	4 (30.8)
	Elevated	0	1 (100)	8 (66.7)	20 (16.5)	3 (50)	11 (64.7)	14 (58.3)	6 (85.7)	13 (54.2)	9 (69.2)

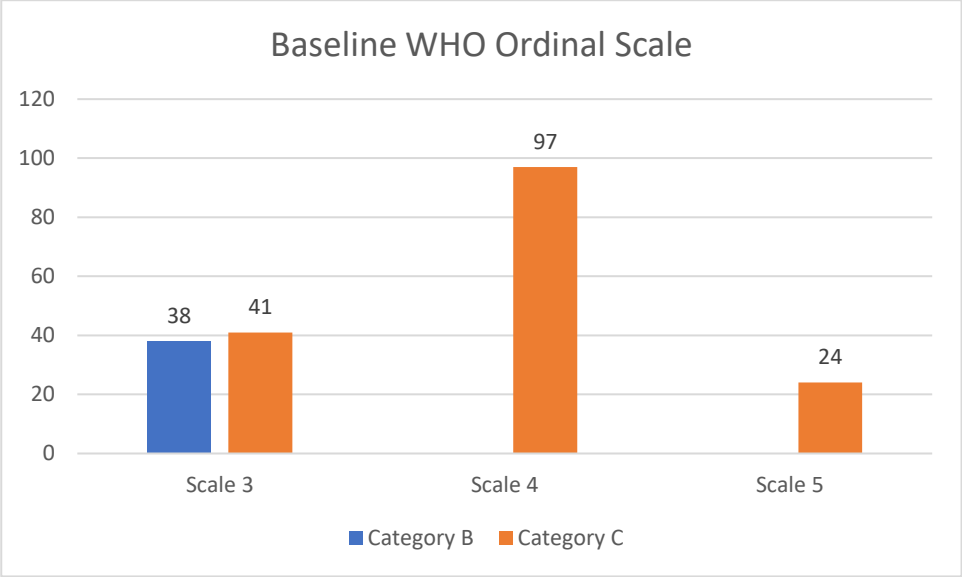

Fig 1: Baseline WHO Ordinal Scale

As shown in Fig 1, at baseline all the patients in Category B had WHO ordinal scale of 3 (hospitalized, no oxygen therapy) while majority 97(59.9%) in Category C had an ordinal Scale of 4 (hospitalized, oxygen mask or nasal prongs). After the initiation of the combination therapy the outcome was measured by the number of days taken to achieve a 2-point step down from the WHO ordinal scale.

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Table 4: Outcome based on Category of patients

Outcome	Category B	Category C	p Value (95% CI of difference)
Mean Hospital Days	9.47 ± 3.4	13.28 ± 7.03	0.001(-6.12 - -1.48)
Mean Intensive Care Unit Days	0.11± 0.65	3.90 ± 6.21	<0.001(-5.8- -1.8)
Mean Oxygen Days	4.29±3.68	5.30 ± 4.26	0.181(-2.48 -0.47)
Mean Non-Re Breathing Mask days	0.13± 0.67	1.62 ± 2.96	0.003(-2.44 - -0.53)
Mean High Flow Oxygen Days	0.11± 0.65	1.97 ± 4.16	0.007(-3.2 - -0.52)
Mean Non-Invasive Mechanical Ventilation Days	0	1.67±3.45	0.003(-2.77- -0.56)
Mean WHO 2 step down days	5.95± 2.7	8.17± 6.76	0.049 (-3.58- -0.86)

Out of the 200 patients, 30 patients died and 6 required mechanical ventilation. Table 4 summarizes the outcome based on Category of patients. As evident, there was statistically significant difference in all except the mean oxygen days. The mean WHO 2 step down days was higher in the Category C as compared to Category B. As shown in Figure 2, the WHO 2 step down days were <10 days for 35 patients (92.1%) in Category B and 97 patients (59.9%) in Category C. Only 6 patients and one patient in Category C required more than 20 days and 30 days respectively for achieving two step downs in the WHO ordinal scale. There was no statistically significant difference in the achievement of two step downs of the WHO ordinal scale gender wise(p=0.74) , age wise(p=0.9) and based on the presence of co-morbidities(p=0.43)

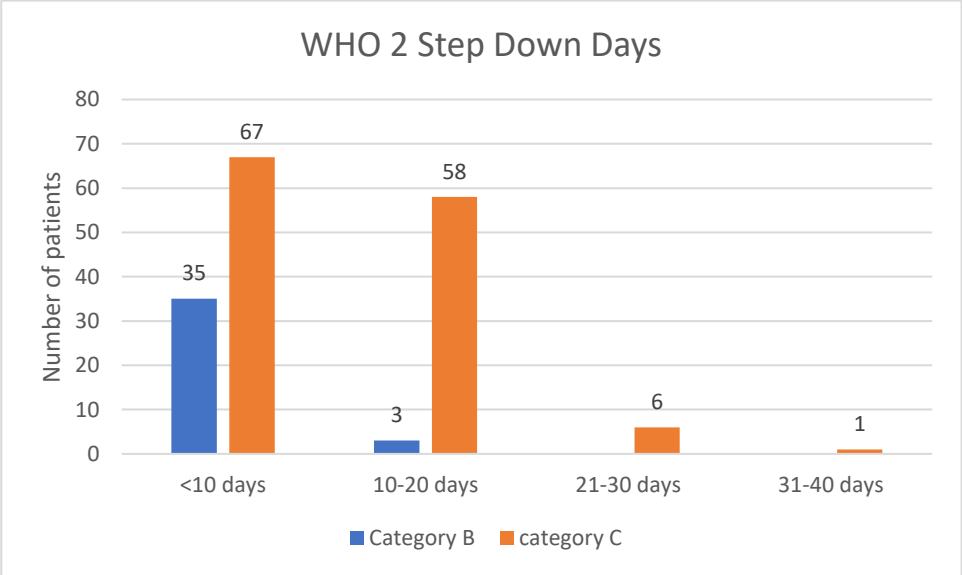

Fig 2: WHO 2 Step Down Days

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Table 5: Outcomes in patients without Remdesivir, anticoagulation without Remdesivir and Anticoagulation with Remdesivir in Category C patient

	Multiple Combinations Without Remdesivir* (n=117)		With Remdesivir and Anticoagulation (n=45)		p (95% Confidence Interval)	Anticoagulation without Remdesivir $ (n=43)		p (95% Confidence Interval)
	Mean	Std. Deviation	Mean	Std. Deviation		Mean	Std. Deviation	
Hospital days	12.53	6.419	15.22	8.196	0.029(-5.1 - -0.28)	13.84	7.761	0.42(-4.7- -2)
Ferritin at Discharge	401.20	362.706	742.58	582.855	<0.001(-491 - -190.8)	662.53	473.506	0.48(113.5- -305.69)
LDH at discharge	344.62	356.399	712.44	617.475	<0.001(-521- -214)	606.19	450.321	0.36(115.6- -336.16)
ICU days	1.50	3.221	10.13	7.677	<0.001(-10.31- -6.94)	3.84	4.225	<0.001(-8.9- -3.6)
Oxygen days	6.43	4.316	2.36	2.238	<0.001(3.04 -5.1)	5.53	4.621	<0.001(1.65-4.7)
NRBM days	1.25	2.849	2.58	3.086	0.14(-2.14- -0.28)	2.60	3.717	0.97(-1.4- -1.4)
High Flow Oxygen days	.79	2.169	5.04	6.135	<0.001(-6,14 - -2.37)	1.93	2.995	0.003(-5.1- -1.1)
NIMV	.62	2.113	4.40	4.594	<0.001(-5.2- -2.3)	1.56	3.254	0.001(-4.5- -1.1)
IMV days	.09	.557	.09	.468	0.95(-0.16- 0.17)	.26	.902	0.28(-4.4- -1.1)
Mean WHO 2 step down days	8.07	5.846	7.35	9.167	0.56(-2.39- 3.8)	7.62	7.199	0.88(-3.4-3.9)

*Total Category C patients is 162 of which 45 received Remdesivir and 117 did not receive Remdesivir

$Total Category C patients who received anticoagulation is 88 of which 45 received it with Remdesivir, while 43 received anticoagulation alone without Remdesivir

As shown in Table 5, the mean was higher in the 45 patients who received Remdesivir as compared to other combinations for hospital stay, Intensive Care Unit days, Ferritin and LDH at discharge, NRBM, High flow oxygen, NIMV days whereas the oxygen days and mean WHO 2 step down days were lower. Out of the 88 patients who received anticoagulation among Category C patients, 76 received steroids. Of the 45 patients who received Remdesivir all received anticoagulation, 42 received steroids, 26 received convalescent plasma and 7 received monoclonal antibodies. While comparing the 88 patients who received anticoagulation with and without Remdesivir, the mean Oxygen days, NRBM days and WHO 2 step down days were lower in those who received remdesivir with anticoagulation.

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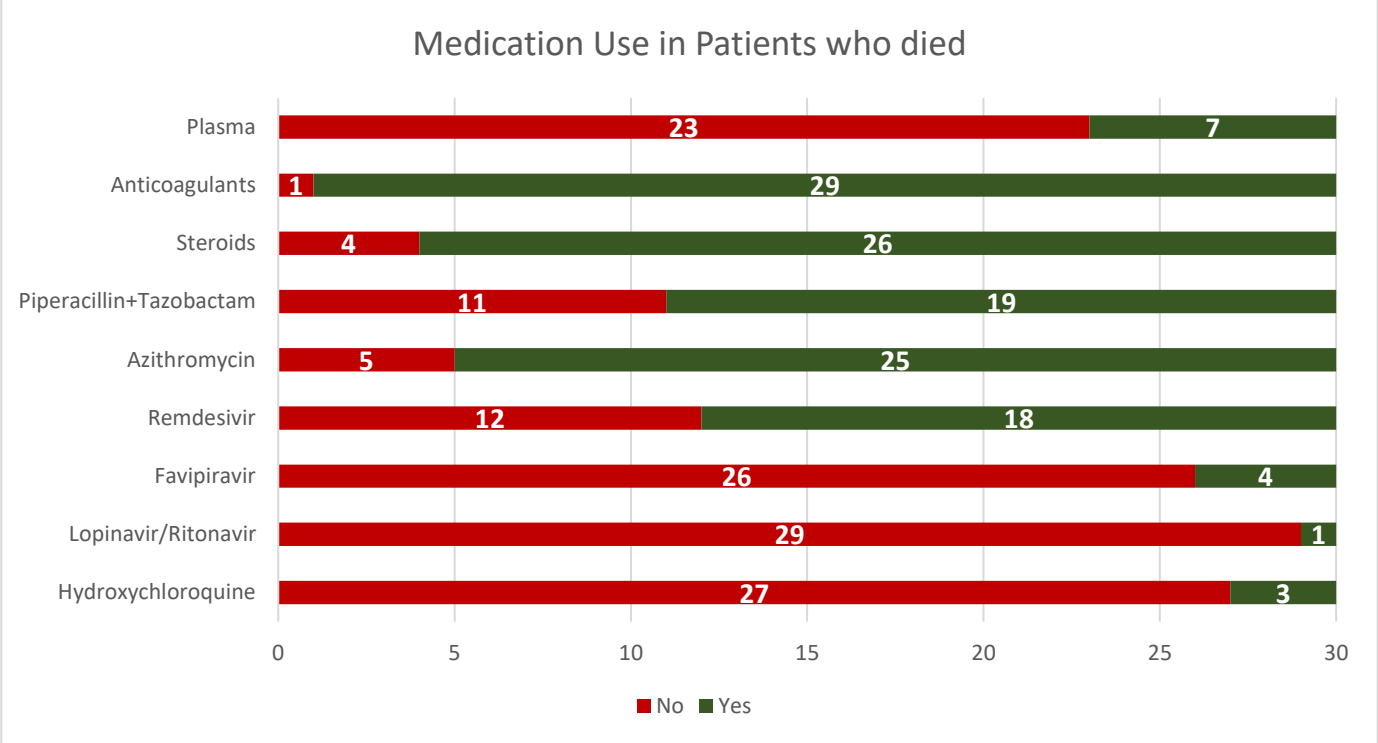

Fig 3: Medication use in participants who died of COVID

As shown in Fgure 3, of the 30 participants who succumbed to COVID majority of them had received anticoagulants(29), steroids(26), azithromycin (25). Seven received plasma, 4 received favipiravir,1 received Lopinavir/Ritonavir, 2 HCQ and 18 received remdesivir.

The common adverse reactions encountered in the patients were diarrhoea 5(2.5%), hypoglycemia 2(1%), new onset diabetes mellitus 14(7%). Oral hypoglycemics were changed over to Insulin in 66(33%) and the insulin dose was escalated in 19(9.5%). Hematuria was observed in 17(8.5%). In the patients who complained of diarrhoea the suspected drug was azithromycin. Those who developed new onset diabetes were on steroids and those who developed hematuria had anticoagulants.

Discussion

Coronavirus disease 2019 (COVID-19), first identified in the China Wuhan of the Hubei Province is now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was declared a pandemic in January 2020.[8] For the treatment of COVID 19 many drugs were repurposed and used, of which HCQ was among the firsts, however the proof of the clinical benefit was not proven. Numerous antivirals and immunotherapies were adopted and still continue to be tested.[8] The interim guidelines for the treatment of COVID patients was released by the Government of Kerala in March 2020 and the second version was released in August 2020.[7,9] This study was conducted during the initial year of COVID and hence explores the effectiveness of the combinations of drugs used and the adverse effects attributed to these drugs in a designated COVID hospital. The Kerala model for combating COVID 19 was discussed and accepted worldwide for adopting the World Health Organisation's test, trace, isolate and treat policy.[10]

The mean age of the participants was 51.4±17.63 years and the male: female ratio was 2.1: 1. Jaya et al., describing the epidemiology of COVID 19 pandemic in Kerala states that of those affected in Kerala, males were 51.7%, females were 46.1% and transgenders 2.2%. Majority were in the age group 21-40 followed by 41.60 years.[11] In similar studies done

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elsewhere, the majority of the participants were in the age group 41-60 years and males were more than females which is comparable to ours.[12–14] The guidelines that existed during the time of study had identified the risk of getting COVID 19 infection in patients based on the level of comorbidities and in this study we identified 58% patients with associated comorbidities.[7]

Hydroxychloroquine 400 mg orally twice daily on the first day followed by 200mg twice daily for the next 4 days along with azithromycin 500 mg orally (Intravenous stat for Category C) on Day 1 and 250 mg for the next 4 days was recommended by the interim guideline for Category B and C patients.[7] Addition of favipiravir 1800mg orally for two doses then 800mg twice daily for total 7 to 10 days instead of azithromycin or the use of Tablets Lopinavir / Ritonavir (400/100) twice daily for 14 days or for 7 days after becoming asymptomatic were recommended in the revised Version 2 released in August 2020.[9] It also recommended the use injection remdesivir 200 mg IV on day 1 followed by 100 mg IV daily for total 5 days If duration of symptoms is less than 10 days along with steroids, convalescent plasma and anticoagulation. In this study out of the 200 patients 125 received hydroxychloroquine and 121 received azithromycin. As shown in table 3, out of the 38 category B patients, 29 received azithromycin, 1 received amoxicillin + clavulanic acid , 10 received steroids and three convalescent plasma along with hydroxycloroquine. In the Category C, hydroxychloroquine was combined with atleast one of these drugs i.e., Lopinavir/Ritonavor (2), favipiravir (1), remdesivir (12), azithromycin (121), pipercaillin+ tazobactam (17), anticoagulants (24), monoclonal antibody (7), steroids (14) and convalescent plasma (10). The latest guideline of Ministry of Health and Welfare, Government of Kerala released in April 2021 however doesn't recommends use of hydroxychloroquine and azithromycin in Category B or C replacing it with oral ivermectin 200mcg/kg/day (not exceeding 12mg) daily for 3-5 days in both categories. The latest guideline also retained the use of favipiravir and remdesivir in Category C. [15]

The therapeutic approaches in COVID 19 include treatment with antiviral drugs (favipiravir, remdesivir), anti-inflammatory agents (dexamethasone, hydroxychloroquine), and immuno-modulators. Currently, combination treatment of remdesivir with dexamethasone and immune therapies, is considered the optimal treatment strategy. [16] Studies analysing the prescription pattern in COVID 19 elsewhere state that corticosteroids, anticoagulants, colchicine as well as azithromycin, ivermectin, and hydroxychloroquine were frequently prescribed.[12,14] A study done in Germany states that remdesivir was used in 31.3% , corticosteroids in 61.7%, and monoclonal antibodies in 2.3%. Dexamethasone combined with remdesivir administration was the most common therapeutic approach during the second pandemic wave while corticosteroids predominated during the third wave with a significant lower mortality with the combination.[17]

From Table 2 , its is evident that out of the 200 patients, 192 received azithromycin; so 67 patients who didn't receive hydroxycloroquine received azithromycin. Favipiravir was initiated in 1 Category B and 20 Category C patients and remedesivir was prescribed for 2 Category B and 34 Category C patients without combining with hydroxychloroquine. In a multi-hospital assessment, treatment with hydroxychloroquine alone and in combination with azithromycin was found to reduce COVID-19 associated mortality.[4] However a review by Alam et al., points out several articles that shows that the effect of hydroxychloroquine is inconclusive even though it was widely used because of the easy availability at the start of the pandemic.[18]A rapid review on the use of azithromycin says that there is little evidence that warrants the use of azithromycin for the treatment of COVID-19 unless there is bacterial super-infection. There is an equally negative evidence depicting possible synergy between azithromycin and hydroxychloroquine.[5]

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Coppock et al., evaluating the effect of combinations and its association with mortality in a large multisite health care system found that the use of anticoagulation alone was solely associated with decreased mortality in patients admitted in the Intensive Care Units. In addition the combinations of anticoagulation with remdesivir, corticosteroids and both were associated with lower mortality.[19] In this study, a higher mean was obtained in the Category C patients who received a combination of remdesivir and anticoagulation for total hospital days, Intensive Care Unit days, Non Invasive Ventilation days and the values of ferritin and LDH at the time of discharge. This could be due to the fact that these combinations were given in patients who were more critical. It is noticeable that the mean 2 step down of the WHO ordinal scale and the oxygen days were lower in these patients.Sahai et al., states that regular screening of coagulation profile and anticoagulant therapy should be started early ias per the standard guidelines so that comlications of COVID can be avoided.[20] The WHO severity scale has been a good classifying and predictive tool for COVID 19 outcome measurement. However the limitations of the tool includes its inability to classify patients based on the criticality of oxygen requirements.[6]

Remdesivir and Favipiravir inhibits the RNA-dependent RNA polymerase and has shown its efficacy against SARS-CoV-1 through the improvement of lung infection.[12,21] In their review Hossain et al., points out several studies which demotes that early treatment with this drug shorten recovery and discharge time and it has good safety and good tolerability.[21] Terada et al., found that the combination of favipiravir, camostat and ciclesonide decreases hospital days without safety concerns.[22] However Hossain et al., pointed out that HCQ has a bad safety profile as compared to remdesivir.[21] We did not record any adverse events suspected due to the antivirals. The observed adverse effects included azithromycin induced diarrhoea , steroid induced diabetes mellitus and hematuria due to anticoagulation. A review on the safety of drugs used during the first covid wave showed that the most frequent adverse reactions were gastrointestinal and the drugs more frequently involved included Lopinavir/ritonavir ,hydroxychloroquine and azithromycin.[23]

Limitations of this study include that it was a single centre study and was restricted to the first pandemic wave. The WHO ordinal scale step down used for outcome measurement has some drawbacks in the classification of patients.

Conclusion

Our study puts forward an analysis regarding the effectiveness and safety of combination of drugs during the first wave of COVID 19 pandemic. The majority of patients received Hydroxychloroquine and Azithromycin with or without Anticoagulants, Corticosteroids, Antiviral drugs, Monoclonal antibodies and Convalescent plasma according to severity of disease. The combination of Remdesivir with Anticoagulation was found to reduce the severity grade of COVID 19 infection faster compared to Anticoagulation alone and those without Remdesivir in Category C patients. Even though there is no conclusive evidence showing the efficacy of Hydroxychloroquine and Azithromycin in COVID 19 infection, these were very commonly used during the first wave of pandemic. Anticoagulant induced hematuria and Corticosteroid induced hyperglycemia were the the commonest adverse effects observed during the course of treatment. Most of the adverse effects were mild to moderately severe and largely self limiting; but, we suggest follow up of the patients to know about the sequelae due to the disease as well as drugs.

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