# A RETROSPECTIVE, CROSS-SECTIONAL, OBSERVATIONAL STUDY COMPARING THE EFFICACY OF VARIOUS COVID-19 TREATMENT PROTOCOLS



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## ABSTRACT:

Purpose and Background: The goal of this study is to examine the efficacy of various medications that are recommended for the treatment of patients in India who are suffering from mild-to-severe cases of corona virus disease 2019 (COVID-19).

Methods: In study carried out a retrospective, cross-sectional, observational and descriptive study. Patients diagnosed with COVID-19 ranging from mild, moderate and severe were given as part of this treatment. The primary objectives are to compare the categorical treatment protocols for COVID-19 (as per NIH Treatment Guidelines) infected mild, moderate and severe patients. To evaluate the efficacy of the drugs on the basis of at the time of discharge improvement in SPO2, RR, D-Dimer, PCT, CRP and Ferritin Values.

Results: A total of 266 patients included in this study mild to severe COVID 19 infection led to significant improvement in SPO2, Respiratory rate (RR), D-Dimer, Procalcitonin (PCT), C-Reactive Protein (CRP) and Ferritin level.

Conclusion: Adult patients with mild, moderate and severe COVID- 19 infection, when treated with different drug combination, were more likely to improve in terms of inflammatory markers and disease severity markers and were more likely to have a better clinical profile at the end of the treatment period.

**Keywords:** Antiviral, Corona virus, COVID-19, SARS-CoV-2 patients, Retrospective, Cross-sectional, Observational Descriptive study and Categorical treatment

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## Introduction:

Corona viruses (CoVs) are a group of positive single-stranded (+ss) RNA viruses that belong to the family Corona viridae [1]. Different CoVs have been isolated from multiple species of mammals and birds [2]. Based on the genome sequence and the animal species they infect, CoVs have been classified into four genera: Alpha corona virus, Beta corona virus, Gamma corona virus, Delta corona virus [1]. Alpha corona viruses and beta corona viruses are known to exist in mammals, whereas gamma and delta

corona viruses circulate in birds and mammals [2]. The first human CoVs (HCoVs) were discovered in the 1960s and to date, seven HCoVs are known to cause respiratory diseases with varying severity [3,4].

Four HCoVs (HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoV-NL63) cause 15% of common colds with mild symptoms, whereas three viruses cause severe respiratory diseases with viral pneumonia [3,4]. These three HCoVs include Severe Acute Respiratory Syndrome-CoV (SARS-CoV), Middle East Respiratory Syndrome-CoV (MERS-CoV) and the most recently described SARS-CoV-2 [3, 4]. SARS-CoV-2 causes the COVID-19 disease, which has resulted in thousands of deaths to date [5]. SARS-CoV-2 was first isolated from critically ill patients in December 2019 [4].

These patients were connected to the Huanan Seafood Market in Wuhan, China [4]. Similar to SARS-CoV, bats have been suggested as the primary host of SARS-CoV-2; however, an intermediate host is yet to be identified [6, 7]. Before the discovery of SARS-CoV, there was no urgency in the development of anti-CoV therapeutics. However, the high fatality rate in SARS-CoV, MERS-CoV, and SARS-CoV-2 outbreaks necessitates the development of effective drugs. Genetic sequencing has shown that SARS-CoV-2 shares 79% identity with SARS-CoV [7]. Based on this finding, efforts to discover antiviral drugs against SARS-CoV-2 have been guided by our understanding of SARS-CoV and the discovery of several anti-SARS-CoV drugs. In patients with COVID-19, they test medications such as hydroxychloroquine, azithromycin, remdesivir, favipiravir, corticosteroids, ivermectin and other drugs to determine how effective. Although the majority of the aforementioned medications have been researched for their effects on a variety of parameters for COVID-19 patients in a number of countries, very little information regarding the efficacy of these drugs has been gathered from Indian patients. The current research project was carried out with the goal of determining whether or not the aforementioned medications are effective in the treatment of COVID-19 patients.

**Methods:**



Study design

This is a retrospective, cross-sectional, observational and descriptive study.

Study setting

The study was conducted at Department of Pharmacology, Santosh Medical College, Santosh University, Ghaziabad, NCR Delhi and Heritage IMS, Varanasi, India.

Study duration

From June, 2020 to July, 2021 and who full fill the required criteria.

Sample size

266 patients (these number of patients fulfilled our study inclusion criteria)

Statistical analysis

Continuous variables were described using mean and slandered deviation (SD). Mean variables was compared using student t-test. P-value ≤ 0.05 was considered as statistically significant. SPSS 16.0 version and Microsoft Excel was used for data analysis.

Data recorded were collected from health record from the tertiary care hospital who fulfilled the required criteria and excluded Pregnant or breast-feeding patients, Patients who are of age ≤ 18 years and Patients file of death occurred during study period

Data of Medication administered was collected from those patients who used them during the study period. Different categories of patient used different drug combinations. In the mild categories Doxycycline along with other drug was used, in moderate categories cefixime, Methylprednisolone along with other drugs were used and the severe group Favipiravir, ceftriaxone along with other drugs were used.

RESULTS

Patients in the Mild Group (Table- 01) category who were prescribed Doxycycline along with other drugs showed significant improvement in SPO2, RR, D-Dimer, PCT, CRP and Ferritin Values.

| MILD GROUP | | | |
|---|---|---|---|
| Doxycycline + Ivermactin + Montelukast + Levocetirizine + Atorvastatin + Fenofibrate | | | |
| | BEFORE (MEAN±SD) | AFTER (MEAN±SD) | p –VALUE* (95 % CONFIDENCE INTERVAL) |
| SPO2 | 94.69 ± 5.94 | 96.37 ± 1.85 | < 0.0001 (0.872 to 2.488) |
| RR | 20.22 ± 2.70 | 17.60 ± 1.27 | < 0.0001 (-3.007 to -2.233) |
| D-DIMER | 1.26 ± 0.65 | 0.34 ± 0.14 | < 0.0001 (-1.006 to -0.834) |
| PCT | 0.27 ± 0.10 | 0.04 ± 0.00 | < 0.0001 (-0.24299 to -0.21701) |
| CRP | 13.47 ± 5.27 | 2.41 ± 0.90 | < 0.0001 (-11.754 to -10.366) |
| FERRITIN | 1044.77 ± 286.98 | 309.83 ± 48.37 | < 0.0001 (-772.734 to -697.146) |
| TOTAL NUMBER OF PATIENTS =229<br>*P≤0.05 CONSIDERD AS SIGNIFICANT | | | |

TABLE – 01

- The SPO2 value raised to 96.37 ± 1.85 at the time of discharge from the value of 94.69 ± 5.94 at the time of admission (p < 0.0001; CI 0.87 to 2.48).
- The RR came down to 17.60 ± 1.27 from the initial rate of 20.22 ± 2.70 (p < 0.0001; CI -3.00 to -2.23).
- D- Dimer value at the time of admission was 1.26 ± 0.65 but at the time of discharge it was 0.34 ± 0.14 (p < 0.0001; CI -1.00 to -0.83).
- PCT value at the time of admission was 1.27 ± 0.10 but at the time of discharge it was 0.04 ± 0.00 (p < 0.0001; CI -0.24 to -0.21).
- CRP value at the time of admission was 13.47 ± 5.27 but at the time of discharge it was 2.41 ± 0.90 (p < 0.0001; CI -11.75 to -10.36).
- Ferritin value at the time of admission was 1044.77 ± 286.98 but at the time of discharge it was 309.83 ± 48.37 (p < 0.0001; CI -772.73 to -697.146).

Patients in the Moderate Group 2 (Table-02) category who were prescribed Cefixime, Methylprednisolone along with other drugs showed significant improvement in SPO2, RR, D-Dimer, PCT, CRP and Ferritin Values.

| MODERATE GROUP | | | |
|---|---|---|---|
| Cefixime + Hydroxycloroquine + Montelukast + Levocetirizine + Atorvastatin + Fenofibrate + Methylprednisolone + Formoterol + Budesonide | | | |
| | BEFORE (MEAN±SD) | AFTER (MEAN±SD) | p –VALUE * (95 % CONFIDENCE INTERVAL) |
| SPO2 | 90.09 ± 8.00 | 96.45 ± 2.62 | = 0.0051 (2.062 to 10.658) |
| RR | 23.09 ± 2.33 | 18.81 ± 1.04 | < 0.0001 (-5.583 to -2.977) |
| D-DIMER | 1.32 ± 0.87 | 0.49 ± 0.12 | = 0.0007 (-1.278 to -0.382) |
| PCT | 0.45 ± 0.11 | 0.045 ± 0.0001 | < 0.0001 (-0.46116 to -0.34884) |
| CRP | 13.89 ± 5.42 | 2.38 ± 1.24 | < 0.001 (-15.007 to -8.013) |

| | | | |
|---|---|---|---|
| FERRITIN | 1279.8 ± 388.76 | 307.02 ± 40.17 | < 0.001 (-1223.589 to -731.971) |
| TOTAL NUMBER OF PATIENTS = 16<br>*P≤0.05 CONSIDERD AS SIGNIFICANT | | | |

TABLE – 02



- The SPO2 value raised to 96.45 ± 2.62 at the time of discharge from the value of 90.09 ± 8.00 at the time of admission (p = 0.0051; CI 2.06 to 10.65).
- The RR came down to 18.81 ± 1.04 from the initial rate of 23.09 ± 2.33 (p < 0.0001; CI -5.58 to -2.97).
- D- Dimer value at the time of admission was 1.32 ± 0.87 but at the time of discharge it was 0.49 ± 0.12 (p = 0.0007; CI -1.27 to -0.38).
- PCT value at the time of admission was 0.45 ± 0.11 but at the time of discharge it was 0.045 ± 0.0001 (p < 0.0001; CI -0.46 to -0.34).
- CRP value at the time of admission was 13.89 ± 5.42 but at the time of discharge it was 2.38 ± 1.24 (p < 0.001; CI -15.00 to -8.01).
- Ferritin value at the time of admission was 1279.8 ± 388.76 but at the time of discharge it was 307.02 ± 40.17 (p < 0.001; CI -1223.58 to -731.97)
- Patients in the Severe Group (Table-03) category who were prescribed Favipiravir along with other drugs showed significant improvement in SPO2, RR, D-Dimer, PCT, CRP and Ferritin Values.

| SEVERE GROUP | | | |
|---|---|---|---|
| Ceftriaxone +Favipiravir + Doxycycline + Ivermactin + Montelukast + Levocetirizine + Atorvastatin + Fenofibrate + Methylprednisolone | | | |
| | BEFORE (MEAN±SD) | AFTER (MEAN±SD) | p –VALUE * (95 % CONFIDENCE INTERVAL) |
| SPO2 | 82.85 ± 8.49 | 93.14 ± 1.84 | <0.0001 (6.459 to 14.121) |
| RR | 27.04 ± 1.36 | 18.57 ± 1.33 | <0.0001 (-9.309 to -7.631) |
| D-DIMER | 1.39 ± 0.54 | 1.72 ± 0.11 | <0.0001 (-0.913 to -0.427) |
| PCT | 1.33 ± 0.11 | 0.069 ± 0.11 | <0.0001 (-1.3296 to -1.1924) |
| CRP | 18.12 ± 5.10 | 3.13 ± 0.91 | <0.0001 (-17.275 to -12.705) |
| FERRITIN | 1632.4 ± 371.16 | 336.43 ± 48.19 | <0.0001 (-1461.038 to -1130.902) |
| TOTAL NUMBER OF PATIENTS = 21<br>*P≤0.05 CONSIDERD AS SIGNIFICANT | | | |

TABLE – 03

- The SPO2 value raised to 93.14 ± 1.84 at the time of discharge from the value of 82.85 ± 8.49 at the time of admission (p < 0.0001; CI 6.45 to 14.95).
- The RR came down to 18.57 ± 1.33 from the initial rate of 27.04 ± 1.36 (p < 0.0001; CI -9.30 to -7.63).
- D- Dimer value at the time of admission was 1.39 ± 0.54 but at the time of discharge it was 1.72 ± 0.11 (p < 0.0001; CI -0.91 to -0.11).
- PCT value at the time of admission was 1.33 ± 0.11 but at the time of discharge it was 0.069 ± 0.11 (p < 0.0001; CI -1.32 to -1.19).
- CRP value at the time of admission was 18.12 ± 5.10 but at the time of discharge it was 3.13 ± 0.91 (p < 0.0001; CI -17.27 to -12.70).

- Ferritin value at the time of admission was 1632.4 ± 371.16 but at the time of discharge it was 336.43 ± 48.19 ($p < 0.0001$; CI -1461.03 to -1130.90).

Discussion

A study by Mahmud R *et.al,* 2021 showed that Patients with mild-to-moderate COVID-19 infection treated with ivermectin plus doxycycline recovered earlier, were less likely to progress to more serious disease, and were more likely to be COVID-19 negative by RT-PCR on the day of discharge. The finding of this study is similar to our findings which showed that treatment with ivermectin with doxycycline and other drug in mild to moderate COVID 19 infection led to significant improvement in spo2, Respiratory rate (RR), D-Dimer, Procalcitonin (PCT), C-Reactive Protein (CRP) and Ferritin level. A case report by Khaleel A *et. al,* 2022 illustrated the benefits of combination of azithromycin, cefixim, vitamin C , Zinc and Vit. D for the treatment of moderate COVID 19 symptoms. In our study in mild to moderate cases of COVID 19 infections was found to be beneficial significantly. In the randomized clinical trial done by Chen C *et.al* 2020,[26] Favipiravir significantly improved the latency to relief for pyrexia and cough in COVID 19 patients. In our study also Favipiravir when used in severe cases of COVID -19 patients along with other drugs significantly improved the patients condition. This study is retrospective study so compare to prospective study this study has some limitation. Because of the retrospective aspects of this study there might be some selection bias and information bias. Because of limited number of included studies the external validity of this study might suffer. Because of the retrospective nature of the study be cannot control the covariates and potential confounders.

**Conclusion:**

Adult patients with mild, moderate and severe COVID- 19 infection, when treated with deferent drug combination, were more likely to improve in terms of inflammatory markers and disease severity markers and were more likely to have a better clinical profile at the end of the treatment period.

Although additional research on the effects of different drug combination is warranted, the efficacy and safety of various combination of drugs assessed in this study were found to be acceptable



Conflict of Interest: None

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