Case Report

Different Treatment Approaches, Clinical Outcome, Effectiveness of the Drug towards Covid 19 with 5 Different Cases: A Case Series.

Dr. Shamsudeen Moideen*, Maheshwari.V[1], Syam prakash KR.[1], Dr. Sooraj Rajagopal[2], Dr. S.Haja Sherief[3]
*Consultant Physician, IQRAA International Hospital and Research Centre, Calicut, India.
[1] Pharm D Interns, Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamil Nadu, India.
[2]Associate Professor, Department of Physical Medicine and Rehabilitation, Calicut, India.
[3]HOD, Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamil Nadu, India.
*Corresponding author's E-mail: maheshwarivengat@gmail.com

ABSTRACT

An outbreak of a novel corona virus disease-19 (nCoV-19) infection began in December 2019 in Wuhan, China, and now involved in the whole word. Globally around 20 million peoples are been infected by novel corona virus. With its staggering world wide morbidity and mortality, the scientific community has been under extra ordinary pressure to find safe and effective treatment, pending the availability of a vaccine. Certain medications, for example, dexamethasone, antimalarials (chloroquine/hydroxychloroquine), antiviral (remdesivir), and IL-6 receptor blocking monoclonal antibodies (tocilizumab) are used in various combinations as off-label medications to treat COVID-19. Here we are discussing 5 cases of covid 19 with different treatment approaches, and analyze the clinical outcome and effectiveness of the drug towards Covid 19.

Keywords: Anti-Viral, Corona Virus, Monoclonal Antibody, Remdesivir, Toclizumab.

INTRODUCTION

Covid 19 which emerged in late 2019 is an infectious disease caused by SARS-CoV-2 zoonotic virus. This virus was identified first in the Wuhan province of China and by the month of march, covid 19 has been declared as a pandemic by WHO. As of now approximately 28 million people across 188 countries have been affected by this zoonotic virus with the death toll around 1 milllion.[1]

SARS CoV2 is enveloped; positive sense single stranded RNA virus with a glycoprotein spike in the surface. This glycoprotein spike helps in receptor binding and cell entry during infection[2]. Exposure to SARS CoV2 can result in range clinical outcomes varying from asymptomatic to severe acute respiratory distress and death. Covid 19 can affect both upper and lower respiratory tract. This virus can access the host cells via angiotensin converting enzyme II which are seen mostly in lung, heart and GI organs thus making them more vulnerable to COVID 19 infection. The symptoms of covid 19 shows variability but common symptoms include fever, loss of appetite, fatigue, cough, shortness of breath, myalgia and loss of smell[3]. In severe stage of infection the patients are also experiencing, difficulty in walking, confusion, persistent chest pain, decreased WBC, kidney failure, and coughing up blood. About 40 % of patients lose their sense of smell (anosmia).[4]

Covid 19 spread primarily when people are in close contact and one person inhales aerosols that are able to stay suspended in the air for longer period of time. Experiments shows that the virus can survive in the air for up to 3 hours.[5]

Although WHO has published several testing protocols for this disease, the standard method of testing involves Real time reverse transcription polymerase chain reaction (Rrt-PCR) with samples collected by nasopharyngeal swab. clinical laboratory findings of elevated IL-2, IL-7, IL-6, granulocyte-macrophagecolony-stimulating factor (GM-CSF), interferon-γ inducible protein 10 (IP-10), monocyte chemo attractant protein 1 (MCP-1), macrophage inflammatory protein 1-α (MIP-1α), and tumor necrosis factor-α (TNF-α) indicative of cytokine release syndrome (CRS) suggest an underlying immunopathology.. Radiographic findings can also demonstrate remarkable data in Covid patients, which include bilateral air space consolidation and peripheral ground glass opacities.[6]

The treatment varies according to the severity of the patient. The decision for inpatient and outpatient monitoring setting should be made on case by case basis. This would rather depend upon the patient's clinical presentation, requirement for supportive care and potential risk factors. Patients with a light clinical presentation (absence of viral infection and hypoxia) might not initially require hospitalization. Patient's with severe disease such as, pneumonia, ARD/hypoxemic respiratory failure, cardiomyopathy and

arrhythmia, AKI, secondary bacterial infections, thromboembolism and bleeding are treated according to the treatment protocol which would vary in different countries. The treatment mainly involves hydroxychloroquine, azithromycin, fluvir, favipiravir, and other multivitamins. Thromboembolism can be treated with either with NOACS or unfractioned heparin.

CASE REPORTS

Case 1 (COVID-19)

A 52-year-old male patient was admitted in hospital with low grade fever (100°F), complaints of cough and fatigability for past 7 days. No history of sore throat and dysuria. After the admission patient feel loss of taste functions. Patient has no travel history and no history of contact with positive covid 19 cases. Patient had a known case of varicose ulcer on Right foot and he is on regular treatment. On clinical examination patient was alert, on general examination pulse was 90 beats/min, RR: 24mins, SPO2 was 95% On room air, BP was 120/80 mmHg, temperature was 100 F. Rapid Antigen test for covid 19 shows positive and the patient was shift to the covid hospital for further management. Based on signs and symptoms, patient was under category B. Further lab investigation showed that patient Hb was 13.1gm/dL, Total count was 5,500cells/cumm, CRP was increased 20.30 mg/l, D dimer level was also increased 1347.97 ng/ml. On liver function test AST level was 26U/L ALT 27 U/L. On chest X RAY lung patches was noted, suggested of possible pneumonia infection.

Figure 1: Chest X ray of patient 1

Patient was managed with INJ. CEFOTAXIM 1gm IV Q8H for 3 days. T. AZITHROMYCIN 500 mg OD for 5 days, T. TAMIFLU 75mg BD for 5 days, T. PANTOPRAZOLE 40 mg OD, T. ZINC ACETATE 50mg OD and T.CALCIUM AND VIT D3 OD. Patient was on SPO2 monitoring. Patient D Dimer level was increased so added INJ. ENOXAPARINE 40 s/c OD. After two days patient have breathing difficulty and continuous cough so add SYP. ASCORYL 10ml TDS and T. MONTEC LC OD After 5 days of treatment regimen add T. FAVIPIRAVIR 1800 mg BD for 1 day followed by 800 mg BD for 6 days. After that, patient feels better and no other fresh complaints. The patient was tested covid 19 negative on day 10 following the next day the patient got discharged and was sent to home quarantine for 7 days.

Case 2 (COVID 19)

A 45 year old male patient was admitted with complaints of cough, fever and headache for past 1 day. Patient has no co morbidities. Patient has no travel history and no history of contact with positive covid 19 cases. On clinical examination patient was alert, on general examination pulse was 87beats/min, RR: 22mins, SPO2: 96% on room air. BP: 110/80 mmHg TEMP: 100 °F. Rapid Antigen test for covid 19 was POSITIVE. And the patient was shifted to the covid hospital for further management. Based on signs and symptoms, patient was under category B. Further lab investigation showed that patient Hb was 16.lgm/dl, Total count was 4,400 cells/cumm, CRP was increased 15.30 mg/l, D Dimer level was also increased 507.93 ng/ml. Liver function test, AST level was increased to 66U/L, ALT 94 U/L. and total bilirubin also increased to 1.47 mg/dl. After 2 days of the admission, patient had complaint of headache which was managed by T.PARACETAMOL 650mg.

Patient was managed with T. AZITHROMYCIN 500mg OD for five days, T. VITAMIN C 500mg BD, T.ZINC ACETATE OD, T.CALCIUM AND VITAMIN D3 OD, T. HYDROXY CHLOROQUINE 200mg BD, T.PANTOPRAZOLE 40mg OD. As per the treatment protocol, he was tested again for covid antigen and showed negative results. Hence the patient was discharged and shifted for home quarantine.

Case 3 (COVID 19)

A 66 year old male female patient was admitted with complaints of throat pain, cough, myalgia, Patient had no comorbidities. Patient has no travel history neither history of contact with positive covid 19 cases (son). On clinical examination patient was alert, on general examination pulse was 83 beats/min, RR: 21mins, SPO2: 97% on room air. BP: 128/86mmhg TEMP: 98°F. SARS COV2 RT PCR-TRUENAT was POSITIVE detected medium and the patient was shift to the covid hospital for further management. Based on signs and symptoms patient was under category A. Lab investigations showed that patient Hb was 13.0gm/dl, Total count was 6,800 cells/cumm, CRP was increased 10.30 mg/l, D Dimer level was normal 267.69 ng/ml. Liver function tests revealed that AST level was normal 13U/L ALT 15U/L and total bilirubin also normal 0.33 mg/dl. Patient HBA1C was 6.85% newly diagnosed diabetes mellitus. Patient has SARS-COV2 and X-RAY shows no infiltration present.

Patient was managed with T.VITAMIN C OD, T.MULTIVITAMIN OD, T.AZITHROMYCIN 500 mg OD for 5 days. T. OSELTAMIVIR 75mg BD for 5 days. T. PANTOPRAZOLE 40mg OD. T. TELMISARTAN, T.METFORMIN OD, T.GLIMEPIRIDE 1mg BD. After 2 weeks SARS COV2 RT PCR- TRUENAT was NEGATIVE and patient was shifted to institutional quarantine for 7 days.
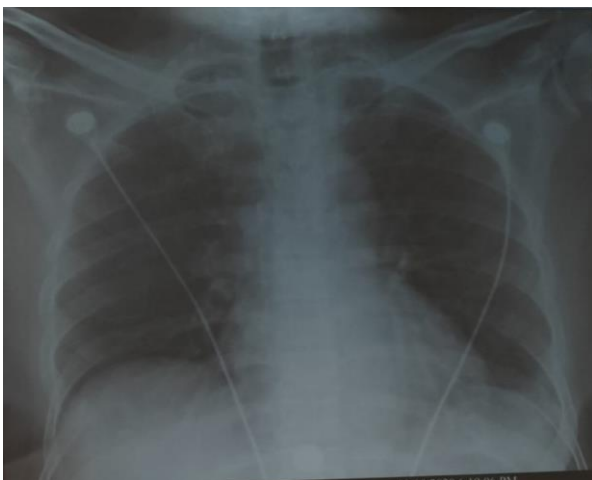
Figure 2: Chest X ray of patient 3

Case 4 (COVID 19)

A 58 year old male patient was admitted in hospital for complaint of chest pain since 1 day and complaint of fever, cough and breathing difficulty. On admission pulse rate was 52 beats/min BP: 74/92 RR: 24/ min SPO2: 94%. On rapid antigen test COVID 19 Positive. Patient was managed in COVID –ICU with DAPT, STATINS, HEPARIN and other supportive care was on dual ionotrops supportive and was under cardiology surveillance. Patient improved significantly and shifted into covid hospital. Patient has no travel history, and history of contact with covid positive. After 2 days patient have complaint of cough. Patient have a known case of CAD ACS- STEMI. On general examination pulse: 94 beats/min, temp: 98 F, RR: 22/min. SPO2: 93% on room air, BP: 117/76 mmHg.

Further lab investigation showed that patient Hb was 11.2gm/dl, Total count was 6,300 cells/cumm, CRP was increased 98.70 mg/l, D Dimer level was also increased 1786.77 ng/ml. Serum ferritin was also increased 1421.69 ng/ml on liver function test AST level was increased 48U/L ALT 36 U/L and total bilirubin also increased 1.46 mg/dl. Blood culture shows Pseudomonas aeruginosa.

Figure 3: Chest X ray of patient 4

Patient was managed with INJ.HEPARIN 5000IU/ Q6H for 2 more days, T. ASPIRIN 75mg OD, T.CLOPILET 75mg OD, T.ATORVASTATIN 20mg OD, T.ZINC ACETATE BD,

T.VITAMIN C 500mg OD, T.METOPROLOL XL 25mg BD. T.METFORMIN 500mg BD.   T. FABIFLU 1800 mg BD for 1 day, followed by 800mg BD for 6 days.

On 3rd day of admission, patient have high grade fever 102^{0}F and dysuria probably UTI. Patient was managed with T. PARACETAMOL 650 mg. INJ. CEFOPERAZONE+ SULBACTAM 1.5gm IV BD for 7 days.

On the 4th day patent have constipation and high grade fever with breathing difficulty, the patient again shifted to ICU, stopped FABIFLU and started INJ. REMDESIVIR 100 mg in 250 ml NS IV over 90 min for 4 days, INJ. DEXAMETHASONE 8mg IV BD. INJ. ENOXAPARIN 40 S/C OD, INJ. FRUSIMIDE 40mg IV OD. After 5 days patient shifted to ward. SARS COV2 RT PCR- TRUENAT on following was NEGATIVE. Hence the patient was shifted to nearest hospital for cardiology consultation.

Case 5 (COVID 19)

A 60 year old male patient who has tested positive admitted in hospital with complaints of severe breathlessness. On admission patient his pulse rate is 78 bpm, respiratory rate 24/min, saturation 95 % BP 110/70 mmHg. Patient is known case of ST elevated Myocardial Infarction and has done percutaneous coronary intervention. Patient was diagnosed with covid 19 with type 1 respiratory failure and was categories into Category B. Patient was immediately transferred to intensive care unit.

Further lab investigation showed that patient CRP was 61.06 Mg/L. Patients Hb count was 12.4 gm/dl. Liver function test shows elevated ALT and AST level which are 121 and 99 U/L respectively. Platelet, RBC, WBC count does not shows much variation and are found normal.

Figure 4: Chest X ray of patient 5

Chest x-ray shows diffuse infiltrates lung Due to type 1 respiratory failure and the patient was managed under ICU monitoring. Patient was initially provided with T.favipiravir 1800 mg bd, Inj.cefoperazone with sulbactum bd, Inj.Pan 40 mg od, Inj.Dexamethasone 8 mg BD, T.Warfarin 5 mg

OD, T.Concor 2.5 mg OD, T.Aldactone 25 OD, T.Lasix 40 mg OD, T.Ivabrid 5 mg ½ tab BD, T.Ecospirin Gold OD. On day 2, the dose of T.favipiravir was changed to 800 mg BD. INR monitoring was done on second day shows 2.10 but was elevated to 3.02 hence T.Warfarin was put on hold for 1 day .T.Concor was put on hold in day 4 when patient has reported with low BP. Along with these drugs patient was also provided with T.Vit C and T.Ascazinc.

Patient was shifted out in day 7 from ICU and shifted to ward. Antibiotic regimen was given for a total of 10 days. Favipiravir was given for total of 6 days, dexamethasone for 5 days and vitamin C for 5 days.

Patient was tested covid 19 negative on 14 th day and was subsequently discharged from hospital.

DISCUSSION

Corona virus Disease 2019 (COVID-19) is a novel viral disease with over 28 million affected individuals in the world till now. Fatality rate in general population is about 1-6%. Out of the seven subtypes of corona virus, beta corona virus is associated with potentially severe diseases. The naming of this virus as SARS-CoV 2 has been done by international committee of taxonomy of viruses and WHO called this as a Covid 19. SARS-CoV-2 is closely related to the SARS-CoV and MERS-CoV, which were responsible for significant morbidity and mortality in their past outbreaks[7].

Due its staggering effect on mortality and morbidity, it's now a global need to evaluate and assess available evidences about this disease that could further support in the process of upgrading the treatment protocol for this disease.

Here we are discussing five cases of covid 19 with different treatment approaches, and analyze the clinical outcome and effectiveness of the drug towards covid 19. Depending up on the signs and symptoms, patients were classified into three categories i.e., category A, category B, category C. All the above cases are from either from category A or from category B. In category A, the patients have only mild sore throat, cough, rhinitis, and diarrhea. In our case, the patients have complaint of mild throat pain, cough and comes under category A. On the other hand, if a patient has complaints of fever or severe sore throat, cough, diarrhea or else if a patient has lung, liver, heart, kidney, neurological disease, hypertension, AIDS, hematological disorder or long-term steroid, immunosuppressive drug, or she is pregnant or his/her age above 60 are grouped as category B. In this case series cases 1 and 2 falls under category B. On the other hand, if a patient is having moderate to severe symptoms along with the drastic fall in oxygen saturation and with major comorbidity, he or she will be categorized under category C. Patient in category C are among the high risk category because of their underlying co morbidities.
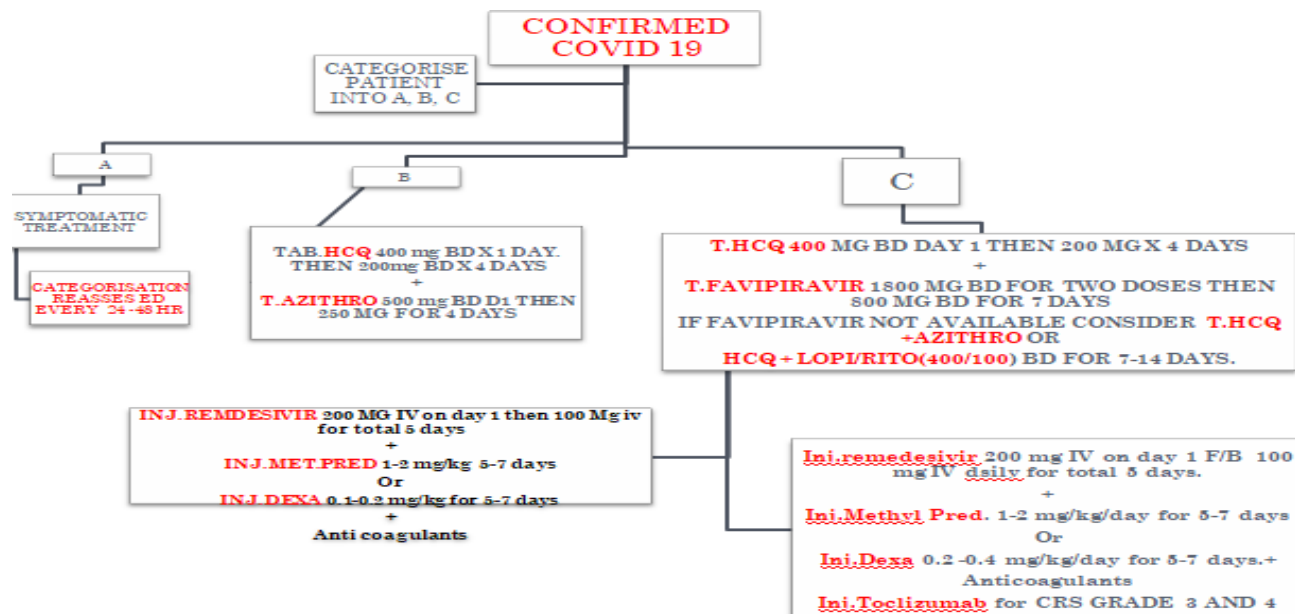
Figure 5: Treatment approach for Covid 19

In all the cases, patient's were managed with T. Multivitamins, Hydroxychloroquine, Azithromycin, Fluvir and Favipiravir. Preclinical data suggests that Hydroxychloroquine has in vitro antiviral activity, blocking the entry of the virus into cells, decreasing pH within cells and attenuating cytokine production. The in vivo efficacy of Hydroxychloroquine has not yet been assessed[8]. Even with the limited evidences with HCQ regimen on Covid 19 treatment. One patient (case 2) was treated with HCQ at a dose 200 mg twice daily for 4 days along with

T.Azithromycin 500 mg OD. Faster recovery was also reported in this patient.

In all the cases, D-dimer value of patient has been elevated. IFCC guidelines on COVID-19 recently published strongly recommends D-dimer testing in covid 19 patients after studies showed a high association between incidence and outcome of covid 19 in patient with elevated Ddimer level[9]. In extreme cases, even disseminated intravascular coagulation can evolve despite enabled coagulation in covid

19. Increased D-dimer levels as a predictor of development of acute respiratory distress in COVID-19 refers to the likelihood of micro pulmonary embolism especially in severe forms of COVID-19[8]. Increased D dimer level was managed by giving INJ. ENOXAPARIN. In case 1, 4 and 5 the patient liver enzymes were elevated. Significant impairment of liver function or overt liver failure as the cause of death in COVID-19 rarely occurs. There was no direct evidence of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) hepatic infections.

In all patients C - reactive protein was increased. Latest study found that, as the disease progresses, CRP levels and the diameter of the largest lung lesion increases. Levels of CRP were associated positively with lung lesion and seriousness of the disease. This indicated that CRP levels might indicate lung lesions and disease severity in the early phase of covid 19.

Favipiravir is one of the antiviral agents used in treatment of COVID 19. The drug which is well known for its rapid reduction in viral load, faster fever resolution, faster resolution of chest changes as well as faster clinical recovery. Since this drug is reported to cause teratogenicity, the use of favipiravir was restricted among pregnant women. In our case series, cases 1, 4 and 5 are provided with favipiravir with a starting dose of 1800 mg BD followed by a maintenance dose of 800 mg BD for 6 days because both the patients are experiencing mild to moderate covid 19 symptoms which mainly include breathlessness. Liver function test for both these patients were closely monitored during favipiravir treatment because of elevated liver enzymes due to this drug. Remdesivir which is a pro drug for its active form GS 441524 which bind to RNA dependent RNA polymerase evades the proof reading and decreases the Viral RNA. This drug given to Category C patient (case 4) under Intensive Care Unit (ICU) supervision. In our case 4, the patient has shifted to ICU and immediately started with Inj.Remdisivir at a dose of 100 mg in 250 ml NS IV in 90 min for 4 days. This regimen must only begin after stoping T.Favipiravir. Introduction of Remdesivir resulted at a sudden decrease in viral load of the patient.

Intravenous administration of dexamethasone for up to 10 days has evidently proven to reduce the mortality [10]. In our case series patient in case 4 and 5 has experienced severe breathlessness and has been treated with Inj.Dexamethasone 8 mg IV 1-0-1. The patient has become symptomatically far better than before after giving the first dose, which also supports the available data regarding its efficacy in modulating inflammation mediated lung injury and thereby reducing progression to respiratory failure and death[10].

Multivitamins mainly Vitamin D and C are also given to the patient irrespective of the category of their severity. Vitamin D serves as a modulator of the immune system by offering an efficient physical barrier and enhancing both innate and adaptive immunity. It preserves the integrity of epithelial barriers by restoring tight junctions, gap junctions and adhering junctions. In addition to this, Vitamin D enhances innate immunity by increasing the production of Antimicrobial Peptides such as cathelicidin (LL-37) in respiratory epithelial cells which has the ability to disrupt bacterial membranes via electrostatic interactions. It also increases the production of anti-inflammatory cytokines and suppresses pro-inflammatory cytokines such as TNF alpha and interferon gamma. This prevents the generation of cytokine storm which is the underlying mechanism of acute respiratory distress syndrome. Moreover, it also affects the adaptive immunity by decreasing the production of pro-inflammatory cytokines during both TH1 and TH2 response and suppresses the pro-inflammatory Th17 cells. In addition to this, it binds to the non-coding region of FoxP3 increasing the production of regulatory Treg cells and IL-10, thus reducing inflammation. Studies indicate that vitamin D has a potential role to play in protecting against viral respiratory infections, especially from enveloped viruses.

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