

PHARMACOTHERAPEUTIC EVALUATION OF COVID-19 PATIENTS WITH CO-MORBIDITIES

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Article Received on 18/10/2022

Article Revised on 08/11/2022

Article Accepted on 28/11/2022

ABSTRACT

Treatment approach for COVID-19 is complicated by many factors, evaluating the effectiveness of drug therapy is crucial to improve health related quality of life of COVID-19 patients. Elderly people and People with multiple disease states are more likely to suffer with severe COVID-19 infection hence, appropriate treatment approach for such vulnerable patients is required. The main objective of the study is to determine therapeutic appropriateness with respect to age and disease state of the patients. A prospective observational cohort study was conducted in a tertiary care hospital for duration of 6 months involving 184 COVID-19 affected patients with various co-morbidities. The study re-evaluates the drug therapy and assesses the quality of life of recovered COVID-19 patients by providing them with a questionnaire to fill, and following up with them for 1-2 months from the time of recovery for proper assessment of the questionnaire. The questionnaire is designed in such a manner that it is easy to answer and evaluates the patient in various physical, mental and social domains. Statistical analysis i.e. t test was carried out on inflammatory biomarkers values obtained before and after treatment to assess improvement in COVID patients. Primary outcomes were re-evaluating the drug therapy, quality of life assessment of patients recovered from COVID-19, survival rate and mortality rate. Secondary outcomes were focused on drug-drug interactions, adverse effects, need of mechanical ventilation, estimation of ICU stay and hospital stay, association between co-morbidities and COVID-19, evaluating laboratory findings and association of complications with age and co-morbidities.

KEYWORDS: COVID-19, co-morbidities, Quality of life, Therapeutic appropriateness, Complications, Mortality rate.

INTRODUCTION

On 31st December 2019 a large number of cases of pneumonia of SARS-COV-2 were reported in the city of Wuhan, Hubei province in China since then, SARS-COV-2 has spread throughout the world in a very short period of time making WHO to declare coronavirus diseases (COVID -19) as a pandemic in March 2020.^[1]

Coronavirus

Coronaviruses are a family of viruses that cause respiratory diseases and gastrointestinal diseases. Respiratory diseases can range from the common cold to more severe illness such as pneumonia e, g.

- Middle East Respiratory Syndrome (MERS-CoV)
- Severe Acute Respiratory Syndrome (SARS-CoV).^[2]

The novel coronavirus (nCoV) is a new strain which has not been identified in humans previously. Once scientists resolved exactly what coronavirus it is, they give it a name as SARS-CoV-2 causing COVID -19).

The core genetic material of the virus is surrounded by an envelope with protein spikes. This gives it the appearance of a crown. The word Corona in Latin means "crown". One of the main biological characteristics of SARS-CoV-2, as well as many other viruses is present of spike proteins which helps these viruses to penetrate host cells and cause infection. Coronaviruses are zoonotic^[3] as the viruses are transmitted between animals and humans. It has been determined that MERS-CoV was transmitted from

dromedary camels to humans and SARS-CoV from civet cats to humans.^[2]

Clinical manifestations

Laboratories confirmed 55,924 cases of COVID-19 had

- Fever (87.9%),
- Dry cough (67.7%),
- Fatigue (38.1%),
- Sputum production (33.4%),
- Difficulty breathing (18.6%),
- Sore throat (13.9%),
- Chills (11.4%),
- Nasal congestion (4.8%),
- Haemoptysis (0.9%)^[4]

A smaller number of people will present with more severe symptoms and will be in need of hospitalisation, most often with pneumonia, and in some cases, the illness can include ARDS, sepsis and septic shock. Emergency warning signs where immediate medical attention is required include-

- Difficulty is breathing
- Pain or pressure in chest
- Bluish lips, nails and skin
- Confusion or inability to arouse.^[5]

High risk population

The virus infects all age groups. However, based on the evidence three groups of people are at a higher risk of getting COVID-19 disease.

- 1) Older people (age >70 years)
- 2) People with co morbidities and chronic illnesses
 - Cancer
 - Diabetes
 - Hypertension
 - Cardiovascular diseases
 - Chronic respiratory diseases
 - Chronic liver diseases
- 3) Physically inactive people.^{[6][7]}

Transmission of covid-19

Evidence indicates that human-human transmission is occurring, the disease spread through large respiratory droplets with direct or indirect contact with infected person. People who are in close proximity to infected person are most likely to get infected.^[8]

There are higher changes of transmission in case of

- 1) Crowded places
- 2) Close – contact settings, especially when people having conversations while being very near to each other.
- 3) Place where ventilation is poor.^[9]

The incubation period for COVID- 19 is estimated to be between 2 to 14 days^[10], this means that if a person remains well after coming in contact with the infected person in that duration then he is not infected.

Special population consideration

• Children

A study on 72,314 cases published by the Chinese Centre for Disease Control and Prevention stated that 0.9% of the total patients were between 0 and 9 years of age, and 1.2% of the total patients were between 10 and 19 years of age. The most common symptoms reported in children are cough (46%), fever, (59%), gastrointestinal symptoms (12%), and some cases (26%) showed no specific symptoms initially with ground glass opacities and patchy consolidation in CT chest findings.^[11]

• In pregnant women

The most common symptoms which are found in pregnant women are fever (61.96%), cough (38.04%), malaise (30.49%), myalgia (21.43%), sore throat (12%), and dyspnea (12.05%). Other symptoms reported in pregnant women are diarrhoea and nasal congestion.^[12]

• Immune compromised patients

Because of their impaired immune response, it is expected that immunocompromised patients infected with COVID-19 might be at higher risk of developing severe disease and co-infections in comparison to normal populations. However, a recent studies stated that the association between the overreaction of the immune system with COVID-19 and cytokine storm syndrome raises the possibility that immune deficient states might increase the over expression of the host immune system and thereby prevent deadly forms of the disease. In one study just like the general population, HIV and immunocompromised patients were having no different infection in terms of clinical manifestation or severity. However, more studies are recommended to be conducted to establish the link between this particular group of patients with severity of the disease.^[13]

Laboratory findings

Most Common laboratory findings among hospitalized patients with COVID-19 include elevated aminotransaminase levels, lymphopenia, elevated lactate dehydrogenase levels, elevated inflammatory markers (eg, C-reactive protein, ferritin and erythrocyte sedimentation rate), and coagulation abnormalities in tests.^[14]

Lymphopenia is mostly common, even though the total white blood cell count can vary. As an example, in a study on 393 adult patients hospitalized with COVID-19 in New York City, 90% had a lymphocyte count <1500/microL; leukocytosis and leukopenia were each reported in approximately 15% of the patients.^[15]

On admission, many patients with pneumonia had normal serum procalcitonin levels; however, in those who needed ICU care, procalcitonin levels are more likely to be elevated.^[14]

In Several laboratory findings more severe lymphopenia and high D-dimer levels have been associated with critical illness or mortality.^[16]

Imaging findings

- **Chest radiography**- In most of the cases the chest radiographs are normal in early stages. In a retrospective study was conducted on 64 COVID-19 patients who lived in Hong Kong, 20% of them did not have any chest radiograph abnormalities at any time of the illness.^[17] The most Common abnormal findings were Consolidation and ground-glass opacities, with peripheral, bilateral, and lower lung zones; the severity involving lung will be increases during the course of illness, with more severity observed at 10 to 12 days after the onset of symptoms. Pneumothorax is also been observed although it is not that common. In a retrospective study review on 70,000 COVID-19 patients evaluated in emergency departments in Spain, 40 patients were identified with spontaneous pneumothorax.^[18]
- **CT scan** — chest computed tomography (CT) is considered more sensitive than chest radiograph.

A systemic review study was conducted on 2700 patients with COVID-19, the following abnormalities

Were observed:

- 83% patients showed - Ground-glass opacities
- 58% patients showed- Ground-glass opacities with mixed consolidation
- 52% patients showed - Adjacent pleural thickening
- 48% patients showed - Interlobular septal thickening
- 46% patients showed- Air bronchograms.^[19]

- **CO-RADS score**

There are seven categories of CO-RADS (CO-RADS 0 to CO-RADS 6) which indicates the level of suspicion and increasing risk of covid-19 infection.

- CO-RADS 0 = the scan does not have the diagnostic quality that would allow the radiologist to either examine or exclude the other CO-RADS categories, this happens due to serious artifacts or missing part of lungs. It should not be taken as a final assessment and one should repeat the scan if possible.
- CO-RADS 1 = one has a normal chest CT scan or one has abnormalities in scan attributed to non infectious diseases
- CO-RADS 2 = abnormal findings consistent with infection other than covid-19 or the abnormality attributes to an infection other than covid-19, example- other lung infections
- CO-RADS 3 = abnormalities associated with covid-19 lung involvement but these abnormalities are also found in other viral pneumonias and non-infectious diseases of the lungs. Unclear whether covid-19 is present or not.
- CO-RADS 4 = abnormal findings in lungs typically associated with covid-19 infection.
- CO-RADS 5 = typical covid-19 infection with mandatory abnormal findings such as ground-glass opacities, this levels signifies very high suspicion of covid-19 lung involvement.

- Co-RADS 6 = indicates proven covid-19 after a positive RT-PCR for the virus.^[20]

Treatment and management

Initially, when the pandemic of covid-19 started, the understanding of COVID-19 and its therapeutic treatment was limited, creating an emergency to subside this new viral illness with drug repurposing and experimental therapies. Since then, due to the intense efforts of the clinical researchers globally to understand not only COVID-19 and its management but this has also resulted in development of new conventional therapies and vaccines at an extraordinary speed.

Pharmacological management of covid-19 in adults

Currently, a number of therapeutic options are available that include

- Anti-viral drugs (eg-Remdesivir)
- Anti-inflammatory drugs (eg- dexamethasone)
- Anti-SARS-CoV-2 monoclonal antibodies (eg- Bamlanivimab/Etesevimab, Casirivimab/Imdevimab)
- Immunomodulators agents (e.g., baricitinib, tocilizumab) are approved by FDA for Emergency Use.^[21]

The clinical uses of these treatments are very specific and are given based on the severity of infection or based on certain risk factors. The clinical phase of the COVID-19 infection occurs in 2 stages, an early stage when SARS-CoV-2 virus replicates in greater amounts before or soon after the onset of symptoms. Anti-viral medications and antibody-based treatments are more likely to be therapeutically effective during the stage of viral replication. The later stage of the infection is controlled by a hyperinflammatory state due to the release of cytokines and prothrombotic state is achieved due to activation of coagulation system. Anti-inflammatory drugs such as corticosteroids, immunomodulating drugs or a combination of these therapies is used to fight this hyper inflammatory state than the use of antiviral therapies.^[22]

- **Remdesivir** is a broad-spectrum antiviral agent that was previously used against SARS-CoV-2 in vitro.^[23] Based on three randomized, controlled clinical trials studies remdesivir showed to be effective and was superior to placebo in shortening the time to recovery and treating mild-to-severe COVID-19 infection in adults patients who were hospitalised. The Food and Drug Administration (FDA) US- approved the use of remdesivir in adults and paediatric patients who are over age 12 years and weighing at least 40 kilograms in treatment of covid-19 in hospital environment^[24]. However, a study of WHO SOLIDARITY conducted at 405 hospitals across 40 countries on 11,330 COVID-19 patients who randomly received remdesivir (2750) or no drug (4088) have shown that remdesivir had little or no role on overall mortality, mechanical

ventilation, and length of hospital stay^[25]. However, there is no evidence available regarding the effectiveness of remdesivir against the new SARS-CoV-2 variants.

- **Ivermectin repurposed** for Covid 19 treatment and got approval for the same by Food and Drug Administration is an anti-parasitic drug. It is given approval based on an in vitro study conducted that showed inhibition of SARS-CoV-2 virus replication.^[26]
- **Corticosteroids:** In Severe COVID-19 infection the patient is in hyper inflammatory state due to release of cytokines which is associated with lung injury, to treat this hyper inflammatory state corticosteroids are used. During the early pandemic glucocorticoids role in treatment of COVID-19 patients was not well explained. However dexamethasone is shown to be effective in patients who were on invasive mechanical ventilation or oxygen support but not in patients who were not receiving any respiratory support. Based on this study trial results, dexamethasone is currently considered as the standard of care either alone or in combination with remdesivir in treating severely ill hospitalized patients who require supplemental oxygen or invasive or non-invasive mechanical ventilation.^[27]
- **Tocilizumab** is an anti-interleukin-6 receptor alpha receptor monoclonal antibody that has been used in variety of rheumatological diseases. The data regarding the use of tocilizumab is mixed. A randomized control trial conducted on 438 patients who were hospitalized and had severe COVID-19 pneumonia, among which 294 were randomly received tocilizumab and 144 patients received placebo, showed that tocilizumab did not showed significant improvement in clinical status of the patient or on the mortality rate compared to placebo^[28]. Results from another randomized, double-blind placebo-controlled trial conducted on 243 severe COVID-19 patients who randomly received tocilizumab or placebo showed that tocilizumab does not play a role in preventing intubation or death rate.^[29] On the other side, based on two studies conducted over a large population showed significant benefit of tocilizumab in patients with severe respiratory distress.^[30]

Management of covid-19 in severe/ critical infection

Patients who are critically ill require hospitalisation.

- Considering that patients with severe COVID-19 are at increased risk of prolonged critical illness and mortality, taking right and early therapeutic decisions and discussing care goals should be done right away.
- Patients with COVID-19 are at a high risk of developing clots and prophylactic use of appropriate anti-coagulants to prevent thromboembolic events.

- Clinicians and healthcare staff should wear proper protection while interacting with the covid-19 patients, protection like appropriate PPE that include gloves, gowns, mask and eye protection when performing aerosol producing procedures on patients with COVID-19 in the ICU, such as bronchoscopy, tracheostomy, endotracheal intubation, manual ventilation before intubation, physical proning of the patient or giving critical patient care such as nebulisation, upper airway suctioning, disconnecting the patient from the ventilator, and non invasive positive pressure ventilation.
- Renal replacement therapy should be given to patients who are suffering from renal failure.
- In patients who do not require intubation, HFNC or NIPPV can be considered.
- Covid-19 Treatment Guidelines given by The National Institutes of Health (NIH) strongly suggest using dexamethasone in hospitalized patients who are on oxygen support via ventilation. Using combination therapy of dexamethasone with remdesivir can also be a good option.
- Covid-19 Treatment Guidelines given by The National Institutes of Health (NIH) strongly suggest tocilizumab given as a single intravenous dose in recently hospitalized patients who are exhibiting severe respiratory discomfort due to COVID-19.
- Future respiratory failure should be recognized as soon as possible and endotracheal intubation with invasive mechanical Ventilation must be commenced.
- Empiric antibiotic therapy should be considered in case of secondary bacterial infection. Reassessment of antibiotics should be done on daily basis for evaluation of appropriateness of medication on the basis of diagnosis.
- Management of COVID-19 patients with ADRs should be done in the same manner in which the other patient would have been managed if they had encountered the same ADR.
- Appropriate management of sepsis according to COVID-19 management guidelines.^[31]

Quality of life

COVID-19 has a devastating effect on patient's life. Apart from the complications of the infection, COVID-19 infection affects a person physical health as well as their mental health and social health. As COVID-19 therapeutic management is still under evaluation, the medication appropriateness in accordance to disease prevalence is a major concern. Getting a satisfactory treatment is the main goal for any patient with respect to the symptoms, drug therapy and hospital stay. In this regard, the quality life of the patients was assessed with the help of a "Quality of life assessment questionnaire for the COVID-19 patients with co-morbidities".

Quality of life assessment questionnaire

A health related quality of life (HRQOL) questionnaire was prepared to assess the quality of life in recovered COVID-19 patients who had co morbidities. The questionnaire is designed by using The Short Form 36 Health Survey Questionnaire (SF-36) and sickness impact profile (SIP) Questionnaire as a reference and consisted of questions about major impairment, symptoms, mental health and general quality of life. Patients who had poor prognosis were found to score low. Their mental health suffered due to their health related anxiety and economic burden related to hospitalisation. The questionnaires were prepared keeping in mind the most common problems individuals

suffering from a particular disease would face and to meet the requirements of the considered parameters. Parameters were related to patient satisfaction with respect to treatment and outcome. The questionnaire was simple and formulated in such a way that a part of it should be filled by the patient or his/her care giver at the time of discharge and the rest of it was filled during the follow up. Patients were followed up for 1-2 months after their recovery through telecommunication for proper assessment of the questionnaire. A score was given after the completion of the questionnaire which determined the quality of life. Higher the score, higher the quality of life. Patients who scored less were counselled at many intervals.

Interpretation

Table 1: questionnaire interpretation.

Sr. no.	Score	Indication	Measures
1.	0 to 3	Poor health related quality of life	Counselled on multiple occasions
2.	4 to 6	Fair health related quality of life	Received counselling
3.	7 to 10	Good health related quality of life	Counselling given only when help was sought

MATERIALS AND METHOD

Study site: The study was conducted at Aster Prime Hospital, Telangana, India

Study design: The study is a prospective observational cohort study. During the study period a total of 184 patients were questioned with physical, mental and treatment queries with the help of a questionnaire, the information was collected from the patients and analyzed.

Study period: 6 months

Sample size: The study was conducted on 184 patients.

Study criteria

Inclusion criteria

- Study includes both male and female are included who are willing to present their consent
- Population equal to and above 18 years of age is considered.
- patients suffering with covid-19 and underlying health conditions:
 - High blood pressure
 - Endocrine disorders (e.g. - diabetes, Hypothyroidism)
 - Cardiovascular illness
 - Chronic respiratory illness
 - Chronic disease (liver disease, kidney disease)
 - Neurological disorders
 - Immune compromised state

Exclusion criteria

- Population of below 18 years is not considered.
- People who are not suffering from COVID-19.
- Patients without any above mentioned health conditions.
- Patient who are not willing to present their consent.

Sources of data

The following data was collected:

1. Patient Case sheets
2. Patient Laboratory reports
3. Quality of life questionnaire.
4. Information gathered through counseling the patient.

Data collection

The study was conducted in Aster prime hospital, Ameerpet, Hyderabad, India. The data was collected using case report forms and the quality of life questionnaire for COVID-19 patients, designed to satisfy the parameters of study.

Ethical consideration

Before commencing the project, ethical approval was taken from the ethical committee of the hospital as well as inform consent were obtained from the patients.

Study Procedure and Monitoring

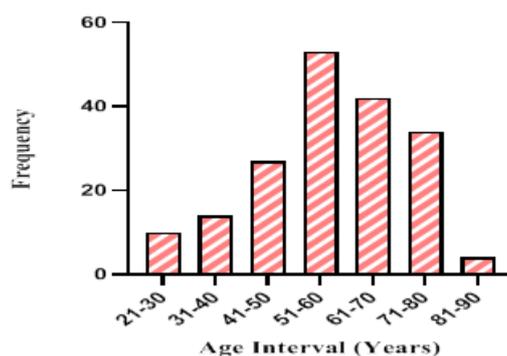
Research information was gathered everyday using case report form, all the required patient info was collected and monitored. The activities were reviewed often to spot gaps and problems which could be resolved early and to avoid any interference within the research.

Statistical analysis

Microsoft Excel was use to compile the collected information and statistical analysis on the data was carried out using SPSS software version 20 and the data was presented in tabular form and graphical representations.

RESULTS**1) Age distribution****Table 2: Age wise distribution.**

Sr. No.	Age Interval (years)	No. of Patients (N)	Percentage %
1.	21-30	10	5
2.	31-40	14	8
3.	41-50	27	15
4.	51-60	53	29
5.	61-70	42	23
6.	71-80	34	18
7.	81-90	4	2

**Fig. 1: Age wise distribution.**

All the patients greater than or equal to 18 years of age suffering with covid-19 and co morbidities were considered for the study. It has been found that the highest number of patients (N=53) fell under the age group of 51-60 years with a total percentage of 29%. The

least number of patients (N=4) fell under the age group of 81-90 years with a total percentage of 2%. The age groups of 21-30, 31-40, 41-50, 61-70 and 71-80 had patients with percentage of 5%, 8%, 15%, 23% and 18%.

2) Gender wise distribution**Table 3: Gender distribution.**

Sr. No	Gender	No. of patients (N)	Percentage
1.	Male	117	64
2.	Female	67	36

Both males and female patients were considered for the study and it has been found that out of a total of 184

patients 64% of the patients were male and 36% of the patients were female.

3) CO-RADS level**Table 4: Distribution Based on CORAD Score.**

Sr. No	Co-rads level	no. of patients (n)	Percentage %
1.	1	0	0
2.	2	2	1
3.	3	3	2
4.	4	21	11
5.	5	102	55
6.	6	56	30

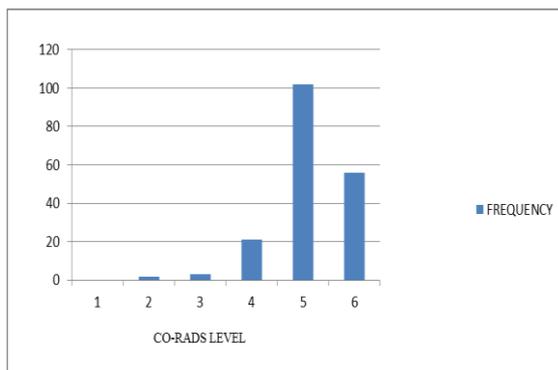


Fig. 2: Distribution based on CO-RADS level.

It has been found that highest number of patients (N=102) had CO-RADS 5 with a total percentage of 55%, followed by 56 patients (N=56) had CO-RADS 6 with a total percentage of 30%, followed by 21 patients

(N=21) had CO-RADS 4 with a total percentage of 11% and rest of patients had CO-RADS 3 and CO-RADS 2 with a percentage of 2% and 1%.

4) Hospital stay

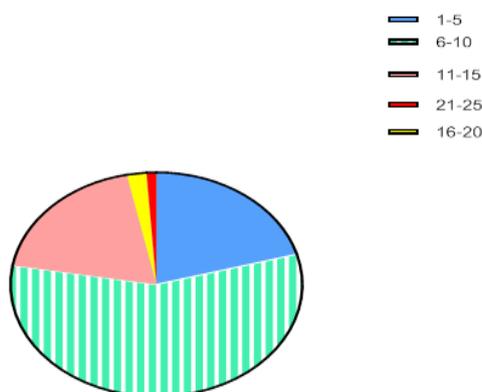


Fig. 3: Hospital stay.

Table 5: Hospital stay.

Sr. No	No. of Days	No. of patients (N)	Percentage%
1.	1-5	38	21
2.	6-10	105	57
3.	11-15	35	19
4.	16-20	4	2
5.	21-25	2	1

The highest number of patients (N=105) with a total percentage of 57% had a hospital stay of 6-10 days, followed by 38 patients (N=38) with a percentage of 21% had a hospital stay of 1-5 days, followed by 35 patients with a percentage of 19% had a hospital stay of

11-15 days, followed by 4 patients (N=4) with a percentage of 2% had hospital stay of 16-20 days, the rest of the 2 patients (N=2) with a percentage of 1% had hospital stay of 21-25 days

5) RT-PCR report

Table 6: Report of RT-PCR.

Sr. No	Report	No. of patients (N)	Percentage %
1.	Positive	165	90
2.	Negative	19	10

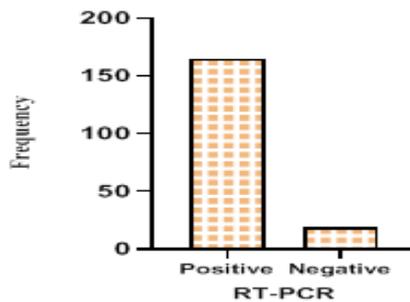


Fig. 4: Report of RT-PCR.

Out of 184 patients, 165 patients (N=165) were tested COVID-19 positive in RT-PCR report with a total

percentage of 90% and 19 patients (N=19) were tested negative in RT-PCR report with a percentage of 10%.

6) Co- morbidities seen in study population

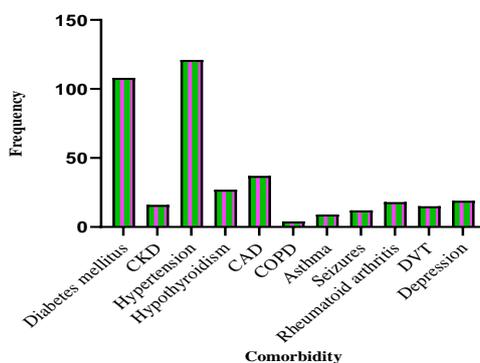


Fig. 5: Co morbidities seen in this study population.

Table 7: Co morbidities seen in this study population.

Sr. No	Co morbidity	No. of patients (N)	Percentage %
1.	Diabetes mellitus	108	59
2.	Hypertension	121	66
3.	Hypothyroidism	27	15
4.	CAD	40	22
5.	COPD	4	2
6.	Asthma	9	5
7.	Parkinson disease	6	3
8.	Seizures	12	7
9.	Rheumatoid arthritis	18	10
10.	Anemia	5	3
11.	Depression	19	10
12.	Schizophrenia	4	2
13.	DVT	15	8
14.	Stroke	5	3
15.	Liver disorder	7	4
16.	Gout	6	3
17.	Psoriasis	2	1
18.	CKD	16	9
19.	BPH	5	3

The highest number of patients (N=121) have hypertension as a co-morbidity with a total percentage of 66%, followed by 108 patients (N=108) who have diabetes mellitus as a co- morbidity with a total percentage of 59%, followed by 40 patients (N=40) who have coronary artery disease as a co-morbidity with a

total percentage of 22%, followed by 27 patients (N=27) who have hypothyroidism as a co-morbidity with a total percentage of 15%. The least common co-morbidity is psoriasis with a percentage of 1% happened to a single patient (N=2).

7) Disease burden in covid-19 patients

It has been found that out of 184 patients, 40 patients (N=40) had a single co-morbidity with a total percentage of 22%, 70 patients (N=70) had 2 co-morbidities with a total percentage of 38%, 62 patients (N=62) had three

co-morbidities with a total percentage of 34%, 9 patients (N=9) had four co-morbidities with a total percentage of 5% and 3 patients (N=3) had five co-morbidities with a total percentage of 2%.

Table 8: Number of co-morbidities in a single patient.

Sr. No	Number of co-morbidities	Number of patients (N)	Percentage %
1.	1	40	22
2.	2	70	38
3.	3	62	34
4.	4	9	5
5.	5	3	2

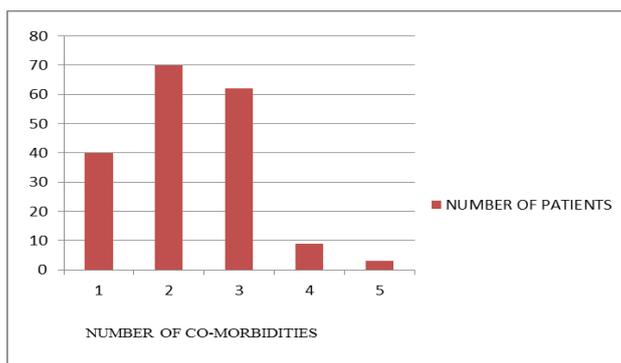


Fig. 6: no of co-morbidities in a single patient.

8) Comparison of inflammatory markers Before and After treatment

Table 9: Comparison of Inflammatory Markers before and after Treatment.

Sr. No	Parameter	Treatment		P value
		Before	After	
1.	CRP	9.26±7.23	4.96±2.56	0.0093
2.	IL-6	91.48±45.32	44.38±22.7	0.0456
3.	Ferritin	664.6±490.6	432.7±212.3	0.0321
4.	D-dimer	647.2±341.8	296.7±102.4	<0.001
5.	LDH	455.6±257.5	279.7±197.2	<0.001

Significant difference exists in the markers Before and After treatment

Taking into consideration CRP, IL-6, Ferritin, D-dimer and LDH and their values before treatment and after treatment and performing dependent T-test on them, it has been found that there exists a significant difference

in the inflammatory markers before and after treatment. The inflammatory markers were significantly high before treatment and there values have been reduced after treatment was given. Confidence interval is 95%, hence the p value < 0.05 is considered significant.

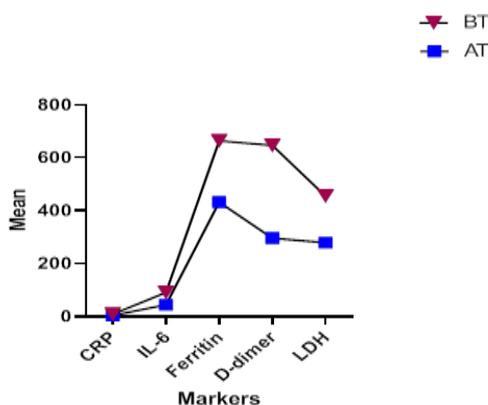


Fig. 7: Comparison of Inflammatory Markers Before and After Treatment.

9) Patient outcome

Table 10: patient outcome.

Sr. No	Outcome	No. of patients (N)	Percentage %
1.	Symptomatically improved	147	80
2.	Death	27	15
3.	Poor prognosis	10	5

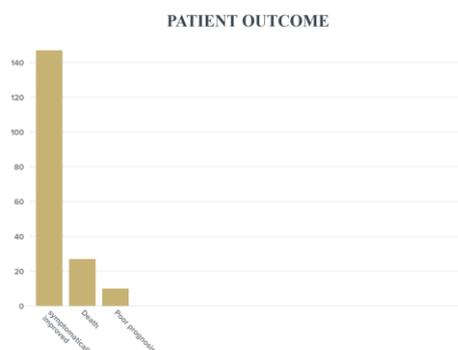


Fig. 8: Based on patient's outcome.

It has been found out that out of 184 patients, 147 patients (N=147) were symptomatically improved and hemodynamically stable with a total percentage of 80%, 27 patients (N=27) were death comprising a total percentage of 15%, 10 patients (N=10) had poor prognosis after the treatment but they were alive comprising a percentage of 5%.

10) Quality of life assessment by the QOL questionnaire score

Based on the analysis of the questionnaire, it has been found that out of 184 patients, 110 patients (N=110) had good quality of life with a total percentage of 70%, 36 patients (N=36) had fair quality of life with a total percentage of 23% and 11 patients (N=11) had poor quality of life with a percentage of 7%.

Table 11: QOL score.

Sr. No	Score	No. of patients (N)	Percentage %
1.	0-3(Poor)	11	7
2.	4-6(Fair)	36	23
3.	7-10(Good)	110	70

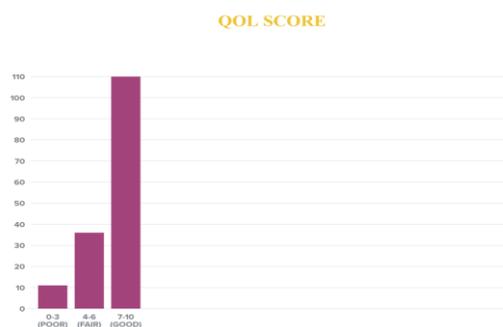


Fig. 9: QOL score.

11) ICU stay

Table 12: ICU stays.

Sr. No	ICU stay	No. of patients (N)	Percentage %
1.	Yes	129	70
2.	No	55	30

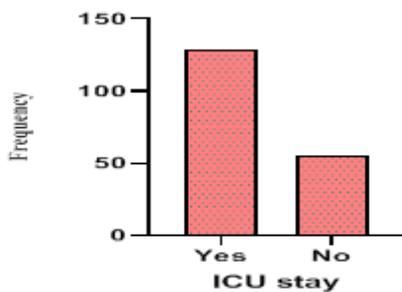


Fig. 10: ICU stay.

It has been found that out of 184 patients, 129 patients (N= 129) were admitted in ICU with a total percentage

of 70% and 55 patients (N= 55) were not admitted in ICU with a total percentage of 30%.

12) Mechanical ventilation

Table 13: Mechanical ventilation.

Sr. No	Need	No. of patients (N)	Percentage%
1.	Yes	40	22
2.	No	144	78

It has been found that out of 184 patients, 40 patients (N=40) required mechanical ventilation with a total percentage of 22% and 144 (N=144) patients did not

require mechanical ventilation with a total percentage of 78%.

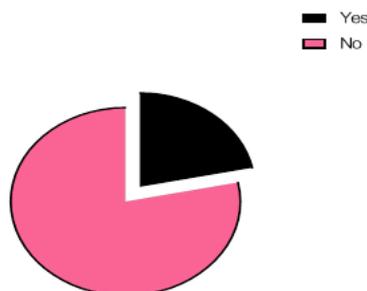


Fig. 11: Mechanical ventilation.

13) Relationship between hospital stay and co-morbidities

Table 14: Average hospital stay.

No of co-morbidities	Average hospital stay
1	4 days
2	7 days
3	10 days
4	14 days
5	17 days

AVERAGE HOSPITAL STAY IN COMPARISON TO DISEASE BURDEN

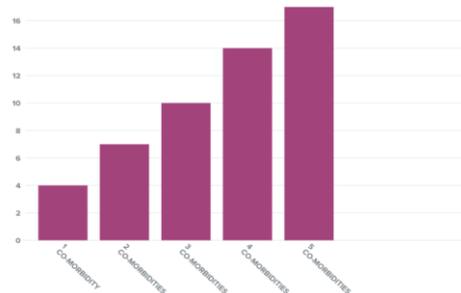


Fig. 12: Average hospital stay.

It has been found that, the most patients who had the highest number of co morbidity had the longest stay in

hospital with a average hospital stay of 17 days when compared to patients who had lesser co morbidities.

14) Complications in covid-19 patients

Table 15: complications.

Sr. No	Complication	No. of patients (N)	Percentage %
1.	Acute Respiratory failure	76	41
2.	Pneumonia	146	79
3.	Acute respiratory distress (ARDS)	42	23
4.	Liver injury	16	9
5.	Cardiac injury	49	27
6.	Kidney injury	19	10
7.	Sepsis	71	39
8.	Diabetic ketoacidosis	6	3
9.	Hyperkalemia	13	7
10.	Hyponatremia	18	10
11.	Hypernatremia	1	1
12.	Uncontrolled diabetes	76	41
13.	Cardiac arrest	9	5
14.	Embolism	1	1
15.	Psychosis	10	5
16.	Secondary infections	42	23
17.	Severe hypotension	5	3
18.	Severe hypoglycemia	6	3
19.	DVT	38	21

It has been found out that, the most common complications is Pneumonia occurred in 146 patients (N=146) with a total percentage of 79%, followed by Sepsis occurred in 71 patients (N=71) with a total percentage of 39%, followed by Acute respiratory failure occurred in 76 patients (N= 76) with a total percentage of 41%, followed by Uncontrolled diabetes mellitus occurred in 76 patients (N=76) with a total percentage of 41%, followed by Cardiac injury occurred in 49 patients (N=49) with a total percentage of 27%, followed by Acute respiratory distress occurred in 42 patients (N=42) with a total percentage of 23%, followed by Secondary

infections occurred in 42 patients (N=42) with a total percentage of 23%, followed by DVT occurred in 38 patients (N=38) with a total percentage of 21%, followed by kidney injury occurred in 19 patients (N=19) with a percentage of 10%, followed by Hyponatremia occurred in 18 patients (N=18) with a percentage of 10%, followed by Liver injury occurred in 16 patients (N=16) with a percentage of 9%, followed by Hyperkalemia occurred in 13 patients (N=13) with a percentage of 7%, followed by Psychosis occurred in 10 patients (N=10) with a percentage of 5%.

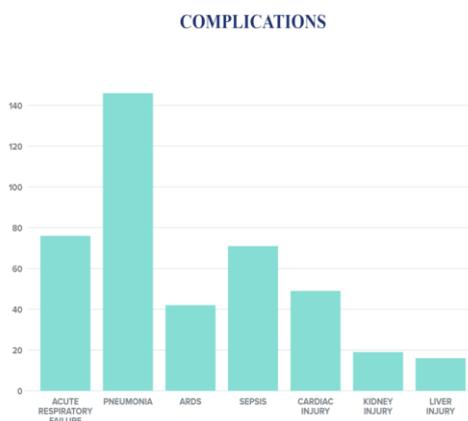


Fig. 13: complications.

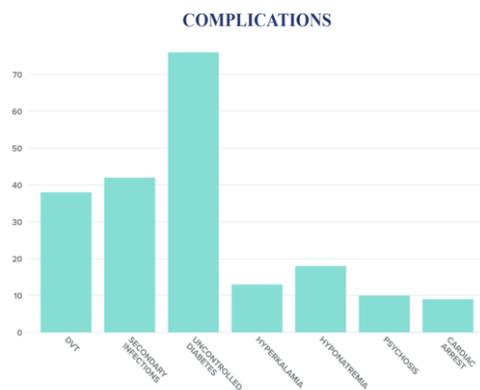


Fig 14: Complications.

15) Lab values

Table 16: Blood count.

Sr. No	Blood Parameter	Normal Count		Abnormal Count	
		N	%	N	%
1.	Hb	94	51	90	49
2.	WBC	90	49	94	51
3.	Neutrophils	106	58	78	42
4.	Lymphocytes	82	45	102	55

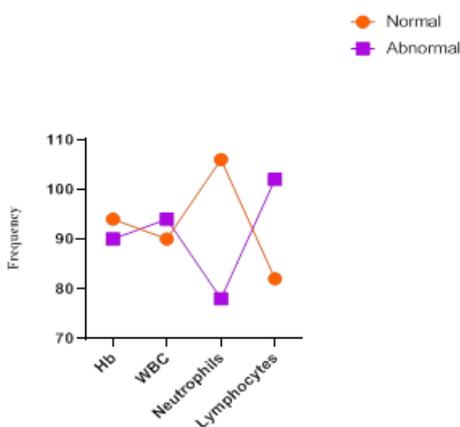


Fig. 15: Blood count.

- 1) It has been found that out of 184 patients, 94 patients (N=94) had normal hemoglobin levels with a total percentage of 51% and 90 patients (N=90) had low hemoglobin levels with a percentage of 49%.
- 2) It has been found that out of 184 patients, 90 patients (N=90) had normal WBC count with a total percentage of 49% and 94 patients (N=94) had leukocytosis (high WBC count) with a total percentage of 51%.
- 3) It has been found that out of 184 patients, 106 patients (N=106) had normal neutrophil count with a total percentage of 58% and 78 patients (N=78) had neutrophilia (high percentage of neutrophils) with a total percentage of 42%.
- 4) It has been found that out of 184 patients, 82 patients (N=82) had normal lymphocyte count with a total percentage of 45% and 102 patients (N=102) had lymphocytosis (high lymphocyte count) and lymphocytopenia (low lymphocyte count) with a total percentage of 55%.

16) Covid-19 treatment

Table 17: Anti-viral drugs.

Sr. No	Drug	Drug given to No. of patients (N)	Percentage
1.	Remdesivir	143	77
2.	Favipiravir	9	5
3.	Oseltamivir	21	11

• **Anti-viral drugs**

It has been found that out of 184 patients, 143 patients (N=143) were prescribed with Remdesivir with a total percentage of 77%, followed by 21 patients (N=21) were

prescribed with Oseltamavir with a total percentage of 11% and 9 patients (N=9) were prescribed with Favipiravir with a percentage of 5%.

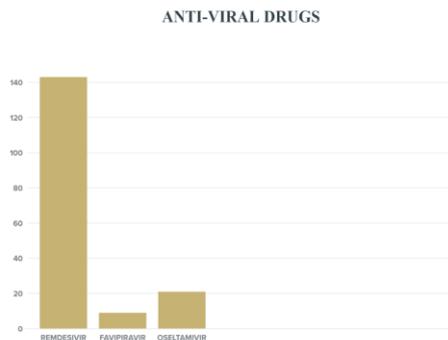


Fig. 16: Anti-viral drugs.

• **Steroids**

Table 18: Steroids.

Sr. No.	Drug	Drug given to No. of patients (N)	Percentage %
1.	Methylprednisolone	158	86
2.	Dexamethasone	28	15
3.	Deflazacort	12	7
4.	Budesonide	21	11

It has been found that out of 184 patients, 158 patients (N=158) were prescribed with Methylprednisolone with a total percentage of 86%, followed by 28 patients (N=28) were prescribed with Dexamethasone with a

percentage of 15%, followed by 12 patients (N=12) prescribed with Deflazacort with a percentage of 7% and 21 patients (N=21) were prescribed with Budesonide with a percentage of 11%.

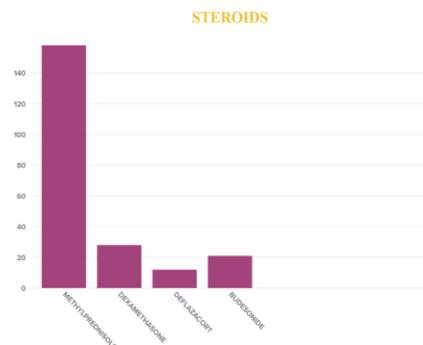


Fig. 17: Steroids.

• **Antibiotics**

Table 19: Antibiotics.

Sr. No	Drug	Drug given to No. of patients (N)	Percentage
1.	Cefopodoxime proxetil	52	28
2.	Meropenem	72	39
3.	Cefoperazone + Sulbactam	59	32
4.	Doxycycline	70	38
5.	Azithromycin	52	28
6.	Piperacillin + Tazobactam	109	59
7.	Clarithromycin	69	38
8.	Teicoplanin	17	9
9.	Linezolid	7	4
10.	Tigecycline	20	11

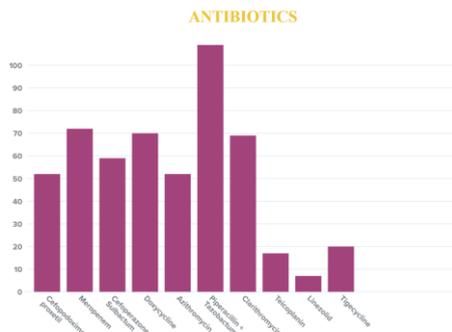


Fig. 18: Antibiotic.

It has been found that the most prescribed Antibiotic is piperacillin + tazobactam, given to 109 patients (N=109) with a total percentage of 59%, followed by Meropenem given to 72 patients (N=72) with a total percentage of 39%, followed by Doxycycline given to 70 patients (N=70) with a total percentage of 38%, followed by Clarithromycin given to 69 patients (N=69) with a total

percentage of 38%, followed by Cefoperazome + salbactam given to 59 patients (N=59) with a total percentage of 32%, followed by Azithromycin and cefopodoxime proxetil given to 52 patients with a percentage of 28%. Lastly, Tigecycline, teicoplanin and linezolid was prescribed to 20,17,7 patients comprising a percentage of 11%, 9%, 4%.

• **Anti-coagulants**

Table 20: Anti-coagulants.

Sr. No	Drugs	Drug given to No. of patients (N)	Percentage %
1.	Enoxaparin	158	86
2.	Heparin	32	17
3.	Fondaparinux	4	2

It has been found that out of 184 patients, 158 patients (N=158) were given enoxaparin with a total percentage of 86%, followed by heparin was given to 32 patients

(N=32) with a percentage of 17% and fondaparinux was given to 2 patients (N=2) with a percentage of 2%.

• **Ivermectin and hydroxychloroquine**

Table 21: Ivermectin and HCQ.

Sr. No	Drug	Drug given to No. of patients (N)	Percentage %
1.	Ivermectin	57	31
2.	Hydroxychloroquine	10	5

It has been found that out of 184 patients, 57 patients (N=57) were prescribed with ivermectin with a total percentage of 31% and 10 patients (N=10) were

prescribed with hydroxychloroquine with a percentage of 5%.

• **Tocilizuman and Pirfenidone**

Table 22: Tocilizumab and pirfenidone.

Sr. No.	Drugs	Drug given to No. of patients (N)	Percentage %
1.	Tocilizumab	41	22
2.	pirfenidone	52	28

It has been found that out of 184 patients, 41 patients (N=41) were prescribed with tocilizumab with a

percentage of 22% and 52 patients (N=52) were prescribed with pirfenidone with a percentage of 28%.

• **Supplements**

Table 23: Supplements.

Sr. No	Drugs	Drug given to No. of patients (N)	Percentage %
1.	Vitamin C	184	100
2.	Vitamin D	145	79
3.	Calcium carbonate + Vit D3	32	17
4.	Zinc	17	9

5.	Thiamine+Vitamin B6+Panthenol	77	42
6.	Zincovit	165	90
7.	Cap Becosules	158	86

- It has been found that all the 184 patients (N=184) were prescribed with Vitamin C with a total percentage of 100%
- It has been found that out of 184 patients, 145 patients (N=145) were prescribed with Vitamin D with a total percentage of 79%.
- It has been found that out of 184 patients, 32 patients (N=32) were prescribed with Calcium carbonate + Vitamin D3 with a total percentage of 17%.
- It has been found that out of 184 patients, 17 patients (N=17) were prescribed with zinc with a total percentage of 9%.
- It has been found that out of 184 patients, 77 patients (N=77) were prescribed with Thiamine + Vitamin B6 + Panthenol with a total percentage of 42%.
- It has been found that out of 184 patients, 165 patients (N=165) were prescribed with Zincovit with a total percentage of 90%.
- It has been found that out of 184 patients, 158 patients (N=158) were prescribed with Cap Becosules with a total percentage of 86%.

• Anti-fungal drugs

Table 24: Anti-fungal drugs.

Drugs	Drug given to No. of patients (N)	Percentage %
Fluconazole	73	40%

It has been found that out of 184 patients, 73 patients (N=73) were prescribed with Fluconazole with a total percentage of 40%.

• Miscellaneous drugs

The other drugs prescribed for symptomatic treatment of covid-19 with frequency and percentage.

Table 25: Miscellaneous drugs.

Sr. No	Drug	Drug given to No. of patients (N)	Percentage %
1.	Paracetamol	133	72
2.	Levodropriopizine+ chlorpheniramine maleate	58	32
3.	Montelukast+levocetrizine	116	63
4.	Syp Ambroxol	45	24
5.	Syp Lactulose	36	20
6.	N- Acetylcysteine	88	48
7.	Acebrophyllin	71	39
8.	Pantoprazole	171	93
9.	Colchicine	67	36
10.	Ipratropium+Salbutamol	32	17
11.	Ondanstron	166	90
12.	N-Acetylcysteine+Acebrophyllin	4	2
13.	Lactic acid/Sporlac	19	10
14.	Ornidazole	2	1
15.	Diclofenac	2	1
16.	Aceclofenac	1	1
17.	Buscopan	2	1

17) Treatment of co morbidities

• Hypertension

Table 26: Hypertensive drugs.

Sr. No	Drug	Drug given to No. of patients (N)	Percentage %
1.	Hydrochlorothiazide	3	2
2.	Spiranolactone	3	2
3.	Olmesartan	6	5
4.	Metoprolol	16	13
5.	Torsemide	22	18

6.	Amlodipine	37	31
7.	Telmisartan	59	49
8.	Losartan	2	1

It has been found that the most prescribed drug for hypertension is Telmisartan given to 59 patients (N=59) with a total percentage 49% and the least used Drug is

Losartan given to 2 patients (N=2) with a total percentage of 1%.

- **Diabetes mellitus (type-2)**

Table 27: Diabetes treatment.

Sr. No	Drugs	Drug given to No. of patients (N)	Percentage %
1.	Reneive Plus	2	2
2.	Metformin + Empaglifozin	18	17
3.	H.Mix 70/30	19	18
4.	Glimepiride	22	20
5.	Metformin + Glimepiride	49	45
6.	Vildagliptin + Metformin	32	30
7.	H.Mix 50/50	20	19
8.	Hai Insulin	90	83
9.	Metformin	62	57

It has been found that the most used drug for diabetes mellitus (type 2) was metformin given to 62 patients (N=62) with a total percentage of 57% , the most used insulin was HAI (Human actrapid insulin) given to 90 patients (N=90) with a total percentage of 83%. The least

used drug used was metformin+empaglifozin combination given to 18 patients (N=18) with a total percentage of 17% and the least used insulin is Human mixtard 70/30 given to 19 patients (N=19) with a total percentage of 18%.

- **CAD (Coronary artery diseases)**

Table 28: CAD drugs.

Sr. No	Drugs	Drug given to No. of patients (N)	Percentage %
1.	Isosorbide Mononitrate	3	8
2.	Spirolactone	4	10
3.	Ticagrelor	5	13
4.	Aspirin + Atorvastatin	15	38
5.	Clopidogrel	6	15
6.	Rosuvastatin	7	18
7.	Aspirin	8	20
8.	Atorvastatin	19	48

It has been found that the most prescribed drug for CAD was Atorvastatin given to 19 pateints (N=19) with a total

percentage of 48% and the least prescribed drug for CAD was isosorbide mononitrate.

- **Hypothyroidism**

Table 29: Hypothyroidism.

Drugs	Drug given to No. of patients (N)	Percentage %
levothyroxine	27	100

It has been found that all the patients with hypothyroidism were prescribed with levothyroxine.

- Respiratory illness

Table 30: Respiratory illness drugs.

Sr. No	Co morbidity	Drug	Drug given to No. of patients (N)	%
1.	COPD	Salmeterol+ fluticasone	1	25
		Theophylline	3	75
2.	ASTHMA	Formoterol + budesonide	1	11
		Salmeterol+ fluticasone	4	44
		Syrup Terbutaline	3	33
		Budesonide	5	55
		Acebrophylline	4	44

➤ It has been found that COPD patients were prescribed with Salmeterol+ fluticasone and Theophylline.

➤ It has been found that Asthma patients were prescribed with Formoterol + budesonide, Salmeterol+ fluticasone, Syrup Terbutaline, Budesonide, Acebrophylline.

- Mental disorders

Table 31: Schizophrenia drugs.

Comorbidity	Drug	Drug given to no. Of patients (n)	%
Schizophrenia	Clozapine	2	50
	Risperidone	2	50

Table 32: depression drugs.

Comorbidity	Drug	Drug given to no. Of patients (n)	%
Depression	Risperidone	2	11
	Amitriptyline	2	11
	Escitalopram	3	16
	Duloxetine	5	26
	Fluvoxamine	6	32

➤ It has been found that the schizophrenia patients were prescribed with Clozapine and Risperidone.

➤ It has been found that the patients who were suffering from depression were prescribed with Risperidone, Amitriptyline, Escitalopram, Duloxetine, Fluvoxamine.

- Other chronic diseases

Drugs prescribed for the following co morbidities with their frequencies and percentage-

Table 33: Other chronic diseases treatment.

Sr. No.	Co morbidity	Drug	Drug given to no. of patients (n)	%
1.	Parkinson	Carbidopa	4	100
		Levodopa	4	100
2.	Seizure	Clonazepam	1	8
		Lorazepam	2	17
		Phenytoin	2	17
		Levetiracetam	7	58
3.	Anemia	Human erythropoietin	2	40
		Ferrous sulphate	2	40
		Iron sucrose	1	20
		Folic acid	2	40
4.	Arthritis	Diclofenac	1	6
		Dexamethasone	2	11
		Teriparatide	2	11
		Azathioprine	4	22
		Flupirtine maleate	2	11

		Hydroxychloroquine	7	39
5.	Dvt	Enoxaparin	10	67
		Rivaroxaban	5	33
		Aspirin	10	67
		Heparin infusion	3	20
6.	Stroke	Eplerenone	2	40
		Atorvastatin	3	60
		Clopidogrel	3	60
7.	Liver diseases	Rifaximin	1	14
		H.albumin	2	29
		Inj vit k	2	29
		Syp. Liv 52	2	29
		L-ornithine	2	29
		Torsemide	2	29
		Ursodeoxycholic acid	7	100
8.	Gout	Allopurinol	6	100
9.	Psoriasis	Lupifit	2	100
10	Ckd	Amlodipine	1	6
		Spiranolactone	1	6
		Calcium supplement	2	13
		Alpha ketoanalogue	2	13
		Torsemide	2	13
11	Bph	Prazosin	1	20
		Dutasteride	3	60
		Tamsulosin	4	80

18) Drug-drug interactions

Table 34: Drug-drug interactions.

Sr. No	Severity	Frequency (N)	Percentage
1.	Mild	19	20
2.	Moderate	32	35
3.	Severe	42	45

DRUG -DRUG INTERACTIONS

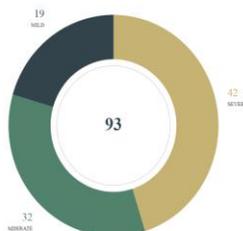


Fig. 19: Drug- Drug interactions.

It is found that total 93 drug-drug interactions were founded out of which 42 were severe with a total percentage of 45%, followed by 32 were moderate with a

total percentage of 35 and 19 were mild with a percentage of 20%.

19) ADRs (Adverse drug reactions)

Table 35: Adverse drug reactions.

Sr. No	ADR	Frequency	Percentage
1.	Constipation	35	11
2.	Diarrhea	12	4
3.	Hepatotoxicity	18	6
4.	Nausea	25	8

5.	Increased creatinine	15	5
6.	Abdominal pain/Epigastric pain	14	5
7.	QT interval prolongation	11	3
8.	Fungal infection/Oral thrush	7	2
9.	Hyperglycemia	132	43
10.	Insomnia/headache	18	6
11.	Bleeding	2	0.7
12.	Anxiety	17	5

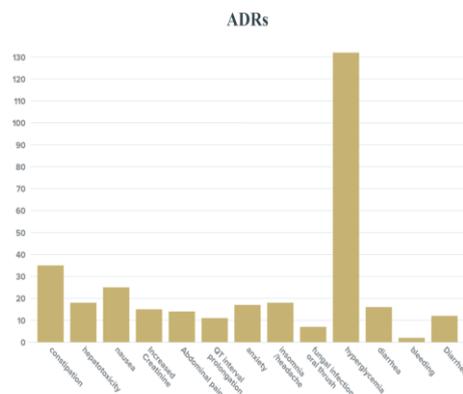


Fig. 20: Adverse drug reactions.

A total of 306 ADRs were found the most common ADR was hyperglycemia (43%), followed by constipation (11%), followed by nausea (8%), followed by insomnia and hepato-toxicity (6%), followed by increased creatinine, abdominal pain and anxiety (5%), followed by prolong QT interval (3%), followed by oral thrush (2%) and the least common ADR was bleeding (0.7%).

DISCUSSION

A prospective observational cohort study was conducted in Aster prime Hospital in Hyderabad. This study aims to evaluate the therapeutic management of COVID-19 patients who already have co-morbidities. A total of 184 patients affected with COVID-19 were considered in this study. The study consisted of 117 males and 67 females. The study included patients from the age of 21 to 90.

Maximum number Of Patients were of the age group of 51 to 60 years and the least number of patients were seen in the age group of 81 to 90 years.

Maximum number of patients had CORADS level of 5 and 6 which primarily indicates CT findings of typical COVID-19 and definite COVID-19. About 90 percent of patients showed positive on RT-PCR report and only 10% were negative. The negative RT-PCR results may be attributed to less viral load in such patients or decreased sensitivity of this technique in these patients.

The most common co morbidity was hypertension and diabetes mellitus, coronary artery disease and hypothyroidism well as the least common was psoriasis. The study included patients with mental and psychotic disorders, history of stroke, musculoskeletal and chronic autoimmune disorders genitourinary diseases, kidney and liver disorders, anaemia, VTE, seizures, respiratory

disorders, neurodegenerative disorders. It was found that the patients who had more co-morbidities, had a longer hospital stay and more complications.

Quality of life of the patient and therapeutic effectiveness was the primary outcome of the study. Primary outcomes were measured by Quality of life questionnaire, survival rate, mortality rate, and decrease in inflammatory biomarkers, assessment of complications and drug-drug interactions and adverse drug reactions occurred and difference in condition of patients before and after treatment. We also assessed how co-morbidity may affect the disease progression in COVID-19 as the patients who had more number of co-morbidities had longer hospital stay and severe COVID-19 infection compared to those who were having less co-morbidities.

The secondary outcomes of this study are: quantifying patients requiring mechanical ventilation and estimation of ICU stay or hospital stay, assessment of haemoglobin, WBC's, neutrophils and lymphocytes indicating infections and disease progression, association of complications with age and co morbidities.

Before and after treatment values of the Inflammatory markers like CRP, IL-6, Ferritin, D-dimer and LDH was noted and a dependent t-test using 95% confidence interval was performed using SPSS software, the results had P values lesser than 0.05 that is CRP(p=0.0093), IL-6(p=0.0456), Ferritin (p=0.0321), D-dimer(p value less than 0.01) and LDH(p value less than 0.01). Since the p value for all parameters is less than 0.05 it indicates that there exist a significant difference in the values before and after treatment , around 20% of the total patients had

persistently elevated markers after the treatment and the rest had decreased inflammatory markers after the treatment, we can infer that the results were statistically significant. The Biomarkers value was in normal range upon admission in mild disease and abnormal values were seen for moderate to severe disease. Only dead patients and patients with very poor prognosis had abnormal levels throughout their hospital stay (20%) while the remaining 80% improved symptomatically and were discharged, indicating appropriate therapy was given to them.

A questionnaire was prepared to assess the "to access the HRQOL (health related quality of life) of the patient with respect to physical, social and mental well being and to assess patient satisfaction with respect to the treatment. Patients were asked to fill a part of the questionnaire at the time of discharge. For the proper assessment of the questionnaire, follow up was done with the patients for 1-2 months through telecommunication for filling the remaining part of the questionnaire. The total score of this questionnaire gives an overview of how patients' life has significantly changed after COVID-19 and it is a measure of how well the treatment was given to the patient during the hospital stay. Based on the analysis of the questionnaire, 110 patients (70%) were found to have a good quality of life and 36 patients (23%) patients had fair quality of life and 11 patients (7%) of patients had poor quality of life. Majority of patients with poor quality of life had chronic conditions, multiple diseases, and poor mental health.

In this study, it has been found that out of 184 patients, 147 patients (80%) were improved symptomatically, 27 patients (15%) were dead and 10 patients (5%) had poor prognosis. It was noticed that around 70% patients were admitted in ICU and 22% needed mechanical ventilation. Patients with multiple co-morbidities and old age required serious interventions during the hospital stay.

The success rate of treatment was 80% with 143 patients treated and hemodynamically stable and is attributed to both pharmacological and non pharmacological interventions.

Parameters from Complete Blood Count also helped us to arrive at conclusion. Haemoglobin, white blood cell count, neutrophils and lymphocytes were taken as parameters. These CBC parameters helped us to get secondary outcomes. Leukocytosis is an indicator of ongoing infection and inflammation, and it can be used to monitor the action of medication on infection. Lymphocytopenia have been associated with patients who had poor prognosis and relates to higher mortality rate. Lymphocytosis was seen in only few patients and resolved eventually but lymphocytopenia was seen in severe disease state and not in mild disease state. Neutrophilia predicts severe respiratory damage, inflammatory condition, viral infection state, and patients with this finding were observed to have poor outcomes.

Low haemoglobin levels were mostly seen in older patients with chronic conditions and in women in our study and we infer that low haemoglobin levels may complicate the treatment approach.

Treatment for COVID-19 most commonly consisted of antiviral drugs with remdesvir and favipiravir in majority cases; around 86% were given steroids of which methylprednisolone and dexamethasone constitute majority. Dexamethasone was preferred for severe disease or those with increased need for oxygen supplementation. Also anticoagulant like enoxaparin was given to around 86% patients. Other drugs like ivermectin(31%), hydroxychloroquine(5%) were also given. Drugs like tocilizumab (22%) for immunomodulatory action and pirfenidone (28%) for anti-fibrotic and anti-inflammatory action were given. Around 10 different antibiotic usages were observed. Antibiotics commonly given were piperacillin+tazobactam (59%), meropenem (39%), doxycycline (38), clarithromycin (38%). The least common antibiotics were tigecycline, teicoplanin and linezolid. The treatment also consisted of supplements majority of which constituted vitamin c, vitamin d, zincovit and capsule becosules.

Symptomatic treatment was given to all patients and mostly comprised of antipyretics, antitussives, antiemetic, pain killers, antidiarrheals, pro-biotics, mucolytics anti-inflammatory drugs, nebulizers, medications for acidity. The most common antitussive was the combination drug of monteleukast +levocetrizine, most common antipyretic and pain killer prescribed was paracetamol, most common prescribed antiemetic was ondansetron, medication for acidity majorly constituted pantoprazole and most common mucolytic was N-acetylcysteine. Prophylactically antibiotics and antifungal drugs like fluconazole were prescribed.

Most patients with hypertension were mostly prescribed with telmisartan (Angiotensin receptor blocker) as SARS-CoV-2 virus affects mostly ACE2 receptors. Patients with diabetes received mostly insulin preparations like HAI and H.Mixtard and most prescribed oral hypoglycemic agents was metformin. Patients with Coronary artery disease were most commonly prescribed a combination of aspirin+atorvastatin. All of the Parkinson patients were prescribed carbidopa and levodopa. The most commonly used antiepileptic drug in seizures was levetiracetam. Patients with anemia were prescribed human erythropoietin, ferrous sulphate and folic acid. Rheumatoid arthritis patients were mostly prescribed hydroxychloroquine. Most prescribed drug for DVT (deep vein thrombosis) was enoxaparin and aspirin, while heparin infusion was given to some patients. Among patients with stroke history were most commonly prescribed clopidogrel and atorvastatin. Patients with liver disorders were most commonly prescribed

ursodeoxycholic acid. All gout patients were given allopurinol. All psoriasis patients were given lupifit. CKD patients were prescribed torsemide, alpha ketoanalogue, calcium supplement, amlodipine and spirinolactone. BPH (benign prostatic hyperplasia) patients were prescribed tamsulosin and prazosin. All patients with hypothyroidism were given levothyroxine. Patients with COPD received theophylline mostly. Asthma patients were mostly given budesonide inhaler. Patients with schizophrenia were given antipsychotic drugs like risperidone and clozapine. The drug prescribed for depression was fluvoxamine.

Patients with co-morbidities had various complications during hospital stay, most patients had pneumonia, sepsis, acute respiratory failure and uncontrolled diabetes mellitus as major complications. Other Complications included acute respiratory distress, secondary infections, Venous thromboembolism, kidney and liver injury, cardiac injury, electrolyte disturbances like hyperkalemia, hyponatremia and hypernatremia, denovo diabetes. Some patients died of complications like cardiac arrest, septic shock and diabetic ketoacidosis. Patients with intensive steroid therapy due to high susceptibility developed fungal infections and were given fluconazole. Steroid induced denovo diabetes was controlled by HAI (insulin preparation). During the hospital stay few patients were reported to develop psychosis. Many complications were mostly seen in people who had 3 to 5 co-morbidities, patients who were admitted in ICU and patients who had hospital stay ranging from 11 to 25 days. These patients had old age group as a common factor in which severe disease progression was seen, thus severity in complications increase with age and co-morbidity.

For respiratory distress and failure oxygen therapy was given. For secondary infections antibiotics like meropenem and piperacillin+ tazobactam, clarithromycin and anti fungal drugs like fluconazole was given. For severe hypotension noradrenaline, IV fluids were given. For hyperkalemia: calcium polystyrene sachets were given. For severe hypoglycemia: 5 %dextrose was given. For Diabetic ketoacidosis: insulin and IV fluids were given. For DVT anticoagulants like enoxaparin was given. Uncontrolled diabetes mellitus was treated with both oral hypoglycemic and insulin preparation (H.mixtard, HAI infusion) and pneumonia was treated with macrolide and tetracycline antibiotics.

Counselling was given to the patients and their attendees during the hospital stay, at the time of discharge and during the follow up. During counselling, it was observed that a group of patients were anxious and were with poor social and mental well being. Discharged Patients were counselled to home isolate themselves for few days and advised to have a teleconsultation after 7-10 days and a follow up after 1 month with their physician and report to them their health status and narrate any problems in drug therapy. They were also

advised to virtually interact with their friends and family in order to improve their social health, prevent stress and decrease chances of post traumatic disorders. The counselling had a significant impact on majority of patients as it provided satisfaction to the patient with respect to treatment and mental well-being.

A total of 93 drug-drug reactions were found out of which 19 were mild drug interactions, 32 were moderate drug interactions and 42 were severe drug interactions.

- The severe interactions reported were: fluvoxamine+clopidogrel (concurrent use of these two drugs increased the risk of bleeding, contraindicated), vitamin c+ doxycycline (concurrent use may decrease doxycycline efficacy). fluconazole+ondansetron(concurrent use of these two drugs increases risk of qt prolongation).
- Moderate interactions reported were: methylprednisolone+enoxaparin (corticosteroids decrease anticoagulant effect by increasing blood coagulability), ondansetron+metformin (ondansetron increases the levels of metformin), aspirin+solumedrol(concurrent use of these drugs increases risk of gastrointestinal ulcers and decreases aspirin levels).
- Mild interactions seen were piperacillin+furosemide (piperacillin increases the rate of furosemide metabolism resulting in decreased level of furosemide), ticagrelor+rosuvastatin (metabolism of rosuvastatin decreased when combined with ticagrelor), methylprednisolone+ colchicines concurrent administration decreases level of colchicines by altering its metabolism).

The most common adverse drug reactions reported was hyperglycemia, insomnia, constipation and anxiety attributed to methylprednisolone. Qt prolongation due to use of drugs like hydroxychloroquine, abnormal liver function tests due to drugs like enoxaparin and remdesvir, increased creatinine due to remdesvir, diarrhoea due to antibiotics and headache due to drugs like clarithromycin and nebulizers (ipratropium+salbutamol, budesonide), Fungal infection or oral thrush due to tocilizumab, Abdominal pain due to azithromycin. Ondansetron was used for nausea, *Saccharomyces boulardii* was used for diarrhoea, lactulose for constipation, and alprazolam was given for anxiety.

CONCLUSION

This prospective cohort study includes 184 patients with COVID 19 infection with co morbidities, 117 of which were males and about 67 were female. Patients greater than or equal to 18 years of age were considered. The study aims to determine the health related quality of life (HRQOL) in COVID 19 patients who have multiple diseases or co morbid conditions adding to their disease burden. Therapeutic strategies employed for management of COVID 19 and other co morbid conditions were also assessed.

The health related quality of life of the patients was determined by the analysis of the questionnaire, with 70% patients falling under the category of “good quality of life” indicating therapeutic appropriateness and patient satisfaction with the treatment during the hospital stay and 23% patients falling under the category of “fair quality of life” and 12% patients falling under the category of “poor quality of life”, Hence the conclusion is that majority of the patients were therapeutically treated well.

Mortality rate was 15% and 5% of the patient had poor prognosis after the treatment while, 80% of patients were symptomatically improved and hemodynamically stable.

To assess the drug effectiveness and appropriateness, patient’s treatment plan was assessed for therapeutic indication, adverse drug reactions and interactions (mild, moderate and severe). The severe interactions were reported. Management of adverse drug reactions was taken into account. Factors predisposing a particular group of patients to adverse drug reactions were studied. A thorough analysis was done to know which drugs were most commonly prescribed for COVID 19 infection and for co morbidities treatment. Combination drugs prescribed were identified. Prophylactic therapy in high risk patients was identified. Among all anti-viral drugs remedesvir was most given anti-viral drug. Among all the steroids methylprednisolone was most given steroid. Piperacillin+tazobactam were the most common antibiotic given. The study also included few repurposed drugs for COVID 19.

COVID-19 Drugs effectiveness was also evaluated based on levels of inflammatory markers before and after treatment. Treatment was continued until patient was symptomatically better and hemodynamically stable. Abnormally high inflammatory markers were seen in dead patients, poor prognosis patients.

The effectiveness of co-morbidity treatment, supportive care and symptomatic care was assessed by analysis of the questionnaire. Factors like patient satisfaction, patient compliance, medication adherence and mental state were reviewed and their effect on success of therapy and change in patient outcome was determined. Majority patients experienced anxiety and only few patients were non compliant. Reasons for failure of therapy were noted. The studied intensively monitored patients with higher risk factors and patients in special population category.

A potential link between COVID 19 and co morbidities was also determined; Patients with multiple co morbidities had prolonged hospital stay and severe progression of COVID 19 disease. Patients requiring mechanical ventilation and other kinds of serious interventions were also quantified. Elderly patients with multiple co morbidities, complications and poor prognosis required mechanical ventilation most

commonly. The association between age and disease progression was explored. Old age patients were found to have more complications and severe COVID-19 disease and prolonged hospital stay.

Lab parameters like hemoglobin, WBCs, neutrophils and lymphocytes were also assessed for abnormalities, which mostly where low hemoglobin count, leukocytosis, neutrophilia, lymphocytosis and lymphopenia

The major challenges found in this study were patients’ limited awareness about COVID-19 and health implications, anxiety in infected patients with COVID-19, poor mental and social health.

ACKNOWLEDGEMENT

The intention and desire to learn is an integral part of research work. This original research work is our teams ‘attempt to learn and grow in various aspects. This research couldn’t be possible without the discipline, great focus, perseverance, passion and commitment. This project has been possible only by the will of Allah, therefore we express our sincere gratitude to our lord. We thank our guide Dr. Mohammed Ashfaq Hussain Sir, Assistant professor Sultan–UI–Uloom College of Pharmacy, for sharing his valuable time in providing knowledge, guidance and excellent support for the successful completion of our project. We would like to express sincere gratitude to our beloved principal, Dr.Anupama Koneru Maam, Mpharm, Ph.D., for providing us with opportunity to carry out this project so efficiently and with an ease. We would like to express our sincere gratitude to the nurses and all hospital staff of Aster Prime hospital for all the support and co-operation during this project work. We would also like to express our gratitude towards the authors, editors, publishers of the articles, journal and other publications reviewed in this paper.

Funding and Support

None

Conflict of interest

None

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