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Clinical characteristics, pharmacotherapy and outcome of hospitalized COVID-19 patients in a tertiary care teaching hospital in south India

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Abstract

The corona virus disease 2019 (COVID-19) initially identified in Wuhan city of China's Hubei province, has become an alarming pandemic affecting the world's population in morbidity and mortality. Though initially the disease manifested as respiratory symptoms, later it involved many other organs and systems and the presentation varied in terms of clinical, laboratory, computerized tomography (CT) findings, and different treatment categories is being tried and used. So this single center retrospective study was undertaken with the objective of characterizing the clinical, diagnostic, treatment and clinical outcome of hospitalized patients diagnosed with COVID-19 in a tertiary hospital. We included the case records of all RTPCR positive COVID-19 patients admitted to the tertiary hospital for which the data were available from admission to discharge irrespective of age, gender and co- morbidities. The data were analyzed using descriptive statistics. Among the 300 patients, 68 COVID-19presented with respiratory symptoms, 88 patients with non-respiratory symptoms and 44 were asymptomatic. We observed elevated ESR in 24%, elevated levels of CRP (43%), LDH (28.76%), D-dimer, (48.2%), fibrinogen (35.3%) and ferritin in 16% of our patients. 72.5% of the patients had findings suggestive of COVID in CT chest.In our study though 26.6% of patients had >3 Neutrophil, Lymphocyte Ratio (NLR) and 28.3% Platelet Lymphocyte Ratio (PLR) more than 180, they did not progress to severe disease. Most common pharmacotherapeutic agents used were Azithromycin, Oseltamivir, Remdesivir, HCQ, Ivermectin, Tocilizumab and Convalescent plasma. Glucocorticoids were used in 54 patients among the 300 patients. Out of 300 patients 285 patients recovered and were discharged. 15 patients were referred to other hospitals upon request. One patient died out of the 285 patients and the mortality was 0.35%. The lower mortality rate could be because of early detection and hospitalization and most patients had mild to moderate disease.

Keywords: COVID-19, treatment, laboratory, CT chest, clinical outcomes

Introduction

Corona virus disease 2019 (COVID-19) is a major pandemic and the most infectious viral disease the world has seen in 2020.The spectrum of clinical presentation of COVID-19 ranges from an asymptomatic infection to a life-threatening disease. It affects all age groups of the population. The acute infection is categorized based on WHO criteria as asymptomatic, mild, moderate, severe, and critical disease [1]. The common symptoms are fever, cough and tiredness. However there is a wide variation in the symptoms involving any system or organ of the body. As there is no definite drug therapy for COVID-19, the patients have been treated with many repurposed drugs like Azithromycin, Hydroxychloroquine, Remdesivir, Tocilizumab Lopinavir/Ritonavir, Favipiravir, Glucocorticoids, Interferons, Ivermectin, traditional medicines as well as convalescent plasma and other drugs depending on the symptoms and signs of the disease and the treating physician's decision. In this scenario of varied presentation and treatment options we studied the clinical, laboratory and radiological profile, the pharmaco-therapeutic management of hospitalized COVID-19 patients and the treatment outcome in a tertiary care teaching hospital.

Objectives

- To study the clinical characteristics and symptoms in COVID- 19 patients
- To assess the laboratory parameters in COVID-19 patients
- To evaluate the pharmacological treatment and the clinical outcome in these patients.

Methodology

This study was a retrospective study conducted at Chettinad Hospital & Research Institute (CHRI), Chettinad Academy of Research and education, TamilNadu, India after obtaining the Institutional Human Ethics Committee approval.

Inclusion Criteria

- The case records of all RTPCR positive COVID-19 patients admitted to CHRI for whom the data were available from admission to discharge irrespective of age, gender and co- morbidities.

Exclusion criteria

- Patients who did not have laboratory confirmation.
- Pregnant and Lactating women

Sample Size

Sample size was calculated using the formula:

$N=Z^2pq/d^2$

p=proportion of symptomatic COVID patients (66.67% or 0.67) (based on the Indian study done by Sudhir Bhandari *et al*., [2]

q= 1-p (0.33)

d=precision (6%)
Z=1.96 (for 95% confidence level)
The sample size calculated was 235 and it was increased to 300 to increase the validity of the outcome.

Data collection

300 case records of COVID- 19 patients admitted to CHRI between May and October 2020 were selected for review based on the inclusion criteria. The data on demographic details, clinical symptoms and signs, laboratory investigations carried out, the drugs used and the clinical outcome were collected in the data collection form & entered in excel sheet.
The data were analyzed using descriptive statistics.

Results

Age and Gender

The number of men affected with COVID-19 washigher (69%) than women (31%) and the age group mainly affected was between 31 and 40 years (24%) followed by 51-60 years (20.3%). 6.3% of patients were between 71-80 years and only one patient was above 80 years. The gender and age distribution are shown in figures 1 and 2.

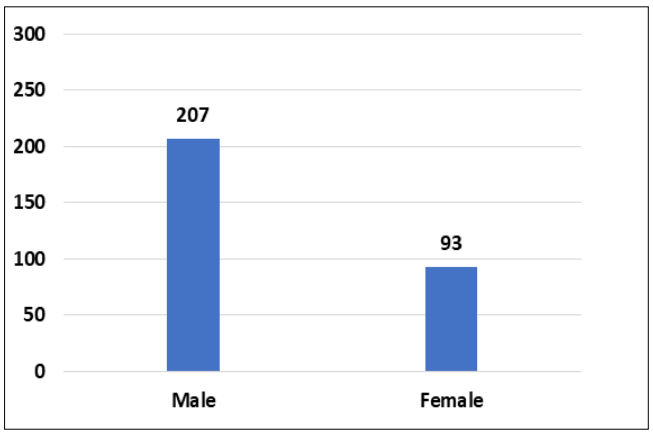

Fig 1: Gender distribution

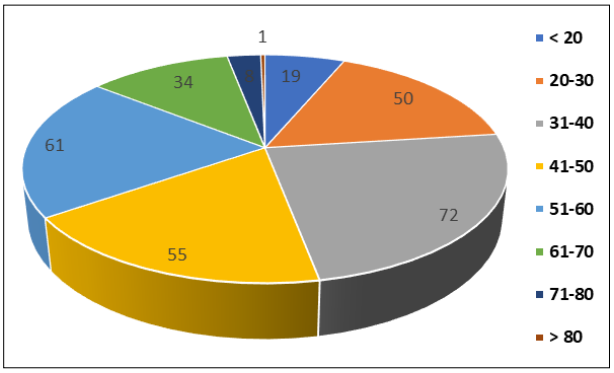

Fig 2: Age distribution

Symptoms

Among the 300 patients, 256 (85.3%) were symptomatic at the time of admission.168 (56%) presented with respiratory symptoms, 88 (29.3%) patients with non-respiratory symptoms and 44 (14.7%) were asymptomatic. The respiratory symptoms included fever, cough, sore throat, and dyspnoea. The non- respiratory symptoms were myalgia, loose stools, anosmia, vomiting, dysgeusia, fatigue, headache and abdominal pain. The details of the symptoms are shown in table 1.

Table 1: Symptoms in COVID-19 patients

Symptoms	Number of patients
Fever	175
Cough	113
Sore throat	60
Headache	33
Myalgia	32
Dyspnoea	30
Loose stools	20
Anosmia	14
Vomiting	10
Loss of taste	9
Fatigue	8
Cold	8
Running nose	8
Abdominal pain	7
Asymptomatic	44

Exposure history

50.3% of patients did not report history of exposure, 35.6% had history of exposure to COVID patients and the contact history was unknown for the remaining patients (figure 3).

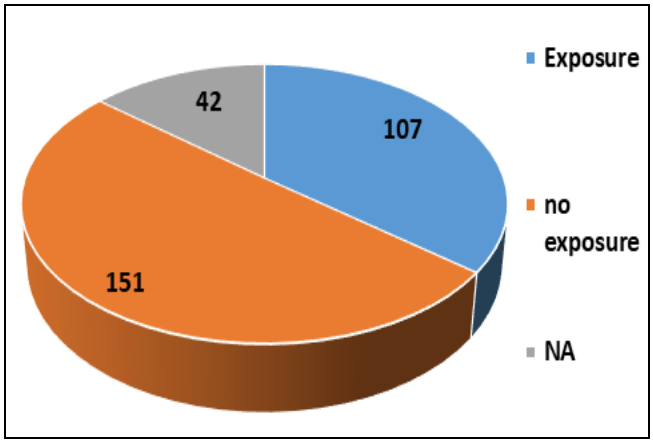

Fig 3: Exposure status

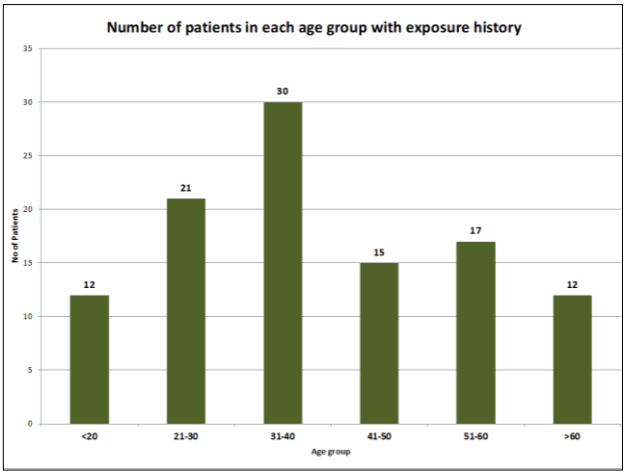

Fig 4

Among those who had the exposure, the maximum number of patients exposed was in the age
Group 31-40 years.

COVID severity

86% of the patients were found to have mild COVID, and only a few patients had moderate to severe COVID.10 % of the patients were asymptomatic. The number of patients in each grade is represented in figure 4. None of the patients progressed to severe disease. None of them needed ventilatory support. Only 18 patients had Spo_2less than 94% and the remaining patients more than 94%.

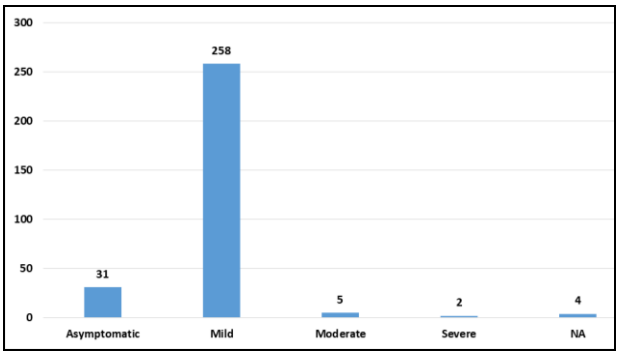

Fig 4: COVID severity

Laboratory findings

The laboratory parameters assessed include Complete Blood Count, the inflammatory markers, hepatic and renal parameters, ECG and Chest CT.

Table 2: *Selected Bio markers*

NLR		CRP		ESR –mm		D-dimer-ng/ml		Ferritin -ng/ml		Fibrinogen ng/ml	
> 3	< 3	Reactive	Non-Reactive	> 30	< 30	>250	< 250	>350	<350	>350	< 350
26.6	73.4	43.2	56.8	24	76	48.2	51.8	16	84	35.3	64.7
The frequency values are in percentage.											

Erythrocyte Sedimentation Rate (ESR) was elevated in 24% of the patients and CRP was found to be reactive in 43% of the patients. LDH was elevated above 280 mg in 28.76%. Elevation of D-dimer, fibrinogen plus ferritin levels were seen in 48.2%, 35.3% and 16% respectively (Table 2). When the two relatively specific parameters for COVID, NLR and D-dimer were assessed they were found increased in 22.8% of patients with mild COVID. Both were elevated in patients with moderate and severe disease.

CT chest findings

72.5% of the patients had findings suggestive of COVID in CT chest while the remaining 27.5% did not have any features suggestive of COVID.

Comorbidities

41.3% (124) of the patients had co morbidities such as diabetes, hypertension, hypothyroidism, asthma, cardio vascular disease, etc. It was observed that diabetes was the commonest co morbidity in about 25.6% of the patients, followed by hypertension (21.3%) and hypothyroidism (4.3%). Dyslipidemia, coronary artery disease (CAD) and chronic kidney disease (CKD) were seen in 9.3% patients. The data regarding co morbid diseases are shown in the table 3.

Table 3: Comorbidities in COVID -19

Co morbid conditions	Number of patients (out of 124)	
DM	77	
HT	64	
Hypothyroidism	13	
Asthma	8	
Dyslipidemia	7	
CAD	10	
CKD	3	

Pharmacotherapy

With regard to the drug treatment, 149 patients (49.7%) were given the repurposed drugs for COVID and the remaining 151 (50.3%) had been treated symptomatically.
The drugs used in COVID treatment were Azithromycin, Hydroxychloroquine, Ivermectin, Oseltamivir, Remdesivir, Tocilizumab and Convalescent plasma. Among these, Azithromycin was the most commonly used drug. 43% of the patients received Azithromycin and among them, Azithromycin was used alone in 36.4% and the remaining 63.6% were given Azithromycin in combination with other drugs. Oseltamivir was given to 93 patients (31%). Among them, less than 1% received Oseltamivir alone and the remaining 99% received Oseltamivir in combination with other drugs. 4% received Remdesivir, 1% received Hydroxychloroquine, Ivermectin 0.6%, and tocilizumab & Convalescent plasma was given to one patient each. The number of patients under each drug category is given in table 4. 64 patients received single drug, 81 patients received combination of 2 drugs and 4 patients received combination of 3 drugs. 51.7% of the patients received Azithromycin + Oseltamivir combination.

Table 4: Pharmacotherapy of COVID

Azithromycin(AZT)	47
Oseltamivir	10
Remdesivir	6
Ivermectin	1
Azithromycin + Oseltamivir	77
Ivermectin + Convalescent plasma	1
Oseltamivir + Hydroxychloroquine (HCQ)	1
Remdesivir + AZT	1
Remdesivir + Oseltamivir	1
AZT + HCQ + Oseltamivir	2
AZT + Oseltamivir + Tocilizumab	1
Remdesivir + Oseltamivir + AZT	1

Steroid therapy

Steroids were administered to 54 patients (18%). The steroids used were Dexamethasone, Methyl prednisolone, Prednisolone and Hydrocortisone. Dexamethasone was the main steroid used (71.9%). (Figure. 5).More than 90 % of patients treated with steroid had increased NLR and D-dimer.

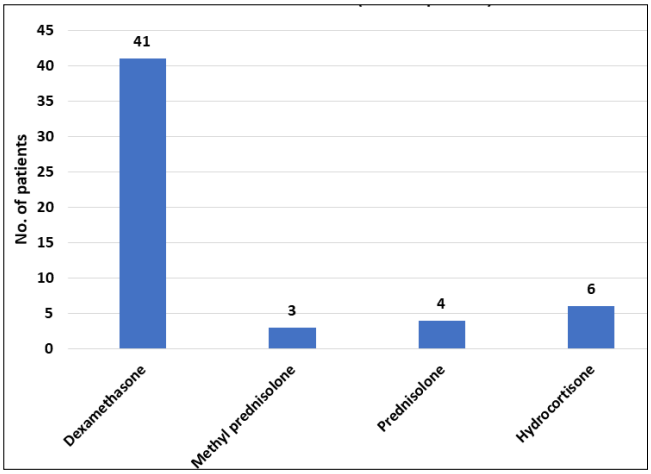

Fig 5: Anti-inflammatory treatment with steroids (Total 54 patients)

Outcome

Mortality was observed in one patient who had severe COVID (0.3%). All the patients were discharged with the advice of home quarantine. The length of hospital stay ranged from 1 to 20 days. 53.7% of the patients were discharged within 7 days, 41.3% between 8 and 14 days and 5%discharged after 15 to 20 days. The details are shown in figure 6.

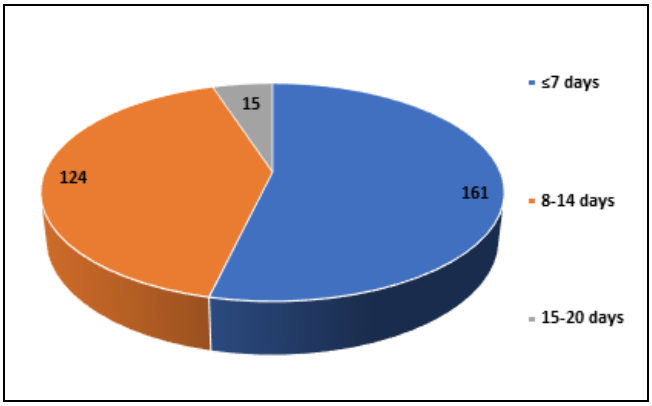

Fig 6: Duration of hospital stay

Discussion

COVID-19 emerged as a sudden pandemic starting in China in December 2019, spreading across continents, affecting more than 200 countries. The clinical presentation is widening from the initial symptoms of fever, cough and breathlessness to the presentation involving gastrointestinal, cardiac, neurological, ocular and dermatological systems. Until now different groups of currently available drugs are used for therapy. Antiviral drugs such as Oseltamivir, Remdesivir, Favipiravir, Ritonavir, Lopinavir, anti-inflammatory agents such as Hydroxychloroquine, glucocorticoids, antimicrobials like Azithromycin and antiprotozoals have been used. Frequent hand wash, wearing facemask, physical distancing, and quarantine are in practice all over the world to reduce the spread. In spite of all these measures the disease is still spreading.

A mutant strain of SARS-CoV-2 has been reported in UK in November 2020 and the infection caused by this strain accounts for 60% of recent infections that occurred in London. The risk associated with this mutant strain is its potential to spread faster and escape detection [3].

In this scenario of varying clinical presentation and non-availability of definite drug therapy, this study was undertaken to find out the clinical features, laboratory findings, the drug treatments, length of hospital stay and clinical outcome as well as assess the correlation among these parameters.

Age and Gender

Our analysis of 300 COVID-19 patient records showed that there is a male preponderance in the occurrence of COVID-19 similar to the earlier reported studies. The age group predominantly affected is 31 to 40 years followed by 51 to 60 years. The mean age affected was 42.85. Gupta *et al* had observed in their study a male preponderance and the mean age of the patients was 40.3 years [4]. Jahan *et al* found that the COVID-19 was higher in the age group 20–59 years with the higher occurrence in the male gender [5].

According to the data published by Statista Research Department, India dated Oct 16, 2020 the majority of COVID-19 patients in India were between the ages 45 and 74 years as of July 9, 2020 [6]. In China the common age affected was 50-59 years [7]. However, in our study the common age group affected is 31 to 40 years and 51 to 60 years indicating the probable liability of these two age groups to get affected in this region. Abbasi J has attributed the increased chances of exposure, higher BMI as well as genetic factors, the reasons for the current higher prevalence of COVID-19 in younger adults [8]. Exposure to COVID patients has contributed for the infection in 35.6% of patients in our study.

Symptomatology

Among the 300 patients 168 presented with respiratory symptoms, 88 patients with non- respiratory symptoms and 44 did not have any symptom. The symptoms reported were similar to the previous studies (table.1)

Loss of smell and taste are the two symptoms that contribute to early identification and help differentiate COVID from other viral infections. Smell disorders are more common due to the anatomical distribution and the vulnerability of the olfactory nerve. Gustatory disturbance without olfactory dysfunction is a unique peculiarity of SARS-CoV-2 as it binds to ACE receptors present in the taste buds and inactivate them [9]. Ibekwe TS *et al* in their systematic review have observed that the global pooled prevalence of loss of smell was 48.47% and loss of taste was 41.47% [10]. In our study 46.66% of patients experienced loss of smell similar to the previous studies. However only 3% experienced loss of taste. Though impairment of smell is common in viral infections due to adenovirus, rhinovirus, influenza and coronavirus, it can be an isolated symptom in COVID-19. A wide variation from 5 to 98% has been observed in the incidence of smell and/or taste disorders in different studies [11].

Anosmia is associated with less severity of COVID -19 and lower in-hospital mortality [12, 13]. In our study also all the

patients had mild COVID and the mortality was very low (0.33%).

Exposure history

35.6% had history of exposure to COVID and the contact history was unknown for the remaining patients. The exposure status correlated with the incidence of COVID, the maximum number of patients exposed and the maximum number affected was in the age group 31-40 years.

Johansson *et al*, have estimated that at least 50% of transmission has occurred by transmission from asymptomatic patients [14]. Similar finding has been observed in our study. 50.3% of patients did not give a history of exposure and they would have got the infection from asymptomatic patients. Among the 107 exposed patients 69 were men and 38 were women. The reason for the higher number of men getting exposed may be due to their free mobility and not adopting the preventive measures.

Lab findings

Liu, J*et al*. have identified Neutrophil lymphocyte ratio (NLR) as an independent risk factor for severe COVID -19 [15]. Yang AP *et al*. have reported the optimal cut-off values for NLR (Neutrophil - Lymphocyte Ratio), and PLR (Platelet Lymphocyte Ratio) were 3.3, and 180, respectively. They have predicted that if the age is ≥ 49.5 years and NLR ≥ 3.3, 46.1% of the patients with mild COVID may progress to severe disease in a mean duration of 6.3 days whereas when age is < 49.5 years and NLR < 3.3, patients with mild disease can be cured and discharged in about 13.5 days [16].

In our study 73.4 % of patients NLR was <3 and in 71.7% PLR was less than 180 correlating with the mild disease in majority of the patients. Though 26.6% of patients had >3 NLR and 28.3% PLR more than 180, they did not progress to severe disease.

The most common changes observed in previous studies were the increase in the levels of inflammatory markers CRP, IL-6 and LDH as well as ESR along with lymphopenia and decreased albumin and eosinophils. Zhang ZL *et al* in their systematic review and meta-analysis involving 4662 patients have observed increased CRP in 73.6%, ESR in 61.2% and LDH in 46.2% of patients and concluded that patients with increased CRP, lymphopenia, and increased LDH may require intensive treatment [17].

Ji P *et al* in their meta-analysis concluded that increased levels of inflammatory markers like WBC, ESR, CRP, PCT, IL-6, and IL-10 are associated with severe COVID-19 and these markers can be used as prognostic indicators of COVID -19 [18].

The normal D-dimer level is less than 0.50 [19]. Zou *et al* have observed a link between high D-dimer levels and severity of COVID-19 and that D-dimer levels in mild disease was < 2 and >10 in severe infection [20].

Artifoni *et al* observed a positive predictive value of 44% and 67% for D-dimer level ≥1.0 µg/mL and ≥3.0 µg/ mL, respectively [21].

We have observed elevated ESR in 24%, CRP in 43%, LDH 28.76%, D-dimer, 48.2%, fibrinogen, 35.3% and ferritin in 16% of patients. Comparatively lower percentage of patients had elevated laboratory markers in our study, which could be because most of them had mild disease.

CT Chest

Bao *et al*. found that Ground Glass Opacity was the commonest manifestation, reported in 83.31% of patients. The sensitivity of CT for the diagnosis of COVID-19 ranges from 60–98% [22, 23]. In our study 72.5% of the patients had CT chest findings diagnostic of COVID, in line with earlier observations.

Among the co-morbid conditions diabetes and hypertension were the most prevalent disorders and this finding is in conformity to the previous reports [24].

The pharmaco therapeutic agents used in the treatment were AZT, Oseltamivir, Remdesivir, HCQ, Ivermectin, Tocilizumab and Convalescent plasma. Among these, Azithromycin was the most commonly used drug. 43% of the patients were treated with AZT and among them, 36.4% received AZT alone and the rest were given AZT in combination with other drugs.

Oseltamivir was given to 93 patients (31%). Among them, less than 1% received Oseltamivir alone and the remaining 99% received Oseltamivir in combination with other drugs.

4% received Remdesivir, 1% received HCQ, Ivermectin 0.6%, and Tocilizumab & Convalescent plasma was given to 1 patient each (table 4).

The reason for using Azithromycin in COVID is its antiviral activity. It appears to act through multiple mechanisms. It decreases the virus entry into cells [25, 26], enhances the immune response against viruses by up-regulating the production of type I and III interferons [27] and and genes involved in virus recognition. These actions are responsible for its action against SARS-CoV-2.

HCQ causes similar effects as that of chloroquine in its anti-viral and anti-inflammatory effects and the difference between the two is safety. HCQ is safer than chloroquine. With the addition of hydroxyl molecule, HCQ becomes less permeable to blood-retinal barrier and carries a lesser risk to cause retinal toxicity [28, 29]. Hence HCQ is preferred over chloroquine. Oseltamivir (Tamiflu), a neuraminidase inhibitor, is approved by FDA for prophylaxis and treatment of acute, uncomplicated influenza A and B. It prevents the release of virus particles. Though its effect in COVID -19 is not proven, early administration within 24 hours was found to reduce the time taken for fever reduction in suspected COVID patients without hypoxia [30]. The combination of Azithromycin and Oseltamivir administered to our patients would have resulted in a synergic anti-viral effect resulting in favorable outcome.

Glucocorticoids were used in 54 patients among the 300 patients. 41 patients received Dexamethasone. Steroids are used because of their anti-inflammatory activity and the benefit seen in clinical trials [31]. Van Paassen *et al* have concluded from the findings of observational studies and RCTs that corticosteroids have beneficial effects on short-term mortality and in reducing the need for mechanical ventilation. In their systematic review they observed that methylprednisolone was the most frequently prescribed steroid [32]. However in our patients, dexamethasone was the most prescribed one.

The other drugs, Remdesivir, Ivermectin, tocilizumab & Convalescent plasma were used only for a few patients.

Outcome

Out of 300 patients 285 patients recovered well and discharged.15 patients were referred to other hospitals based on their request. One patient died out of the 285 patients and

the mortality is 0.35%.The mortality rate is much lesser in our Institute than the crude death rate reported in TamilNadu, 2.44% [33] and in India, which is 1.44% as of January 22, 2021 [34].The lower mortality rate could be because all the patients had mild to moderate infection. The length of hospital stay ranged from 1 to 20 days. 53.7% of the patients were discharged within 7 days, 41.3% between 8 and 14 days and only 5% discharged after 15 to 20 days.

Conclusions

The following conclusions are drawn from this study:

- The common age group affected was 31-40 and 51-60 years.
- Male preponderance was found among the COVID–19 patients.
- 86% of patients had mild COVID infection.
- 72.5% had CT changes positive for COVID.
- Patients who had elevated inflammatory markers did not develop severe disease.
- Diabetes and hypertension were the commonest co-morbidities.
- Azithromycin, Oseltamivir and Dexamethasone were the drugs used mainly.
- The clinical outcome was good with the mortality of 0.35%

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Author contributions

All the authors contributed equally to the content of the manuscript.

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None declared.

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