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Original Research Article

Recovery of 157 COVID-19 patients with tailored treatment regime: a single centre study at dedicated COVID hospital in India

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ABSTRACT

Background: The regimen in treatment of COVID-19 disease patients is quite variable, with wide range of outcomes. We present our successful recovery rates of COVID-19 disease patients with our tailored treatment based on comorbidity and clinical symptoms.
Methods: We retrospectively analysed 157 consecutive discharged patients with COVID-19 from 20th March 2020 to 20th May 2020. They were admitted and treated at Pandit Bhimsen Joshi general hospital.
Results: The Gender distribution was 86 (54.8 %) males and 71 (45.2%) females. Mean length of hospital stay was 13 days. Among the total of 157 patients, 41(26.1%) had co-morbidities. Study results revealed that patients with comorbidities have three times (OR=2.92) higher risk of death compared with patients without any comorbidities. Diabetic patients have four times (OR=4.1) higher risk of death compared with patients without any comorbidities. X-ray of patients showed 88% had no pulmonary involvement, 6.3% bilateral alveolar shadow, 3.18% unilateral alveolar shadow and 2.54% unilateral consolidation.
Conclusions: Generally, focus is on fever as primary symptom, our majority patients were asymptomatic. Three tailor made regimens approach for asymptomatic, mild cases and moderate to severe COVID-19 cases yielded in good recovery rate. Study results revealed that patients with comorbidities have three times (OR=2.92) higher risk of death compared with patients without any comorbidities. Diabetic patients have four times (OR=4.1) higher risk of death compared with patients without any comorbidities.

Keywords: COVID-19, SARS-cov-2, Coronavirus, Pandemic

INTRODUCTION

In 1960, coronavirus was first discovered.[1] It is a species of enveloped positive-sense RNA and can be classified broadly in four categories namely, alphacoronavirus, betacoronavirus, gammacoronavirus, and deltacoronavirus, based on the basis of genomic and serological properties. SARS CoV-2 is now classified in to betacoronavirus.[2,3]

The novel coronavirus disease (COVID-19) has been spreading at a rapid rate across the world, which made world health organization (WHO) to declare it as a pandemic disease. Globally, as of 3:47 pm CEST, 7th June 2020, there have been 6,799,713 confirmed cases of COVID-19, including 397,388 deaths, reported to WHO.

On January 30, 2020, first case of coronavirus was reported in India when one of the medical students

returning from Wuhan University was tested positive in Kerala.[4] In Initial phases of COVID-19, testing was done at 78 national reference laboratories under supervision of ICMR.[5] As on 8th June 2020, 08:00 IST, in India active cases are 124981, recovered cases are 124429 and 7200 deaths are reported due to COVID-19. Testing for SARS-CoV-2 is being conducted at 742 labs led by Indian council of medical research (ICMR).

The clinical manifestations of COVID-19 vary from asymptomatic form to different symptomatic forms. The clinical presentations of COVID-19 include mild and moderate symptoms like fever, dry cough and sore throat. Severe forms present like acute respiratory distress syndrome commonly in elderly and patients with comorbidities. Such presentation leads to systemic manifestations like septic shock and multiple organ dysfunction (MOD) syndromes.[6]

Although several clinical trials are going on to evaluate possible therapies and treatment regimen, the worldwide response to the COVID-19 outbreak has been largely limited to containment.[7]

Current Treatment regimens offered worldwide are mostly limited to treat symptoms which includes giving respiratory support (oxygen therapy, mechanical ventilation), antibiotics, anti-inflammatory and antiviral therapies. Many of the medical interventions for COVID-19 were administered to treat symptoms on the basis of their ability to cure similar symptoms in other diseases like influenza and were not specifically designed to treat COVID-19.[8]

In this retrospective study, we are presenting outcome of tailored treatment administered to COVID-19 positive patients, associated comorbidities and their clinical symptoms.

METHODS

In this retrospective study, data of 157 consecutive discharged patients who were diagnosed with Covid-19 disease were analysed. These patients were admitted in civic general hospital from 20th March 2020 to 20th May 2020 and included all genders and all age groups. All these patients were laboratory confirmed for COVID-19 by rRT-PCR (nucleic acid amplification test). All the patients had history of contact with COVID-19 cases. All patients in this study were diagnosed for COVID-19 according to ICMR guidelines. All patients received appropriate supportive care and regular clinical and laboratory monitoring, Data involving demography, clinical presentation, treatment regimens, nCoronavirus rRT-PCR reports and other laboratory results were extracted from medical records. This study was approved by the Bhaktivedanta hospital ethics committee for bio-medical and health research.

Investigator collected demographic details and other data parameters of discharged/death patients including age, gender and date of admission and discharge, treatment details (list of medications used to treat COVID-19), COVID-19 rRT PCR test reports, clinical features (fever, cough, cold, breathlessness, body ache, chest pain, diarrhoea, loss of taste, loss of smell, rashes on body), comorbidities (diabetes hypertension, ischaemic heart disease, asthma, renal disease, chronic obstructive pulmonary disease, bronchiectasis), radiological examination (X-ray) reports and outcomes details: (discharge/death).

Exclusion criteria for the study excluded patients on ventilator were excluded.

Statistical analysis tools included descriptive statistical analyses were performed for the study sample. This is retrospective observational study. The numeric data was summarized by descriptive statistics like; n and Mean ± SD. The gender and age distribution were presented in percentage, mean and SD respectively. Chi-square test and Fisher Exact Test used for statistical significance determination, event with year wise at 5% level of significant. Statistical analyses were done using the SAS software (version 9.4), unless otherwise indicated.

RESULTS

157 patients were admitted in Pandit Bhimsen Joshi general hospital, Thane, Maharashtra, India, from 20th March 2020 to 20th May 2020. We found that, of all the patients admitted in this hospital, 86 (54.8%) were males and 71 (45.2%) were females. 99 (63.1%) belonged to the age group of less than 40 years of age, 45 (28.7%) between 41 to 60 years of age and 13 (8.3%) to more than 60 years of age (Table 1). Mean age of the patient was 36.56 (SD 17.7%). Mean length of hospital stay was 13 days. There was no statistically significant difference between genders regarding length of hospital stay. Mean length of hospital stay was 13 days.

As shown Figure 1, among total 157 patients, 41 (26.1%) patients had some form of co-morbidities. 32 (20.4 %) had diabetes, 23 (14.6%) hypertension, 7 (4.5%) IHD, 1 (0.6%) CKD, Asthma 4 (2.5%), hypothyroidism 7 (4.4%).

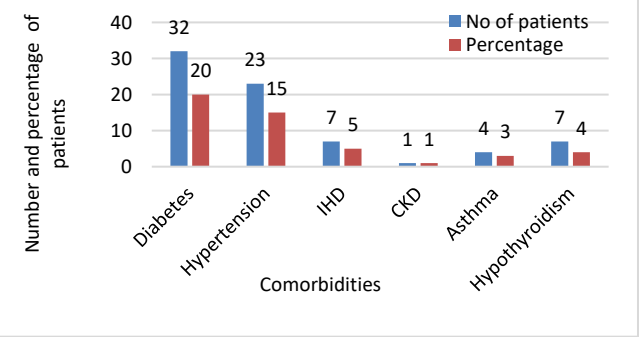

Figure 1: Frequency of comorbid conditions.

Table 1: Number and percentage of patients in different age groups and mean hospital stay.

Age (mean age-36.56 year)	No. of patients	% of patients (%)	Mean hospital stay (p=0.095)
<40	99	63.1	12.71
41 to 60	45	28.7	14.82
>61	13	8.3	11.15

On admission most of the patients were asymptomatic. Remaining patients displayed varying symptoms viz cough, fever, breathlessness, cold and sore throat with different frequencies as shown in Figure 2.

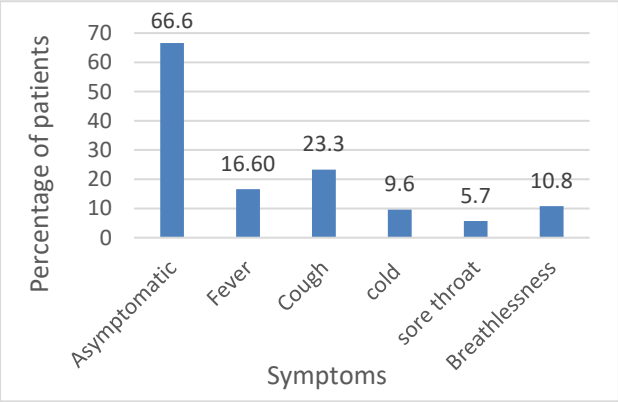

Figure 2: Patients symptoms (percentage wise).

There was no statistically significant difference between diabetes and number of day's hospital admission.

There were 4 deaths in the study group (2.5%). Study results revealed that patients with comorbidities have three times (OR=2.92) higher risk of death compared with patients without any comorbidities. Diabetic patients have four times (OR=4.1) higher risk of death compared with patients without any comorbidities. Due to small sample size, it will be difficult to prove statistical significance. Patients having both diabetes and hypertension were at 4 times more risk of death (OR=4.1) compared to those having neither hypertension nor diabetes.

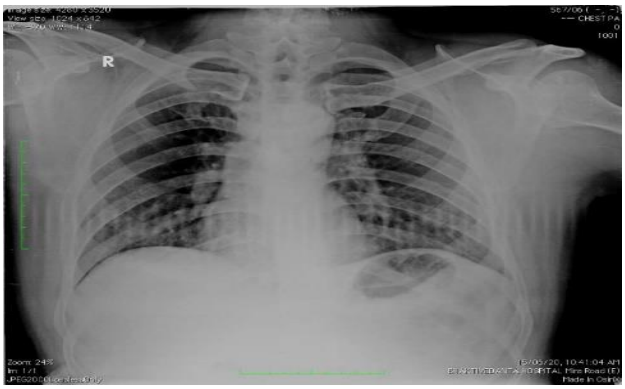

Figure 3: Image depicting bilateral alveolar shadow in COVID-19 patient.

On X-ray (Table 2) 88% of the patients had no pulmonary involvement, 6.3% showed bilateral alveolar shadow (Figure 3), 3.18% unilateral alveolar shadow and 2.54 % unilateral consolidation.

Table 2: X-ray findings.

X-ray findings	No. of patients	Percentage (%)
No pulmonary involvement	138	87.8
Unilateral alveolar shadow	5	3.18
Bilateral alveolar shadow	10	6.3
Unilateral consolidation	4	2.54

DISCUSSION

At our centre we initiated COVID-19 treatment with basic medications namely hydroxychloroquine, azithromycin and vitamin C.

Table 3 (Figure 4) depicts list of medications administered to patients at our centre.

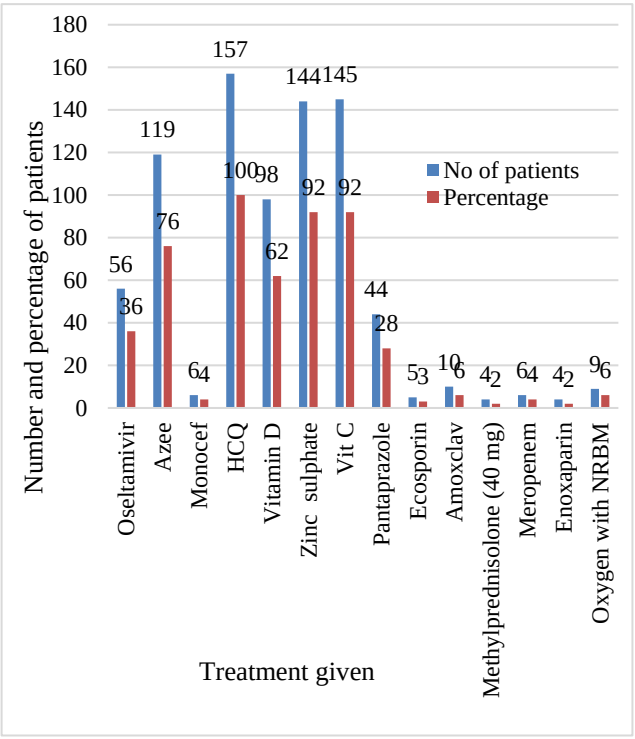

Figure 4: Treatment given at our centre, number and percentage.

Patients in our cohort had several comorbidities with highest incidence of diabetes followed by hypertension, hypothyroidism, asthma and IHD.

In multicentric clinical trials conducted on use of chloroquine phosphate, routinely used for the treatment of Malaria, shown benefit in treating COVID-19 treatment. We used hydroxyl chloroquine sulphate in 157 (100%)

patients.[9,10] Study published from China revealed that Chloroquine phosphate is not only beneficial at entry but also at post-entry stages of the COVID-19.[11]

Table 3: Treatment given to patients.

Treatment	No. of patients (%)
Oseltamivir	56 (35.6)
Azee	119 (75.7)
Monocef	6 (3.82)
HCQ	157 (100)
Vitamin D	98 (62.42)
Zinc sulphate	144 (91.71)
Vit C	145 (92.35)
Pantoprazole	44 (28.02)
Ecosprin	5 (3.18)
Amoxclav	10 (6.36)
Methylprednisolone (40 mg)	4 (2.54)
Meropenem	6 (3.82)
Enoxaparin	4 (2.54)
Oxygen with NRBM	9 (5.73)

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As per the studies published from China, elderly people deteriorated faster. Studies also conclude that with respect to death, median number of days from the appearance of first symptom in elderly patients were shorter when compared.[12,13]

Studies published from Wuhan, China stated that antiviral drugs (neuraminidase inhibitors) such as oseltamivir are in-efficacious, however we treated 56 patients (35.7%) with oseltamivir and found encouraging response with better recovery when administered with hydroxy chloroquine.[14,15] In another study published from Wuhan, 41 COVID-19 patients (93%) of the patients were prescribed antiviral oseltamivir.[16]

Zinc supplement have been shown to improve systematic immunity and inhibit the viral replication which would in turn reduces viral load.[17] We administered 40 mg zinc twice a day to decrease the viral load.

As per our clinical experience and literature data, it is observed that cause of death for most of the COVID-19 patients is sudden cardiac event or pulmonary embolism, severe hypoxia and ferritin deposition, which prompted us to introduce low dose methyl prednisolone (40 mg twice a day), low molecular weight heparin 40 mg once a day and Aspirin 75 mg once a day in moderate to severe patients. Our initial observation showed marked recovery.

We decided to do a controlled study of moderate to severe patients admitted in ICU after our findings in these 157 patients.

Three regimens that COVID-19 patients received at our centre: Hydroxychloroquine in asymptomatic cases, hydroxychloroquine, azithromycin, vitamin C, zinc and vitamin D3 in mild symptomatic cases and hydroxychloroquine, azithromycin, vitamin C, zinc, vitamin D3, methyl prednisolone, Aspirin, low molecular weight heparin, oseltamivir in moderate to severe symptomatic cases.

Protease inhibitors such as lopinavir/ritonavir, along with other antiretroviral drugs such as darunavir/cobicistat have shown reduction of viral load,[18,19] however there is no additional benefit observed in recent studies on hospitalized severe COVID-19 patients. Hence, we didn't consider using these drugs on our patients.[20]

COVID-19 infection generates pro-inflammatory and anti-inflammatory cytokines. By enhancing cellular immunity, vitamin D reduces cytokine storm which is induced by innate immune system.[16,21] COVID-19 patients can be benefited by administrating vitamin D3 as it reduces pro-inflammatory cytokines and increases the expression of anti-inflammatory cytokines by macrophages, vitamin D acts as an immune system modulator, preventing excessive expression of inflammatory cytokines, what we found after thorough literature search that in previous epidemics, level of vitamin D3 if maintained above 30 ng/ml had shown milder version of disease.[22-24] Considering the sudden rush of patients and limited time to build up vitamin D3 level, we decided to give 6 lakh IU of vitamin D3 intramuscular for prophylaxis of health care workers and all patients presenting with COVID-19 symptoms.

As mentioned in the Table 2, in all the studies it is observed that a greater number of males are affected than females which is also the case in our study. This is regarded to be conferred by several immune response genes present on X chromosome and sex hormones, which play an important role in innate and adaptive immunity.[25]

Table 5 depicts our study COVID-19 symptoms comparison with other studies. As per Table 5, number of patients presenting with fever is significantly less in our study, compared to that reported by Chu et al, chi square=35.43 and $p<0.00001$.[26]

Table 4: Depicts comparison of our study with other studies with respect to age, gender and comorbidities.

Study	Media and age (year)	Gender (%)		Prognosis (%)	Comorbidity (%)	Diabetes (%)	Hypertension (%)	IHD (%)
		M	F					
In this study	35	86 (54.8)	71 (45.2)	Discharge-153 (97.45) Death-4 (2.54)	41 (26.1)	32 (20.4)	23 (14.6)	7 (4.5)
Chu et al[26]	39	36 (66.7)	18 (33.3)	-	-	-	-	-
Huang et al[16]	49	30 (73)	11 (27)	Discharge-28 (68) Death-6 (15)	13 (32)	8 (20)	6 (15)	6 (15)
Chen et al[27]	55.5	67 (68)	32 (32)	Discharge-31 (31) Death-11 (11) still hospitalized till end of the study-57 (58)	51	-	-	-
Booth et al[28]	45	56 (38.8)	88 (61)	-	-	16 (11)	-	12 (8)

Table 5: Clinical symptoms comparison with other studies.

Study	Asymptomatic (%)	Fever (%)	Cough (%)	Cold (%)	Sore throat (%)	Breathlessness (%)
In our study	66.90	16.60	22.30	9.60	5.70	10.80
Chu et al[26]	-	66.7	31.5	-	1.9	9.3
Huang et al[16]	-	98	76	-		55
Chen et al [27]		82 (83)	81 (82)	-	5 (5)	31 (31)
Booth et al[28]	-	99.3	69.4	-	12.5	41.7

Limitations

First, due to the retrospective study design, not all laboratory tests were done in all patients. As the study was conducted in a single general hospital, it limits generalizability. Conduct of the study in more diverse settings/populations would certainly further refine for its more general applicability.

CONCLUSION

Three tailor made regimens approach for asymptomatic, mild cases and moderate to severe COVID-19 cases yielded in good recovery rate. Though Indian Government is focussing on fever (as a primary symptom) clinics for detecting coronavirus patients, in our study, we observed that majority patients are asymptomatic and only 16.6% patients had fever as presenting symptom. Study recommends focus on contact tracing over symptomatic screening to identify infected patients and control community spread.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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