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Clinical Profile of COVID-19 Patients Admitted in a COVID Designated Hospital

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ABSTRACT

Background: Pandemic of COVID-19 has engulfed Nepal as well. In this paper, we studied the demographic, clinical, laboratory findings as well as the treatment modalities, prognostic factors and outcome of patients admitted with COVID-19.

Methods: This was an observational cross-sectional study that included all patients admitted to the General Medicine Department of College of Medical Sciences, Bharatpur, during the first wave of COVID-19 from April 2020 to February 2021 after obtaining the ethical clearance. Data analysis was done using statistical packages for social sciences version 16.

Results: A total of 119 patients with mean age of 61.5 years were admitted. They had a mean duration of onset of symptoms of 7.1 days. Commonest symptoms were fever (70.6%), cough (67.2%) and dyspnea (64.7%). Severe COVID-19 at admission with a median CT severity score of 15 was found in 49.7% of them. Total 83.2% patients required ICU care and 10.9% required mechanical ventilation. ARDS and secondary infection occurred in 17.6% each. Median length of hospital stay was 6 days. In total, 56.3% recovered 27.7% left against medical advice and 16.0% expired. Severity of COVID at admission, CT severity score at presentation and D-dimer at admission were found to be significantly associated with mortality ($P<0.05$).Neither of the age, duration of illness, CRP at admission nor the use of remdesivir or convalescent plasma had significant relation with the mortality ($P\geq0.05$).

Conclusions: Severity of illness at presentation, CT severity score and D-dimer level at admission are significantly associated with mortality of the patients admitted with COVID-19.

Keywords: COVID-19; prognosis; SARS-CoV-2

INTRODUCTION

COVID-19 was first diagnosed at Wuhan,China at the end of 2019, which spread rapidly all across the globe and was declared pandemic by WHO on March 11,2020.[1] First case of COVID-19 was diagnosed in Nepal on Jan 13,2020.[2] Cases increased slowly in Nepal and the peak was reached by Mid October in 2020 and decreased by end of January 2021. However, by March 2021 second wave has begun and is ongoing.[3]

There are different factors that have been shown to affect the outcome of COVID-19 patients in different part of the world. However, we do not have much data about the interactions between those different factors in relation to the outcome in Nepalese population. The objective of the research is to study the epidemiology, clinical presentation, laboratory findings, and the outcome of patients with COVID-19 admitted to our hospital during the first wave of COVID-19 in Nepal. We also intended to analyze the factors that affected the in-hopsital mortality of COVID-19 patients.

METHODS

This is an observational cross-sectional study conducted at College of Medical Sciences, Bharatpur, Nepal from April 2020 to February 2021 after obtaining Ethical clearance from the Institutional review board.

1839 patients admitted to various departments from April 2020 to February 2021 screened for COVID-19 infection using RT-PCR. Of these patients, 283 patients were found to have COVID-19 PCR positive. A proportion of these patients along with other patients already diagnosed as COVID at some other centers who were referred for treatment of COVID-19 were admitted to the General Medicine Department. Patients who required sub-speciality care along with COVID management were admitted under sub-speciality department of Nephrology,

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Cardiology and Gastroenterology-Hepatology, and were not included in the study. The total number of cases included in this study is 119.

Epidemiological data, clinical parameters, lab parameters, daily progression of the disease, medications used, oxygen supplementation done and outcome of the patient were tabulated in a structured case sheet.

We treated our patients with oxygen, steroids and anticoagulation along with Remdesivir and Convalescent plasma therapy (CPT). These treatment practices were based on guidelines from various countries and expert opinions from different institutions mostly in Nepal and India as there was no single universal standard guidelines available.

As per the WHO guidelines, the severity of COVID-19 was divided into asymptomatic, mild, moderate, severe and severe in ventilator.[4]

Oxygen was supplemented to maintain a SPo2 >90%.We used Remdesivir and CPT as per guidelines from Nepal Health Research Council to oxygen requiring patients within 10 days of illness.[5]

We assessed the degree of inflammation using the CT severity score (CTSS) in HRCT chest and CRP values at admission. We used high doses of methylprednisolone (4mg /kg loading dose followed by 2 mg/kg/day) in patients who were severe at admission for duration of 5 days maximum. We then decreased dose to 1 mg/kg per day or less once the CRP started to fall or when the CRP <20 mg/L, whichever is the earlier. In Moderate patients, Dexamethasone was used in a dose of 6 mg/day.

Patients with D-dimer <3000 ng/mL and no suspicion for Venous thromboembolism (VTE) received standard thromboprophylaxis with Enoxaparin 40 mg once a day. Patients with D-dimer>3000 ng/mL and no suspicion of VTE received High-intensity prophylactic dose of 40 mg twice daily. Patients with known or suspected VTE, or otherwise unexplained increase in oxygen requirement, or organ failure with concern for microthrombi received therapeutic dosing of 1mg/kg 12 hourly.[6]

Patients with rising CRP after an initial fall with new shadows in chest imaging, new signs and symptoms suggestive of sepsis were presumed to have secondary bacterial infection. Samples sent for microbiology and patients were put on empirical antibiotics to cover nosocomial infections till a definite culture report is obtained, after which the spectrum of antibiotic was narrowed. Patients of high dose of steroids were also evaluated for fungal infection in case of deterioration and antifungal prophylaxis was used whenever clinically warranted.

Statistical analyses were performed using SPSS 16.0. Nominal variables like gender, address, comorbidities, symptoms, severity of COVID at admission, categories of lab values, HRCT findings, several other treatment and outcome parameters were presented in percentages in tables and graphs and measurement variables like age, absolute lab parameters as group means for normally distributed variables and median for skewed distributon . Fischer's Exact test was used to compare nominal variables as the sample size was not very large. Comparison between nominal and measurement variables was done using one-way anova followed by Post Hoc using Tukey test. Correlation was used for comparing measurement variables. P value of less than 0.5 was considered significant.

RESULTS

The mean age of the patients was 61.5±17.0 years. The age distribution was as shown in Figure 1.

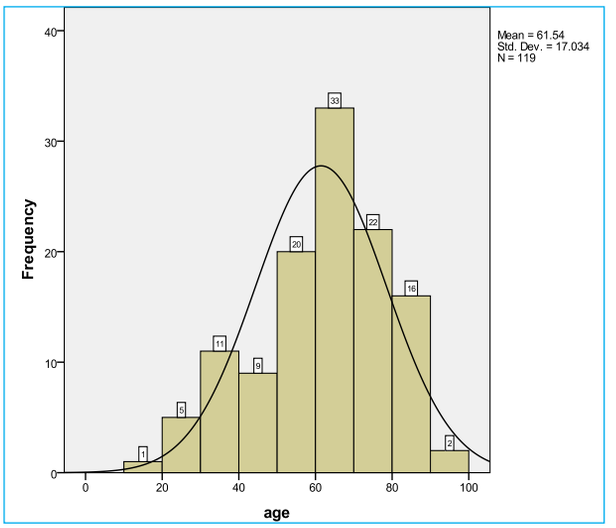

Figure 1. Age distribution of the study population.

Of all admitted patients, 58.8% of patients were male. 36.9% of patients were from Chitwan, 17.6% from Nawalparasi and 15.2% from Makwanpur. 92% of the patients had clinical suspicion of COVID-19 before being tested with PCR, the rest were found to have COVID during admission for other reasons. 40.3% of the patients were hypertensive and 17.6% were diabetic. Fever (70.6%), cough (67.2%) and dyspnea (64.7%) were the most common symptoms. Patients presented to hospital after a mean duration of 7.1 days of onset of illness. 47.9% were having severe COVID-19 at admission(Table 1).

Table 1. Demographic and clinical variables.

Variables	Frequency (%) (N=119)
Sex ratio (Male:Female)	70 : 49 (59 : 41)
Address	
Chitwan	44 (36.9)
Nawalparasi	21 (17.6)
Makwanpur	18 (15.2)
Nawalpur	10 (8.4)
Others	26 (21.8)
Comorbidities	
Hypertension	48 (40.3)
Diabetes	21 (17.6)
COPD	19 (16.0)
others	5 (4.2)
Symptoms	
Fever	84 (70.6)
Cough	80 (67.2)
Shortness of breath	77 (64.7)
Diarrhea	9 (7.6)
Nausea/Vomiting	8 (6.7)
Headache and Myalgia	6 (5.0)
Severity of COVID at admission	
Asymptomatic	3 (2.5)
Mild	17 (14.3)
Moderate	35 (29.4)
Severe	57 (47.9)
Severe in Ventilator	7 (5.9)

Complete blood count reports showed that 50.5 % of the patients have absolute lymphocyte count < 1800 /cumm, the lower limit of normal for adults, of which 16% had a value < 800/cumm. AST and ALT was elevated among 67.2% of the patients. D-dimer reports were available for only 73.9% of the patients with a median value of 880 ng/mL, among which 76% had D-dimer elevated with 54% of them having a level > 1000 ng/mL. Of 93 patients who had CRP measured at admission, 70(75.3%) had a CRP value > 20 mg/L. The median CRP value of those patients was 73.7 mg/L (Table 2).

Out of 93 patients, whose CRP values at admission were available, 71 patients had CRP measured sequentially. Even after treatment with steroids, CRP kept rising in 9 out of those 71(12.7%) patients. However, 62 patients showed declining trend in CRP. Of those 62, 24(38.7%) patients had a secondary rise in CRP while 38 (61.3%) continued to have a steady fall in CRP, with the CRP reaching <20 mg/L at a mean duration 4.5±1.8 days.

Of 105 patients who underwent HRCT chest on admission, 97(92.3%) had finding suspicious of COVID-19. Among those 97 patients with HRCT suspicious of COVID-19, 29 had CTSS>10, 19 had CTSS >15 and 12 patients had CTSS>20. (Table 3)

At admission 82.4% of patients required oxygen supplementation of which 25.2% required each of Face masks and NRMB with 100% FiO2. Only 2.5% were on High Flow Nasal Cannula (HFNC) at admission, but with treatment escalation, 17.6% required supplemental oxygen with HFNC. 4.2% of the patients were on Non-invasive ventilation, whereas 10.9% were mechanically ventilated. 108 patients (90.8%) were treated with steroids. 19.3% were prescribed Low dose dexamethasone, while 71.5 % patients, who were relatively sick, were prescribed high dose methylprednisolone for a mean duration of initial 5.0±3.4 days before tapering to lower dosage. 21(17.6%) patients received convalescent plasma therapy (CPT) while 22(18.5%) received Remdesivir. Prophylactic doses of anticoagulation was given to 52.1% of the patients while 35.3% patients received therapeutic anticoagulation (Table 3).

Of all 119 patients, 83.2% received ICU care at different points of time. Median duration of ICU stay of such patients was 4 days. ARDS (17.6%), secondary bacterial infection (17.6%) and AKI (14.3%) were the commonest complications. Median duration of hospital stay of our patients was 6 days. 67 out of 119 patients (56.3%) recovered, 33(27.7%) patients left against medical advice and 19(16.0%) patients succumbed to COVID-19. (Table 3)

Data were cross tabulated and subjected to Fischer's Exact Test to study if there is any relationship of changes in severity of COVID-19 during treatment (static, improvement or deterioration of severity) to the severity of COVID-19 at admission. Of 57 patients who were severe at admission, 26(45.6%) patients deteriorated while 7(12.3%) showed no signs of improvement. Similarly, none of the 7 patients who were on ventilator at admission improved. The rate of improvement in patients presenting in moderate and mild severity is significantly better (68.6% and 76.5% respectively) Fischer's Exact Test: (G= 32.224, 8 d.f., P <0.001)Mean duration to decrease in severity by one severity scale among those who showed an improvement is 5.2±3.4 days (Figure 2).

Table 2. Laboratory parameters.

Variables	Frequency (%) (N=119)	Variables	Frequency (%) (N=119)
Hemoglobin in g/dL (Mean ± SD)	12.4 ± 1.8	**D-dimer at presentation (ng/mL) (median 880)**	
Total leukocyte count (per cumm)		Reports not available	31 (26.1)
Less than 4000	8 (6.7)	Reports available (N = 88)	
4000 to 12000	82 (68.9)	Normal (<500)	24 (27.3)
More than 12000	29 (24.4)	500 to 1000	22 (25.0)
Platelets count (per cumm)		1000 to 3000	24 (27.3)
Less than 100,000	4 (3.4)	3000 to 10000	10 (11.4)
100,000 to 150,000	13 (10.9)	More than 10000	8 (9.1)
More than 150,000	102 (85.7)	**CRP at presentation mg/L (Median 73.7 mg/L)**	
Absolute lymphocyte count (per cumm)		Reports not available	26 (21.8)
Less than 800	19 (16.0)	Reports available (N= 93)	
800 to 1800	41 (34.5)	Less than 20	23 (24.7)
1800 to7700	56 (47.1)	20 to 50	15 (16.1)
More than 7700	3 (2.5)	50 to 100	16 (17.3)
Creatinine in mg/dL(Mean ± SD)	1.12 ± 0.62	More than 100	39 (41.9)
AST (U/L)		**Procalcitonin at presentation microgram/L (Median 0.37)**	
Normal (7-40)	39 (32.8)	Reports not available	34 (28.6)
1-3 X UNL	71 (59.7)	Reports available (N= 85)	
3-5 X UNL	6 (5.0)	Less than 0.5	49 (57.6)
>5 X UNL	3 (2.5)	0.5 to 1.0	17 (20.0)
ALT (U/L)		1.0 to 2.0	8 (9.4)
Normal (7-35)	39 (32.8)	2.0 to 10.0	7 (8.3)
1-3 X UNL	66 (55.4)	More than 10.0	4 (4.7)
3-5 X UNL	10 (8.4)		
>5 X UNL	4 (3.4)		

Table 3. Imaging, treatment and outcome parameters.

Variables	Frequency (%) (N=119)	Variables	Frequency (%) (N=119)
HRCT finding at admission		**Steroid**	
Reports not available	14 (11.8)	Not used	11 (9.2)
Reports available (N= 105)		Low dose Dexamethasone	23 (19.3)
Normal	3 (2.9)	Methylprednisolone	85 (71.5)
Abnormal but not suggestive of COVID	5 (4.8)	**Duration for which high dose methylprednisolone used (mean±SD)**	5.0 ± 3.4 days
Ground glass opacities suggestive of COVID	97 (92.3)	**Convalescent plasma therapy done**	21 (17.6)
CTSS severity not reported	23 (23.7)	**Remdesivir used**	22 (18.5)
CTSS reported (N=74)(Median= 15)		**Anticoagulation used**	
CTSS 5 or less	2 (2.7)	None	15 (12.6)
CTSS 6 to 10	12 (16.2)	Prophylactic dose	62 (52.1)

CTSS 11 to 15	29 (39.2)	Therapeutic dose	42 (35.3)
CTSS 16 to 20	19 (25.7)	**Total patient requiring ICU care**	99 (83.2%)
CTSS 21 and above	12 (16.2)	**Length of ICU stay (Median days)**	4 days
Oxygen delivery devices on admission		**Complications**	
Not required	21 (17.6)	ARDS	21 (17.6)
Nasal prongs	10 (8.4)	Secondary bacterial infection (Suspected or microbiologically confirmed)	21 (17.6)
Face masks	30 (25.2)	Acute Kidney injury	17 (14.3)
Venturi Mask	18 (15.1)	Septic shock	5 (4.2)
NRBM	30 (25.2)	Pulmonary embolism	1 (0.8)
HFNC	3 (2.5)	Myocardial infarction	1 (0.8)
Mechanically ventilated	7 (5.9)	Median duration of hospital stay	6.0 days
Total patients where HFNC used during treatment	21 (17.6)	**Outcome**	
Non invasive ventilation done	5 (4.2)	**Discharged after improvement**	**67 (56.3)**
Total patients intubated during course of treatment	13 (10.9)	Left against medical advice	33 (27.7
		Expired	19 (16.0)

Table 4. Comparison of outcome of the patients with different variables.

Variables			Outcome (N=119)			G or F value *	P value
			Recovered (N=67)	LAMA (N=33)	Expired (N=19)		
Fischer's Exact test	Severity at presentation	Asymptomatic	2 (66.6%)	1(33.3%)	0	36.178	<0.001
		Mild	14 (82.4%)	3 (17.6%)	0		
		Moderate	26 (74.3%)	9 (25.7%)	0		
		Severe	25(43.9%)	19(33.3%)	13(22.8%)		
		Severe in ventilator	0	1(14.3%)	6(85.7%)		
	Remdesivir given	Yes	15(68.2%)	3(13.6%)	4(18.2%)	2.545	0.314
		No	52(54.2%)	29(30.2%)	15(15.6%)		
	CPT done	Yes	15(71.4%)	4(19.0%)	2(9.5%)	1.93	0.397
		No	52(53.6%)	28(28.9%)	17(17.5%)		
One-way anova	Age of the patient (in years)	Mean	57.6	64.7	69.9	4.971	0.008
		SD	16.6	16.4	16.6		
	Duration of illness at presentation (in days)	Mean	6.89	7.87	6.47	1.369	0.259
		SD	3.22	3.03	3.61		
	CTSS at presentation	Mean	13.57	17.61	18.5	9.899	<0.001
		SD	4.72	3.5	2.9		
	CRP at admission (mg/L)	Mean	77.21	111.56	94.43	1.819	0.168
		SD	66.96	95.21	64.95		
	D-dimer at presentation (ng/mL)	Mean	1527.5	3245.1	5633.3	8.062	<0.001
		SD	2268.9	3694.3	5767.4		

** G value in case of Ficher's Exact test and F value in case of One-way anova*

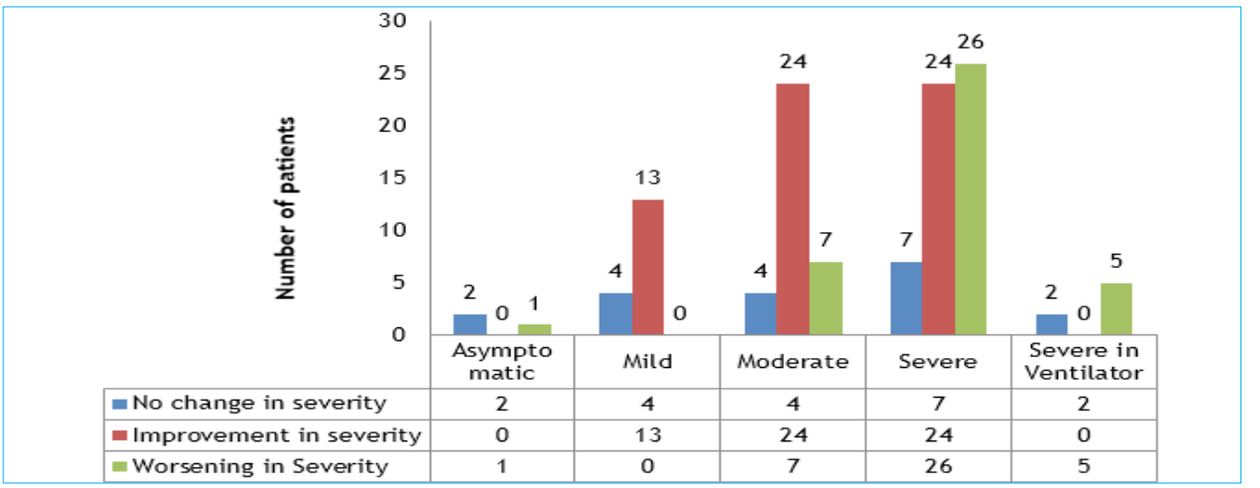

Figure 2. Change in Severity of COVID during treatment.

Increase in severity at presentation was associated with worse outcome. None of the patients who presented with mild to moderate severity had in-hospital mortality. Only 43.8% of patients who were severe at presentation survived, while none of those on ventilator survived. (Fischer's Exact Test:G=36.178, 8 d.f., P<0.001)(Table 4).

Outcome of the patients had no relation with the duration of illness (DOI) at presentation. The mean DOI among those who recovered (6.89±3.22) was similar to those who went on LAMA (7.87±3.03) and to those who expired (6.47±3.61).(One-way anova, $F_{2,111}$=1.369, P= 0.259) Post Hoc anaylsis with Tukey Test also didn't show any significant difference between pairs among any of the three outcome groups (Table 4).

Patients who had lower CTSS on HRCT at admission had better outcome. The mean CTSS of recovered group was 13.57±4.7 as compared to 17.61±3.50 in those on LAMA and 18.5± 2.91 in those who expired.(One-way anova, $F_{2,71}$=9.899, P <0.001) Post Hoc analysis with Tukey test, showed that there is a statistically significant difference in CTSS score of the recovered group with both the the LAMA group(P=0.003) and Expired group(P=0.002). But there is no difference between LAMA group and Expired group in terms of CTSS at presentation.(P=0.838) (Table 4).

Comparing the D-dimer level at presentation with the outcome, it was found that the mean level among those who recovered was 1527.5 + 2268.9 as compared to a mean level of 3245.1±3694.9 among those who left on LAMA and a mean level of 5633.3±5767.3 among those who expired. (One-way anova, $F_{2,85}$=8.062, P <0.001) Post Hoc anaylsis with Tukey Test showed that the difference in between the D-dimer value is significant only in between Recovered group and Expired group (p=001), whereas there is no significant difference in D-dimer value between the other pairs of outcome group (Table 4).

The outcome was found to have no relation with either the age of the patient (One-way anova, $F_{2,90}$=1.819, P = 0.168) or the CRP at admission (One-way anova, $F_{2,116}$=4.971, P <0.008). Post Hoc anaylsis with Tukey Test also didn't show any significant difference between pairs among any of the three outcome groups (Table 4).

Similarly, the outcome was found to have no significant relation to the use of neither Remdesivir (Fischer's Exact Test: G= 2.545, 2 d.f., P= 0.314), nor CPT (Fischer's Exact Test: G= 1.930, 2 d.f., P= 0.397) (Table 4).

On running a Pearson correlation study, it was found that the CTSS is not associated with either of duration of illness at presentation (R^2= 0.01, P=0.375), CRP level at admission (R^2= 0.038, P=0.099) or D-dimer level at admission (R^2=0.029, P= 0.171) (Table 4).

Table 5. Correlation of CTSS with other measurement variables using Pearson correlation.

Correlation of CTSS with	Pearson correlation coefficient (R)	P value
Duration of illness	0.105	0.375
CRP level at admission	0.196	0.099
D-dimer level at admission	0.172	0.171

DISCUSSION

In Nepal, the highest incidence of COVID-19 is among the people of age group 21-40 years of age.[3] Mean age of patients admitted with us was 61.54 years. 60-69 was commonest age among both the hospitalized(24.6%) and the ICU admitted patients(27.4%) in a study done in California.[7]

Our study showed no difference in outcome in relation to the age of the patient.(P = 0.008) Other studies have however, shown the older age to be a risk factor for mortality. In a study done in 11721 patients, it was found thatthat the odds of mortality was higher in patients of age group 41-60, as compared to those aged 18-40. (OR,2.6; 95% CI, 1.9-3.5).[8] Smaller sample size in our study might be the cause of this discrepancy.

In our center, mean DOI at admission was 7.1 days. 47.9% patients were already having severe COVID-19 at admission. Although there was no significant relation between the outcome and the DOI at presentation (P=0.259), the study showed that severity of illness at admission has significant effect on the outcome. (P<0.001) Those who presented with mild to moderate disease tend to have improvement in severity (76.5% and 68.6% respectively) more than the patients presenting in severe COVID-19 and those who were intubated at admission. All these findings dictate the importance of careful monitoring and early hospitalization. A study from California found that 30.0% of their patients required requiring ICU at admission and 29.2% required mechanical ventilation at admission.[7]

Lymphopenia has been described as predictors of severe disease. An absolute lymphocyte count <800/cumm has been found to predict ICU admission in COVID-19 patients.[9] Neutrophilia has been found to have a hazard ratio of 3.26 as a risk factor to the development of ARDS in COVID-19.[10]

D-dimer value >1000 ng/mL was seen in 54% of our patients. Our study showed that higher value of D-dimer at presentation is associated with higher incidence of mortality(P=001). Data from California also mentioned that the mean D-dimer level was 1160 ng/mL among patients developing ARDS as compared to a mean of 520 ng/mL among those not developing ARDS.[7] Severe cases of COVID-19 are thought to be associated with infection induced coagulopathy and secondary hyper-fibrinolysis.[11]

Our study failed to show any relation between the CRP at admission with the CTSS on HRCT(P= 0.099) neither with the outcome(P= 0.168).However, CRP has been used in different centers as a marker of severity of inflammation in COVID-19 and is used for follow-up as well. A meta-analysis found a significant role of CRP in COVID-19 infection outcome (SD in means = 1.371, P= 000). [12] Another study demonstrated a positive correlation between CRP level and diameter of the largest lung lesion in patients with severe COVID-19 (R=0.873, 0.734, P <0.001).[13]

Our study demonstrated that CTSS on HRCT at admission has a significant relation to the outcome in between those who recovered (13.57±4.7) and those who expired (18.5±2.91) or went on LAMA (17.61±3.50)(P <0.001). A study done by Raoufi et al, showed that the mean CTSS of cases who expired was significantly higher than the survivors (13.68±4.59 versus 8.72±4.42; P<0.0001).[14]

We found no difference in the outcome regardless of use of Remdesivir (P=0.314) or convalescent plasma therapy (P=0.397). Solidarity trial randomized 2750 patients to receive Remdesivir and found that it had no effect on mortality (rate ratio, 0.95; 95% CI, 0.81 to 1.11; P=0.50).[15] In regards to CPT, a meta-analysis of four different trials couldn't demonstrate a significant mortality benefit of CPT as compared to placebo or standard of care (RR 0.93, 95% CI, 0.63-1.38).[16]

We used low dose dexamthasone in our moderate patients (19.3% of 108 patients requiring steroids). Recovery trial authors found that use of dexamethasone 6 mg per day lowered the 28 days mortality in patients receiving oxygen support (23.3 versus 26.2%, RR 0.82, 95% CI 0.72-0.94).[17] We used high dose methylprednisolone (71.5% of 108 patients) for the initial few days in our sicker patients followed by tapering. A study conducted in Iran demonstrated significant better clinical outcomes in term of improvement in clinical status, need of ventilator and the duration of hospital stay, when methylprednisolone 2 mg/kg/day was compared to dexamethasone 6 mg/day.[18]

We found no significant correlation of CTSS at presentation with either of DOI, CRP level or the D-dimer level at admission. A study done to compare the CT findings in COVID-19 with the DOI showed that CTSS increased upto 9 days and then remained high, with the CTSS in first 4 days being 2.8±3.1 as compared to a CTSS of 6±4.6 in between days 5 to 9 (P <0.01).[19] Observations that the extent of lung abnormalities peak by day 6-11 has also been done by Wang et al.[20] As the mean duration of illness was already 7.1 days among our patients, the CTSS might not be changing as rapidly to be statistically significant.

Our study had few limitations. We studied those patients which were admitted to our department only, missing a fraction of patients with renal, cardiac and liver problems who were expected to do worse. We also had a significant proportion of the patients who left the hospital against medical advice before a conclusive outcome. Further, information on the specified variables was not complete for all the patients.

CONCLUSIONS

Our study showed that the severity of illness at presentation, the CTSS and the D-dimer level at presentation are significantly associated with the mortality of the patients. Age of the patients, duration of illness, CRP levels at presentation, and any use of Remdesivir or CPT had no significant relation to the mortality of the patients.

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Competing interests: None declared

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