Tocilizumab improves survival in severe COVID-19 pneumonia with persistent hypoxia: A retrospective cohort study with follow-up from Mumbai, India

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Abstract

Background

Cytokine storm triggered by Severe Corona Virus Disease 2019 (COVID-19) is associated with high mortality. With high 'Interlukin -6' (IL-6) levels reported in COVID-19 related deaths in China[1], IL-6 is considered to be the key player in COVID-19 cytokine storm. Tocilizumab, a monoclonal antibody against IL-6 receptor, is used on compassionate grounds for treatment of COVID-19 cytokine storm. The aim of this study was to assess effect of tocilizumab on mortality due to COVID-19 cytokine storm.

Method

This retrospective, observational study included patients of severe COVID-19 pneumonia with persistent hypoxia (defined as saturation 94% or less on supplemental Oxygen of 15 L per minute through non-rebreathing mask or PaO2/FiO2 ratio of less than 200) who were admitted to a tertiary care center in Mumbai, India, between 31st March to 5th July 2020. In addition to standard care, single Inj. Tocilizumab 400mg was given intravenously to 151 consecutive COVID-19 patients with persistent hypoxia, from 13th May to 5th July 2020. These 151 patients were retrospectively analysed and compared with historic controls, i.e consecutive COVID-19 patients with persistent hypoxia, defined as stated above (N=118, from our first COVID-19 admission on 31st March to 12th May 2020 i.e, till tocilizumab was available in hospital). Univariate and multivariate Cox regression analysis was performed for identifying predictors of survival. Statistical analysis was performed using IBM SPSS version 26.

Results

On multivariate Cox regression analysis, independent predictors of survival were use of tocilizumab (HR 0.621, 95% CI 0.427-0.903, P 0.013) and higher oxygen saturation.

Interpretation: Tocilizumab improved survival in severe COVID-19 pneumonia with persistent hypoxia

Background:

In December 2019, a newly discovered corona virus, SARS-CoV-2 caused the novel corona virus disease (COVID-19), that spread rapidly to become a pandemic. Though around 80% patients have a mild course and overall mortality is 2–3% only, around 20% need hospitalization (14% have severe disease and 5% are critical) [2]. Mortality is high in those with severe acute lung injury. With absence of specific antiviral drugs, treatment is essentially empirical, supportive and symptomatic, with

- antiviral - Lopinavir/ Ritonavir[3], Remdesivir[4], Favipiravir, Oseltamavir, Interferons, Ivermectin[5] (in vitro reduction in viral load)
- Convalescent plasma with passive antiviral antibodies transfer,

- drugs to reduce virus induced inflammatory response including Methyl Prednisolone and IL-6 blockade with Tocilizumab[6,7,8,9], JAK-inibitors[10]
- conventional or Low Molecular Weight Heparin (LMWH) for virus induced coagulopathy[11,12]
- Hydroxychloroquin and Azithromycin
- supportive – Oxygen therapy/ high flow nasal cannula, non-invasive ventilation, mechanical ventilator, extracorporeal membrane oxygenation, antibiotics (to treat secondary infection), inotropic support and renal replacement.

Autopsy studies from deaths due to corona virus infection suggested that aberrant host immune response results in a lethal inflammatory cytokine storm.[13] Increased alveolar exudates caused by aberrant host immune response and inflammatory cytokine storm probably impedes alveolar gas exchange and contributes to the mortality of severe COVID-19 patients. IL-6 is one of the most important cytokines involved in COVID-19 cytokine storm. Therefore tocilizumab, a humanized monoclonal antibody against IL-6 receptor (IL-6R) is investigated in treatment of seriously ill COVID-19 patients with cytokine storm. Untreated cytokine storm can progress from respiratory failure, to cardiovascular collapse, multiorgan dysfunction, and death.

Methods:

Study design and participants: This is a retrospective, observational study done at a single tertiary care center in Mumbai, India. The study population included adults of age more than 18 years with a positive nasopharyngeal swab for COVID-19 by RT-PCR, admitted from 31st March-5th July 2020.

Inclusion criteria were:

- persistent hypoxia (defined as saturation 94% or less on supplemental Oxygen of 15 L per minute through non-rebreathing mask or PaO2/FiO2 ratio of less than 200),
- bilateral pulmonary infiltrates on chest x-ray and
- raised inflammatory markers (C-Reactive Protein, Lactose Dehydrogenase, Ferritin)

Tocilizumab was available to us (free through the Municipal Corporation of Greater Mumbai) from 13th May onwards and was used in patients satisfying inclusion criteria from 13th May to 5th July. Although all three inclusion criteria were mandatory in tocilizumab group, in the historic control group the only two mandatory inclusion criteria applied were persistent hypoxia as defined above and presence of bilateral alveolar shadows. High C-reactive Protein could not be applied as inclusion criterion in the historic control group due to non availability of this test in our institute at that time, with prevalent financial constraints at that time.

Exclusion Criteria were:

- altered sensorium

- hypotension requiring multiple inotropic agents or multisystem organ failure (MSOF)
- patients suffering from terminal malignancy
- cardiomyopathy with ejection fraction less than 20%

Clinical features, co-morbidities, laboratory investigations and treatment details of all patients satisfying inclusion criteria were recorded. We have follow up of 55 days after last patient enrolment. Historic control group consisted of patients with COVID-19 infection satisfying inclusion criteria, from 31st March to 12th May (i.e, from first COVID-19 admission to our hospital till tocilizumab became available).Their data was obtained from indoor papers medical records. The study was approved by the Institutional Ethical Committee. Written consent for compassionate use of tocilizumab was obtained from patient or relative, and a consent waiver was permitted by institutional ethics committee for this retrospective study.

Procedures:

All patients received standard treatment consisting of antibiotics (Piperacilin-Tzobactum or Meropenem/ Vancomycin in view of critical condition), hydroxychloroquine 400 mg once daily, ivermectin 12 mg once daily, oseltamivir 75 mg twice daily, low molecular weight heparin 1 mg/ kg subcutaneously once daily (twice daily if D-dimer > 3000 ng/mL), methylprednisolone 125–500 mg intravenously once daily, and other supportive care as needed (Oxygen through non-rebreathing mask, High Flow Nasal Canula, Noninvasive or invasive ventilator support, inotropic support, renal replacement therapy). In addition to standard treatment, tocilizumab group received single intravenous dose of 400 mg tocilizumab.

Outcomes: Primary outcome was death or recovery.

Statistical analysis: Comparison of the characteristics of the patients who received tocilizumab versus the control group, and comparison of characteristics of patients who survived versus those who died was performed. For comparison of categorical data, chi square test was used while for ordinal or continuous data, independent samples Mann Whitney U test was used. A p value of less than 0.05 was considered as significant.

Univariate and multivariate Cox regression analysis and logistic regression were performed for identifying predictors of survival. Log rank test was used to compare survival between patients who received tocilizumab versus the control group. Survival time was calculated from the date of giving tocilizumab to avoid immortal time bias. Statistical analysis was performed using IBM SPSS version 26.

Results:

From 31st March to 5th July 2020, a total of 2183 COVID-19 patients were admitted under Medicine department. Three hundred and ninety seven had persistent hypoxia (defined as saturation 94% or less on supplemental Oxygen of 15 L per minute through non-rebreathing mask or PaO2/FiO2 ratio of less than 200); of them 128 died within 24 hours of admission and were not included in the study. A total of 269

patients with persistent hypoxia were included in the study. One fifty one received single intravenous infusion of tocilizumab 400 mg and 118 who did not, were historic controls.

Their characteristics are shown in Table 1. Tocilizumab group was younger (53 years v/s 55 years), but had lower mean Oxygen saturation of 86% (82–92%) v/s 91% (88–93%) in the control group. In tocilizumab group 63.6% had at least one co-morbidity and 36.4% were without any co-morbidity, where as in the control group 74.6% had at least one co-morbidity and 25.4% were without any comorbidity. Tocilizumab group had more patients with obesity and less proportion of patients with hypertension than the control group.

Table 1
Comparison of the characteristics of the patients who received tocilizumab versus those who did not.

Variable	Tocilizumab (n = 151)	Control (n = 118)	P value
Age	53 (44–60)	55 (47–64)	0.007
Male sex	107 (70.9)	69 (58.5)	0.034
Hypertension	40 (26.5)	53 (44.9)	0.002
Diabetes	78 (51.7)	59 (50)	0.788
Obesity	14 (9.3)	0 (0)	0.001
Other comorbidities	5 (3.3)	13 (11)	0.012
Number of comorbidities	1 (0–1)	1 (1–2)	0.031
No comorbidities	55 (36.4)	28 (23.7)	0.035
Category*	125 (82.8)	108 (91.5)	0.036
E	26 (17.2)	10 (8.5)	
F			
Oxygen saturation	86 (82–92)	91 (88–93)	0.001
Respiratory rate	34 (30–40)	30 ((27–38)	0.137
Serum creatinine	1 (1-1.9)	1.3 (1-1.7)	0.002
Non-invasive ventilation	56 (37.1)	0 (0)	0.001
Invasive ventilation	22 (14.6)	8 (6.8)	0.044
Deaths	79 (52.3)	74 (62.7)	0.088

*Revised guidelines on clinical management of COVID-19.Ministry of health & family welfare,directorate general of health services, government of India, (2020). https://www.mohfw.gov.in/pdf/Revised National Clinical Management Guideline for-COVID1931032020.pdf

Non invasive ventilation was used in 56/151 patients from tocilizumab group (15 of them later required invasive ventilation) but in none from control group (as a rule, it was avoided initially due to fear of aerosolization with increased risk to health care workers). Overall, 30 patients required invasive ventilation (22 from tocilizumab group and 8 from control group). Inotropic support was required in 11 patients from tocilizumab group and 7 patients from control group. In tocilizumab group, 79 out of 151 died (52.3% mortality) and in control group 74 out of 118 died (62.7%). Figure 1 depicts effect of tocilizumab on overall survival. (The median survival in the tocilizumab group was significantly longer than in the control group; 18 days (95% CI: 11.3 to 24.7) versus 9 days (95% CI: 5.7 to 12.3); log rank p 0.007). From tocilizumab group 72 out of 151 patients (47.7%) were discharged, whereas from the control group 44 out of 118 (37.3%) were discharged. Tocilizumab was well tolerated and no adverse drug reactions were noted.

Table 2 shows comparison of the demographic and laboratory parameters in ‘overall’ survived versus non-survived groups (including both control and tocilizumab groups). Those who survived were significantly younger (52 v/s 55 years, p = 0.029) and had significantly higher Oxygen saturation (91% v/s 88%, p = 0.002), lower respiratory rate (30 v/s 36 breaths per min, p = 0.001) and lower serum creatinine (1 mg/dl v/s 1.3 mg/dl, p = 0.001). The higher average serum creatinine in the non-survived group probably reflected some degree of hypotension with prerenal element.

Table 2
Comparison of the characteristics of the patients who survived versus those who did not (both tocilizumab and control groups)

Variable	Survived (n = 116)	Died (n = 153)	P value
Age	52 (44–60)	55 (47–62)	0.029
Male sex	71 (61.2)	105 (68.6)	0.205
Hypertension	37 (31.9)	56 (36.6)	0.422
Diabetes	55 (47.4)	82 (53.6)	0.315
Obesity	3 (2.6)	11 (7.2)	0.092
Other comorbidities	8 (6.9)	10 (6.5)	0.907
Number of comorbidities	1 (0–1)	1 (0–2)	0.074
Category	105 (90.5)	128 (83.7)	0.10
E	11 (9.5)	25 (16.3)	
F			
Oxygen saturation	91 (86–93)	88 (83–92)	0.002
CRP	97.5 (63.5–159)	90 (56–136)	0.264
Respiratory rate	30 (30–36)	36 (30–40)	0.001
Serum Creatinine	1 (1-1.2)	1.3 (1–2)	0.001
SGOT	49 (37–75)	57 (42–72)	0.169
SGPT	40 (30–58)	44 (28–68)	0.977
LDH	666 (275–990)	978 (369–2000)	1.000
Ferritin	437 (293–947)	690 (369–1257)	0.364
D-dimer	1000 (1000–1927)	1411 (1000–5000)	0.079
IL-6	455 (75–984)	Not available	
WBC counts ($x10^9$/L)	8.9 (5.85–13.6)	8.55 (6.1-12.15)	0.799
Platelet count ($x10^9$/L)	200 (200–300)	200 (200–300)	0.314
CT CORAD	6 (6–6)	6 (6–6)	1.000
CT severity score	21 (17–24)	24 (21–25)	0.343
Thrombosis on CT	2 of 8	1 of 2	0.490
Tocilizumab	72 ((62.1)	79 (51.6)	0.088

Variable	Survived (n = 116)	Died (n = 153)	P value
Day of tocilizumab	3 (2–6)	3 (2–5)	0.865
Non-invasive ventilation	22 (19)	34 (22.2)	0.515
Invasive ventilation	1 (0.9)	29 (19)	0.001

Our patients, on the whole, did not have significant leucopenia (white blood cells less than 4000), lymphopenia or thrombocytopenia.

D-dimer level was higher in the 'not-survived' group, (mean 1411 / ml, range of 1000–5000 / ml) than in those who survived (mean 1000 / ml, range of 1000–1927 / ml), but the difference was not statistically significant (P 0.079).

Total 38 radiological scans (High Resolution CT chest: 26, CT-Pulmonary Angiography: 9, CT-brain: 3) were done in 28 out of 151 patients receiving Tocilizumab. Of these 28 patients, 21 were not on any form of advanced respiratory support at any time. Seven patients had radiological scans done early in the disease and ultimately required advanced respiratory support (HFNC/ NIV/ ventilator). Only 7 out of 68 patients who were on advanced respiratory support (HFNC/ NIV/ Ventilator) had radiological scans done before getting switched to the same. In the 28 patients with radio-imaging available 11 patients expired and 17 were discharged. The CT severity scores were similar in the two groups (median of 21 versus 24; p value of 0.343). The median CORAD score was also 6 in both groups (p 1.000).

Table 3 depicts univariate and multivariate Cox regression analysis. Data on CRP, SGOT, SGPT, LDH, IL-6, WBC and differential count, platelet count, ferritin and d-dimer was not available in all patients in the control group. Data on respiratory rate was available only for 142 patients and d-dimer data was available for 78 patients. Hence these parameters were not included in the multivariate analysis. On multivariate analysis, 'older age' was not detected to be a risk factor for death. Survival was not different in those with or without any co-morbidity.

Table 3
Univariate and multivariate cox regression analysis

Variable	Univariate			Multivariate		
	HR	95%CI	P value	HR	95%CI	P value
Age	1.017	1.002–1.032	0.029	1.012	0.994–1.029	0.200
Male Sex	0.813	0.577–1.145	0.237			
Hypertension	0.887	0.638–1.233	0.476			
Diabetes	0.983	0.714–1.353	0.916			
Obesity	0.805	0.435–1.489	0.489			
Other comorbidities	0.926	0.487–1.761	0.815			
Number of comorbidities	1.090	0.903–1.315	0.371			
Oxygen saturation	0.979	0.962–0.996	0.017	0.969	0.950–0.989	0.002
CRP	0.999	0.996–1.002	0.379			
Creatinine	1.157	1.031–1.298	0.013	1.123	0.995–1.267	0.061
Respiratory rate	1.045	1.006–1.084	0.023			
LDH	1.000	0.997–1.003	0.880			
Ferritin	1.000	1.000-1.001	0.626			
D-dimer	1.000	1.000–1.000	0.043			
WBC counts	1.000	1.000–1.000	0.875			
Tocilizumab	0.655	0.476–0.901	0.009	0.621	0.427–0.903	0.013
CT severity score	1.084	0.810–1.449	0.588			
Thrombosis	2.160	0.135–34.608	0.586			
Non-invasive ventilation	0.770	0.525–1.131	0.183			
Invasive ventilation	2.028	1.349–3.049	0.001	2.31	1.442–3.701	0.001
Data on respiratory rate was available only for 142 patients while d-dimer was available for 78 patients. Hence these parameters were not included in the multivariate analysis						

The independent predictors of survival were use of tocilizumab (HR 0.621, 95% CI 0.427–0.903, P 0.013), higher oxygen saturation (HR 0.969, 95% CI 0.950–0.989, p 0.002) and use of invasive ventilation (HR 2.31, 95% CI: 1.442–3.701, p 0.001) on multivariate analysis.

Table 4 depicts comparison of the characteristics of the patients who survived (N = 72) versus those who did not (N = 79), in the tocilizumab group. Tocilizumab was administered on 2nd to 5th day of admission (average 3rd day) in both groups. Those who ‘survived’ had higher Oxygen saturation than ‘non-survived group’ (mean 88% with a range of 85–93% v/s mean 85% and range of 79–90%- p = 0.014) and were less tachypnic than ‘non-survived group’(respiratory rate 30 v/s 36 breaths per min, p = 0.002),at the time of enrolment for tocilizumab. Obesity and raised serum creatinine, on the other hand, had adverse effect on survival, p = 0.039 and 0.001 respectively. Blood levels of inflammatory markers were comparable in both groups. D-dimer was higher in those who did not survive than in those who survived, but the difference was not statistically significant. Proportion of patients who required invasive ventilation was significantly more amongst patients who died as compared to those who survived (26.6% versus 1.4%, p 0.001).

Table 4
Comparison of the characteristics of the patients receiving tocilizumab who survived versus those who did not

Variable	Survived (n = 72)	Died (n = 79)	P value
Age	52 (42–59)	55 (46–60)	0.105
Male sex	48 (66.7)	59 (74.7)	0.279
Hypertension	19 (26.4)	21 (26.6)	0.979
Diabetes	33 (45.8)	45 (57)	0.172
Obesity	3 (4.2)	11 (13.9)	0.039
Other comorbidities	2 (2.8)	3 (3.8)	0.727
Number of comorbidities	1 (0–1)	1 (0–2)	0.082
Category	63 (87.5)	62 (78.5)	0.143
E	9 (12.5)	17 (21.5)	
F			
Oxygen saturation	88 (85–93)	85 (79–90)	0.014
CRP	97.5 (63.5–159)	90 (56–136)	0.264
Respiratory rate	30 (30–36)	36 (30–40)	0.002
Serum Creatinine	1 (1–1)	1 (1–2)	0.001
SGOT	49 (37–75)	57 (42–72)	0.169
SGPT	40 (30–58)	44 (28–68)	0.977
LDH	701 (515–988)	608 (462–753)	1.000
Ferritin	437 (293–947)	978 (369–2000)	0.364
D-dimer	1000 (1000–1927)	1411 (1000–5000)	0.079
IL-6	455 (75–984)	Not available	
WBC counts ($x10^9$/L)	8.9 (5.85–13.6)	8.4 (6.1–12.0)	0.799
Neutrophil percentage	72 (65–78)	72 (70–75)	1.000
Lymphocyte percentage	25 (17–29)	23 (10–27)	0.469
Platelet count ($x10^9$/L)	200 (200–300)	200 (200–300)	0.314
Day of tocilizumab	3 (2–6)	3 (2–5)	0.865
Non-invasive ventilation	22 (30.6)	34 (43)	0.113

Variable	Survived (n = 72)	Died (n = 79)	P value
Invasive ventilation	1 (1.4)	21 (26.6)	0.001

Discussion:

We found a significant reduction in risk of death in severe COVID-19 pneumonia with persistent hypoxia receiving a single dose of intravenous tocilizumab 400 mg, compared with those treated with standard care alone. The hazards of dying in the tocilizumab group was 0.621 times of that in the control group. We reported 47.1% mortality in our first 70 patients of severe COVID-19 pneumonia with persistent hypoxia treated with tocilizumab till 5th June 2020, compared with 67% mortality in 90 controls (three weeks prior to availability of tocilizumab) with persistent hypoxia due to severe COVID pneumonia[14]. At three weeks follow-up 11 / 151(15.7%) patients were still hospitalized. Two of them died later, increasing mortality to 50% in tocilizumab group. In a retrospective observational study in COVID 19 patients treated in ICU in New Jersey, Noa et al[15] reported 49% mortality in 210 patients treated with tocilizumab and 61% mortality in 256 patients who did not receive tocilizumab. In present study, 60 out of our 151 patients from tocilizumab group were managed in COVID ICU. Due to non-availability of COVID ICU beds, 15 patients received non-invasive ventilation (NIV) in covid wards, and 7 patients received oxygen through high flow nasal canula (HFNC) in covid wards. Non invasive ventilation was used in 56 patients from tocilizumab group (15 of them later required invasive ventilation) but in none from control group (it was avoided initially due to fear of aerosolization causing increased risk to health care workers).Overall, 30 patients required invasive ventilation (22 from tocilizumab group and 8 from control group. Many investigators, for example Kewan[9], Nicola[8] have used early Tocilizumab in Covid 19 treatment. Nicola et al[7] used tocilizumab in patients with peripheral Oxygen saturation 93% on room air or PaO2/FiO2 less than 300 mm of Hg, and documented reduction in mortality from 50–7.7%. With early use of tocilizumab, Nicola et al[8] could reduce risk of death by 94%. Although more than 70% of our admitted patients were hypoxic (Oxygen saturation less than 95% on ambient air) during hospital stay, the limited availability of tocilizumab made it mandatory for us to formulate strict inclusion criteria for tocilizumab administration. These criteria were formulated by consensus of department members and approved by institutional ethics committee. (saturation 94% or less on 15L per min supplemental Oxygen through non-rebreathing mask or PaO2/FiO2 less than 200). Depending upon inclusion criteria for use of tocilizumab in severe Covid19 pneumonia, various outcomes are reported. Guaraldi et al[7] reported mortality in tocilizumab versus standard care group to be 7% and 20% respectively (P < .0001), with inclusion criteria being respiratory rate more than or equal to 30 per min, Oxygen saturation less than or equal to 93% on room air or PaO2/FiO2 ratio being 300 or less, and bilateral lung infiltrates more than 50% being present within 24 to 48 of admission. Rossotti et al[16] reported tocilizumab use to be associated with a better overall survival (HR 0.499 [95% CI 0.262–0.952], p = 0.035) as compared to control, their inclusion criteria being respiratory rate more than or equal to 30 per min, Oxygen saturation less than or equal to 93% on room air or PaO2/FiO2 ratio being 300 or less.

In the current study, clinical response in terms of reduction in Oxygen requirements and respiratory rate was observed within 24–72 hours of tocilizumab infusion in those who responded. C-reactive Protein improved by day 3 to 4. Amongst patients who received tocilizumab, D-dimer levels were higher in 'non-survived' group than in 'survived' group. Although this difference was not statistically significant, suspicion of terminal pulmonary thromboembolic event was high on clinical grounds in the non-survived group. Zhou et al[17] reported D-dimer more than 1000 nanogram/ml to be a risk factor for mortality. A Chinese group has reported that coagulation abnormalities probably did not improve with tocilizumab[18]. Our clinical impression is that patients in whom clinical improvement in terms of reduced Oxygen requirement did not occur had either extensive lung involvement or high D-dimer or pulmonary thrombi on CT-Pulmonary angiography (imaging could not be performed in all patients due to logistics issues in patients on High Flow Nasal Canula or on non-invasive or mechanical ventilators). In 23/26 patients in whom HRCT chest could be performed, CO-RAD score[19] was 6 (lowest is 1 and highest is 6) and average CT-score[20] was 21 out of 25. CT-pulmonary angiography was performed in 9 patients, and documented pulmonary thrombi in 3 patients. CT-brain was performed in 3 patients and documented brain infracts in all. One patient with pulmonary thrombus developed two large infarcts in brain despite full dose heparin and streptokinase for pulmonary thrombus. Radiological imaging was not possible in the more severely affected patients due to them being on advanced respiratory support.

The possibility of secondary infection due to immunosuppressants (steroids and tocilizumab), contributing to morbidity, also has to be considered in both Tocilizumab and control groups, though higher antibiotics like Piperacilin Tazobactum or Meropenem / Vancomycin were used in all critically ill patients. Procalcitonin levels could not be done due to cost constraints. Presence or absence of any co-morbidity did not affect primary out come in the current study.

Conclusion:

Use of tocilizumab confers a significant survival benefit in COVID19 patients with persistent hypoxia despite optimal supportive care.

One of the limitations of this study was that tocilizumab group was overall younger, but this factor was likely to have been offset by lower average Oxygen saturation level in tocilizumab group.

These preliminary results are encouraging. Randomised controlled trials on use of tocilizumab as rescue therapy in patients of severe COVID-19 pneumonia with hypoxia due to hyperinflammatory state, are warranted.

Abbreviations

1. COVID 19 : Corona Virus Disease 2019
2. IL-6 : Interleukin 6
3. NIV: Non-invasive ventilation

4. HFNC: High Flow nasal canula
5. JAK: Janus kinase
6. RT-PCR: Real time polymerase chain reaction
7. CRP: C- reactive protein
8. SGOT: Serum glutamic-oxaloacetic transaminase.
9. SGPT: Serum glutamic-pyruvic transaminase
10. LDH: Lactose dehydrogenase
11. WBC: White blood Corpuscle
12. CO-RADS: Coronavirus disease 2019 (COVID-19) Reporting and Data System
13. CTPA: Computerised tomography pulmonary angiography
14. HRCT: High resolution computerised tomography

Declarations

- Ethics approval and consent to participate: We confirm that our study was submitted to and approved by our institutional ethics committee.

Full name of the Ethics committee- Institutional Ethics Committee Human Research, Lokmanya Tilak Municipal Medical College and General Hospital, Registration Number- ECR/266/Lokmanya/Inst/MH/2013RR-16

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